HUMAN ANATOMY AND PHYSIOLOGY

John Ulici

Human Anatomy *and* Physiology

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PART 1

Levels of Organization

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1

An Introduction to the Human Body

Chapter Objectives

After studying this chapter, you will be able to:

- Distinguish between anatomy and physiology and identify several branches of each
- Describe the structure of the body, from simplest to most complex, in terms of the six levels of organization
- Identify the functional characteristics of human life
- Identify the four requirements for human survival
- Define homeostasis and explain its importance to normal human functioning
- Use appropriate anatomical terminology to identify key body structures, body regions, and directions in the body

Though you may approach a course in anatomy and physiology strictly as a requirement for your field of study, the knowledge you gain in this course will serve you well in many aspects of your life. An understanding of anatomy and physiology is not only fundamental to any career in the health professions, but it can also benefit your own health.

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1.1 Overview of Anatomy and Physiology

Learning Objectives

By the end of this section, you will be able to:

- Compare and contrast anatomy and physiology, including their specializations and methods of study
- Discuss the fundamental relationship between anatomy and physiology

Human **anatomy** is the scientific study of the body's structures. Some of these structures are very small and can only be observed and analyzed with the assistance of a microscope. Other larger structures can readily be seen, manipulated, measured, and weighed. Like most scientific disciplines, anatomy has areas of specialization. **Gross anatomy** is the study of the larger structures of the body, those visible without the aid of magnification. *Macro-* means "large"; thus gross anatomy is also referred to as macroscopic anatomy. In contrast, *micro-* means "small," and **microscopic anatomy** is the study of structures that can be observed only with the use of a microscope or other magnification devices.

Anatomists take two general approaches to the study of the body's structures: regional and systemic. **Regional anatomy** is the study of the interrelationships of all the structures in a specific body region, such as the abdomen. Studying regional anatomy helps us appreciate the interrelationships of body structures, such as how muscles, nerves, blood vessels, and other structures work together to serve a particular body region. In contrast, **systemic anatomy** is the study of the structures that make up a discrete body system—that is, a group of structures that work together to perform a unique body function. For example, a systemic anatomical study of the muscular system would consider all the skeletal muscles of the body.

Whereas anatomy is about structure, physiology is about function. Human **physiology** is the scientific study of the chemistry and physics of the structures of the body and the ways in which they work together to support the functions of life. Much of the study of physiology centres on the body's tendency toward homeostasis. **Homeostasis** is the state of steady internal conditions maintained by living things.

Form is closely related to function in all living things. For example, the thin flap of your eyelid can snap down to clear away dust particles and almost instantaneously slide back up to allow you to see again. At the microscopic level, the arrangement and function of the nerves and muscles that serve the

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eyelid allow for its quick action and retreat. At a smaller level of analysis, the function of these nerves and muscles likewise relies on the interactions of specific molecules and ions. Even the three-dimensional structure of certain molecules is essential to their function.

1.2 Structural Organization of the Human Body

Learning Objectives

By the end of this section, you will be able to:

- Describe the structure of the human body in terms of six levels of organization
- List the eleven organ systems of the human body and identify at least one organ and one major function of each

Before you begin to study the different structures and functions of the human body, it is helpful to consider its basic architecture—that is, how its smallest parts are assembled into larger structures. It is convenient to consider the structures of the body in terms of fundamental levels of organization that increase in complexity: subatomic particles, atoms, molecules, organelles, cells, tissues, organs, organ systems, organisms, and biosphere (Figure 1.1).

The Levels of Organization

To study the chemical level of organization, scientists consider the simplest building blocks of matter: subatomic particles, known as **atoms and molecules**. All matter in the universe is composed of one or more unique pure substances called elements, familiar examples of which are hydrogen, oxygen, carbon, nitrogen, calcium, and iron. The smallest unit of any of these pure substances (elements) is an atom. Atoms are made up of subatomic particles such as protons, electrons, and neutrons. Two or more atoms combine to form a molecule, such as the water molecules, proteins, and sugars found in living things. Molecules are the chemical building blocks of all body structures.

A **cell** is the smallest independently functioning unit of a living organism. Even bacteria, which are extremely small and independently living organisms, have a cellular structure. Each bacterium is a single cell. All living structures of human anatomy contain cells, and almost all functions of human physiology are performed in cells or are initiated by cells. A human cell typically consists of flexible membranes that enclose cytoplasm, a water-based cellular fluid, together with a variety of tiny functioning units called organelles.

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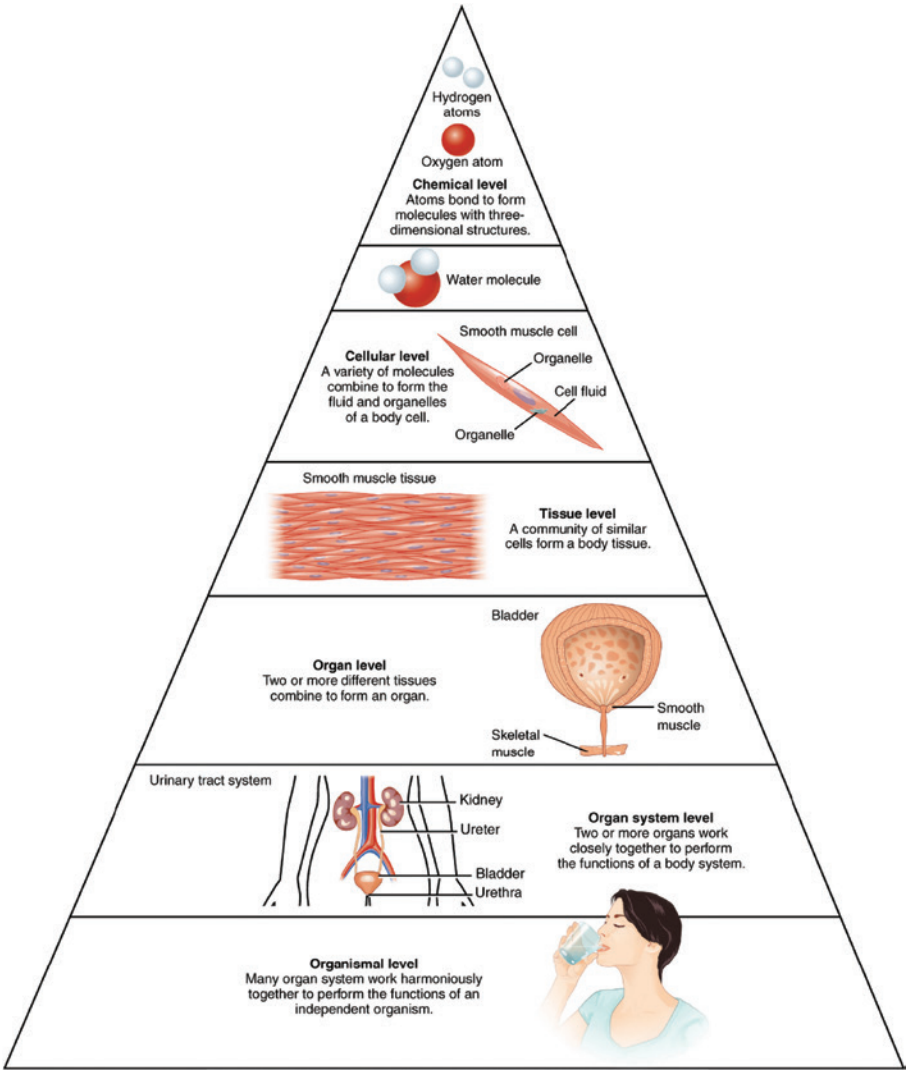


Figure 1.1 Levels of Structural Organization of the Human Body. The organization of the body is often discussed in terms of six distinct levels of increasing complexity, from the smallest chemical building blocks to a unique human organism.

A **tissue** is a group of many similar cells (though sometimes composed of a few related types) that work together to perform a specific function.

An **organ** is an anatomically distinct structure of the body composed of two or more tissue types. Each organ performs one or more specific physiological functions.

An **organ system** is a group of organs that work together to perform major functions or meet physiological needs of the body.

This book covers eleven distinct organ systems in the human body (Figure 1.2 and Figure 1.3). Assigning organs to organ systems can be imprecise,

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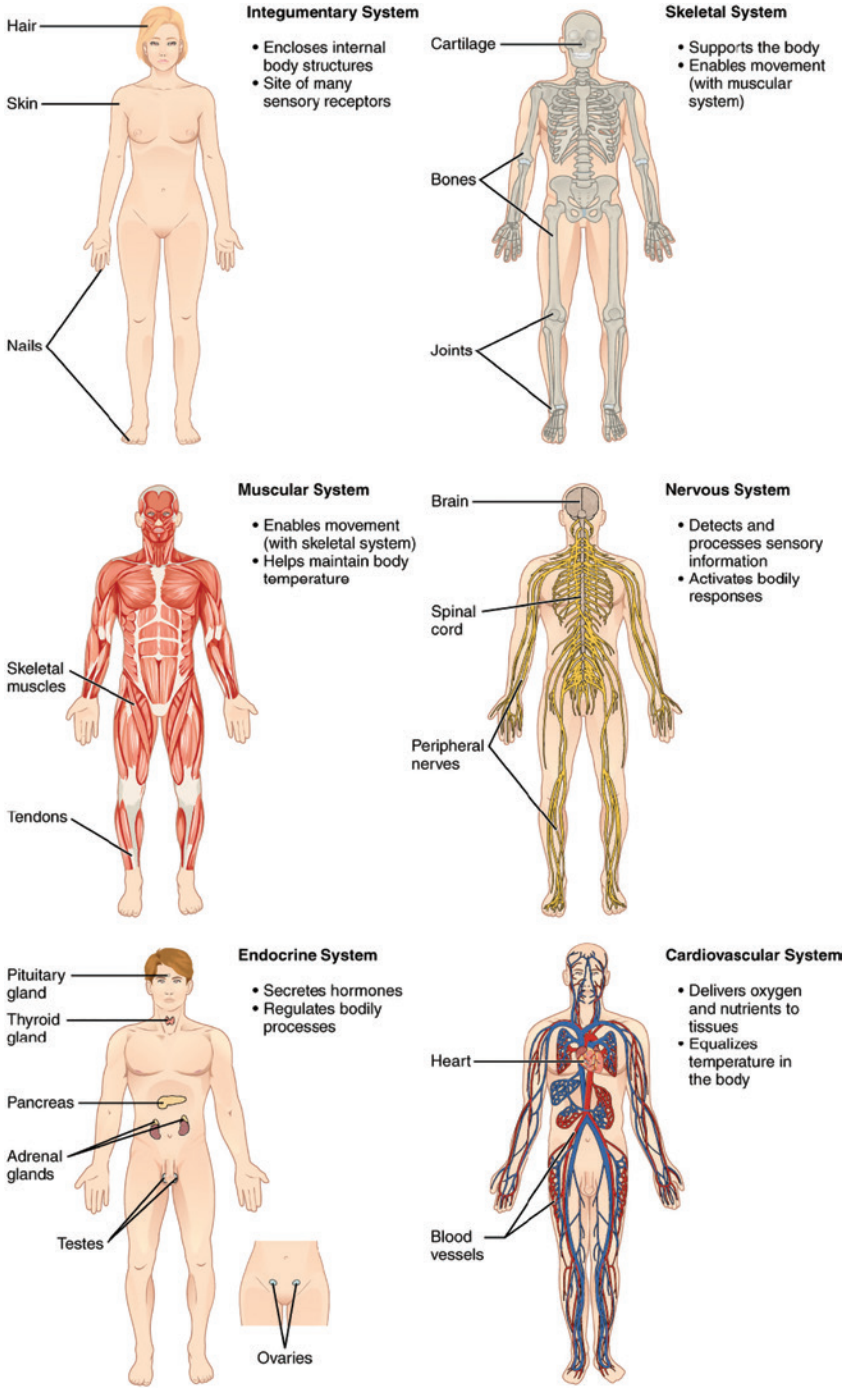


Figure 1.2 Organ Systems of the Human Body. Organs that work together are grouped into organ systems.

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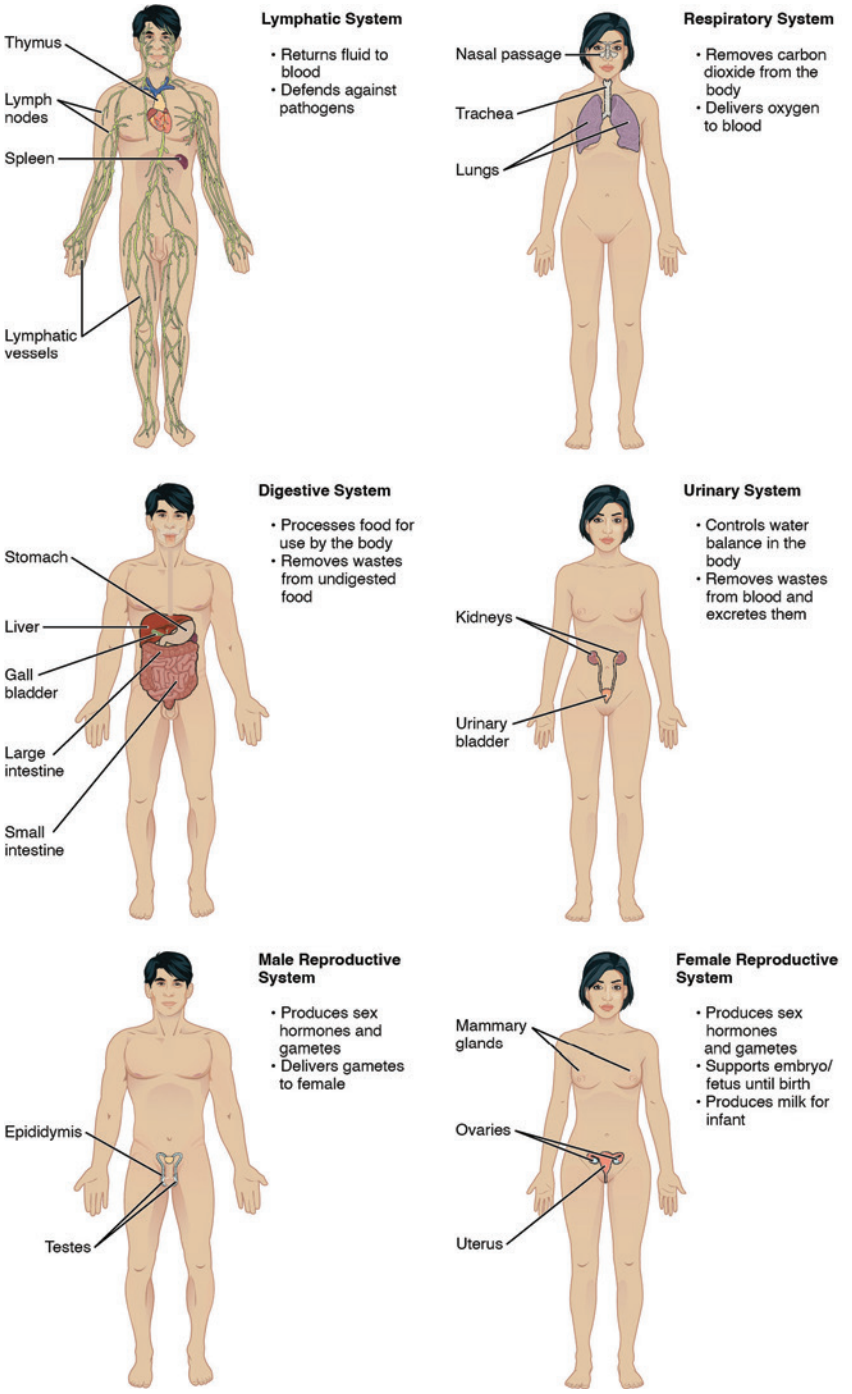


Figure 1.3 Organ Systems of the Human Body (*continued*). Organs that work together are grouped into organ systems.

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since organs that "belong" to one system can also have functions integral to another system. In fact, most organs contribute to more than one system.

In this book and throughout your studies of biological sciences, you will often read descriptions of similarities and differences among biological structures, processes, and health related to a person's biological sex. People often use the words *female* and *male* to describe two different concepts: our sense of gender identity and our biological sex as determined by our chromosomes, hormones, organs, and other physical characteristics. For some people, gender identity is different from biological sex or their sex assigned at birth. Throughout this book, *female* and *male* refer to sex only, and the typical anatomy and physiology of XX and XY individuals are discussed.

The **organism** level is the highest level of organization; it is a living being that has a cellular structure and that can independently perform all physiologic functions necessary for life. In multicellular organisms, including humans, all cells, tissues, organs, and organ systems of the body work together to maintain the life and health of the organism.

1.3 Functions of Human Life

Learning Objectives

By the end of this section, you will be able to:

- Explain the importance of organization to the function of the human organism
- Distinguish between metabolism, anabolism, and catabolism
- Provide at least two examples of human responsiveness and human movement
- Compare and contrast growth, differentiation, and reproduction

The different organ systems each have different functions and therefore unique roles to perform in physiology. These many functions can be summarized in terms of a few that we might consider definitive of human life: organization, metabolism, responsiveness, movement, development, and reproduction.

Organization

A human body consists of trillions of cells organized in a way that maintains distinct internal compartments. These compartments keep body cells separated from external environmental threats and keep the cells moist and nourished. They also separate internal body fluids from the countless microorganisms that

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grow on body surfaces, including the linings of certain passageways that connect to the outer surface of the body. The intestinal tract, for example, is home to more bacterial cells than the total of all human cells in the body, yet these bacteria are outside the body and cannot be allowed to circulate freely inside the body.

Example: Cells have a cell membrane (also referred to as the plasma membrane) that keeps the intracellular environment—the fluids and organelles—separate from the extracellular environment. Blood vessels keep blood inside a closed circulatory system, and nerves and muscles are wrapped in connective tissue sheaths that separate them from surrounding structures. In the chest and abdomen, a variety of internal membranes keep major organs such as the lungs, heart, and kidneys separate from one another.

The body's largest organ system is the integumentary system, which includes the skin and its associated structures, such as hair and nails. The surface tissue of skin is a barrier that protects internal structures and fluids from potentially harmful microorganisms and other toxins.

Metabolism

The first law of thermodynamics holds that energy can be neither created nor destroyed—it can only change form. Your basic function as an organism is to consume (ingest) energy and molecules in the foods you eat, convert some of them into fuel for movement, sustaining your body functions, and building and maintaining your body structures. There are two types of reactions that accomplish this: anabolic and catabolic.

- **Anabolism** is the process whereby smaller, simpler molecules are combined into larger, more complex substances. Your body can assemble, utilizing energy, the complex chemicals it needs by combining small molecules derived from the foods you eat.
- **Catabolism** is the process by which larger, more complex substances are broken down into smaller, simpler molecules. Catabolism releases energy. The complex molecules found in foods are broken down so the body can use their parts to assemble the structures and substances needed for life.

Taken together, these two processes are called metabolism. **Metabolism** is the sum of all anabolic and catabolic reactions that take place in the body (Figure 1.4). Both anabolism and catabolism occur simultaneously and continuously to keep you alive.

Every cell in your body makes use of a chemical compound, adenosine triphosphate (ATP), to store and release energy. The cell stores energy in the synthesis (anabolism) of ATP, then moves the ATP molecules to the location where energy is needed to fuel cellular activities. Then the ATP is broken down

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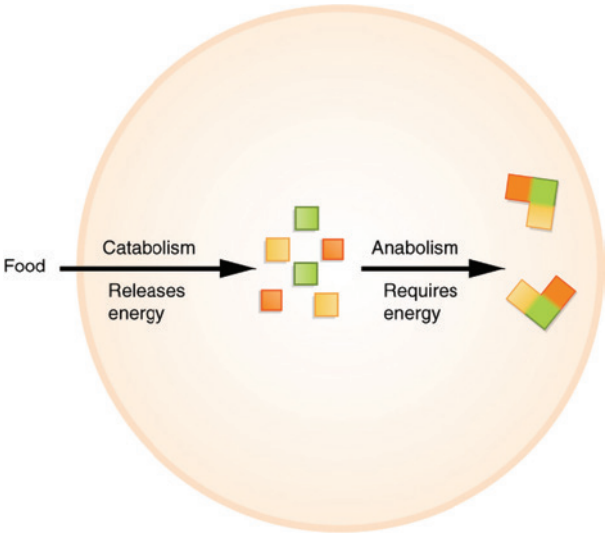


Figure 1.4 Metabolism. Anabolic reactions are building reactions, and they consume energy. Catabolic reactions break down materials and release energy. Metabolism includes both anabolic and catabolic reactions.

(catabolism), and a controlled amount of energy is released, which is used by the cell to perform a particular job.

Interactive Link 1.1

View this video (http://oer.aupress.ca/oer-202505/1.1) to learn more about metabolic processes. Which organs of the body likely carry out anabolic processes? What about catabolic processes?

Responsiveness

Responsiveness is the ability of an organism to adjust to changes in its internal and external environments.

An example of responsiveness to external stimuli could include moving toward sources of food and water and away from perceived dangers. Changes in an organism's internal environment, such as increased body temperature, can cause the responses of sweating and the dilation of blood vessels in the skin in order to decrease body temperature.

Movement

Human **movement** includes not only actions at the joints of the body but also the motion of individual organs and even individual cells.

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Example: Red and white blood cells are moving throughout your body, muscle cells are contracting and relaxing to maintain your posture and to focus your vision, and glands are secreting chemicals to regulate body functions. Your body is coordinating the action of entire muscle groups to enable you to move air into and out of your lungs, to push blood throughout your body, and to propel the food you have eaten through your digestive tract. Consciously, of course, you contract your skeletal muscles to move the bones of your skeleton to get from one place to another and to carry out all the activities of your daily life.

Development, Growth, and Reproduction

Development is all the changes the body goes through in life. Development includes the process of **differentiation**, in which unspecialized cells become specialized in structure and function to perform certain tasks in the body. Development also includes the processes of growth and repair, both of which involve cell differentiation.

Growth is the increase in body size. Humans, like all multicellular organisms, grow by increasing the number of existing cells, increasing the amount of noncellular material around cells (such as mineral deposits in bone), and, within very narrow limits, increasing the size of existing cells.

Reproduction is the formation of a new organism from parent organisms. In humans, reproduction is carried out by the male and female reproductive systems. Because death will come to all complex organisms, without reproduction, the line of organisms would end.

1.4 Homeostasis

Learning Objectives

By the end of this section, you will be able to:

- Discuss the role of homeostasis in healthy functioning
- Contrast negative and positive feedback, giving one physiologic example of each mechanism

Maintaining homeostasis requires that the body continuously monitor its internal conditions. From body temperature to blood pressure to levels of certain nutrients, each physiological condition has a particular set point. A **set point** is the physiological value around which the normal range fluctuates. A **normal range** is the restricted set of values that is optimally healthful and stable.

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Example: The set point for normal human body temperature is approximately 37°C. Physiological parameters, such as body temperature and blood pressure, tend to fluctuate within a normal range that is a few degrees above and below that point.

Control centres in the brain and other parts of the body monitor and react to deviations from homeostasis using negative feedback.

Negative Feedback

Negative feedback is a mechanism that reverses a deviation from the set point, maintaining body parameters within their normal range. The maintenance of homeostasis by negative feedback goes on throughout the body at all times, and an understanding of negative feedback is thus fundamental to an understanding of human physiology. A negative feedback system has three basic components (Figure 1.5a). A **sensor**, also referred to as a receptor, is a component of a feedback system that monitors a physiological value. This value is reported to the control centre. The **control centre** is the component in a feedback system that compares the value to the normal range. If the value deviates too much from the set point, then the control centre activates an effector. An **effector** is the component in a feedback system that causes a change to reverse the situation and return the value to the normal range.

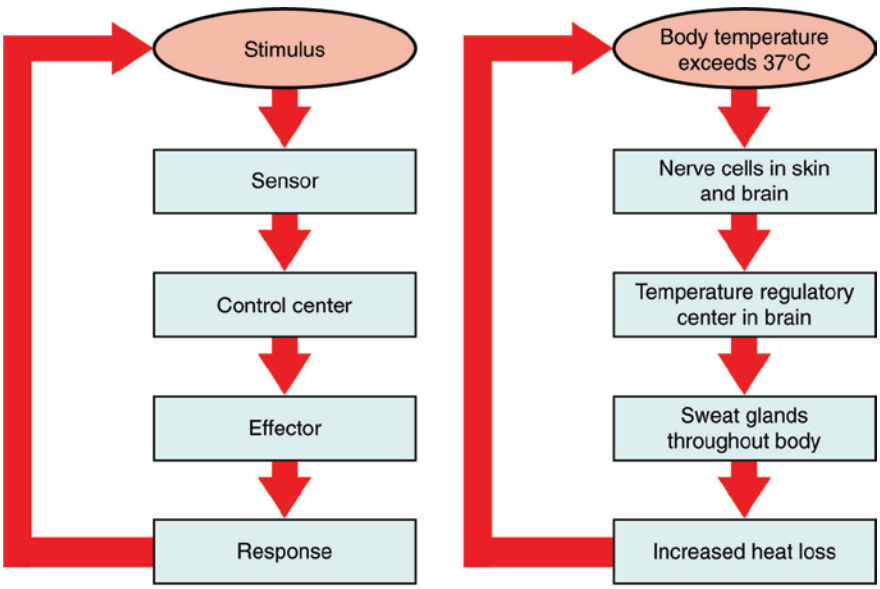


Figure 1.5 Negative Feedback System. In a negative feedback system, a stimulus—a deviation from a set point—is resisted through a physiological process that returns the body to homeostasis. (a) A negative feedback system has five basic parts. (b) Body temperature is regulated by negative feedback.

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In order to set the system in motion, a stimulus must drive a physiological parameter beyond its normal range (i.e., beyond homeostasis). This stimulus is "heard" by a specific sensor.

Example: In the control of blood glucose, specific endocrine cells in the pancreas detect excess glucose (the stimulus) in the bloodstream. These pancreatic beta cells respond to the increased level of blood glucose by releasing the hormone insulin into the bloodstream. The insulin signals skeletal muscle fibres, fat cells (adipocytes), and liver cells to take up the excess glucose, removing it from the bloodstream. As glucose concentration in the bloodstream drops, the decrease in concentration—the actual negative feedback—is detected by pancreatic alpha cells, and insulin release stops. This prevents blood sugar levels from continuing to drop below the normal range.

Humans have a similar temperature regulation feedback system that works by promoting either heat loss or heat gain (Figure 1.5b).

Interactive Link 1.2

Water concentration in the body is critical for proper functioning. A person's body retains very tight control over water levels without conscious control by the person. Watch this video (http://oer.aupress.ca/oer-202505/1.2) to learn more about water concentration in the body. Which organ has primary control over the amount of water in the body?

Positive Feedback

Positive feedback intensifies a change in the body's physiological condition rather than reversing it. A deviation from the normal range results in more change, and the system moves farther away from the normal range. Positive feedback in the body is normal only when there is a definite end point. Childbirth and the body's response to blood loss are two examples of positive feedback loops that are normal but are activated only when needed.

Example: Childbirth at full term is a situation in which the maintenance of the existing body state is not desired. Enormous changes in a person's body are required to expel the baby at the end of pregnancy. And the events of childbirth, once begun, must progress rapidly to a conclusion, or the life of the person giving birth and the baby will be at risk. The extreme muscular work of labour and delivery is the result of a positive feedback system (Figure 1.6).

The first contractions of labour (the stimulus) push the baby toward the cervix (the lowest part of the uterus). The cervix contains stretch-sensitive

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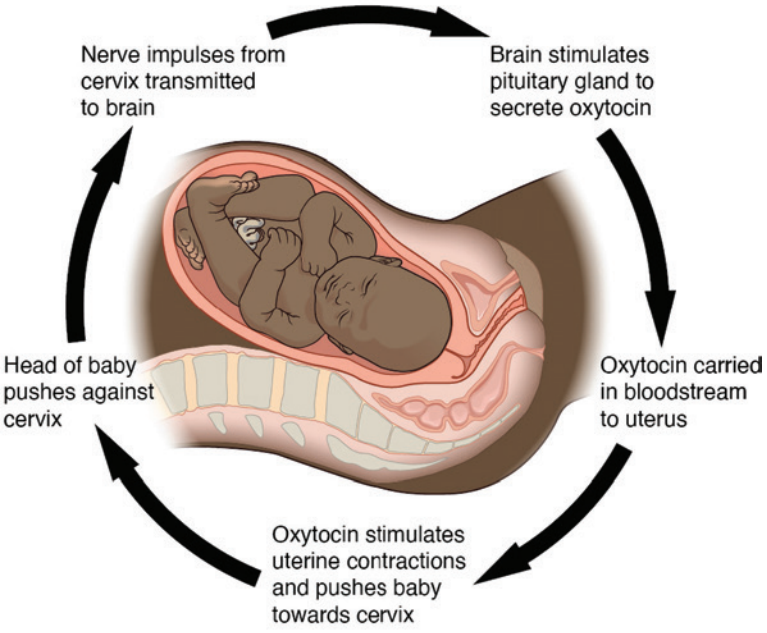


Figure 1.6 Positive Feedback Loop. Normal childbirth is driven by a positive feedback loop. A positive feedback loop results in a change in the body's status rather than a return to homeostasis.

nerve cells that monitor the degree of stretching (the sensors). These nerve cells send messages to the brain, which in turn causes the pituitary gland at the base of the brain to release the hormone oxytocin into the bloodstream. Oxytocin causes stronger contractions of the smooth muscles of the uterus (the effectors), pushing the baby farther down the birth canal. This causes even greater stretching of the cervix. The cycle of stretching, oxytocin release, and increasingly more forceful contractions stops only when the baby is born. At this point, the stretching of the cervix halts, stopping the release of oxytocin.

Example: A second example of positive feedback centres on reversing extreme damage to the body. Following a penetrating wound, the most immediate threat is excessive blood loss. Less blood circulating means reduced blood pressure and reduced perfusion (penetration of blood) to the brain and other vital organs. If perfusion is severely reduced, vital organs will shut down and the person will die. The body responds to this potential catastrophe by releasing substances in the injured blood vessel wall that begin the process of blood clotting. As each step of clotting occurs, it stimulates the release of more clotting substances. This accelerates the processes of clotting and sealing off the damaged area. Clotting is contained in a local area based on the tightly controlled availability of clotting proteins. This is an adaptive, lifesaving cascade of events.

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1.5 Anatomical Terminology

Learning Objectives

By the end of this section, you will be able to:

- Demonstrate the anatomical position
- Describe the human body using directional and regional terms
- Identify three planes most commonly used in the study of anatomy
- Distinguish between the posterior (dorsal) and the anterior (ventral) body cavities, identifying their subdivisions and the representative organs found in each
- Describe the serous membrane and explain its function

Anatomical terms are made up of roots, prefixes, and suffixes. The root of a term often refers to an organ, tissue, or condition, whereas the prefix or suffix often describes the root.

For example, in the disorder hypertension, the prefix *hyper-* means "high" or "over," and the root word *tension* refers to pressure, so the word *hypertension* refers to abnormally high blood pressure.

Anatomical Position

To further increase precision, anatomists standardize the way in which they view the body. Just as maps are normally oriented with north at the top, the standard body "map," or **anatomical position**, is that of the body standing upright, with the feet at shoulder width and parallel, toes forward. The upper limbs are held out to each side, and the palms of the hands face forward as illustrated in Figure 1.7. Using this standard position reduces confusion. It does not matter how the body being described is oriented; the terms are used as if it is in anatomical position.

Example: A scar in the "anterior (front) carpal (wrist) region" would be present on the palm side of the wrist.

The term *anterior* would be used even if the hand were palm-down on a table. A body that is lying down is described as either prone or supine. **Prone** describes a face-down orientation, and **supine** describes a face-up orientation. These terms are sometimes used in describing the position of the body during specific physical examinations or surgical procedures.

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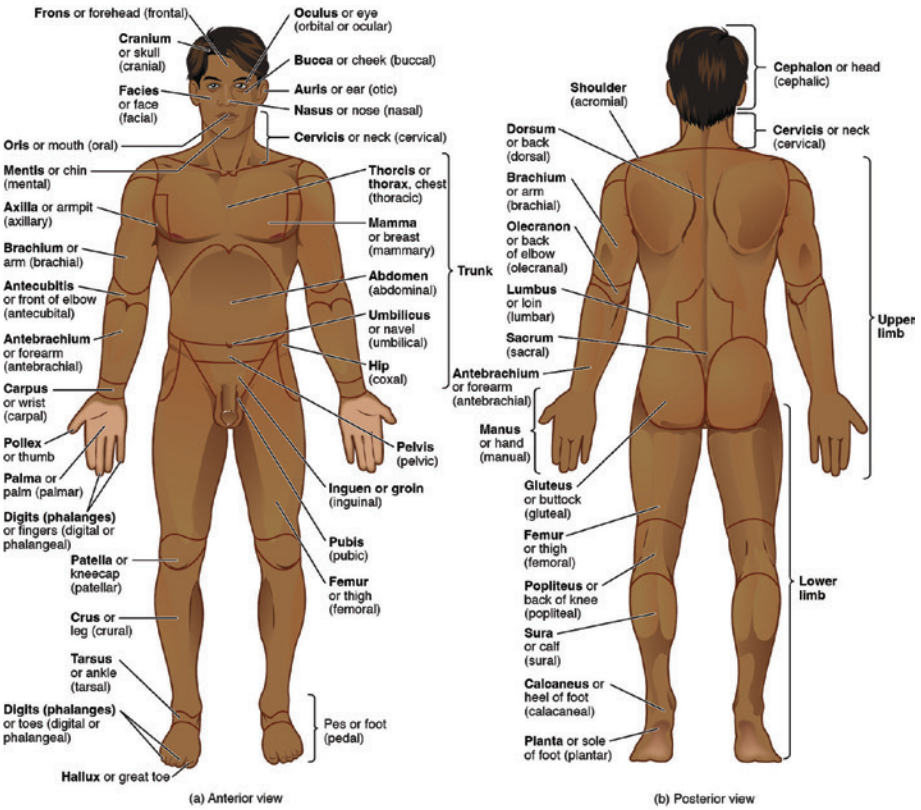


Figure 1.7 Regions of the Human Body. The human body is shown in anatomical position in an (a) anterior view and a (b) posterior view. The regions of the body are labelled in bold.

Regional Terms

The human body's numerous regions have specific terms to help increase precision (see Figure 1.7). Notice that the term *brachium* or *arm* is reserved for the "upper arm," and *antebrachium* or *forearm* is used rather than "lower arm." Similarly, *femur* or *thigh* is correct, and *leg* or *crus* is reserved for the portion of the lower limb between the knee and the ankle. You will be able to describe the body's regions using the terms from the figure.

Directional Terms

Certain directional anatomical terms appear throughout this and any other anatomy textbook (Figure 1.8). These terms are essential for describing the relative locations of different body structures.

Example: An anatomist might describe one band of tissue as "inferior to" another, or a physician might describe a tumor as "superficial to" a deeper body structure.

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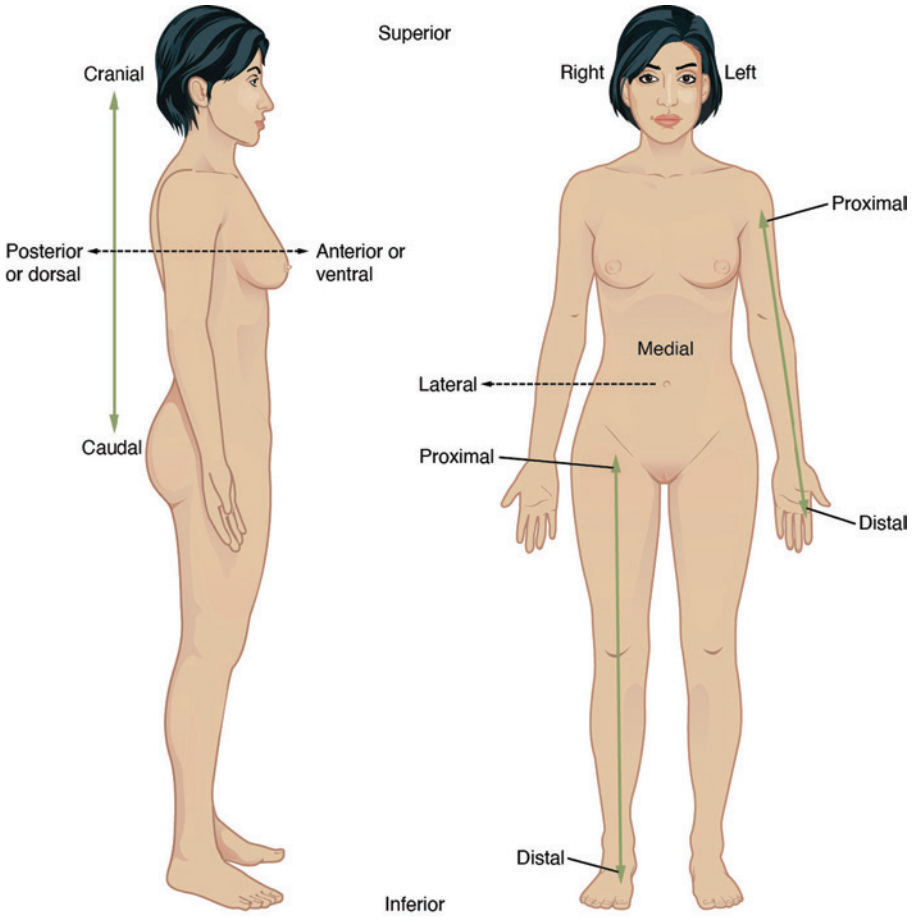


Figure 1.8 Directional Terms Applied to the Human Body. Paired directional terms are shown as applied to the human body.

Commit these terms to memory to avoid confusion when you are studying or describing the locations of particular body parts.

- **Anterior** (or **ventral**) describes the front or direction toward the front of the body. The toes are anterior to the foot.
- **Posterior** (or **dorsal**) describes the back or direction toward the back of the body. The popliteus muscle is posterior to the patella.
- **Superior** (or **cranial**) describes a position above or higher than another part of the body proper. The orbits are superior to the oris.
- **Inferior** (or **caudal**) describes a position below or lower than another part of the body proper, near or toward the tail (in humans, the coccyx, or lowest part of the spinal column). The pelvis is inferior to the abdomen.

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- **Lateral** describes the side or direction toward the side of the body. The thumb (pollex) is lateral to the digits.
- **Medial** describes the middle or direction toward the middle of the body. The hallux is the medial toe.
- **Proximal** describes a position in a limb that is nearer to the point of attachment or the trunk of the body. The brachium is proximal to the antebrachium.
- **Distal** describes a position in a limb that is farther from the point of attachment or the trunk of the body. The crus is distal to the femur.
- **Superficial** describes a position closer to the surface of the body. The skin is superficial to the bones.
- **Deep** describes a position farther from the surface of the body. The brain is deep relative to the skull.

Body Planes

A **section** is a two-dimensional surface of a three-dimensional structure that has been cut. Modern medical imaging devices enable clinicians to obtain "virtual sections" of living bodies. We call these scans. Body sections and scans can only be correctly interpreted, however, if the viewer understands the plane along which the section was made. A **plane** is an imaginary two-dimensional surface that passes through the body. There are three planes commonly referred to in anatomy and medicine, as illustrated in Figure 1.9. Transverse planes produce images referred to as cross sections.

- The **sagittal plane** is the plane that divides the body or an organ vertically into right and left sides. If this vertical plane runs directly down the middle of the body, it is called the **midsagittal or median plane**. If it divides the body into unequal right and left sides, it is called a **parasagittal plane** or, less commonly, a **longitudinal section**.
- The **frontal plane** is the plane that divides the body or an organ into an anterior (front) portion and a posterior (rear) portion. The frontal plane is often referred to as a **coronal plane**.
- The **transverse plane** is the plane that divides the body or an organ horizontally into upper and lower portions.

Body Cavities and Serous Membranes

The body maintains its internal organization by means of membranes, sheaths, and other structures that separate compartments. The dorsal (posterior) cavity and the ventral (anterior) cavity are the largest body compartments

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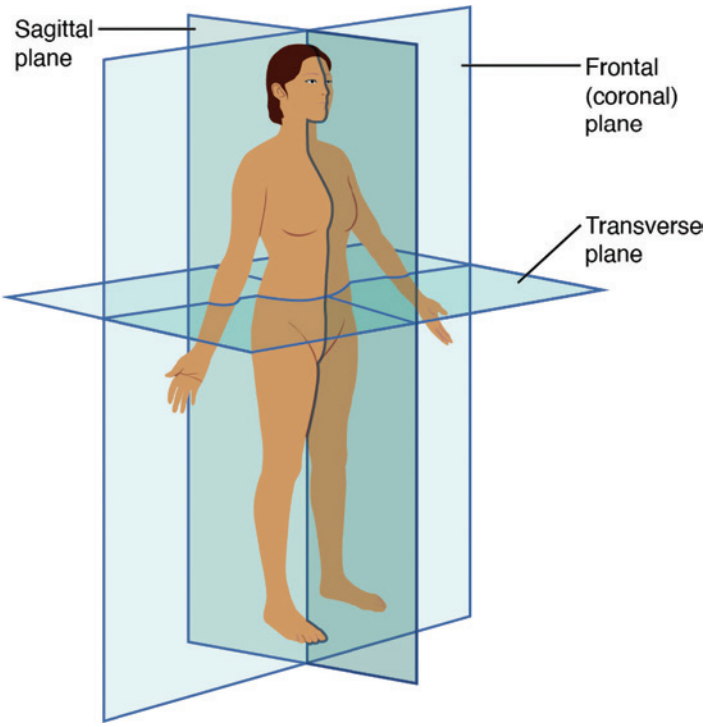


Figure 1.9 Planes of the Body. The three planes most commonly used in anatomical and medical imaging are the sagittal, frontal (or coronal), and transverse planes.

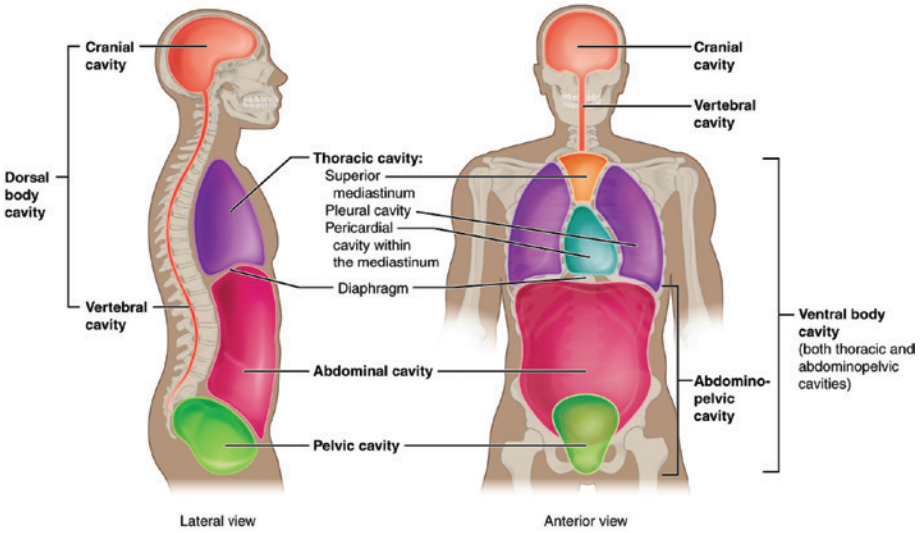


Figure 1.10 Dorsal and Ventral Body Cavities. The ventral cavity includes the thoracic and abdominopelvic cavities and their subdivisions. The dorsal cavity includes the cranial and spinal cavities.

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(Figure 1.10). These cavities contain and protect delicate internal organs, and the ventral cavity allows for significant changes in the size and shape of the organs as they perform their functions. The lungs, heart, stomach, and intestines can expand and contract without distorting other tissues or disrupting the activity of nearby organs.

Subdivisions of the Posterior (Dorsal) and Anterior (Ventral) Cavities

The posterior (dorsal) and anterior (ventral) cavities are each subdivided into smaller cavities. In the **posterior** (**dorsal**) **cavity**, the **cranial cavity** houses the brain, and the **spinal cavity** (or **vertebral cavity**) encloses the spinal cord. Just as the brain and spinal cord make up a continuous, uninterrupted structure, the cranial and spinal cavities that house them are also continuous. The brain and spinal cord are protected by the bones of the skull and vertebral column and by cerebrospinal fluid, a colourless fluid produced by the brain, which cushions the brain and spinal cord within the posterior (dorsal) cavity.

The **anterior** (**ventral**) **cavity** has two main subdivisions: the thoracic cavity and the abdominopelvic cavity (see Figure 1.10). The **thoracic cavity** is the more superior subdivision of the anterior cavity, and it is enclosed by the rib cage. The thoracic cavity contains the lungs and the heart, which is located in the mediastinum. The diaphragm forms the floor of the thoracic cavity and separates it from the more inferior abdominopelvic cavity. The **abdominopelvic cavity** is the largest cavity in the body. Although no membrane physically divides the abdominopelvic cavity, it can be useful to distinguish between the abdominal cavity, the division that houses the digestive organs, and the pelvic cavity, the division that houses the organs of reproduction.

Abdominal Regions and Quadrants

To promote clear communication—for instance, about the location of a patient's abdominal pain or a suspicious mass—health care providers typically divide up the cavity into either nine regions or four quadrants (Figure 1.11).

The more detailed regional approach subdivides the cavity with one horizontal line immediately inferior to the ribs, another horizontal line immediately superior to the pelvis, and two vertical lines drawn as if dropped from the midpoint of each clavicle (collarbone). There are nine resulting regions. The simpler quadrants approach, which is more commonly used in medicine, subdivides the cavity with one horizontal and one vertical line that intersect at the patient's umbilicus (navel).

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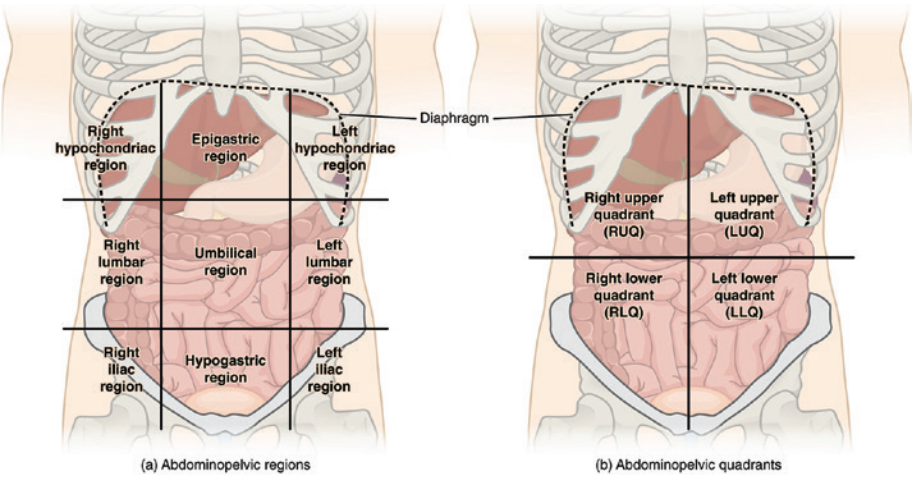


Figure 1.11 Regions and Quadrants of the Peritoneal Cavity. There are (a) nine abdominal regions and (b) four abdominal quadrants in the peritoneal cavity.

Membranes of the Anterior (Ventral) Body Cavity

A **serous membrane** (also referred to as **serosa**) is one of the thin membranes that cover the walls and most of the organs in the thoracic and abdominopelvic cavities. The **parietal layer** of the membrane lines the walls of the body cavity. The **visceral layer** of the membrane covers the organs (the viscera). Between the parietal and visceral layers is a very thin, fluid-filled serous space, or cavity (Figure 1.12).

There are two serous cavities in the thoracic cavity with their associated membranes. The **pleura** is the serous membrane that encloses the **pleural cavity** with both layers, parietal (on the wall of the thoracic cavity) and visceral (covering the lungs); the pleural cavity surrounds the lungs. The **pericardium** is the serous membrane that encloses the **pericardial cavity**, which is a cavity in the thoracic cavity that surrounds the heart.

The abdominopelvic cavity has the **peritoneum**, which is the serous membrane that encloses the peritoneal cavity with both layers, parietal (on the wall of the abdominopelvic cavity) and visceral (covering the abdominopelvic organs); the peritoneal cavity surrounds several organs in the abdominopelvic cavity.

The serous membranes form fluid-filled sacs, or cavities, that are meant to cushion and reduce friction on internal organs when they move, such as when the lungs inflate or the heart beats. Both the parietal and visceral serosa secrete the thin, slippery serous fluid located within the serous cavities. The pleural cavity reduces friction between the lungs and the body wall. Likewise, the pericardial cavity reduces friction between the heart and the wall of the

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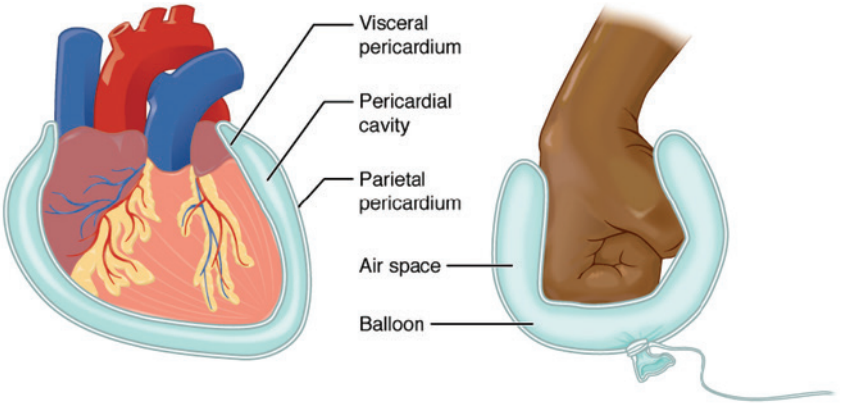


Figure 1.12 Serous Membrane. A serous membrane lines the pericardial cavity and reflects back to cover the heart, in much the same way that an underinflated balloon would form two layers surrounding a fist.

pericardium. The peritoneal cavity reduces friction between the abdominal and pelvic organs and the body wall.

Therefore, serous membranes provide additional protection to the viscera they enclose by reducing friction that could lead to inflammation of the organs.

Key Terms

abdominopelvic cavity: Division of the anterior (ventral) cavity that houses the abdominal and pelvic viscera.

anabolism: Assembly of more complex molecules from simpler molecules.

anatomical position: Standard reference position used for describing locations and directions on the human body.

anatomy: Science that studies the form and composition of the body's structures.

anterior: Describes the front or direction toward the front of the body; also referred to as ventral.

anterior cavity: Larger body cavity located anterior to the posterior (dorsal) body cavity; includes the serous membrane–lined pleural cavities for the lungs, pericardial cavity for the heart, and peritoneal cavity for the abdominal and pelvic organs; also referred to as ventral cavity.

atoms and molecules: The smallest unit of any pure substance (element) is an atom; molecules are the chemical building blocks of all body structures.

catabolism: Breaking down of more complex molecules into simpler molecules.

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caudal: Describes a position below or lower than another part of the body proper, near or toward the tail (in humans, the coccyx, or lowest part of the spinal column); also referred to as inferior.

cell: Smallest independently functioning unit of all organisms; in animals, a cell contains cytoplasm, composed of fluid and organelles.

control centre: Compares values to their normal range; deviations cause the activation of an effector.

coronal plane: Two-dimensional, vertical plane that divides the body or organ into anterior and posterior portions; also referred to as frontal plane.

cranial: Describes a position above or higher than another part of the body proper; also referred to as superior.

cranial cavity: Division of the posterior (dorsal) cavity that houses the brain.

deep: Describes a position farther from the surface of the body.

development: Changes an organism goes through during its life.

differentiation: Process by which unspecialized cells become specialized in structure and function.

distal: Describes a position farther from the point of attachment or the trunk of the body.

dorsal: Describes the back or direction toward the back of the body; also referred to as posterior.

dorsal cavity: Posterior body cavity that houses the brain and spinal cord; also referred to as the posterior body cavity.

effector: Organ that can cause a change in a value.

frontal plane: Two-dimensional, vertical plane that divides the body or organ into anterior and posterior portions; also referred to as coronal plane.

gross anatomy: Study of the larger structures of the body, typically with the unaided eye; also referred to as macroscopic anatomy.

growth: Process of increasing in size.

homeostasis: Steady state of body systems that living organisms maintain.

inferior: Describes a position below or lower than another part of the body proper, near or toward the tail (in humans, the coccyx, or lowest part of the spinal column); also referred to as caudal.

lateral: Describes the side or direction toward the side of the body.

medial: Describes the middle or direction toward the middle of the body.

metabolism: Sum of all the body's chemical reactions.

microscopic anatomy: Study of very small structures of the body using magnification.

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midsagittal or median plane: Vertical plane that runs directly down the middle of the body.

movement: Actions at the joints of the body and the motion of individual organs and even of individual cells.

negative feedback: Homeostatic mechanism that tends to stabilize an upset in the body's physiological condition by preventing an excessive response to a stimulus, typically as the stimulus is removed.

normal range: Range of values around the set point that do not cause a reaction by the control centre.

organ: Functionally distinct structure composed of two or more types of tissues.

organism: Living being that has a cellular structure and that can independently perform all physiologic functions necessary for life.

organ system: Group of organs that work together to carry out a particular function.

parasagittal plane (**longitudinal section**): Divides the body into unequal right and left sides.

parietal layer: Serous membrane that lines the walls of the body cavity.

pericardial cavity: Cavity in the thoracic cavity that surrounds the heart.

pericardium: Sac that encloses the heart.

peritoneum: Serous membrane that lines the abdominopelvic cavity and covers the organs found there.

physiology: Science that studies the chemistry, biochemistry, and physics of the body's functions.

plane: Imaginary two-dimensional surface that passes through the body.

pleura: Serous membrane that lines the pleural cavity and covers the lungs.

pleural cavity: Cavity in the thoracic cavity that surrounds the lungs.

positive feedback: Mechanism that intensifies a change in the body's physiological condition in response to a stimulus.

posterior: Describes the back or direction toward the back of the body; also referred to as dorsal.

posterior cavity: Posterior body cavity that houses the brain and spinal cord; also referred to as dorsal cavity.

prone: Face down.

proximal: Describes a position nearer to the point of attachment or the trunk of the body.

regional anatomy: Study of the structures that contribute to specific body regions.

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reproduction: Process by which new organisms are generated.
responsiveness: Ability of an organism or a system to adjust to changes in conditions.
sagittal plane: Two-dimensional, vertical plane that divides the body or organ into right and left sides.
section: A single flat surface of a three-dimensional structure that has been cut through.
sensor (also receptor): Reports a monitored physiological value to the control centre.
serous membrane (serosa): Membrane that covers organs and reduces friction.
set point: Ideal value for a physiological parameter; the level or small range within which a physiological parameter, such as blood pressure, is stable and optimally healthful—that is, within its parameters of homeostasis.
spinal cavity (vertebral cavity): Division of the dorsal cavity that houses the spinal cord; also referred to as the vertebral cavity.
superficial: Describes a position nearer to the surface of the body.
superior: Describes a position above or higher than another part of the body proper; also referred to as cranial.
supine: Face-up.
systemic anatomy: Study of the structures that contribute to specific body systems.
thoracic cavity: Division of the anterior (ventral) cavity that houses the heart, lungs, esophagus, and trachea.
tissue: Group of similar or closely related cells that act together to perform a specific function.
transverse plane: Two-dimensional, horizontal plane that divides the body or organ into superior and inferior portions.
ventral: Describes the front or direction toward the front of the body; also referred to as anterior.
ventral cavity: Larger body cavity located anterior to the posterior (dorsal) body cavity; includes the serous membrane-lined pleural cavities for the lungs, pericardial cavity for the heart, and peritoneal cavity for the abdominal and pelvic organs; also referred to as the anterior body cavity.
visceral layer: Serous membrane that covers the organs (the viscera).

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Chapter Review

1.1 Overview of Anatomy and Physiology

Human anatomy is the scientific study of the body's structures. In the past, anatomy has primarily been studied via observing injuries and later by the dissection of anatomical structures of cadavers, but in the past century, computer-assisted imaging techniques have allowed clinicians to look inside the living body. Human physiology is the scientific study of the chemistry and physics of the structures of the body. Physiology explains how the structures of the body work together to maintain life. It is difficult to study structure (anatomy) without knowledge of function (physiology). The two disciplines are typically studied together because form and function are closely related in all living things.

1.2 Structural Organization of the Human Body

Life processes of the human body are maintained at several levels of structural organization. These include the chemical, cellular, tissue, organ, organ system, and organism levels. Higher levels of organization are built from lower levels. Therefore, molecules combine to form cells, cells combine to form tissues, tissues combine to form organs, organs combine to form organ systems, and organ systems combine to form organisms.

1.3 Functions of Human Life

Most processes that occur in the human body are not consciously controlled. They occur continuously to build, maintain, and sustain life. These processes include organization (in terms of the maintenance of essential body boundaries), metabolism (including energy transfer via anabolic and catabolic reactions), responsiveness, movement, differentiation (including growth and renewal), and reproduction.

1.4 Requirements for Human Life

Humans cannot survive for more than a few minutes without oxygen, for more than several days without water, and for more than several weeks without carbohydrates, lipids, proteins, vitamins, and minerals. Although the body can respond to high temperatures by sweating and to low temperatures by shivering and increased fuel consumption, long-term exposure to extreme heat and cold is not compatible with survival. The body requires a precise atmospheric pressure to maintain its gases in solution and to facilitate respiration—the intake of oxygen and the release of carbon dioxide. Humans also require blood pressure high enough to ensure that blood reaches all body tissues but low enough to avoid damage to blood vessels.

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1.5 Homeostasis

Homeostasis is the activity of cells throughout the body to maintain the physiological state within a narrow range that is compatible with life. Homeostasis is regulated by negative feedback loops and, much less frequently, by positive feedback loops. Both have the same components of a stimulus, sensor, control centre, and effector; however, negative feedback loops work to prevent an excessive response to the stimulus, whereas positive feedback loops intensify the response until an end point is reached.

1.6 Anatomical Terminology

Ancient Greek and Latin words are used to build anatomical terms. A standard reference position for mapping the body's structures is the normal anatomical position. Regions of the body are identified using terms such as *occipital* that are more precise than common words and phrases such as "the back of the head." Directional terms such as *anterior* and *posterior* are essential for accurately describing the relative locations of body structures. Images of the body's interior commonly align along one of three planes: the sagittal, frontal, or transverse. The body's organs are organized in one of two main cavities—dorsal (also referred to as posterior) and ventral (also referred to as anterior)—which are further subdivided according to the structures present in each area. The serous membranes have two layers—parietal and visceral—surrounding a fluid-filled space. Serous membranes cover the lungs (pleural serosa), heart (pericardial serosa), and some abdominopelvic organs (peritoneal serosa).

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2

The Chemical Level of Organization

Chapter Objectives

After studying this chapter, you will be able to:

- Describe the fundamental composition of matter
- Identify the three subatomic particles
- Identify the four most abundant elements in the body
- Explain the relationship between an atom's number of electrons and its relative stability
- Distinguish between ionic bonds, covalent bonds, and hydrogen bonds
- Explain how energy is invested, stored, and released via chemical reactions, particularly those reactions that are critical to life
- Explain the importance of the inorganic compounds that contribute to life, such as water, salts, acids, and bases
- Compare and contrast the four important classes of organic (carbon-based) compounds—proteins, carbohydrates, lipids, and nucleic acids—according to their composition and functional importance to human life

The smallest, most fundamental material components of the human body are basic chemical elements. In fact, chemicals called nucleotide bases are the foundation of the genetic code, with the instructions on how to build and maintain the human body from conception through old age. There are about three billion of these base pairs in human DNA. Life cannot exist without many of the elements that are part of the earth. All the elements that contribute to chemical reactions, to the transformation of energy, and to electrical activity and muscle

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contraction—elements that include phosphorus, carbon, sodium, and calcium, to name a few—originated in stars. These elements, in turn, can form both the inorganic and organic chemical compounds important to life, including, for example, water, glucose, and proteins. This chapter begins by examining elements and how the structures of atoms, the basic units of matter, determine the characteristics of elements by the number of protons, neutrons, and electrons in the atoms. The chapter then builds the framework of life from there.

2.1 Elements and Atoms: The Building Blocks of Matter

Learning Objectives

By the end of this section, you will be able to:

- Discuss the relationships between matter, mass, elements, compounds, atoms, and subatomic particles
- Distinguish between atomic number and mass number
- Identify the key distinctions between isotopes of the same element
- Explain how electrons occupy electron shells and their contribution to an atom's relative stability

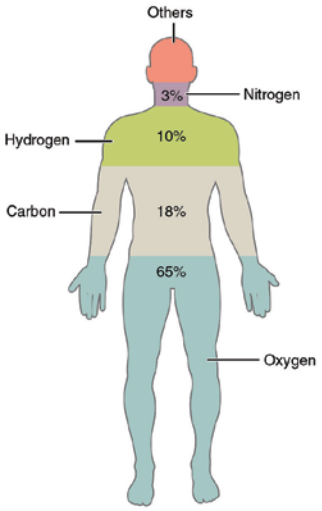
Elements and Compounds

The substance of the universe—from a grain of sand to a star—is called **matter**. All matter in the natural world is composed of one or more of the 92 fundamental substances called elements. An **element** is a pure substance that is distinguished from all other matter by the fact that it cannot be created or broken down by ordinary chemical means. While your body can assemble many of the chemical compounds needed for life from their constituent elements, it cannot make elements. They must come from the environment.

Example: An element that you must take in is calcium (Ca). Calcium is essential to the human body; it is absorbed and used for a number of processes, including strengthening bones. When you consume dairy products, your digestive system breaks down the food into components small enough to cross into the bloodstream. Among these is calcium, which, because it is an element, cannot be broken down further. The elemental calcium in cheese, therefore, is the same as the calcium that forms your bones. Some other elements you might be familiar with are oxygen, sodium, and iron. The elements in the human body are shown in Figure 2.1, beginning with the most abundant: oxygen (O), carbon (C), hydrogen (H), and nitrogen (N). Each element's name

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can be replaced by a one- or two-letter symbol; you will become familiar with some of these during this course. All the elements in your body are derived from the foods you eat and the air you breathe.



Element	Symbol	Percentage in Body
Oxygen	O	65.0
Carbon	C	18.5
Hydrogen	H	9.5
Nitrogen	N	3.2
Calcium	Ca	1.5
Phosphorus	P	1.0
Potassium	K	0.4
Sulfur	S	0.3
Sodium	Na	0.2
Chlorine	Cl	0.2
Magnesium	Mg	0.1
Trace elements include boron (B), chromium (Cr), cobalt (Co), copper (Cu), fluorine (F), iodine (I), iron (Fe), manganese (Mn), molybdenum (Mo), selenium (Se), silicon (Si), tin (Sn), vanadium (V), and zinc (Zn).		less than 1.0

Figure 2.1 Elements of the Human Body. The main elements that compose the human body are shown from most abundant to least abundant.

In nature, elements rarely occur alone. Instead, they combine to form compounds. A **compound** is a substance composed of two or more elements joined by chemical bonds.

Example: The compound glucose is an important body fuel. It is always composed of the same three elements: carbon, hydrogen, and oxygen. Moreover, the elements that make up any given compound always occur in the same relative amounts. In glucose, there are always six carbon and six oxygen units for every twelve hydrogen units. But what, exactly, are these "units" of elements?

Atoms and Subatomic Particles

An **atom** is the smallest quantity of an element that retains the unique properties of that element. In other words, an atom of hydrogen is a unit of hydrogen—the smallest amount of hydrogen that can exist. As you might guess, atoms are almost unfathomably small. The period at the end of this sentence is millions of atoms wide.

Atomic Structure and Energy

Atoms are made up of even smaller subatomic particles, three types of which are important: the proton, neutron, and electron. The sum of positively charged

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protons and noncharged ("neutral") **neutrons** found in an atom's nucleus is its mass number, and the number of protons determines the elements' atomic number. The number of negatively charged **electrons** that "spin" around the nucleus at close to the speed of light equals the number of protons. An electron has about 1/2000th the mass of a proton or neutron.

Example: Figure 2.2 shows two models that can help you imagine the structure of an atom—in this case, helium (He). In one model, helium's two electrons are shown circling the nucleus in a fixed orbit depicted as a ring. Although this model is helpful in visualizing atomic structure, in reality, electrons do not travel in fixed orbits but whiz around the nucleus erratically in a so-called electron cloud.

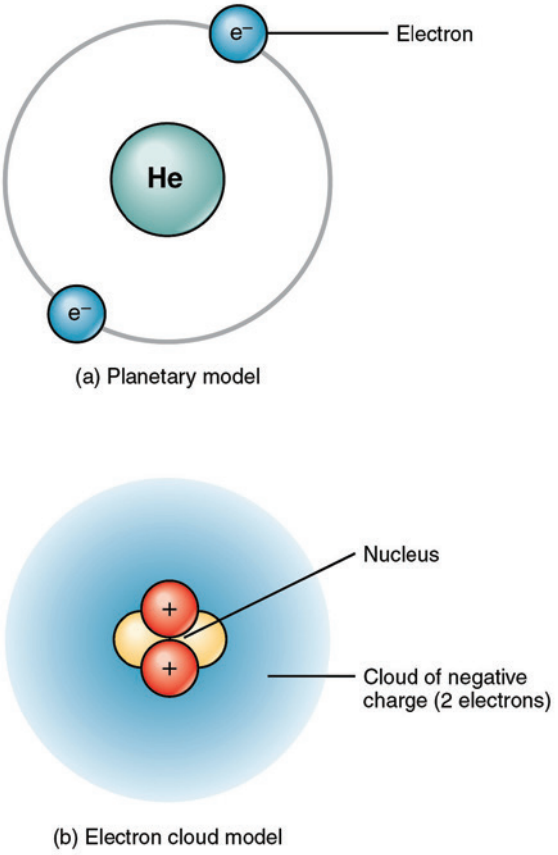


Figure 2.2 Two Models of Atomic Structure. (a) In the planetary model, the electrons of helium are shown in fixed orbits, depicted as rings, at a precise distance from the nucleus, somewhat like planets orbiting the sun. (b) In the electron cloud model, the electrons of helium are shown in the variety of locations they would have at different distances from the nucleus over time.

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An atom's protons and electrons carry electrical charges. Electrons, which have a negative charge, are designated e^-. An atom's neutrons have no charge: They are electrically neutral because they have an equal number of electrons and protons.

Atomic Number and Mass Number

The **atomic number**, which is the number of protons in the nucleus of the atom, identifies the element. Because an atom usually has the same number of electrons as protons, the atomic number identifies the usual number of electrons as well.

In their most common form, many elements also contain the same number of neutrons as protons. An element's **mass number** is the sum of the number of protons and neutrons in its nucleus.

The **periodic table of the elements** is a chart identifying the 92 elements found in nature as well as several larger, unstable elements discovered experimentally.

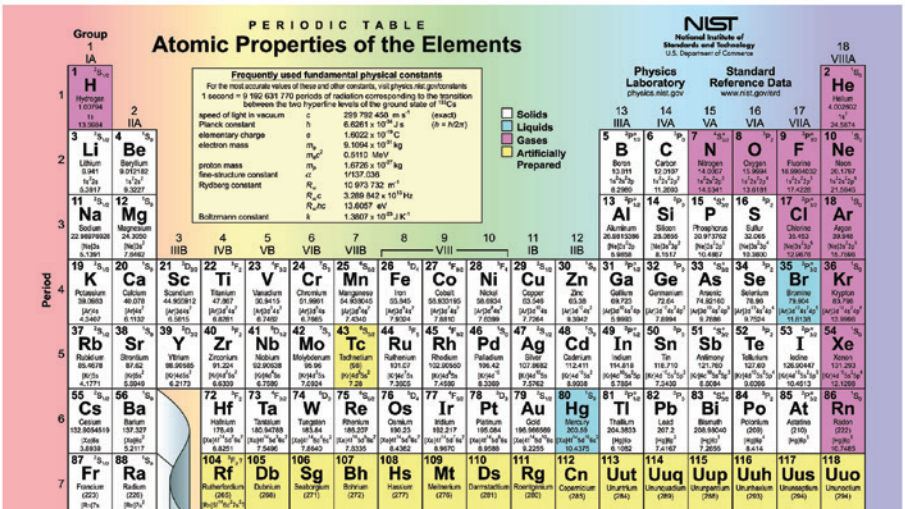


Figure 2.3 The Periodic Table of the Elements. (credit: R. A. Dragoset, A. Musgrove, C. W. Clark, W. C. Martin)

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Interactive Link 2.1

Visit this website (http://oer.aupress.ca/oer-202505/2.1) to view the periodic table. In the periodic table of the elements, elements in a single column have the same number of electrons that can participate in a chemical reaction. These electrons are known as "valence electrons." For example, the elements in the first column all have a single valence electron, an electron that can be "donated" in a chemical reaction with another atom. What is the meaning of a mass number shown in parentheses?

The Behaviour of Electrons

In the human body, atoms do not exist as independent entities. Rather, they are constantly reacting with other atoms to form and break down more complex substances. To fully understand anatomy and physiology, you must grasp how atoms participate in such reactions. The key is understanding the behaviour of electrons.

Although electrons do not follow rigid orbits a set distance away from the atom's nucleus, they do tend to stay within certain regions of space called electron shells. An **electron shell** is a layer of electrons that encircle the nucleus at a distinct energy level.

The atoms of the elements found in the human body have from one to five electron shells, and all electron shells hold eight electrons except the first shell, which can only hold two. This configuration of electron shells is the same for all atoms. The precise number of shells depends on the number of electrons in the atom.

Example: Hydrogen and helium have just one and two electrons, respectively. If you take a look at the periodic table of the elements, you will notice that hydrogen and helium are placed alone on either side of the top row; they are the only elements that have just one electron shell (Figure 2.4). A second shell is necessary to hold the electrons in all elements larger than hydrogen and helium.

The factor that most strongly governs the tendency of an atom to participate in chemical reactions is the number of electrons in its valence shell. A **valence shell** is an atom's outermost electron shell. If the valence shell is full, the atom is stable, meaning its electrons are unlikely to be pulled away from the nucleus by the electrical charges of other atoms. If the valence shell is not full, the atom is reactive, meaning it will tend to react with other atoms in ways that make the valence shell full.

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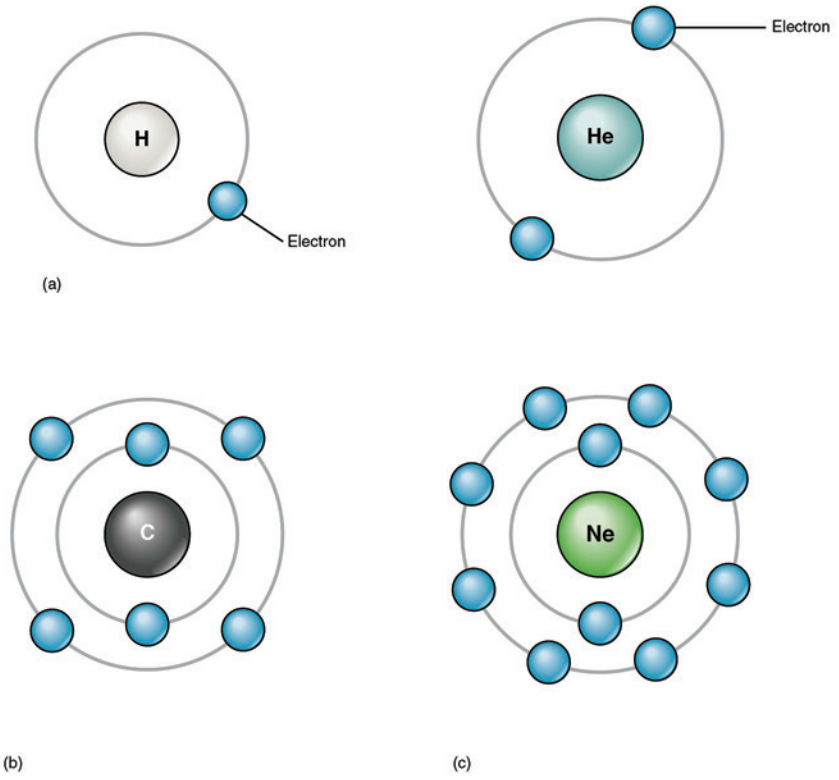


Figure 2.4 Electron Shells. Electrons orbit the atomic nucleus at distinct levels of energy called electron shells. (a) With one electron, hydrogen only half fills its electron shell. Helium also has a single shell, but its two electrons completely fill it. *Disregard b. and c. parts of this figure.*

Example: Consider hydrogen, with its one electron only half filling its valence shell. This single electron is likely to be drawn into relationships with the atoms of other elements so that hydrogen's single valence shell can be stabilized.

All atoms (except hydrogen and helium with their single electron shells) are most stable when there are exactly eight electrons in their valence shell. This principle is referred to as the octet rule, and it states that an atom will give up, gain, or share electrons with another atom so that it ends up with eight electrons in its own valence shell.

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2.2 Chemical Bonds

Learning Objectives

By the end of this section, you will be able to:

- Explain the relationship between molecules and compounds
- Distinguish between ions, cations, and anions
- Identify the key difference between ionic and covalent bonds
- Distinguish between nonpolar and polar covalent bonds
- Explain how water molecules link via hydrogen bonds

Atoms link by forming a chemical bond. A **bond** is a weak or strong electrical attraction that holds atoms in the same vicinity. The new grouping is typically more stable—less likely to react again—than its component atoms were when they were separate. A more or less stable grouping of two or more atoms held together by chemical bonds is called a **molecule**. The bonded atoms may be of the same element, as in the case of H_2, which is called molecular hydrogen or hydrogen gas. When a molecule is made up of two or more atoms of different elements, it is called a chemical **compound**. Thus, a unit of water, or H_2O, is a compound, as is a single molecule of the gas methane, or CH_4.

Three types of chemical bonds are important in human physiology because they hold together substances that are used by the body for critical aspects of homeostasis, signalling, and energy production, to name just a few important processes. These are ionic bonds, covalent bonds, and hydrogen bonds.

Ions and Ionic Bonds

When an atom participates in a chemical reaction that results in the donation or acceptance of one or more electrons, the atom will then become positively or negatively charged. This happens frequently for most atoms in order to have a full valence shell, as described previously. This can happen either by gaining electrons to fill a shell that is more than half full or by giving away electrons to empty a shell that is less than half full, thereby leaving the next smaller electron shell as the new, full valence shell. An atom that has an electrical charge—whether positive or negative—is an **ion**. For example, a potassium ion is written K^+, indicating that it has lost a single electron. A positively charged ion is known as a **cation**. If an element accepts one electron, its electrons will outnumber its protons by one, and it will have an overall negative charge. The ionized form of fluorine is called fluoride and is written as F^-. A negatively charged ion is known as an **anion**

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Interactive Link 2.2

Watch this video (http://oer.aupress.ca/oer-202505/2.2) to learn about electrical energy and the attraction/repulsion of charges. What happens to the charged electroscope when a conductor is moved between its plastic sheets, and why?

Atoms that have more than one electron to donate or accept will end up with stronger positive or negative charges. A cation that has donated two electrons has a net charge of +2. Using magnesium (Mg) as an example, this can be written Mg^{++} or Mg^{2+}. An anion that has accepted two electrons has a net charge of −2. The ionic form of selenium (Se), for example, is typically written Se^{2-}.

The opposite charges of cations and anions exert a moderately strong mutual attraction that keeps the atoms in close proximity, forming an ionic bond. An **ionic bond** is an ongoing close association between ions of opposite charge. As shown in Figure 2.5, sodium commonly donates an electron to chlorine, becoming the cation Na^+. When chlorine accepts the electron, it becomes the chloride anion, Cl^-. With their opposing charges, these two ions strongly attract each other.

Water is an essential component of life because it is able to break the ionic bonds in salts to free the ions. In fact, in biological fluids, most individual atoms exist as ions. These dissolved ions produce electrical charges within the body. The behaviour of these ions produces the tracings of heart and brain function observed as waves on an electrocardiogram (EKG or ECG) or an electroencephalogram (EEG). The electrical activity that derives from the interactions of the charged ions is why they are also called electrolytes.

Covalent Bonds

A **covalent bond** shares electrons in a mutually stabilizing relationship. The atoms do not lose or gain electrons permanently; instead, the electrons move back and forth between the elements. Because of the close sharing of pairs of electrons (one electron from each of two atoms), covalent bonds are stronger than ionic bonds.

Nonpolar Covalent Bonds

The sharing of the negative electrons is relatively equal, as is the electrical pull of the positive protons in the nuclei of the atoms involved. This is why covalently bonded molecules that are electrically balanced in this way are described as nonpolar; that is, no region of the molecule is either more positive or more negative

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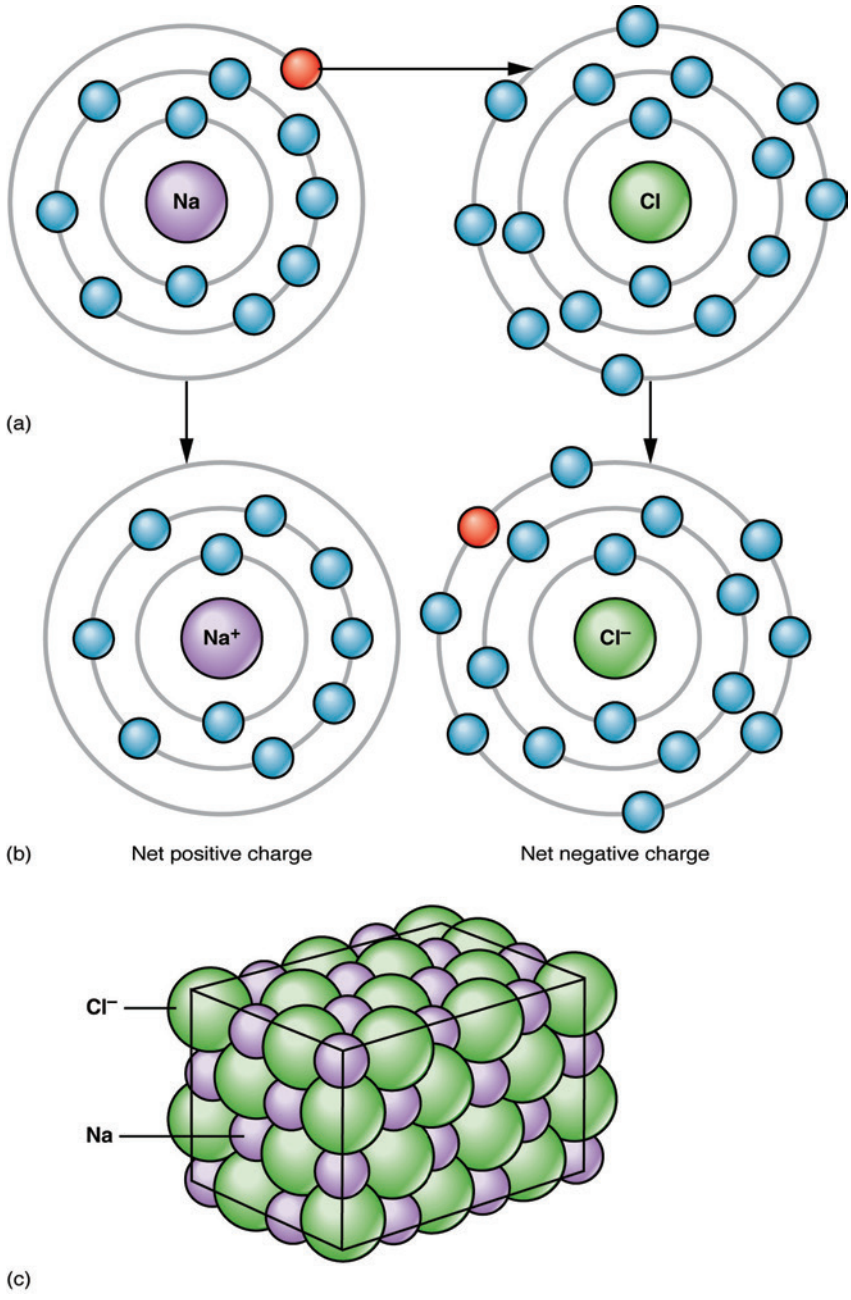


Figure 2.5 Ionic Bonding. (a) Sodium readily donates the solitary electron in its valence shell to chlorine, which needs only one electron to have a full valence shell. (b) The opposite electrical charges of the resulting sodium cation and chloride anion result in the formation of a bond of attraction called an ionic bond. (c) The attraction of many sodium and chloride ions results in the formation of large groupings called crystals.

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than any other (Figure 2.6). In covalent bonds, electrons in the two atoms' overlapping atomic orbitals are shared to fill the valence shells of both atoms, ultimately stabilizing both of the atoms involved. In a single covalent bond, a single electron pair is shared between two atoms, while in a double covalent bond, two pairs of electrons are shared between two atoms. There are even triple covalent bonds, where three electron pairs are shared between two atoms.

Polar Covalent Bonds

A **polar molecule** contains regions that have partial opposite electrical charges. Some elements have a strong "pull" on the electrons of other elements. In a covalent bond, elements do not take electrons from other elements but pull them closer to their own nucleus. Take, for example, a water molecule (Figure 2.7). In this molecule, the nucleus of the oxygen attracts the electrons more strongly than the nuclei of the hydrogen atoms. Because electrons are negative, the oxygen end of their bond becomes slightly more negative than the hydrogen end of their bond. This gives the water molecule partially charged ends.

Hydrogen Bonds

A **hydrogen bond** is a bond between molecules or part of a large molecule. It is formed when a weakly positive hydrogen atom already bonded to one

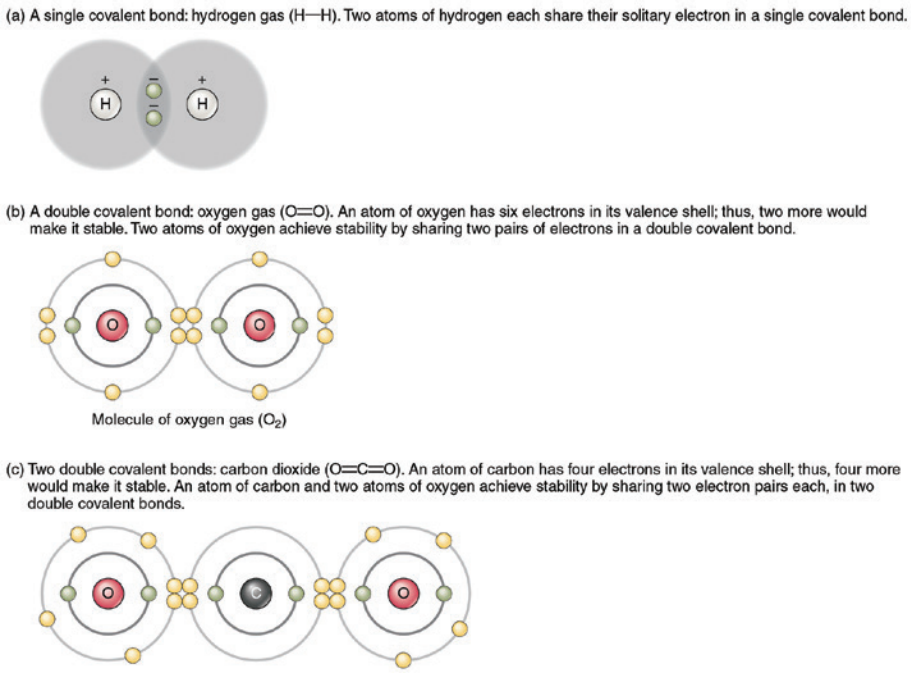


Figure 2.6 Covalent Bonding.

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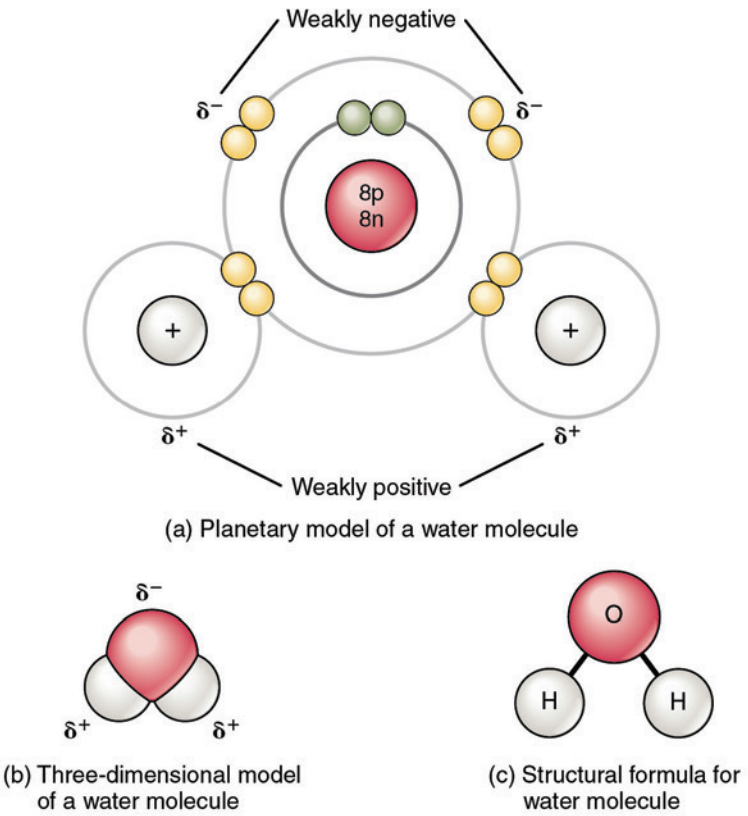


Figure 2.7 Polar Covalent Bonds in a Water Molecule.

electronegative atom (for example, the oxygen in the water molecule) is attracted to another electronegative atom from another molecule. In other words, hydrogen bonds always include hydrogen that is already part of a polar molecule.

Example: The most common example of hydrogen bonding in the natural world occurs between molecules of water. It happens before your eyes whenever two raindrops merge into a larger bead or a creek spills into a river. Hydrogen bonding occurs because the weakly negative oxygen atom in one water molecule is attracted to the weakly positive hydrogen atoms of two other water molecules (Figure 2.8).

Water molecules also strongly attract other types of charged molecules as well as ions.

Example: This explains why "table salt"—a molecule called a "salt" in chemistry, which consists of equal numbers of positively charged sodium (Na^+) and negatively charged chloride (Cl^-) ions—dissolves so readily in water, in this case forming dipole-ion bonds between the water and the electrically charged ions (electrolytes). Water molecules also repel molecules with nonpolar covalent bonds, like fats, lipids, and oils.

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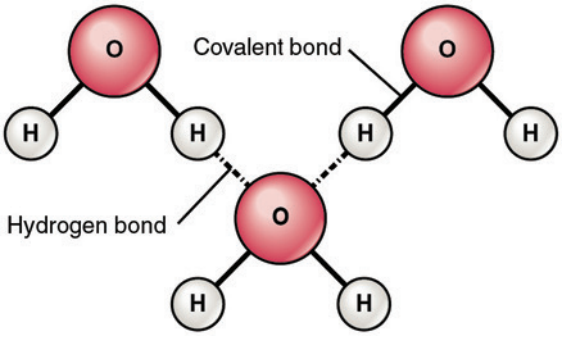


Figure 2.8 Hydrogen Bonds Between Water Molecules. Notice that the bonds occur between the weakly positive charge on the hydrogen atoms and the weakly negative charge on the oxygen atoms. Hydrogen bonds are relatively weak and therefore are indicated with a dotted (rather than a solid) line.

2.3 Chemical Reactions

Learning Objectives

By the end of this section, you will be able to:

- Distinguish between kinetic and potential energy and between exergonic and endergonic chemical reactions
- Identify four forms of energy important in human functioning
- Describe the three basic types of chemical reactions
- Describe how enzymes influence the rate of chemical reactions

One characteristic of a living organism is metabolism, which is the sum of all the chemical reactions that go on to maintain that organism's health and life.

The Role of Energy in Chemical Reactions

Chemical reactions require a sufficient amount of energy to cause the matter to collide with enough precision and force that old chemical bonds can be broken and new ones formed. In general, **kinetic energy** is the form of energy powering any type of matter in motion. Imagine you are building a brick wall. The energy it takes to lift and place one brick atop another is kinetic energy—the energy matter possesses because of its motion. Once the wall is in place, it stores potential energy. **Potential energy** is the energy of position, or the energy matter possesses because of the positioning or structure of its components. If the brick wall collapses, the stored potential energy is released as kinetic energy as the bricks fall. In the human body, potential

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energy is stored in the bonds between atoms and molecules. **Chemical energy** is the form of potential energy in which energy is stored in chemical bonds. When those bonds are formed, chemical energy is invested, and when they break, chemical energy is released. Notice that chemical energy, like all energy, is neither created nor destroyed; rather, it is converted from one form to another. When you eat an energy bar before heading out the door for a hike, the honey, nuts, and other foods the bar contains are broken down and rearranged by your body into molecules that your muscle cells convert to kinetic energy.

Chemical reactions that release more energy than they absorb are characterized as exergonic. The catabolism of the foods in your energy bar is an example. Some of the chemical energy stored in the bar is absorbed into molecules your body uses for fuel, but some of it is released—for example, as heat. In contrast, chemical reactions that absorb more energy than they release are endergonic. These reactions require energy input, and the resulting molecule stores not only the chemical energy in the original components but also the energy that fuelled the reaction.

Because energy is neither created nor destroyed, where does the energy needed for endergonic reactions come from? In many cases, it comes from exergonic reactions.

Forms of Energy Important in Human Functioning

You have already learned that chemical energy is absorbed, stored, and released by chemical bonds. In addition to chemical energy, mechanical, radiant, and electrical energy are important in human functioning.

- Mechanical energy, which is stored in physical systems such as machines, engines, or the human body, directly powers the movement of matter. When you lift a brick into place on a wall, your muscles provide the mechanical energy that moves the brick.
- Radiant energy is energy emitted and transmitted as waves rather than matter. These waves vary in length from long radio waves and microwaves to short gamma waves emitted from decaying atomic nuclei. The full spectrum of radiant energy is referred to as the electromagnetic spectrum.
- Electrical energy, supplied by electrolytes in cells and body fluids, contributes to the voltage changes that help transmit impulses in nerve and muscle cells.

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Characteristics of Chemical Reactions

All chemical reactions begin with a **reactant**, the general term for one or more substances that enter into a reaction. Sodium and chloride ions, for example, are the reactants in the production of table salt. The one or more substances produced by a chemical reaction are called the **product**.

Like energy, mass cannot be created or destroyed in a chemical reaction. This is called the law of conservation of mass. In chemical reactions, the components of the reactants—the elements involved and the number of atoms of each—are all present in the product(s). Similarly, there is nothing present in the products that is not present in the reactants.

A **synthesis reaction** is a chemical reaction that results in the synthesis (joining) of components that were formerly separate. A **decomposition reaction** is a chemical reaction that breaks down or "decomposes" something larger into its constituent parts.

An **exchange reaction** is a chemical reaction in which both synthesis and decomposition occur, chemical bonds are both formed and broken, and chemical energy is absorbed, stored, and released.

Enzymes and Catalysts

In chemistry, a **catalyst** is a substance that increases the rate of a chemical reaction without itself undergoing any change. You can think of a catalyst as a chemical change agent. They help increase the rate and force at which atoms, ions, and molecules collide, thereby increasing the probability that their valence shell electrons will interact. The most important catalysts in the human body are enzymes. An **enzyme** is a biological catalyst primarily composed of either protein (amino acid chains) or ribonucleic acid (RNA) and is specific for a single substrate. More details later in this chapter.

All reactions, whether they are endergonic or exergonic, require a little bit of energy to "get going." This is activation energy. Enzymes work by lowering the level of energy that needs to be invested in a chemical reaction. A chemical reaction's **activation energy** is the "threshold" level of energy needed to break the bonds in the reactants. Once those bonds are broken, new arrangements can form. Without an enzyme to act as a catalyst, a much larger investment of energy is needed to ignite a chemical reaction (Figure 2.9). Enzymes are critical to the body's healthy functioning. They assist, for example, with the breakdown of food and its conversion to energy. In fact, most of the chemical reactions in the body are facilitated by enzymes.

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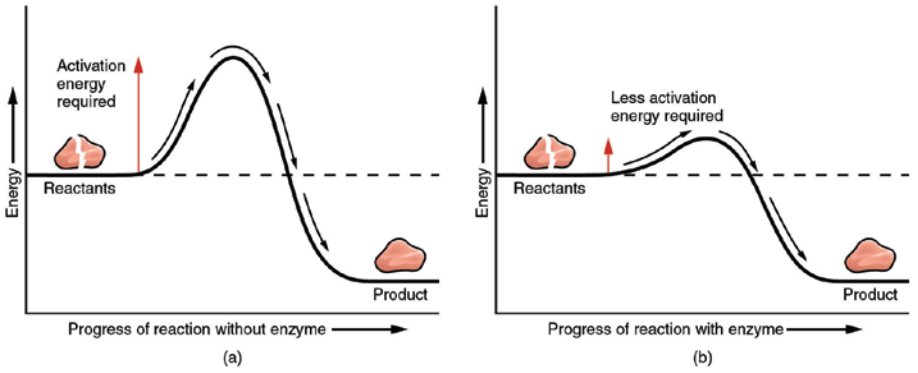


Figure 2.9 Energy Required in Chemical Reactions. Enzymes decrease the activation energy required for a given chemical reaction to occur. (a) Without an enzyme, the energy input needed for a reaction to begin is high. (b) With the help of an enzyme, less energy is needed for a reaction to begin.

2.4 Inorganic Compounds Essential to Human Functioning

Learning Objectives

By the end of this section, you will be able to:

- Compare and contrast inorganic and organic compounds
- Identify the properties of water that make it essential to life
- Explain the role of salts in body functioning
- Distinguish between acids and bases, and explain their role in pH
- Discuss the role of buffers in helping the body maintain pH homeostasis
- Understand the concepts of acidosis and alkalosis

The concepts you have learned so far in this chapter govern all forms of matter and would work as a foundation for geology as well as biology. This section of the chapter narrows the focus to the chemistry of human life—that is, the compounds important for the body's structure and function. In general, these compounds are either inorganic or organic.

- An **inorganic compound** is a substance that does not contain both carbon and hydrogen. A great many inorganic compounds do contain hydrogen atoms, such as water (H_2O) and the hydrochloric acid (HCl) produced by your stomach. In contrast, only a handful of inorganic

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compounds contain carbon atoms. Carbon dioxide (CO_2) is one of the few examples.

- An **organic compound**, then, is a substance that contains both carbon and hydrogen. Organic compounds are synthesized via covalent bonds within living organisms, including the human body. Recall that carbon and hydrogen are the second- and third-most-abundant elements in your body.

The following section examines the three groups of inorganic compounds essential to life: water, salts, and acids and bases. Organic compounds are covered later in the chapter.

Water

As much as 70 percent of an adult's body weight is water. This water is contained both within the cells and between the cells that make up tissues and organs. Its several roles make water indispensable to human functioning.

Water as a Lubricant and Cushion

Water is a major component of many of the body's lubricating fluids.

Example: Water in synovial fluid lubricates the actions of body joints, and water in pleural fluid helps the lungs expand and recoil with breathing. Watery fluids help keep food flowing through the digestive tract and ensure that the movement of adjacent abdominal organs is friction-free.

Water also protects cells and organs from physical trauma.

Example: Water's protective functions include cushioning the brain within the skull, protecting the delicate nerve tissue of the eyes, and cushioning a developing fetus in the mother's womb as well.

Water as a Heat Sink

A heat sink is a substance or object that absorbs and dissipates heat but does not experience a corresponding increase in temperature. In the body, water absorbs the heat generated by chemical reactions without greatly increasing in temperature. Moreover, when the environmental temperature soars, the water stored in the body helps keep the body cool. This cooling effect happens as warm blood from the body's core flows to the blood vessels just under the skin and is transferred to the environment. At the same time, sweat glands release warm water in sweat. As the water evaporates into the air, it carries away heat, and then the cooler blood from the periphery circulates back to the body core.

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Water as a Component of Liquid Mixtures

A mixture is a combination of two or more substances, each of which maintains its own chemical identity. In other words, the constituent substances are not chemically bonded into a new, larger chemical compound.

Example: The concept is easy to imagine if you think of powdery substances such as flour and sugar; when you stir them together in a bowl, they obviously do not bond to form a new compound. The air you breathe is a gaseous mixture containing three discrete elements—nitrogen, oxygen, and argon—and one compound, carbon dioxide.

There are three types of liquid mixtures, all of which contain water as a key component. These are solutions, colloids, and suspensions.

For cells in the body to survive, they must be kept moist in a water-based liquid called a solution. In chemistry, a liquid **solution** consists of a solvent (water) that dissolves a substance called a solute. An important characteristic of solutions is that they are homogeneous; that is, the solute molecules are distributed evenly throughout the solution.

Example: If you were to stir a teaspoon of sugar into a glass of water, the sugar would dissolve into sugar molecules separated by water molecules. The ratio of sugar to water in the left side of the glass would be the same as the ratio of sugar to water in the right side of the glass. If you were to add more sugar, the ratio of sugar to water would change, but the distribution—provided you had stirred well—would still be even.

Water is certainly the most abundant solvent in the body; essentially all the body's chemical reactions occur among compounds dissolved in water. Water is considered the "universal" solvent, and it is thought that life cannot exist without water because of this. Because water molecules are polar, with regions of positive and negative electrical charge, water readily dissolves ionic compounds and, to a lesser degree, polar covalent compounds. Such compounds are referred to as hydrophilic, or "water-loving." As mentioned in the sugar example, sugar dissolves well in water. This is because sugar molecules contain regions of hydrogen-oxygen polar bonds, making them hydrophilic. Nonpolar molecules, which do not readily dissolve in water, are called hydrophobic, or "water-fearing."

Concentrations of Solutes

The concentration of a given solute is the number of particles of that solute in a given space; for example, oxygen makes up about 21 percent of atmospheric air.

A **colloid** is a mixture that is somewhat like a heavy solution. The solute particles consist of tiny clumps of molecules large enough to make the liquid mixture opaque (because the particles are large enough to scatter light).

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Familiar examples of colloids are milk and cream. In the thyroid glands, the thyroid hormone is stored as a thick protein mixture also called a colloid.

A **suspension** is a liquid mixture in which a heavier substance is suspended temporarily in a liquid but, over time, settles out. This separation of particles from a suspension is called sedimentation.

Example: Sedimentation occurs in a blood test that establishes a sedimentation rate, or sed rate. The test measures how quickly red blood cells in a test tube settle out of the watery portion of blood (known as plasma) over a set period of time. Rapid sedimentation of blood cells does not normally happen in the healthy body, but aspects of certain diseases can cause blood cells to clump together, and these heavy clumps of blood cells settle to the bottom of the test tube more quickly than do normal blood cells.

The Role of Water in Chemical Reactions

Two types of chemical reactions involve the creation or the consumption of water: dehydration synthesis and hydrolysis.

- In dehydration synthesis, one reactant gives up an atom of hydrogen and another reactant gives up a hydroxyl group (OH) in the synthesis of a new product. In the formation of their covalent bond, a molecule of water is released as a by-product. This is also sometimes referred to as a condensation reaction.
- In hydrolysis, a molecule of water disrupts a compound, breaking its bonds. The water is itself split into H and OH. One portion of the severed compound then bonds with the hydrogen atom, and the other portion bonds with the hydroxyl group.

These reactions are reversible and play an important role in the chemistry of organic compounds (which will be discussed shortly).

Salts

Salts (broader meaning) are formed when ions form ionic bonds. In these reactions, one atom gives up one or more electrons and thus becomes positively charged, whereas the other accepts one or more electrons and becomes negatively charged—for example, potassium chloride or sodium chloride. You can define a salt as a substance that, when dissolved in water, dissociates into ions other than H^+ or OH^-. This fact is important in distinguishing salts from acids and bases, discussed next.

Example: A typical salt, NaCl, dissociates completely in water. The positive and negative regions on the water molecule (the hydrogen and oxygen ends, respectively) attract the negative chloride and positive sodium ions, pulling

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them away from each other. Again, whereas nonpolar and polar covalently bonded compounds break apart into molecules in solution, salts dissociate into ions. These ions are electrolytes; they are capable of conducting an electrical current in solution. This property is critical to the function of ions in transmitting nerve impulses and prompting muscle contraction.

Many other salts are important in the body. Bile salts produced by the liver help break apart dietary fats, and calcium phosphate salts form the mineral portions of teeth and bones.

Acids and Bases

Acids and bases, like salts, dissociate in water into electrolytes. Acids and bases can very much change the properties of the solutions in which they are dissolved.

Acids

An **acid** is a substance that releases hydrogen ions (H^+) in solution (Figure 2.10a). Because an atom of hydrogen has just one proton and one electron, a positively charged hydrogen ion is simply a proton. This solitary proton is highly likely to participate in chemical reactions. Strong acids are compounds that release all their H^+ in solution; that is, they ionize completely.

Example: Hydrochloric acid (HCl), which is released from cells in the lining of the stomach, is a strong acid because it releases all its H^+ in the stomach's watery environment. This strong acid aids the stomach in killing ingested microbes.

Weak acids do not ionize completely; that is, some of their hydrogen ions remain bonded within a compound in solution. An example of a weak acid is vinegar, or acetic acid; it is called acetate after it gives up a proton.

Bases

A **base** is a substance that releases hydroxyl ions (OH^-) in solution or one that accepts H^+ already present in solution (see Figure 2.10b). Strong bases release most or all of their hydroxyl ions; weak bases release only some hydroxyl ions or absorb only a few H^+.

Example: Food mixed with hydrochloric acid from the stomach would burn the small intestine, the next portion of the digestive tract after the stomach, if it were not for the release of bicarbonate (HCO^-) released by the pancreas, a weak base that attracts H^+. Bicarbonate accepts some of the H^+ protons, thereby reducing the acidity of the solution.

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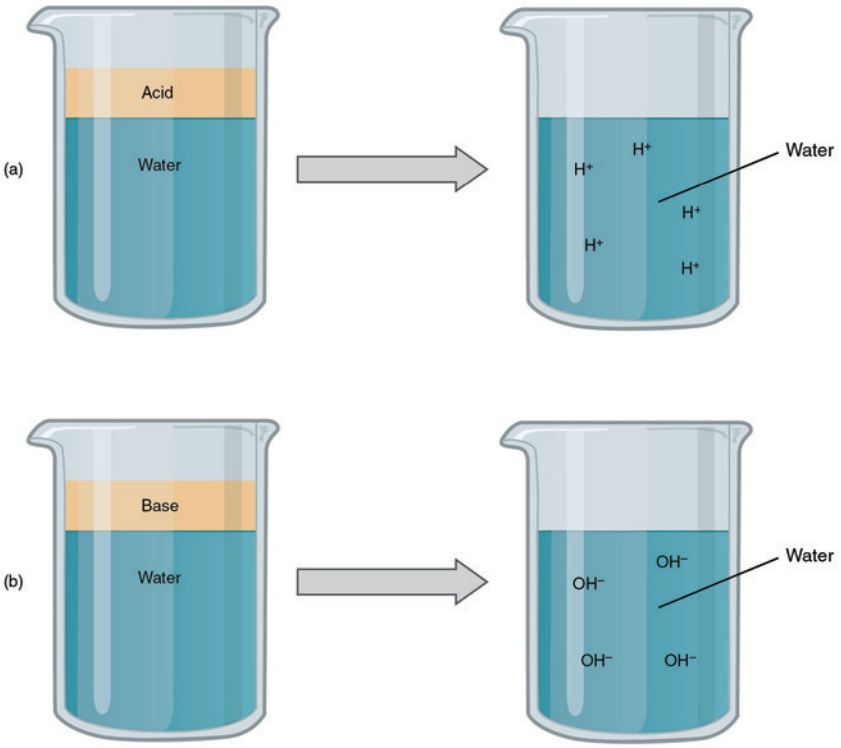


Figure 2.10 Acids and Bases. (a) In aqueous solution, an acid dissociates into hydrogen ions (H^+) and anions. Nearly every molecule of a strong acid dissociates, producing a high concentration of H^+. (b) In aqueous solution, a base dissociates into hydroxyl ions (OH^-) and cations. Nearly every molecule of a strong base dissociates, producing a high concentration of OH^-.

The Concept of pH

The relative acidity or alkalinity of a solution can be indicated by its pH. A solution's **pH** is the negative, base-10 logarithm of the hydrogen ion (H^+) concentration of the solution.

Example: A pH 4 solution has a concentration of H^+ that is ten times greater than that of a pH 5 solution. That is, a solution with a pH of 4 is ten times more acidic than a solution with a pH of 5.

The concept of pH will begin to make more sense when you study the pH scale, as shown in Figure 2.11. The scale consists of a series of increments ranging from 0 to 14. A solution with a pH of 7 is considered neutral—neither acidic nor basic. Pure water has a pH of 7. The lower the number below 7, the more acidic the solution, or the greater the concentration of H^+. The concentration of hydrogen ions at each pH value is 10 times different than the next pH. The higher the number above 7, the more basic (alkaline) the solution, or the lower the concentration of H^+.

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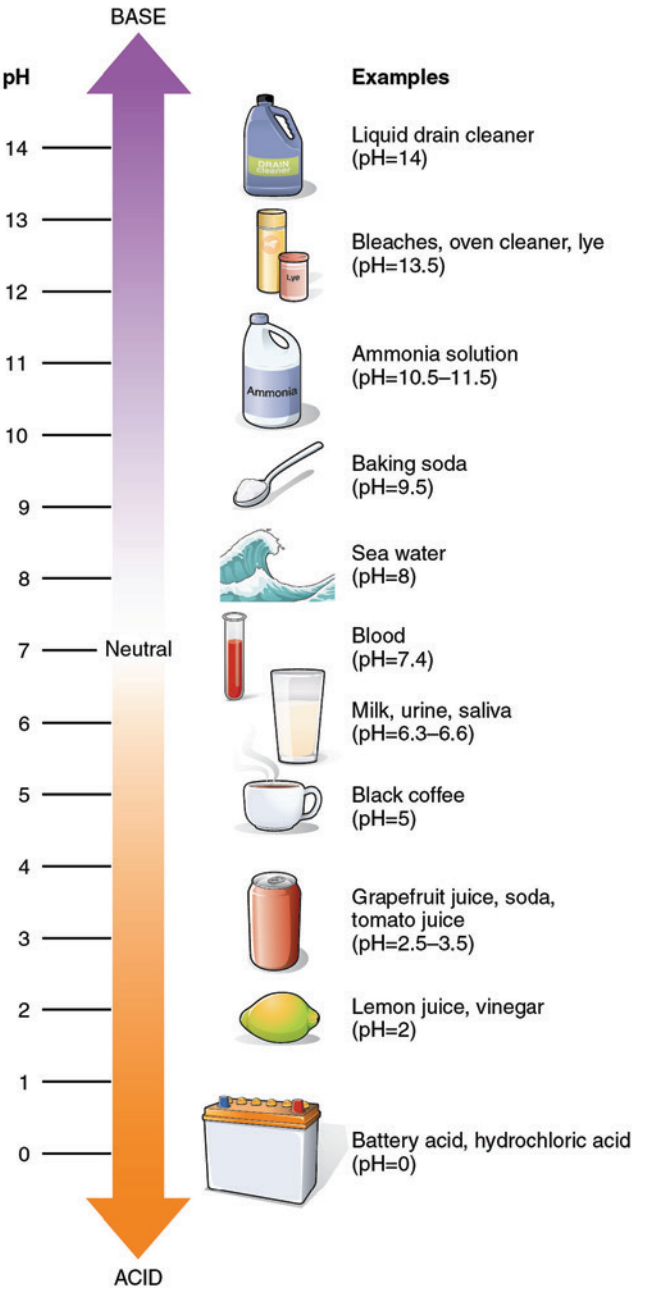


Figure 2.11 **The pH Scale.**

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Example: Human urine is ten times more acidic than pure water, and HCl is 10,000,000 times more acidic than water.

Buffers

The pH of human blood normally ranges from 7.35 to 7.45, although it is typically identified as pH 7.4. At this slightly basic pH, blood can reduce the acidity resulting from the carbon dioxide (CO_2) constantly being released into the bloodstream by the trillions of cells in the body. Homeostatic mechanisms (along with exhaling CO_2 while breathing) normally keep the pH of blood within this narrow range. This is critical because fluctuations—either too acidic or too alkaline—can lead to life-threatening disorders.

All cells of the body depend on homeostatic regulation of acid-base balance at a pH of approximately 7.4. The body therefore has several mechanisms for this regulation, involving breathing, the excretion of chemicals in urine, and the internal release of chemicals collectively called buffers into body fluids. A **buffer** is a solution of a weak acid and its conjugate base. A buffer can neutralize small amounts of acids or bases in body fluids (details in Chapter 25).

Example: If there is even a slight decrease below 7.35 in the pH of a body fluid, the buffer in the fluid—in this case, acting as a weak base—will bind the excess hydrogen ions. In contrast, if pH rises above 7.45, the buffer will act as a weak acid and contribute hydrogen ions.

Excessive acidity of the blood and other body fluids is known as acidosis. Acidosis can also be caused by metabolic problems that reduce the level or function of buffers that act as bases or that promote the production of acids.

Example: With severe diarrhea, too much bicarbonate can be lost from the body, allowing acids to build up in body fluids. In people with poorly managed diabetes (ineffective regulation of blood sugar), acids called ketones are produced as a form of body fuel. These can build up in the blood, causing a serious condition called diabetic ketoacidosis. Kidney failure, liver failure, heart failure, cancer, and other disorders can also prompt metabolic acidosis.

In contrast, alkalosis is a condition in which the blood and other body fluids are too alkaline (basic). As with acidosis, respiratory disorders are a major cause; however, in respiratory alkalosis, carbon dioxide levels fall too low. Lung disease, aspirin overdose, shock, and ordinary anxiety can cause respiratory alkalosis, which reduces the normal concentration of H^+. Metabolic alkalosis often results from prolonged, severe vomiting, which causes a loss of hydrogen and chloride ions (as components of HCl). Medications can also prompt alkalosis. These include diuretics that cause the body to lose potassium ions as well as antacids when taken in excessive amounts—for instance, by someone with persistent heartburn or an ulcer.

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2.5 Organic Compounds Essential to Human Functioning

Learning Objectives

By the end of this section, you will be able to:

- Identify four types of organic molecules essential to human functioning
- Provide examples of three types of carbohydrates and identify the primary functions of carbohydrates in the body
- Discuss four types of lipids important in human functioning
- Describe the structure of proteins and discuss their importance to human functioning
- Identify the building blocks of nucleic acids and the roles of DNA, RNA, and ATP in human functioning

Organic compounds typically consist of groups of carbon atoms covalently bonded to hydrogen, usually oxygen, and often other elements as well. They are found throughout the world in soils and seas, commercial products, and every cell of the human body. The four types most important to human structure and function are carbohydrates, lipids, proteins, and nucleotides.

Carbohydrates

A **carbohydrate** is a molecule composed of carbon, hydrogen, and oxygen. The chemical formula for a "generic" molecule of carbohydrate is $(CH_2O)_n$.

Carbohydrates are referred to as saccharides, a word meaning "sugars." Three forms are important in the body. Monosaccharides are the monomers of carbohydrates. Disaccharides (*di-* = "two") are made up of two monomers. Polysaccharides are the polymers of carbohydrates and can consist of hundreds to thousands of monomers.

Monosaccharides

A **monosaccharide** is a monomer of carbohydrates. Five monosaccharides are important in the body. Three of these are the hexose sugars, so called because they each contain six atoms of carbon. These are glucose, fructose, and galactose. The remaining monosaccharides are the two pentose sugars, each of which contains five atoms of carbon. They are ribose and deoxyribose.

A **disaccharide** is a pair of monosaccharides. Disaccharides are formed via dehydration synthesis, and the bond linking them is referred to as a glycosidic

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bond (*glyco-* = "sugar"). Three disaccharides are important to humans. These are sucrose, commonly referred to as table sugar; lactose, or milk sugar; and maltose, or malt sugar. As you can tell from their common names, you consume these in your diet; however, your body cannot use them directly. Instead, in the digestive tract, they are split into their component monosaccharides via hydrolysis.

Interactive Link 2.3

Watch this video (http://oer.aupress.ca/oer-202505/2.3) to observe the formation of a disaccharide. What happens when water encounters a glycosidic bond?

Polysaccharides

Polysaccharides can contain a few to a thousand or more monosaccharides. Three are important to the body:

- Starches are polymers of glucose. They occur in long chains called amylose or branched chains called amylopectin, both of which are stored in plant-based foods and are relatively easy to digest.
- Glycogen is also a polymer of glucose, but it is stored in the tissues of animals, especially in the muscles and liver. It is not considered a dietary carbohydrate because very little glycogen remains in animal tissues after slaughter; however, the human body stores excess glucose as glycogen, again, in the muscles and liver.
- Cellulose, a polysaccharide that is the primary component of the cell wall of green plants, is the component of plant food referred to as "fibre." In humans, cellulose/fibre is not digestible; however, dietary fibre has many health benefits. It helps you feel full so you eat less, it promotes a healthy digestive tract, and a diet high in fibre is thought to reduce the risk of heart disease and possibly some forms of cancer.

Functions of Carbohydrates

The body obtains carbohydrates from plant-based foods. Grains, fruits, and legumes and other vegetables provide most of the carbohydrates in the human diet, although lactose is found in dairy products.

While most body cells can break down other organic compounds for fuel, all body cells can use glucose. Moreover, nerve cells (neurons) in the brain, spinal cord, and peripheral nervous system, as well as red blood cells, can use only glucose for fuel. In the breakdown of glucose for energy, molecules of adenosine

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triphosphate, better known as ATP, are produced. **Adenosine triphosphate** (**ATP**) is composed of a ribose sugar, an adenine base, and three phosphate groups. ATP releases free energy when its phosphate bonds are broken and thus supplies ready energy to the cell. More ATP is produced in the presence of oxygen (O_2) than in pathways that do not use oxygen. The overall reaction for the conversion of the energy in glucose to energy stored in ATP can be written as follows:

$$C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + ATP$$

In addition to being a critical fuel source, carbohydrates are present in very small amounts in cells' structure. For instance, some carbohydrate molecules bind with proteins to produce glycoproteins, and others combine with lipids to produce glycolipids, both of which are found in the membrane that encloses the contents of body cells.

Lipids

A **lipid** is one of a highly diverse group of compounds made up mostly of hydrocarbons. The few oxygen atoms they contain are often at the periphery of the molecule. Their nonpolar hydrocarbons make all lipids hydrophobic. In water, lipids do not form a true solution, but they may form an emulsion, which is the term for a mixture of solutions that do not mix well.

Triglycerides

A **triglyceride** is one of the most common dietary lipid groups, and the type found most abundantly in body tissues. This compound, which is commonly referred to as a fat, is formed from the synthesis of two types of molecules:

- A glycerol backbone at the core of triglycerides consists of three carbon atoms.
- Three fatty acids, long chains of hydrocarbons with a carboxyl group and a methyl group at opposite ends, extend from each of the carbons of the glycerol.

Triglycerides form via dehydration synthesis. As a group, triglycerides are a major fuel source for the body. Glycerol gives up hydrogen atoms from its hydroxyl groups at each bond, and the carboxyl group on each fatty acid chain gives up a hydroxyl group. A total of three water molecules are thereby released.

Fatty acid chains that have no double carbon bonds anywhere along their length and therefore contain the maximum number of hydrogen atoms are called saturated fatty acids. These straight, rigid chains pack tightly together and are solid or semisolid at room temperature. Butter and lard are examples,

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as is the fat found on a steak or in your own body. In contrast, unsaturated fatty acids are fatty acids with one double carbon bond that are kinked at that bond. These monounsaturated fatty acids are therefore unable to pack together tightly and are liquid at room temperature. Polyunsaturated fatty acids contain two or more double carbon bonds and are also liquid at room temperature. Plant oils such as olive oil typically contain both mono- and polyunsaturated fatty acids.

Finally, trans fatty acids—found in certain processed foods, including some stick and tub margarines—are thought to be even more harmful to the heart and blood vessels than saturated fatty acids. Trans fats are created from unsaturated fatty acids (such as corn oil) when chemically treated to produce partially hydrogenated fats.

Fatty acids are also components of glycolipids, which are sugar-fat compounds found in the cell membrane. Lipoproteins are compounds in which the hydrophobic triglycerides are packaged in protein envelopes for transport in body fluids.

Phospholipids

As its name suggests, a **phospholipid** is a bond between the glycerol component of a lipid and a phosphorus molecule. In fact, phospholipids are similar in structure to triglycerides. However, instead of having three fatty acids, a phospholipid is generated from a diglyceride, a glycerol with just two fatty acid chains. The third binding site on the glycerol is taken up by the phosphate group, which in turn is attached to a polar "head" region of the molecule. Recall that triglycerides are nonpolar and hydrophobic. This still holds for the fatty acid portion of a phospholipid compound. However, the head of a phospholipid contains charges on the phosphate groups as well as on the nitrogen atom. These charges make the phospholipid head hydrophilic. Therefore, phospholipids are said to have hydrophobic tails, containing the neutral fatty acids, and hydrophilic heads, containing the charged phosphate groups and nitrogen atom.

Steroids

A **steroid** compound (referred to as a sterol) has as its foundation a set of four hydrocarbon rings bonded to a variety of other atoms and molecules. Although both plants and animals synthesize sterols, the type that makes the most important contribution to human structure and function is cholesterol, which is synthesized by the liver in humans and animals and is also present in most animal-based foods. Like other lipids, cholesterol's hydrocarbons make it hydrophobic; however, it has a polar hydroxyl head that is hydrophilic. Cholesterol is an important component of bile acids, compounds that help emulsify dietary

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fats. In fact, the word root *chole-* refers to bile. Cholesterol is also a building block of many hormones, signalling molecules that the body releases to regulate processes at distant sites. Finally, like phospholipids, cholesterol molecules are found in the cell membrane, where their hydrophobic and hydrophilic regions help regulate the flow of substances into and out of the cell.

Prostaglandins

Like a hormone, a **prostaglandin** is one of a group of signalling molecules, but prostaglandins are derived from unsaturated fatty acids. One reason that the omega-3 fatty acids found in fish are beneficial is that they stimulate the production of certain prostaglandins that help regulate aspects of blood pressure and inflammation, thereby reducing the risk for heart disease. Prostaglandins also sensitize nerves to pain.

Example: One class of pain-relieving medications called nonsteroidal anti-inflammatory drugs (NSAIDs) works by reducing the effects of prostaglandins.

Proteins

You might associate proteins with muscle tissue, but in fact, proteins are critical components of all tissues and organs. A **protein** is an organic molecule composed of amino acids linked by peptide bonds. Proteins include the keratin in the epidermis of skin that protects underlying tissues as well as the collagen found in the dermis of skin, in bones, and in the meninges that cover the brain and spinal cord. Proteins are also components of many of the body's functional chemicals, including digestive enzymes in the digestive tract, antibodies, the neurotransmitters that neurons use to communicate with other cells, and the peptide-based hormones that regulate certain body functions (for instance, growth hormone). While carbohydrates and lipids are composed of hydrocarbons and oxygen, all proteins also contain nitrogen (N), and many contain sulfur (S) in addition to carbon, hydrogen, and oxygen.

Microstructure of Proteins

Proteins are polymers made up of nitrogen-containing monomers called amino acids. An **amino acid** is a molecule composed of an amino group and a carboxyl group together with a variable side chain. Just 20 different amino acids contribute to nearly all the thousands of different proteins important in human structure and function. Body proteins contain a unique combination of a few dozen to a few hundred of these 20 amino acid monomers. All 20 of these amino acids share a similar structure. Amino acids join via dehydration synthesis to form protein polymers. The unique bond holding amino acids together is called

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a peptide bond. A **peptide bond** is a covalent bond between two amino acids that forms by dehydration synthesis. A peptide, in fact, is a very short chain of amino acids. Strands containing fewer than about 100 amino acids are generally referred to as polypeptides rather than proteins.

The body is able to synthesize most of the amino acids from components of other molecules; however, nine cannot be synthesized and have to be consumed in the diet. These are known as the essential amino acids.

Free amino acids available for protein construction are said to reside in the amino acid pool within cells. Structures within cells use these amino acids when assembling proteins. If a particular essential amino acid is not available in sufficient quantities in the amino acid pool, however, synthesis of proteins containing it can slow or even cease.

Shape of Proteins

A protein's shape is essential to its function, and it is determined, most fundamentally, by the sequence of amino acids of which it is made. The sequence is called the primary structure of the protein. Although some polypeptides exist as linear chains, most are twisted or folded into more complex secondary structures that form when bonding occurs between amino acids with different properties at different regions of the polypeptide.

When they are exposed to extreme heat, acids, bases, and certain other substances, proteins will denature. **Denaturation** is a change in the structure of a molecule through physical or chemical means. Denatured proteins lose their functional shape and are no longer able to carry out their jobs. An everyday example of protein denaturation is the curdling of milk when acidic lemon juice is added.

The contribution of the shape of a protein to its function can hardly be exaggerated.

Example: The long, slender shape of protein strands that make up muscle tissue is essential to their ability to contract (shorten) and relax (lengthen); bones contain long threads of a protein called collagen that acts as scaffolding upon which bone minerals are deposited. These elongated proteins, called fibrous proteins, are strong, durable, and typically hydrophobic.

In contrast, globular proteins are globes or spheres that tend to be highly reactive and are hydrophilic.

Example: Hemoglobin proteins are packed into red blood cells; however, globular proteins are abundant throughout the body, playing critical roles in most body functions; enzymes are examples of this.

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Proteins Function as Enzymes

Without enzymes to catalyze chemical reactions, the human body would be nonfunctional. It functions only because enzymes function.

Enzymatic reactions—chemical reactions catalyzed by enzymes—begin when substrates bind to the enzyme. A **substrate** is a reactant in an enzymatic reaction. This occurs on regions of the enzyme known as active sites (Figure 2.12). Any given enzyme catalyzes just one type of chemical reaction. This characteristic, called specificity, is due to the fact that a substrate with a particular shape and electrical charge can bind only to an active site corresponding to that substrate.

Due to this jigsaw puzzle–like match between an enzyme and its substrates, enzymes are known for their specificity. In fact, as an enzyme binds to its substrate(s), the enzyme structure changes slightly to find the best fit between the transition state (a structural intermediate between the substrate and product) and the active site. This active-site modification in the presence of a substrate, along with the simultaneous formation of the transition state, is called induced fit. Overall, there is a specifically matched enzyme for each substrate and, thus, for each chemical reaction; however, there is some flexibility as well. Some enzymes have the ability to act on several different structurally related substrates.

The binding of a substrate produces an enzyme-substrate complex. It is likely that enzymes speed up chemical reactions in part because the enzyme-substrate complex undergoes a set of temporary and reversible changes that cause the substrates to be oriented toward each other in an optimal position to facilitate their interaction. This promotes increased reaction speed. The enzyme

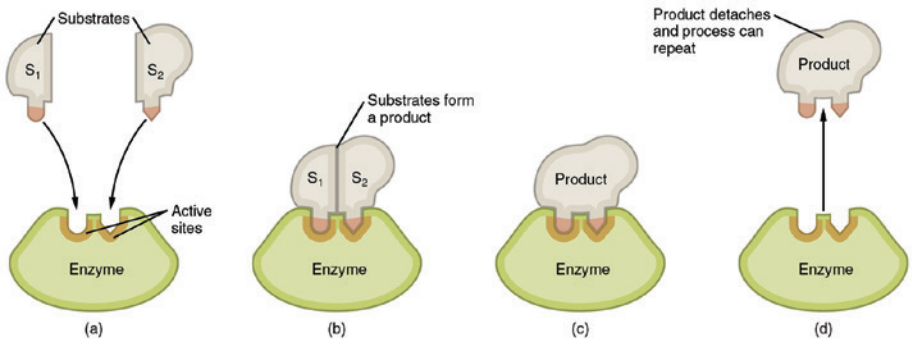


Figure 2.12 Steps in an Enzymatic Reaction. According to the induced-fit model, the active site of the enzyme undergoes conformational changes upon binding with the substrate. (a) Substrates approach active sites on the enzyme. (b) Substrates bind to active sites, producing an enzyme-substrate complex. (c) Changes internal to the enzyme-substrate complex facilitate interaction of the substrates. (d) Products are released, and the enzyme returns to its original form, ready to facilitate another enzymatic reaction.

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then releases the product(s) and resumes its original shape. The enzyme is then free to engage in the process again and will do so as long as substrate remains.

Other Functions of Proteins

Protein is important in building, repairing, and maintaining muscle tissue, but the truth is that proteins contribute to all body tissues, from the skin to the brain cells. Also, certain proteins act as hormones, chemical messengers that help regulate body functions; for example, growth hormone is important for skeletal growth, among other roles.

Their basic and acidic components enable proteins to function as buffers in maintaining acid-base balance, but they also help regulate fluid-electrolyte balance. Proteins attract fluid, and a healthy concentration of proteins in the blood, the cells, and the spaces between cells helps ensure a balance of fluids in these various "compartments." Moreover, proteins in the cell membrane help transport electrolytes in and out of the cell, keeping these ions in a healthy balance. Like lipids, proteins can bind with carbohydrates. They can thereby produce glycoproteins or proteoglycans, both of which have many functions in the body.

The body can use proteins for energy when carbohydrate and fat intake is inadequate and stores of glycogen and adipose tissue become depleted. However, since there is no storage site for protein except in functional tissues, using protein for energy causes tissue breakdown and results in body wasting.

Nucleotides

The fourth type of organic compound important to human structure and function is the nucleotide. A **nucleotide** is one of a class of organic compounds composed of three subunits:

- one or more phosphate groups
- a pentose sugar: either deoxyribose or ribose
- a nitrogen-containing base: adenine (A), cytosine (C), guanine (G), thymine (T), or uracil (U)

Nucleotides can be assembled into nucleic acids (DNA or RNA) or the energy compound adenosine triphosphate.

Nucleic Acids

The nucleic acids differ in their type of pentose sugar. **Deoxyribonucleic acid** (**DNA**) is a polynucleotide that stores genetic information; it serves as long-term storage of information for protein synthesis. DNA contains deoxyribose (so called because it has one less atom of oxygen than ribose) plus one phosphate group and one nitrogen-containing base. The "choices" of base for DNA are adenine,

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cytosine, guanine, and thymine. **Ribonucleic acid** (**RNA**) is a ribose-containing nucleotide that helps manifest the genetic code as protein. RNA contains ribose, one phosphate group, and one nitrogen-containing base, but the "choices" of base for RNA are adenine, cytosine, guanine, and uracil (not thymine).

Bonds formed by dehydration synthesis between the sugar of one nucleic acid monomer and the phosphate group of another form a "backbone" from which the components' nitrogen-containing bases protrude. In DNA, two such backbones attach at their protruding bases via hydrogen bonds. These twist to form a shape known as a **double helix** (Figure 2.13). The sequence of nitrogen-containing bases within a strand of DNA forms the genes that act as a molecular code, instructing cells in the assembly of amino acids into proteins. Humans have almost 22,000 genes in their DNA, locked up in the 46 chromosomes inside the nucleus of each cell (except red blood cells, which lose their nuclei during development). These genes carry the genetic code to build one's body and are unique for each individual, except identical twins.

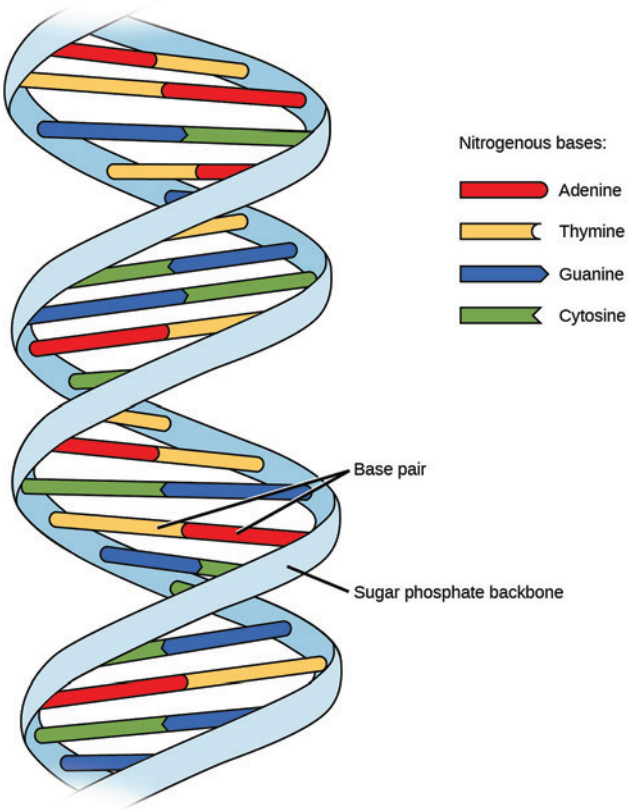


Figure 2.13 DNA. In the DNA double helix, two strands attach via hydrogen bonds between the bases of the component nucleotides.

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In contrast, RNA consists of a single strand of RNA nucleotides of sugar-phosphate backbone studded with bases. Messenger RNA (mRNA) is created during protein synthesis to carry the genetic instructions from the DNA to the cell's protein manufacturing plants in the cytoplasm, the ribosomes.

Adenosine Triphosphate

The nucleotide adenosine triphosphate (ATP) is composed of a ribose sugar, an adenine base, and three phosphate groups. ATP is classified as a high-energy compound because the two covalent bonds linking its three phosphates store a significant amount of potential energy. In the body, the energy released from these high-energy bonds helps fuel the body's activities, from muscle contraction to the transport of substances in and out of cells to anabolic chemical reactions.

When a phosphate group is cleaved from ATP, the products are adenosine diphosphate (ADP) and inorganic phosphate (P_i). This hydrolysis reaction can be written as follows:

$$ATP + H_2O \rightarrow ADP + P_i + \text{energy}$$

Removal of a second phosphate leaves adenosine monophosphate (AMP) and two phosphate groups. Again, these reactions also liberate the energy that had been stored in the phosphate-phosphate bonds. They are reversible, too, as when ADP is formed back into ATP with the addition of energy. **Phosphorylation** is the addition of a phosphate group to an organic compound, in this case resulting in ATP. In such cases, the same level of energy that had been released during hydrolysis must be reinvested to power dehydration synthesis.

Cells can also transfer a phosphate group from ATP to another organic compound. For example, when glucose first enters a cell, a phosphate group is transferred from ATP, forming glucose phosphate ($C_6H_{12}O_6$—P) and ADP.

Key Terms

acid: Compound that releases hydrogen ions (H^+) in solution.
activation energy: Amount of energy greater than the energy contained in the reactants, which must be overcome for a reaction to proceed.
adenosine triphosphate (ATP): Nucleotide containing ribose, an adenine base, and three phosphates; essential in energy transfer.
amino acid: Building block of proteins; characterized by an amino functional group, carboxyl functional groups, and a variable side chain.
anion: Atom with a negative charge.

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atom: Smallest unit of an element that retains the unique properties of that element.

atomic number: Number of protons in the nucleus of an atom.

base: Compound that accepts hydrogen ions (H^+) in solution.

bond: Electrical force linking atoms.

buffer: Solution containing a weak acid or a weak base that opposes wide fluctuations in the pH of body fluids.

carbohydrate: Class of organic compounds built from sugar molecules containing carbon, hydrogen, and oxygen in a 1-2-1 ratio.

catalyst: Substance that increases the rate of a chemical reaction without itself being changed in the process.

cation: Atom with a positive charge.

chemical energy: Form of energy that is absorbed as chemical bonds form, stored as they are maintained, and released as they are broken.

colloid: Liquid mixture in which the solute particles consist of clumps of molecules large enough to scatter light.

compound: Substance composed of two or more different elements joined by chemical bonds.

covalent bond: Chemical bond in which two atoms share electrons, thereby completing their valence shells.

decomposition reaction: Type of catabolic reaction in which one or more bonds within a larger molecule are broken, resulting in the release of smaller molecules or atoms.

denaturation: Change in the structure of a molecule through physical or chemical means.

deoxyribonucleic acid (DNA): Deoxyribose-containing nucleotide that stores genetic information.

disaccharide: Pair of carbohydrate monomers bonded by dehydration synthesis via a glycosidic bond.

double helix: Characteristic of DNA where two strands attach via hydrogen bonds between the bases of the component nucleotides.

electron: Subatomic particle having a negative charge and nearly no mass; found orbiting the atom's nucleus.

electron shell: Area of space a given distance from an atom's nucleus in which electrons are grouped.

element: Substance that cannot be created or broken down by ordinary chemical means.

enzyme: Protein or RNA that catalyzes chemical reactions.

exchange reaction: Type of chemical reaction in which bonds are both formed and broken, resulting in the transfer of components.

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hydrogen bond: Very weak bond between molecules or between parts of large polar molecules like water.

inorganic compound: Substance that does not contain both carbon and hydrogen.

ion: Atom with an overall positive or negative charge.

ionic bond: Attraction between an anion and a cation.

kinetic energy: Energy that matter possesses because of its motion.

lipid: Class of nonpolar organic compounds built from hydrocarbons and distinguished by the fact that they are not soluble in water.

mass number: Sum of the number of protons and neutrons in the nucleus of an atom.

matter: Physical substance; that which occupies space and has mass.

molecule: Two or more atoms covalently bonded together.

monosaccharide: Monomer of carbohydrate; also known as a simple sugar.

neutron: Heavy subatomic particle having no electrical charge and found in the atom's nucleus.

nucleotide: Class of organic compounds composed of one or more phosphate groups, a pentose sugar, and a nitrogen-containing base.

organic compound: Substance that contains both carbon and hydrogen.

peptide bond: Covalent bond formed by dehydration synthesis between two amino acids.

periodic table of the elements: Arrangement of the elements in a table according to their atomic number; elements having similar properties because of their electron arrangements compose columns in the table, while elements having the same number of valence shells compose rows in the table.

pH: Negative logarithm of the hydrogen-ion (H^+) concentration of a solution.

phospholipid: A lipid compound in which a phosphate group is combined with a diglyceride.

phosphorylation: Addition of one or more phosphate groups to an organic compound.

polar molecule: Molecule covalently bonded where one atom is more electronegative and draws electrons toward its nucleus, resulting in slight negative and positive charges.

potential energy: Stored energy matter possesses because of the positioning or structure of its components.

product: One or more substances produced by a chemical reaction.

prostaglandin: Lipid compound derived from fatty acid chains; important in regulating several body processes.

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protein: Class of organic compounds that are composed of many amino acids linked together by peptide bonds.
proton: Heavy subatomic particle having a positive charge and found in the atom's nucleus.
reactant: One or more substances that enter into the reaction.
ribonucleic acid (RNA): Ribose-containing nucleotide that helps manifest the genetic code as protein.
solution: Homogeneous liquid mixture in which a solute is dissolved into molecules within a solvent.
steroid (also sterol): Lipid compound composed of four hydrocarbon rings bonded to a variety of other atoms and molecules.
substrate: Reactant in an enzymatic reaction.
suspension: Liquid mixture in which particles distributed in the liquid settle out over time.
synthesis reaction: Type of anabolic reaction in which two or more atoms or molecules bond, resulting in the formation of a larger molecule.
triglyceride: Lipid compound composed of a glycerol molecule bonded with three fatty acid chains.
valence shell: Outermost electron shell of an atom.

Chapter Review

2.1 Elements and Atoms: The Building Blocks of Matter

The human body is composed of elements, the most abundant of which are oxygen (O), carbon (C), hydrogen (H), and nitrogen (N). You obtain these elements from the foods you eat and the air you breathe. The smallest unit of an element that retains all the properties of that element is an atom. But atoms themselves contain many subatomic particles, the three most important of which are protons, neutrons, and electrons. These particles do not vary in quality from one element to another; rather, what gives an element its distinctive identification is the quantity of its protons, called its atomic number. Protons and neutrons contribute nearly all of an atom's mass; the number of protons and neutrons is an element's mass number. Heavier and lighter versions of the same element can occur in nature because these versions have different numbers of neutrons. Different versions of an element are called isotopes.

The tendency of an atom to be stable or to react readily with other atoms is largely due to the behaviour of the electrons within the atom's outermost electron shell, called its valence shell. Helium and larger atoms with eight electrons in their valence shell are unlikely to participate in chemical reactions because they are stable. All other atoms tend to accept, donate, or share electrons in a

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process that brings the electrons in their valence shell to eight (or in the case of hydrogen, to two).

2.2 Chemical Bonds

Each moment of life, atoms of oxygen, carbon, hydrogen, and the other elements of the human body are making and breaking chemical bonds. Ions are charged atoms that form when an atom donates or accepts one or more negatively charged electrons.

Cations (ions with a positive charge) are attracted to anions (ions with a negative charge). This attraction is called an ionic bond. In covalent bonds, the participating atoms do not lose or gain electrons but rather share them. Molecules with nonpolar covalent bonds are electrically balanced and have a linear three-dimensional shape. Molecules with polar covalent bonds have "poles"—regions of weakly positive and negative charge—and have a triangular three-dimensional shape. An atom of oxygen and two atoms of hydrogen form a water molecule by means of polar covalent bonds. Hydrogen bonds link hydrogen atoms already participating in polar covalent bonds to anions or electronegative regions of other polar molecules. Hydrogen bonds link water molecules, resulting in the properties of water that are important to living things.

2.3 Chemical Reactions

Chemical reactions, in which chemical bonds are broken and formed, require an initial investment of energy. Kinetic energy, the energy of matter in motion, fuels the collisions of atoms, ions, and molecules that are necessary if their old bonds are to break and new ones to form. All molecules store potential energy, which is released when their bonds are broken.

Four forms of energy essential to human functioning are chemical energy, which is stored and released as chemical bonds are formed and broken; mechanical energy, which directly powers physical activity; radiant energy, emitted as waves such as in sunlight; and electrical energy, the power of moving electrons.

Chemical reactions begin with reactants and end with products. Synthesis reactions bond reactants together, a process that requires energy, whereas decomposition reactions break the bonds within a reactant and thereby release energy. In exchange reactions, bonds are both broken and formed, and energy is exchanged.

The rate at which chemical reactions occur is influenced by several properties of the reactants: temperature, concentration, pressure, and the presence or absence of a catalyst. An enzyme is a catalytic protein that speeds up chemical reactions in the human body.

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2.4 Inorganic Compounds Essential to Human Functioning

Inorganic compounds essential to human functioning include water, salts, acids, and bases. These compounds are inorganic; that is, they do not contain both hydrogen and carbon. Water is a lubricant and cushion, a heat sink, a component of liquid mixtures, a by-product of dehydration synthesis reactions, and a reactant in hydrolysis reactions. Salts are compounds that, when dissolved in water, dissociate into ions other than H^+ or OH^-. In contrast, acids release H^+ in a solution, making it more acidic. Bases accept H^+, thereby making the solution more alkaline (caustic). The pH of any solution is its relative concentration of H^+. A solution with pH 7 is neutral. Solutions with a pH below 7 are acids, and solutions with a pH above 7 are bases. A change in a single digit on the pH scale (e.g., from 7 to 8) represents a tenfold increase or decrease in the concentration of H^+. In a healthy adult, the pH of blood ranges from 7.35 to 7.45. Homeostatic control mechanisms important for keeping blood in a healthy pH range include chemicals called buffers, weak acids and weak bases released when the pH of blood or other body fluids fluctuates in either direction outside of this normal range.

2.5 Organic Compounds Essential to Human Functioning

Organic compounds essential to human functioning include carbohydrates, lipids, proteins, and nucleotides. These compounds are said to be organic because they contain both carbon and hydrogen. Carbon atoms in organic compounds readily share electrons with hydrogen and other atoms, usually oxygen and sometimes nitrogen. Carbon atoms also may bond with one or more macromolecules such as carboxyls, hydroxyls, aminos, or phosphates.

Monomers are single units of organic compounds. They bond by dehydration synthesis to form polymers, which can in turn be broken by hydrolysis.

Carbohydrate compounds provide essential body fuel. Their structural forms include monosaccharides such as glucose, disaccharides such as lactose, and polysaccharides, including starches (polymers of glucose), glycogen (the storage form of glucose), and fibre. All body cells can use glucose for fuel. It is converted via an oxidation-reduction reaction to ATP.

Lipids are hydrophobic compounds that provide body fuel and are important components of many biological compounds. Triglycerides are the most abundant lipid in the body and are composed of a glycerol backbone attached to three fatty acid chains. Phospholipids are compounds composed of a diglyceride with a phosphate group attached at the molecule's head. The result is a molecule with polar and nonpolar regions. Steroids are lipids formed of four

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hydrocarbon rings. The most important is cholesterol. Prostaglandins are signalling molecules derived from unsaturated fatty acids.

Proteins are critical components of all body tissues. They are made up of monomers called amino acids, which contain nitrogen joined by peptide bonds. Protein shape is critical to its function. Most body proteins are globular. An example is enzymes, which catalyze chemical reactions.

Nucleotides are compounds with three building blocks: one or more phosphate groups, a pentose sugar, and a nitrogen-containing base. DNA and RNA are nucleic acids that function in protein synthesis. ATP is the body's fundamental molecule of energy transfer. Removal or addition of phosphates releases or invests energy.

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3

The Cellular Level of Organization

Chapter Objectives

After studying this chapter, you will be able to:

- Describe the structure and function of the cell membrane, including its regulation of materials into and out of the cell
- Describe the functions of the various cytoplasmic organelles
- Explain the structure and contents of the nucleus, as well as the process of DNA replication
- Explain the process by which a cell builds proteins using the DNA code
- List the stages of the cell cycle in order, including the steps of cell division in somatic cells
- Discuss how a cell differentiates and becomes more specialized
- List the morphological and physiological characteristics of some representative cell types in the human body

A primary responsibility of each cell is to contribute to homeostasis, a term used in biology that refers to a dynamic state of balance within parameters that are compatible with life. For example, living cells require a water-based environment to survive in, and there are various physical (anatomical) and physiological mechanisms that keep all the trillions of living cells in the human body moist. This is one aspect of homeostasis. When a particular parameter, such as blood pressure or blood oxygen content, moves far enough *out* of homeostasis (generally becoming too high or too low), illness or disease—and sometimes death—inevitably results.

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In this chapter, you will learn about the major components and functions of a prototypical, generalized cell and discover some of the different types of cells in the human body.

3.1 The Cell Membrane

Learning Objectives

By the end of this section, you will be able to:

- Describe the molecular components that make up the cell membrane
- Explain the major features and properties of the cell membrane
- Differentiate between materials that can and cannot diffuse through the lipid bilayer
- Compare and contrast different types of passive transport with active transport, providing examples of each

Despite differences in structure and function, all living cells in multicellular organisms have a surrounding cell membrane. As the outer layer of your skin separates your body from its environment, the cell membrane (also known as the plasma membrane) separates the inner contents of a cell from its exterior environment. This cell membrane provides a protective barrier around the cell and regulates which materials can pass in or out.

Structure and Composition of the Cell Membrane

The **cell membrane** is an extremely pliable structure composed primarily of back-to-back phospholipids (a "bilayer") composed of a head (phosphate group) and tails (fatty acids). Cholesterol is also present, which contributes to the fluidity of the membrane, and there are various proteins embedded within the membrane that have a variety of functions.

A single phospholipid molecule has a phosphate group on one end, called the "head," and two side-by-side chains of fatty acids that make up the lipid tails (Figure 3.1). The phosphate group is negatively charged, making the head polar and hydrophilic. A **hydrophilic** molecule (or region of a molecule) is one that is attracted to water. The phosphate heads are thus attracted to the water molecules of both the extracellular and intracellular environments. The lipid tails, on the other hand, are uncharged, or nonpolar, and are hydrophobic. A **hydrophobic** molecule (or region of a molecule) repels and is repelled by water. Some lipid tails consist of saturated fatty acids, and some contain unsaturated fatty acids. This combination adds to the fluidity of the tails that are constantly in motion.

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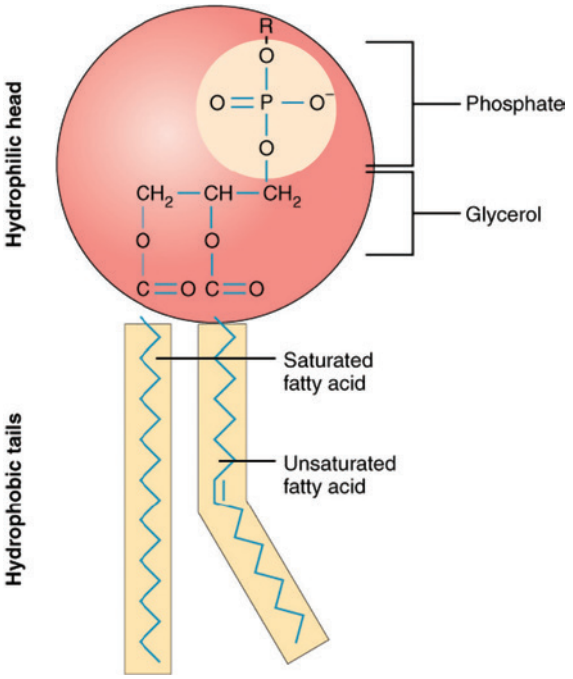


Figure 3.1 Phospholipid Structure. A phospholipid molecule consists of a polar phosphate "head," which is hydrophilic, and a nonpolar lipid "tail," which is hydrophobic. The tails can be any mixture of saturated and unsaturated fatty acids. Unsaturated fatty acids result in kinks in the hydrophobic tails.

Phospholipids are thus amphipathic molecules. An **amphipathic** molecule is one that contains both a hydrophilic and a hydrophobic region.

The cell membrane consists of two adjacent layers of phospholipids. The lipid tails of one layer face the lipid tails of the other layer, meeting at the interface of the two layers. The phospholipid heads face outward, one layer exposed to the interior of the cell and one layer exposed to the exterior (Figure 3.2). Because the phosphate groups are polar and hydrophilic, they are attracted to water in the intracellular fluid. **Intracellular fluid** (**ICF**) is the fluid interior of the cell. The phosphate groups are also attracted to the extracellular fluid. **Extracellular fluid** (**ECF**) is the fluid environment outside the enclosure of the cell membrane. **Interstitial fluid** (**IF**) is the term given to extracellular fluid not contained within blood vessels. Because the lipid tails are hydrophobic, they meet in the inner region of the membrane, excluding watery intracellular and extracellular fluid from this space. The cell membrane has many proteins, as well as other lipids (such as cholesterol), that are associated with the phospholipid bilayer. An important feature of the membrane is that it remains fluid; the lipids and proteins in the cell membrane are not rigidly locked in place.

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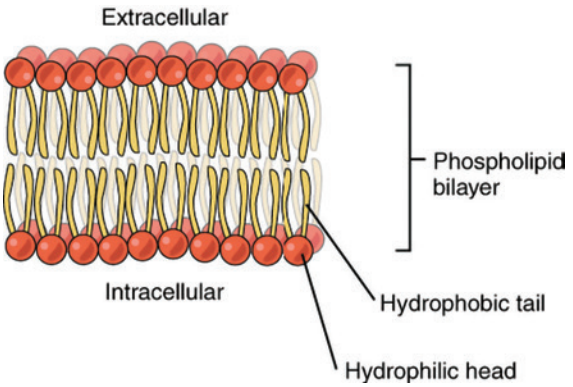


Figure 3.2 Phospholipid Bilayer. The phospholipid bilayer consists of two adjacent sheets of phospholipids, arranged tail to tail. The hydrophobic tails associate with one another, forming the interior of the membrane. The polar heads of the phospholipids contact the fluid inside and outside of the cell.

Membrane Proteins

The lipid bilayer forms the basis of the cell membrane, but it is peppered throughout with various proteins.

Two different types of proteins that are commonly associated with the cell membrane are the integral proteins and peripheral proteins (Figure 3.3). As its name suggests, an **integral protein** is a protein that is embedded in the membrane. A **channel protein** is an example of an integral protein that selectively allows particular materials, such as certain ions, to pass into or out of the cell.

Another important group of integral proteins is cell recognition proteins, which serve to mark a cell's identity so that it can be recognized by other cells. A **receptor** is a type of recognition protein that can selectively bind a specific molecule outside the cell (e.g., hormones, neurotransmitters), and this binding induces a chemical reaction within the cell. A **ligand** is the specific molecule that binds to and activates a receptor. Some integral proteins serve dual roles as both a receptor and an ion channel.

Example: A receptor-ligand interaction is seen in the receptors on nerve cells that bind neurotransmitters, such as dopamine. When a dopamine molecule binds to a dopamine receptor protein, a channel within the transmembrane protein opens to allow certain ions to flow into the cell.

Some integral membrane proteins are glycoproteins. A **glycoprotein** is a protein that has carbohydrate molecules attached, which extend into the extracellular matrix. The attached carbohydrate molecules on glycoproteins aid in cell recognition. The carbohydrates that extend from membrane proteins and even from some membrane lipids collectively form the glycocalyx. The

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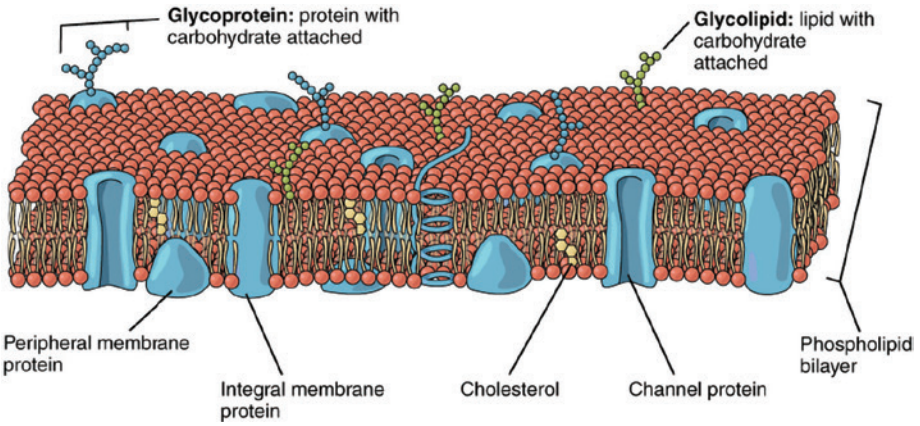


Figure 3.3 Cell Membrane. The cell membrane of the cell is a phospholipid bilayer containing many different molecular components, including proteins and cholesterol, some with carbohydrate groups attached.

glycocalyx is a fuzzy-appearing coating around the cell formed from glycoproteins and other carbohydrates attached to the cell membrane. The glycocalyx can have various roles.

Example: It may have molecules that allow the cell to bind to another cell, it may contain receptors for hormones, or it might have enzymes to break down nutrients.

The glycocalyces found in a person's body are products of that person's genetic makeup. They give each of the individual's trillions of cells the "identity" of belonging in the person's body. This identity is the primary way that a person's immune defence cells "know" not to attack the person's own body cells, but it is also the reason organs donated by another person might be rejected.

Peripheral proteins are typically found on the inner or outer surface of the lipid bilayer but can also be attached to the internal or external surface of an integral protein. These proteins typically perform a specific function for the cell. Some peripheral proteins on the surface of intestinal cells, for example, act as digestive enzymes to break down nutrients to sizes that can pass through the cells and into the bloodstream.

Transport Across the Cell Membrane

One of the great wonders of the cell membrane is its ability to regulate the concentration of substances inside the cell. These substances include ions such as Ca^{++}, Na^{+}, K^{+}, and Cl^{-}; nutrients including sugars, fatty acids, and amino acids; and waste products, particularly carbon dioxide (CO_2), which must leave the cell.

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The membrane's lipid bilayer structure provides the first level of control. The phospholipids are tightly packed together, and the membrane has a hydrophobic interior. This structure causes the membrane to be selectively permeable. A membrane that has **selective permeability** allows only substances meeting certain criteria to pass through it unaided. In the case of the cell membrane, only relatively small, nonpolar materials can move through the lipid bilayer (remember, the lipid tails of the membrane are nonpolar). Some examples of these are other lipids, oxygen and carbon dioxide gases, and alcohol. However, water-soluble materials—like glucose, amino acids, and electrolytes—need some assistance to cross the membrane because they are repelled by the hydrophobic tails of the phospholipid bilayer. All substances that move through the membrane do so by one of two general methods, which are categorized based on whether or not energy is required. **Passive transport** is the movement of substances across the membrane without the expenditure of cellular energy. In contrast, **active transport** is the movement of substances across the membrane using cellular energy from adenosine triphosphate (ATP).

Passive Transport

In order to understand *how* substances move passively across a cell membrane, it is necessary to understand concentration gradients and diffusion. A **concentration gradient** is the difference in concentration of a substance across a space. Molecules (or ions) will spread/diffuse from where ions are more concentrated to where ions are less concentrated until they are equally distributed in that space. (When molecules move in this way, they are said to move *down* their concentration gradient.) **Diffusion** is the movement of particles from an area of higher concentration to an area of lower concentration of themselves.

Example: Imagine being inside a closed bathroom. If a bottle of perfume were sprayed, the scent molecules would naturally diffuse from the spot where they left the bottle to all corners of the bathroom, and this diffusion would go on until no more concentration gradient remains. Another example is a spoonful of sugar placed in a cup of tea. Eventually, the sugar will diffuse throughout the tea until no concentration gradient remains.

In both cases, if the room is warmer or the tea hotter, diffusion occurs even faster as the molecules bump into each other and spread out faster than at cooler temperatures. Having an internal body temperature around 37°C thus also aids in the diffusion of particles within the body.

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Interactive Link 3.1

Visit this link (http://oer.aupress.ca/oer-202505/3.1) to see diffusion and how it is propelled by the kinetic energy of molecules in solution. How does temperature affect diffusion rate, and why?

Whenever a substance exists in greater concentration on one side of a selectively permeable membrane, such as a cell membrane, any substance that can move down its own concentration gradient across the membrane will do so.

Example: Substances that can easily diffuse through the lipid bilayer of the cell membrane include the gases oxygen (O_2) and CO_2. O_2 generally diffuses into cells because it is more concentrated outside of them, and CO_2 typically diffuses out of cells because it is more concentrated inside of them. Neither of these examples requires any energy on the part of the cell, and therefore they use passive transport to move across the membrane.

Before moving on, you need to review the gases that can diffuse across a cell membrane. Because cells rapidly use up oxygen during metabolism, there is typically a lower concentration of O_2 inside the cell than outside. As a result, oxygen will diffuse from the interstitial fluid directly through the lipid bilayer of the membrane and into the cytoplasm within the cell. On the other hand, because cells produce CO_2 as a by-product of metabolism, CO_2 concentrations rise within the cytoplasm; therefore, CO_2 will move from the cell through the lipid bilayer and into the interstitial fluid, where its concentration is lower. This mechanism of molecules moving across a cell membrane from the side where they are more concentrated to the side where they are less concentrated is a form of passive transport called **simple diffusion** (Figure 3.4).

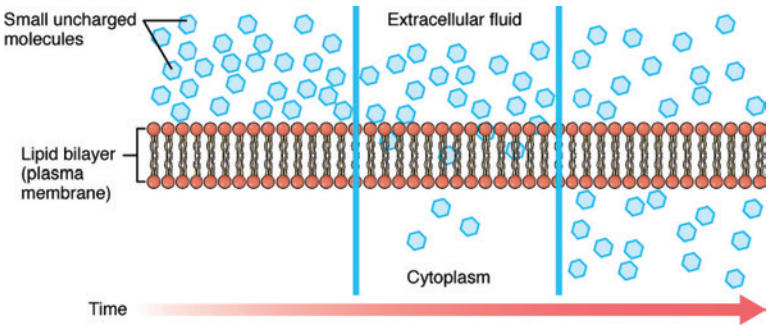


Figure 3.4 Simple Diffusion Across the Cell (Plasma) Membrane. The structure of the lipid bilayer allows small, uncharged substances such as oxygen and carbon dioxide, and hydrophobic molecules such as lipids, to pass through the cell membrane, down their concentration gradient, by simple diffusion.

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Large polar or ionic molecules, which are hydrophilic, cannot easily cross the phospholipid bilayer. Very small polar molecules, such as water, can cross via simple diffusion due to their size. Charged atoms or molecules of any size cannot cross the cell membrane via simple diffusion, as the charges are repelled by the hydrophobic tails in the interior of the phospholipid bilayer. Solutes dissolved in water on either side of the cell membrane will tend to diffuse down their concentration gradients, but because most substances cannot pass freely through the lipid bilayer of the cell membrane, their movement is restricted to protein channels and specialized transport mechanisms in the membrane. **Facilitated diffusion** is the diffusion process used for those substances that cannot cross the lipid bilayer due to their size, charge, and/or polarity (Figure 3.5).

Example: Facilitated diffusion moves glucose into the cell, where it is used to make ATP. Although glucose can be more concentrated outside of a cell,

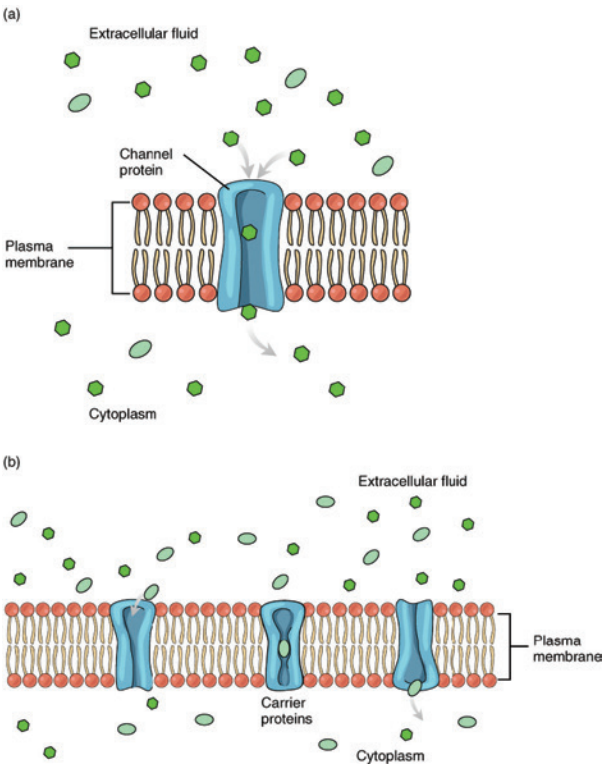


Figure 3.5 Facilitated Diffusion. (a) Facilitated diffusion of substances crossing the cell (plasma) membrane takes place with the help of proteins such as channel proteins and carrier proteins. Channel proteins are less selective than carrier proteins and usually mildly discriminate what they allow through based on size and charge. (b) Carrier proteins are more selective, often only allowing one particular type of molecule to cross.

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it cannot cross the lipid bilayer via simple diffusion because it is both large and polar.

To resolve this, a specialized carrier protein called the glucose transporter will transfer glucose molecules into the cell to facilitate (assist) its inward diffusion.

Example: Even though sodium ions (Na^+) are highly concentrated outside of cells, these electrolytes are charged and cannot pass through the nonpolar lipid bilayer of the membrane. Their diffusion is facilitated by membrane proteins that form sodium channels (or "pores") so that Na^+ ions can move down their concentration gradient from outside the cells to inside the cells.

There are many other solutes that must undergo facilitated diffusion to move into a cell, such as amino acids, or to move out of a cell, such as wastes. Because facilitated diffusion is a passive process, it does not require energy expenditure by the cell.

Water can also move freely across the cell membranes of all cells, either through protein channels or by slipping between the lipid tails of the membrane itself. **Osmosis** is the diffusion of water from a biologic compartment with a lower concentration of solutes to one with a higher concentration of solutes (down its concentration gradient) through a selectively permeable membrane (Figure 3.6).

Tonicity is a measure of a solution's ability to change the volume of cells by altering their water content. The movement of water molecules is not itself regulated by some cells, so it is important that these cells are exposed to an environment in which the concentration of solutes outside of the cells (in the extracellular fluid) is equal to the concentration of solutes inside the

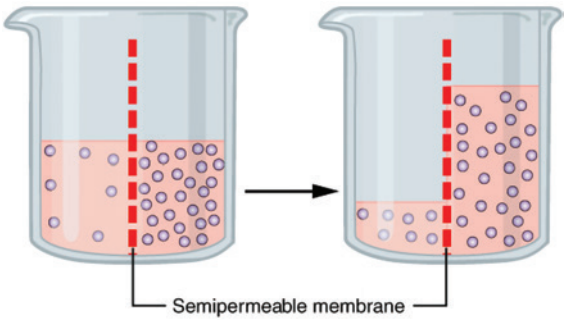


Figure 3.6 Osmosis. Osmosis is the diffusion of water through a selectively permeable (semipermeable) membrane down its concentration gradient. If a membrane is permeable to water, though not to a solute, water will equalize its own concentration by diffusing to the side of lower water concentration (and thus the side of higher solute concentration). In the beaker on the left, the solution on the right side of the membrane is hypertonic. Water "follows" salt.

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cells (in the cytoplasm). Two solutions that have the same concentration of solutes are said to be **isotonic** (equal tension). When cells and their extracellular environments are isotonic, the concentration of water molecules is the same outside and inside the cells, and the cells maintain their normal shape (and function).

Osmosis occurs when there is an imbalance of solutes outside of a cell versus inside the cell. A solution that has a higher concentration of solutes than another solution is said to be **hypertonic**, and water molecules tend to diffuse into a hypertonic solution (Figure 3.7). Cells in a hypertonic solution will shrivel as water leaves the cell via osmosis. In contrast, a solution that has a lower concentration of solutes than another solution is said to be **hypotonic**, and water molecules tend to diffuse out of a hypotonic solution. Cells in a hypotonic solution will take on too much water and swell, with the risk of eventually bursting. A critical aspect of homeostasis in living things is to create an internal environment in which all the body's cells are in an isotonic solution. Various organ systems, particularly the kidneys, work to maintain this homeostasis.

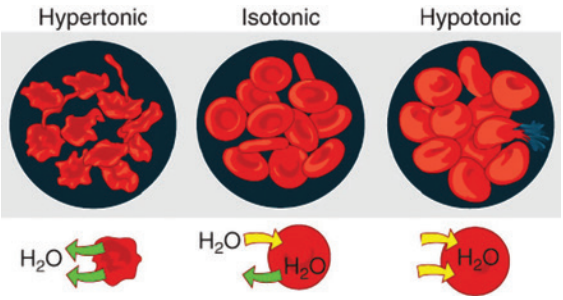


Figure 3.7 Concentration of Solutions. A hypertonic solution has a higher solute concentration than another solution. An isotonic solution has a solute concentration equal to that of another solution. A hypotonic solution has a lower solute concentration than another solution.

Active Transport

There are two types of active transport, primary and secondary.

For all the transport methods described in the previous section, the cell expends no energy. Membrane proteins that aid in the passive transport of substances do so without the use of ATP. During primary active transport, ATP is required to move a substance across a membrane, often with the help of protein carriers and usually *against* its concentration gradient.

One of the most common types of active transport involves proteins that serve as pumps. The word *pump* probably conjures up thoughts of using energy

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to pump up the tire of a bicycle or a basketball. Similarly, energy from ATP is required for these membrane proteins to transport substances—molecules or ions—across the membrane, usually against their concentration gradients (from an area of low concentration of itself to an area of high concentration of itself).

The **sodium-potassium pump**, which is also called **Na^+/K^+ ATPase**, transports sodium ions out of a cell while moving potassium ions into the cell. The Na^+/K^+ pump is an important ion pump found in the membranes of many types of cells. These pumps are particularly abundant in nerve cells, which are constantly pumping out sodium ions and pulling in potassium ions to maintain an electrical gradient across their cell membranes. An **electrical gradient** is a difference in electrical charge across a space. In the case of nerve cells, for example, the electrical gradient exists between the inside and outside of the cell, with the inside being negatively charged (at around −70 mV) relative to the outside.

The negative electrical gradient is maintained because each Na^+/K^+ pump moves three Na^+ ions out of the cell and two K^+ ions into the cell for each ATP molecule that is used (Figure 3.8). This process is so important for nerve cells that it accounts for the majority of their ATP usage.

Active transport pumps can also work together with other active or passive transport systems to move substances across the membrane.

Example: The sodium-potassium pump maintains a high concentration of sodium ions outside of the cell. Therefore, if the cell needs sodium ions, all it

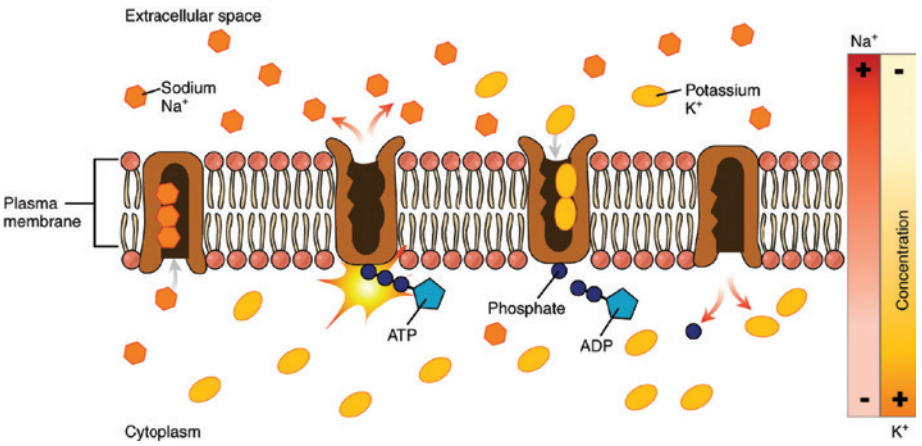


Figure 3.8 Sodium-Potassium Pump. The sodium-potassium pump is found in many cell (plasma) membranes. Powered by ATP, the pump moves sodium and potassium ions in opposite directions, each against its concentration gradient. In a single cycle of the pump, three sodium ions are extruded from and two potassium ions are imported into the cell.

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has to do is open a passive sodium channel, as the concentration gradient of the sodium ions will drive them to diffuse into the cell.

Secondary active transport harnesses an electrochemical gradient that was established by primary active transport to drive the transport of a second molecule. **Symporters** are secondary active transporters that move two substances in the same direction.

Example: The sodium-glucose symporter uses sodium ions to "pull" glucose molecules into the cell. Because cells store glucose for energy, glucose is typically at a higher concentration inside the cell than outside. However, due to the action of the sodium-potassium pump, sodium ions will easily diffuse into the cell when the symporter is opened. The flood of sodium ions through the symporter provides the energy that allows glucose to move through the symporter and into the cell, against its concentration gradient.

Conversely, **antiporters** are secondary active transport systems that transport substances in opposite directions.

Example: The sodium-hydrogen ion antiporter uses the energy from the inward flood of sodium ions to move hydrogen ions (H^+) out of the cell. The sodium-hydrogen antiporter is used to maintain the pH of the cell's interior.

Other Types of Active Transport

Other forms of active transport do not involve membrane carriers. **Endocytosis** is the process of a cell ingesting material by enveloping it in a portion of its cell membrane and then pinching off that portion of membrane (Figure 3.9). Once pinched off, the portion of membrane and its contents becomes an independent, intracellular vesicle. A **vesicle** is a membranous sac—a spherical and hollow organelle bounded by a lipid bilayer membrane embedded with proteins. Endocytosis often brings materials into the cell that must be broken down or digested.

Phagocytosis is the endocytosis of large particles. Many immune cells engage in phagocytosis of invading pathogens. Like a little Pac-Man, an immune cell's job is to patrol body tissues for unwanted matter such as invading bacterial cells, phagocytize them, and digest them. In contrast to phagocytosis, **pinocytosis** brings fluid containing dissolved substances into a cell through membrane vesicles.

Phagocytosis and pinocytosis take in large portions of extracellular material, and they are typically not highly selective in the substances they bring in. Cells regulate the endocytosis of specific substances via **receptor-mediated endocytosis**, or endocytosis by a portion of the cell membrane that contains many receptors that are specific for a certain substance. Once the surface receptors have bound sufficient amounts of the specific substance (the receptor's

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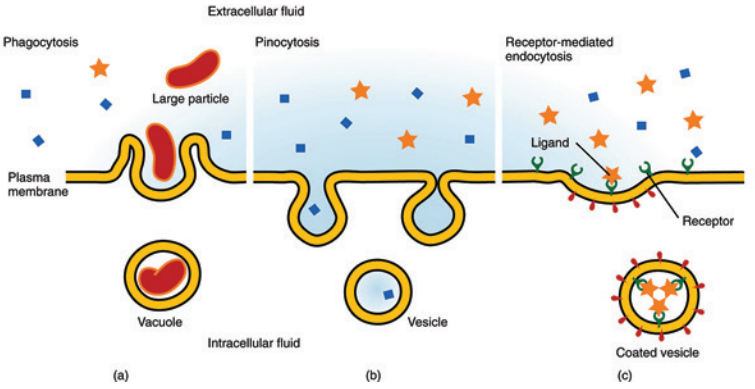


Figure 3.9 Three Forms of Endocytosis. Endocytosis is a form of active transport in which a cell envelops extracellular materials using its cell membrane. (a) In phagocytosis, which is relatively nonselective, the cell takes in a large particle. (b) In pinocytosis, the cell takes in small particles in solution. (c) In contrast, receptor-mediated endocytosis is quite selective. When external receptors bind a specific ligand, the cell responds by endocytosing the ligand.

ligand), the cell will bring in the entire part of the cell membrane containing the receptor-ligand complexes.

Example: Iron, a required component of hemoglobin, is endocytosed by red blood cells in this way. Iron is bound to a protein called transferrin in the blood. Specific transferrin receptors on red blood cell surfaces bind the iron-transferrin molecules, and the cell endocytoses the receptor-ligand complexes.

In contrast with endocytosis, **exocytosis** is the process of a cell exporting material using vesicles (Figure 3.10). Many cells manufacture substances that must be secreted; these substances are typically packaged into membrane-bound vesicles within the cell. When the vesicle membrane fuses with the cell membrane, the vesicle releases its contents into the interstitial fluid. The vesicle membrane then becomes part of the cell membrane. Cells of the stomach and pancreas produce and secrete digestive enzymes through exocytosis. Endocrine cells produce and secrete hormones that are sent throughout the body, and certain immune cells produce and secrete large amounts of histamine, a chemical important for immune responses.

Interactive Link 3.2

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/3.2) to explore the tissue sample in greater detail.

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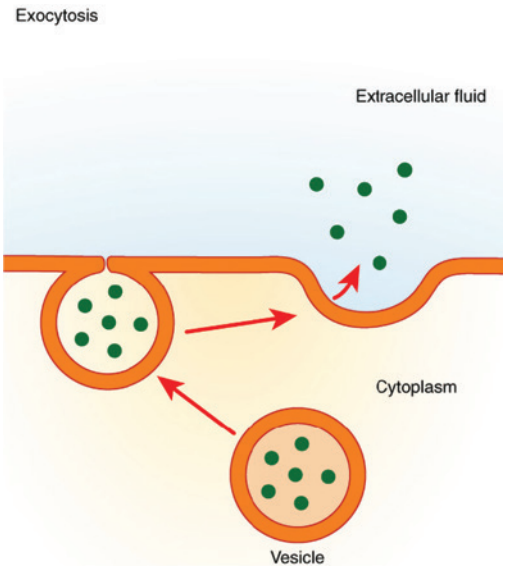


Figure 3.10 Exocytosis. Exocytosis is much like endocytosis in reverse. Material destined for export is packaged into a vesicle inside the cell. The membrane of the vesicle fuses with the cell membrane, and the contents are released into the extracellular space.

3.2 The Cytoplasm and Cellular Organelles

Learning Objectives

By the end of this section, you will be able to:

- Describe the structure and function of the cellular organelles associated with the endomembrane system, including the endoplasmic reticulum, the Golgi apparatus, and lysosomes
- Describe the structure and function of mitochondria and peroxisomes
- Explain the three components of the cytoskeleton, including their composition and functions

All living cells in multicellular organisms contain an internal cytoplasmic compartment and a nucleus within the cytoplasm. **Cytosol**, the jellylike substance within the cell, provides the fluid medium necessary for biochemical reactions. Eukaryotic cells, including all animal cells, also contain various cellular organelles. An **organelle** is one of several different types of membrane-enclosed bodies in the cell, each performing a unique function. Just as the various bodily organs work together in harmony to perform all of a human's functions, the many different cellular organelles work together to keep the cell

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healthy and performing all its important functions. The organelles and cytosol, taken together, compose the cell's **cytoplasm**. The **nucleus** is a cell's central organelle, which contains the cell's DNA (Figure 3.11).

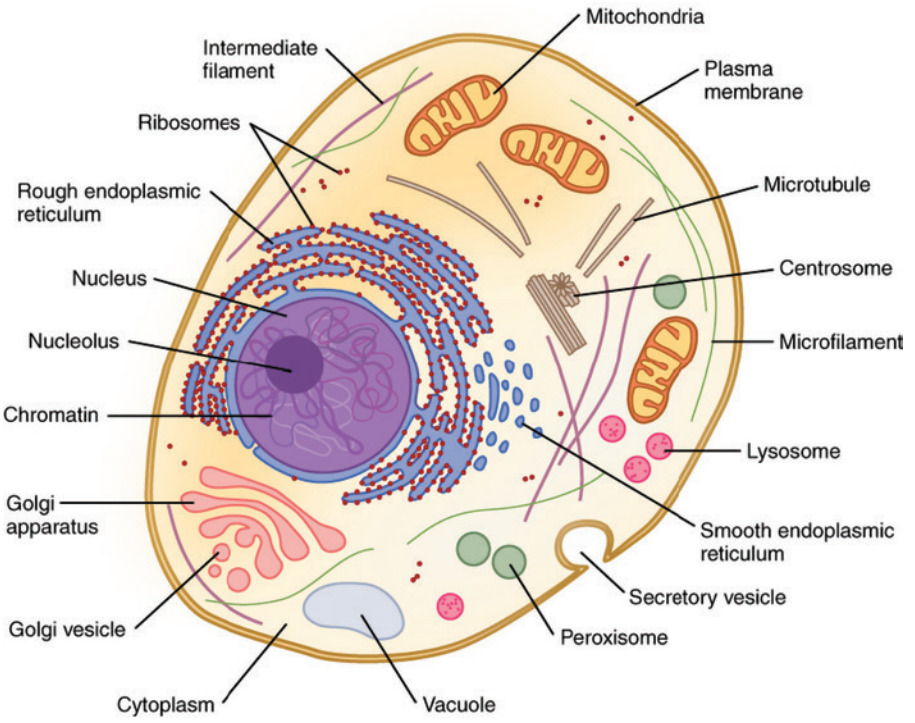


Figure 3.11 Prototypical Human Cell. While this image is not indicative of any one particular human cell, it is a prototypical example of a cell containing the primary organelles and internal structures.

Organelles of the Endomembrane System

A set of three major organelles together forms a system within the cell called the endomembrane system. These organelles work together to perform various cellular jobs, including the task of producing, packaging, and exporting certain cellular products. The organelles of the endomembrane system include the endoplasmic reticulum, Golgi apparatus, and vesicles.

Endoplasmic Reticulum

The **endoplasmic reticulum** (**ER**) is a system of channels that is continuous with the nuclear membrane (or "envelope") covering the nucleus and composed of the same lipid bilayer material. The ER can be thought of as a series of winding thoroughfares similar to the waterway canals in Venice.

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The ER provides passages throughout much of the cell that function in transporting, synthesizing, and storing materials. The winding structure of the ER results in a large membranous surface area that supports its many functions (Figure 3.12).

Endoplasmic reticulum can exist in two forms: rough ER and smooth ER. These two types of ER perform some very different functions and can be found in very different amounts depending on the type of cell. **Rough ER** (**RER**) is so called because its membrane is dotted with embedded granules—organelles called ribosomes—giving the RER a bumpy appearance. A **ribosome** is a tiny, non-membrane-bound, free-floating organelle that serves as the site of protein synthesis. It is composed of two ribosomal RNA subunits consisting of ribosomal RNA (rRNA) and proteins that wrap around messenger RNA (mRNA)

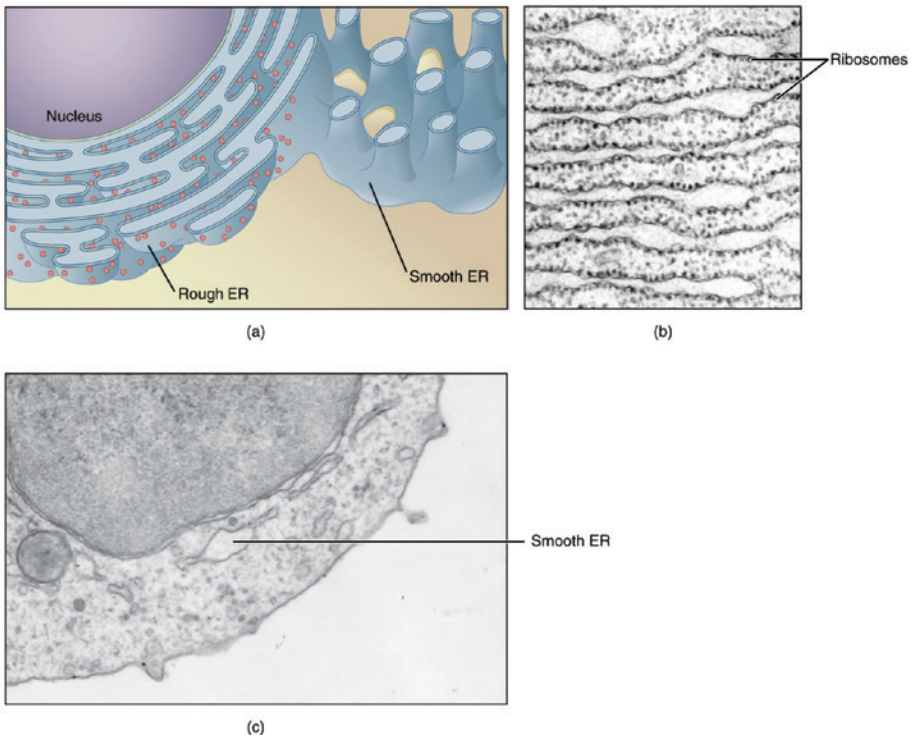


Figure 3.12 Endoplasmic Reticulum (ER). (a) The ER is a winding network of thin membranous sacs found in close association with the cell nucleus. The smooth and rough endoplasmic reticula are very different in appearance and function (source: mouse tissue). (b) Rough ER is studded with numerous ribosomes, which are sites of protein synthesis (source: mouse tissue). EM × 110,000. (c) Smooth ER synthesizes phospholipids, steroid hormones, regulates the concentration of cellular Ca^{++}, metabolizes some carbohydrates, and breaks down certain toxins (source: mouse tissue). EM × 110,510. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)

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to start the process of translation, followed by protein synthesis for use in the cytosol of the cell.

Smooth ER (**SER**) lacks these ribosomes. One of the main functions of the SER is in the synthesis of lipids. The SER synthesizes phospholipids, the main component of biological membranes, as well as steroid hormones. For this reason, cells that produce large quantities of steroid hormones, such as those of the female ovaries and male testes, contain large amounts of SER. In addition to lipid synthesis, the SER also sequesters (i.e., stores) and regulates the concentration of cellular Ca^{++}, a function extremely important in skeletal muscle cells, where Ca^{++} is the trigger for muscle contraction. The SER additionally metabolizes some carbohydrates and performs a detoxification role, breaking down certain toxins.

In contrast with the SER, the primary job of the RER is the synthesis and modification of proteins destined for the cell membrane or for export from the cell. For this protein synthesis, many ribosomes attach to the ER (giving it the studded appearance of RER). Typically, a protein is synthesized within the ribosome and released inside the channel of the RER, where sugars can be added to it (by a process called glycosylation) before it is transported within a vesicle to the next stage in the packaging and shipping process: the Golgi apparatus.

The Golgi Apparatus

The **Golgi apparatus** is responsible for sorting, modifying, and shipping off the products that come from the rough ER, much like a post office.

The Golgi apparatus looks like stacked, flattened discs, almost like stacks of oddly shaped pancakes. Like the ER, these discs are membranous. The Golgi apparatus has two distinct sides, each with a different role. One side of the apparatus receives products in vesicles. These products are sorted through the apparatus, and then they are released from the opposite side after being repackaged into new vesicles. If the product is to be exported from the cell, the vesicle migrates to the cell surface and fuses to the cell membrane, and the cargo is secreted (Figure 3.13).

Lysosomes

Some of the protein products packaged by the Golgi include digestive enzymes that are meant to remain inside the cell for use in breaking down certain materials. The enzyme-containing vesicles released by the Golgi may form new lysosomes or fuse with existing lysosomes. A **lysosome** is an organelle that contains enzymes that break down and digest unneeded cellular components, such as damaged organelles. **Autophagy** is the process of a cell digesting its own structures.

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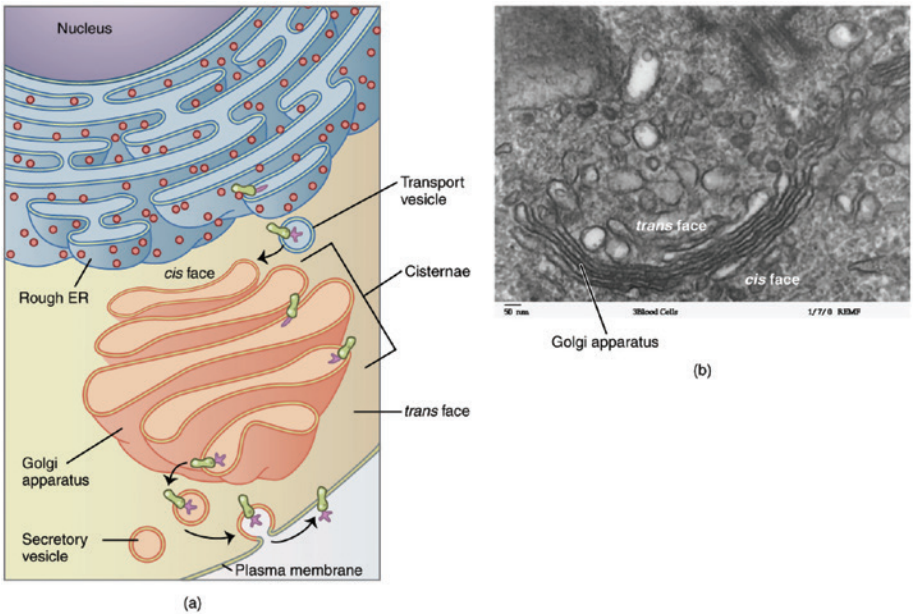


Figure 3.13 Golgi Apparatus. (a) The Golgi apparatus manipulates products from the rough ER and also produces new organelles called lysosomes. Proteins and other products of the ER are sent to the Golgi apparatus, which organizes, modifies, packages, and tags them. Some of these products are transported to other areas of the cell for inclusion in cell membranes, including the plasma membrane, and some are exported from the cell through exocytosis. Enzymatic proteins are packaged as new lysosomes (or packaged and sent for fusion with existing lysosomes). (b) An electron micrograph of the Golgi apparatus.

Example: When certain immune defence cells (white blood cells) phagocytize bacteria, the bacterial cell is transported into a lysosome and digested by the enzymes inside. As one might imagine, such phagocytic defence cells contain large numbers of lysosomes.

Under certain circumstances, lysosomes perform a more grand and dire function. In the case of damaged or unhealthy cells, lysosomes can be triggered to open up and release their digestive enzymes into the cytoplasm of the cell, killing the cell. This "self-destruct" mechanism is called **autolysis** and makes the process of cell death controlled (a mechanism called **apoptosis**).

Interactive Link 3.3

Watch this video (http://oer.aupress.ca/oer-202505/3.3) to learn about the endomembrane system, which includes the rough and smooth ER and the Golgi apparatus as well as lysosomes and vesicles. What is the primary role of the endomembrane system?

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Organelles for Energy Production and Detoxification

In addition to the jobs performed by the endomembrane system, the cell has many other important functions. Just as you must consume nutrients to provide yourself with energy, so must each of your cells take in nutrients, some of which convert to chemical energy that can be used to power biochemical reactions. Another important function of the cell is detoxification. Humans take in all sorts of toxins from the environment and also produce harmful chemicals as by-products of cellular processes. Cells called hepatocytes in the liver detoxify many of these toxins.

Mitochondria

A **mitochondrion** (plural = mitochondria) is a membranous, bean-shaped organelle that is the "energy transformer" of the cell. Mitochondria consist of two lipid bilayer membranes (Figure 3.14). The inner membrane is highly folded into winding structures with a great deal of surface area, called cristae. The middle of the mitochondrion contains a fluid-filled substance called the matrix. The inner membrane and the matrix are locations for many of the reactions that convert energy stored in nutrient molecules (such as glucose) into adenosine triphosphate (ATP), which provides usable energy to the cell.

Cells use ATP constantly, so the mitochondria are constantly at work. Oxygen molecules are required during cellular respiration, which is why you must constantly breathe them in. One of the organ systems in the body that uses huge amounts of ATP is the muscular system because ATP is required to sustain

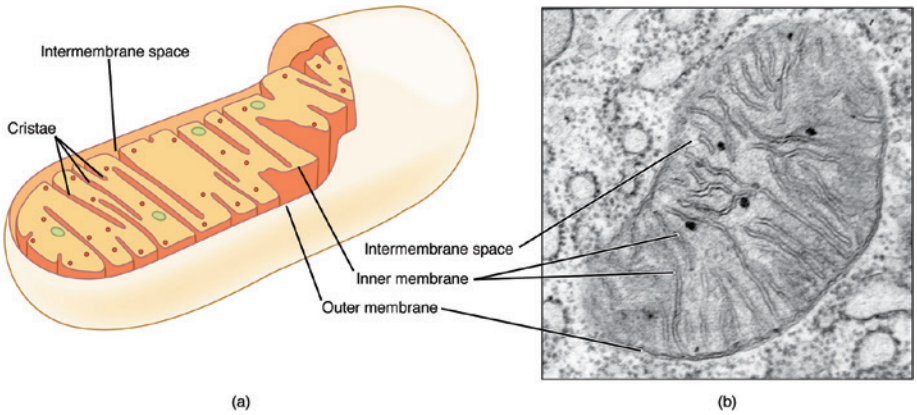


Figure 3.14 Mitochondrion. The mitochondria are the energy-conversion factories of the cell. (a) A mitochondrion is composed of two separate lipid bilayer membranes. Along the inner membrane are various molecules that work together to produce ATP, the cell's major energy currency. (b) An electron micrograph of mitochondria. EM × 236,000. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

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muscle contraction. As a result, muscle cells are packed full of mitochondria. Nerve cells also need large quantities of ATP to run their sodium-potassium pumps. Therefore, an individual neuron will be loaded with over a thousand mitochondria. On the other hand, a bone cell, which is not nearly as metabolically active, might only have a couple hundred mitochondria.

Peroxisomes

Like lysosomes, a **peroxisome** is a single-layer membrane-bound cellular organelle that contains mostly enzymes. Peroxisomes perform a couple of different functions, including lipid metabolism and chemical detoxification. In contrast to the digestive enzymes found in lysosomes, the enzymes within peroxisomes serve to transfer hydrogen atoms from various molecules to oxygen, producing hydrogen peroxide (H_2O_2). In this way, peroxisomes neutralize poisons such as alcohol.

The Cytoskeleton

Much like the bony skeleton structurally supports the human body, the cytoskeleton helps the cells maintain their structural integrity. The **cytoskeleton** is a group of fibrous proteins that provide structural support for cells, but this is only one of the functions of the cytoskeleton. Cytoskeletal components are also critical for cell motility, cell reproduction, and the transportation of substances within the cell.

The cytoskeleton forms a complex threadlike network throughout the cell, consisting of three different kinds of protein-based filaments: microfilaments, intermediate filaments, and microtubules (Figure 3.15).

A **microtubule** is the thickest of the three; it is a structural filament composed of subunits of a protein called tubulin. Microtubules maintain cell shape and structure, help resist compression of the cell, and play a role in positioning the organelles within the cell. Microtubules also make up two types of cellular appendages important for motion: cilia and flagella. **Cilia** are found on many cells of the body, including the epithelial cells that line the airways of the respiratory system. Cilia move rhythmically; they beat constantly, moving waste materials such as dust, mucus, and bacteria upward through the airways, away from the lungs, and toward the mouth. Beating cilia on cells in the female fallopian tubes move egg cells from the ovary toward the uterus. A **flagellum** (plural = flagella) is an appendage larger than a cilium and specialized for cell locomotion. The only flagellated cell in humans is the sperm cell that must propel itself toward female egg cells.

A very important function of microtubules is to set the paths (somewhat like railroad tracks) along which the genetic material can be pulled (a process requiring

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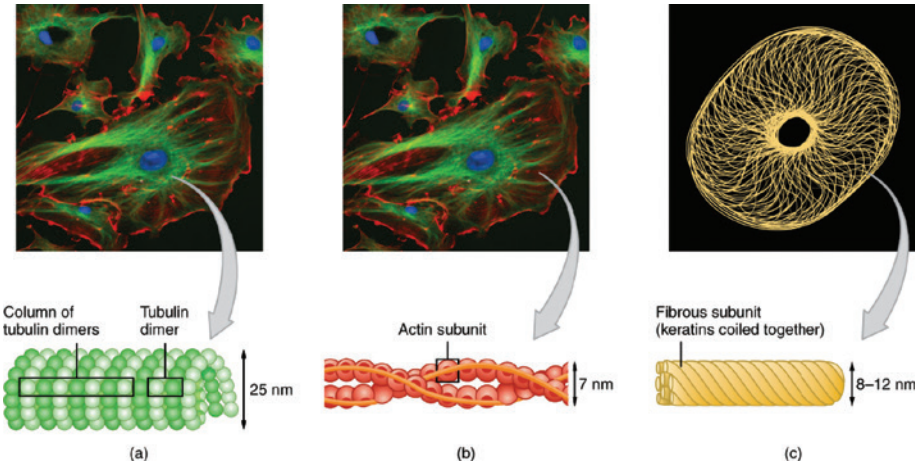


Figure 3.15 The Three Components of the Cytoskeleton. The cytoskeleton consists of (a) microtubules, (b) microfilaments, and (c) intermediate filaments. The cytoskeleton plays an important role in maintaining cell shape and structure, promoting cellular movement, and aiding cell division.

ATP) during cell division so that each new daughter cell receives the appropriate set of chromosomes. Two short, identical microtubule structures called centrioles are found near the nuclei of cells. A **centriole** can serve as the cellular origin point for microtubules, extending outward as cilia or flagella, or can assist with the separation of DNA during cell division. Microtubules grow out from the centrioles by adding more tubulin subunits, like adding additional links to a chain.

In contrast with microtubules, **microfilaments**, or actin filaments, are a thinner type of cytoskeletal filament (see Figure 3.15b). Like microtubules, actin filaments are long chains of single subunits (called actin subunits). Actin fibres as well as the protein called myosin are responsible for muscle contraction. Actin also has an important role during cell division. When a cell is about to split in half during cell division, actin filaments work with myosin to create a cleavage furrow that eventually splits the cell down the middle, forming two new cells from the original cell.

An **intermediate filament**, as its name would suggest, is a filament intermediate in thickness between the microtubules and microfilaments (see Figure 3.15c). Intermediate filaments are made up of long fibrous subunits of proteins such as keratin, which are wound together like the threads that compose a rope. Intermediate filaments, in concert with the microtubules, are important for maintaining cell shape and structure. Unlike the microtubules, which resist compression, intermediate filaments resist tension—the forces that pull apart cells. There are many cases in which cells are prone to tension, such as when epithelial cells of the skin are compressed, tugging them in different

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directions. Intermediate filaments help anchor organelles together within a cell and also link cells to other cells by forming special cell-to-cell junctions.

3.3 The Nucleus and DNA Replication

Learning Objectives

By the end of this section, you will be able to:

- Describe the structure and features of the nuclear membrane
- List the contents of the nucleus
- Explain the organization of the DNA molecule within the nucleus
- Describe the process of DNA replication

The **nucleus** is the largest and most prominent of a cell's organelles (Figure 3.16). The nucleus is generally considered the control centre of the cell because it stores as DNA most of the genetic instructions for manufacturing protein. Interestingly, some cells in the body, such as muscle cells, contain more than one nucleus (Figure 3.17); these are known as multinucleated cells. Other cells, such as mammalian red blood cells (RBCs), do not contain nuclei at all. RBCs eject their nuclei as they mature, making space for the large numbers of hemoglobin

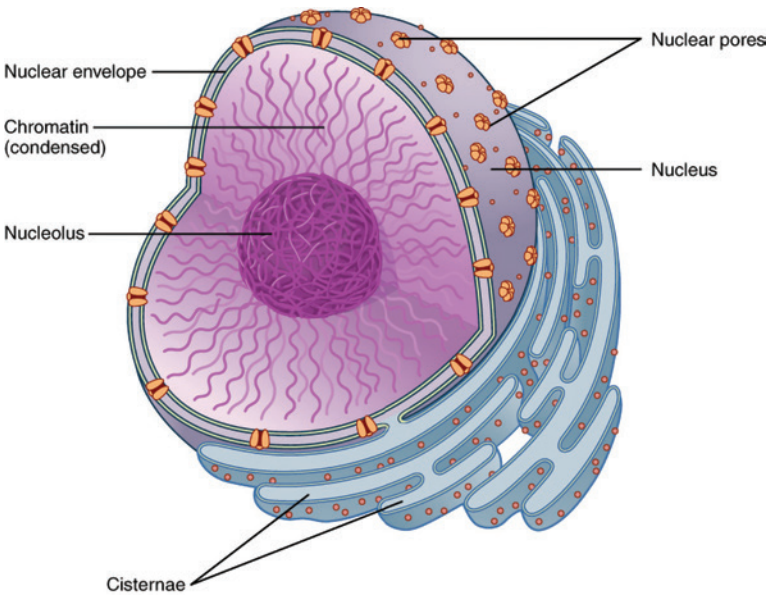


Figure 3.16 The Nucleus. The nucleus is the control centre of the cell. The nucleus of living cells contains the genetic material that determines the entire structure and function of that cell.

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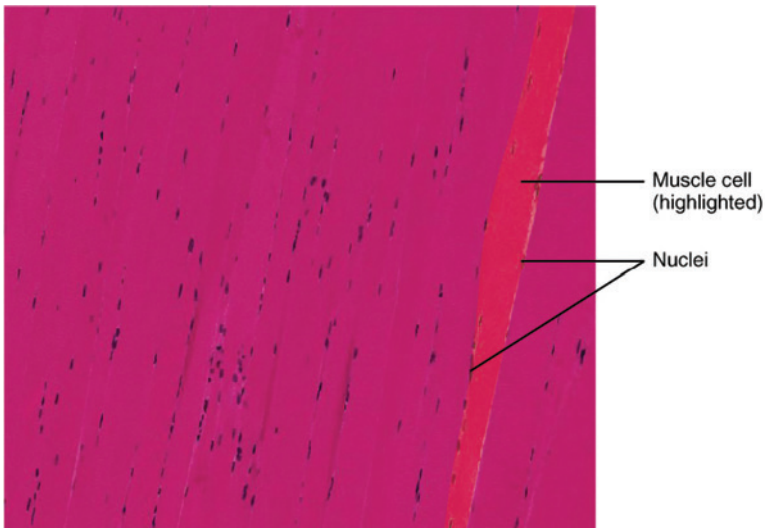


Figure 3.17 Multinucleate Muscle Cell. Unlike cardiac muscle cells and smooth muscle cells, which have a single nucleus, a skeletal muscle cell contains many nuclei and is referred to as "multinucleated." These muscle cells are long and fibrous (often referred to as muscle fibres). During development, many smaller cells fuse to form a mature muscle fibre. The nuclei of the fused cells are conserved in the mature cell, thus imparting a multinucleate characteristic to mature muscle cells. LM × 104.3. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

molecules that carry oxygen throughout the body (Figure 3.18). Without nuclei, the lifespan of RBCs is short, so the body must produce new ones constantly.

Interactive Link 3.4

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/3.4) to explore the tissue sample in greater detail.

Interactive Link 3.5

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/3.5) to explore the tissue sample in greater detail.

Inside the nucleus lies the blueprint that dictates everything a cell will do and all the products it will make. Each cell in your body (with the exception of germ cells) contains the complete set of your DNA. When a cell divides, the DNA must be duplicated so that each new cell receives a full complement of DNA through DNA replication. The nucleus is also the site of RNA production.

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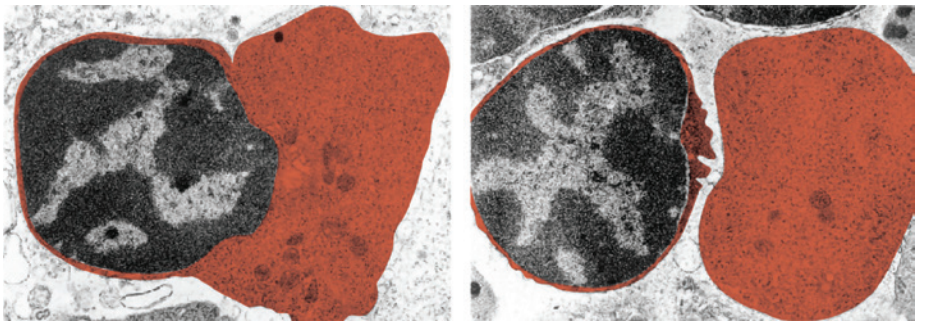


Figure 3.18 Red Blood Cell Extruding Its Nucleus. Mature red blood cells lack a nucleus. As they mature, erythroblasts extrude their nucleus, making room for more hemoglobin. The two panels here show an erythroblast before and after ejecting its nucleus, respectively. (credit: modification of micrograph provided by the Regents of University of Michigan Medical School © 2012)

Messenger RNA, or mRNA, carries the "message" of the DNA out of the nucleus to the cytosol. This is known as transcription. The following section will explore the structure of the nucleus and its contents as well as the process of DNA replication.

Organization of the Nucleus and Its DNA

Like most other cellular organelles, the nucleus is surrounded by a membrane, called the **nuclear envelope**. This membranous covering consists of two adjacent lipid bilayers with a thin fluid space in between them. Spanning these two bilayers are nuclear pores. A **nuclear pore** is a tiny passageway for the passage of proteins, RNA, and solutes between the nucleus and the cytoplasm. Proteins called pore complexes lining the nuclear pores regulate the passage of materials into and out of the nucleus.

Inside the nuclear envelope is a gel-like nucleoplasm with solutes that include the building blocks of nucleic acids. There can also be a dark-staining mass often visible under a simple light microscope, called a **nucleolus** (plural = nucleoli). The nucleolus is a region of the nucleus that is responsible for manufacturing the RNA necessary for the construction of ribosomes, called ribosomal or rRNA. Once synthesized, newly made ribosomal subunits exit the cell's nucleus through the nuclear pores.

The genetic instructions that are used to build and maintain an organism are arranged in an orderly manner in strands of DNA. DNA in the nucleus is always found with proteins called histones. This DNA and protein structure is called **chromatin** (Figure 3.19).

Along the chromatin threads, the DNA is wrapped around a set of **histone** proteins. When a cell is in the process of division, the chromatin condenses into chromosomes so that the DNA can be safely transported to the "daughter

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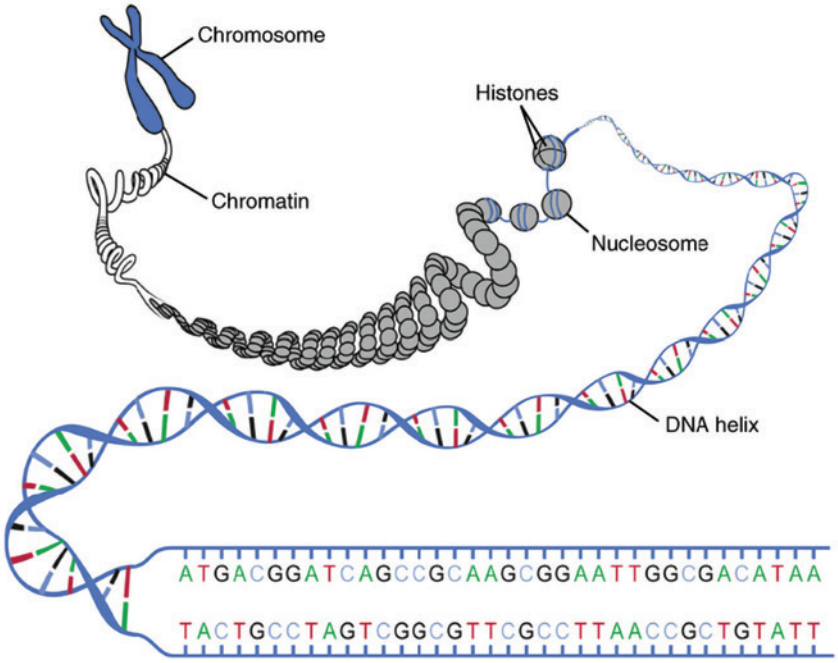


Figure 3.19 DNA Macrostructure. Strands of DNA are wrapped around supporting histones. These proteins are increasingly bundled and condensed into chromatin, which is packed tightly into chromosomes when the cell is ready to divide.

cells." The **chromosome** is composed of DNA and proteins; it is the condensed form of chromatin. It is estimated that humans have almost 22,000 genes distributed on 46 chromosomes.

DNA Replication

In order for an organism to grow, develop, and maintain its health, cells must reproduce themselves by dividing to produce two new daughter cells, each with the full complement of DNA as found in the original cell. Billions of new cells are produced in an adult human every day. Only very few cell types in the body do not divide, including nerve cells, skeletal muscle fibres, and cardiac muscle cells. The division time of different cell types varies. Epithelial cells of the skin and gastrointestinal lining, for instance, divide very frequently to replace those that are constantly being rubbed off the surface by friction.

A DNA molecule is made of two strands that "complement" each other in the sense that the molecules that compose the strands fit together and bind to each other, creating a double-stranded molecule that looks much like a long, twisted ladder. This double helix can be constructed easily because the two strands are antiparallel, meaning the two strands run in opposite directions. Each side rail of the DNA ladder is composed of alternating sugar

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and phosphate groups (Figure 3.20). The two sides of the ladder are not identical but complementary. These two backbones are bonded to each other across pairs of protruding bases, each bonded pair forming one "rung," or cross member. The four nitrogen-containing bases of a nucleotide in DNA are adenine (A), thymine (T), cytosine (C), and guanine (G). Because of their shape and charge, the two bases that compose a pair always bond together. Adenine always binds with thymine, and cytosine always binds with guanine. The particular sequence of bases along the DNA molecule determines the genetic code. Therefore, if the two complementary strands of DNA were pulled apart, you could infer the order of the bases in one strand from the bases in the other, complementary strand. For example, if one strand has a region with the sequence AGTGCCT, then the sequence of the complementary strand would be TCACGGA.

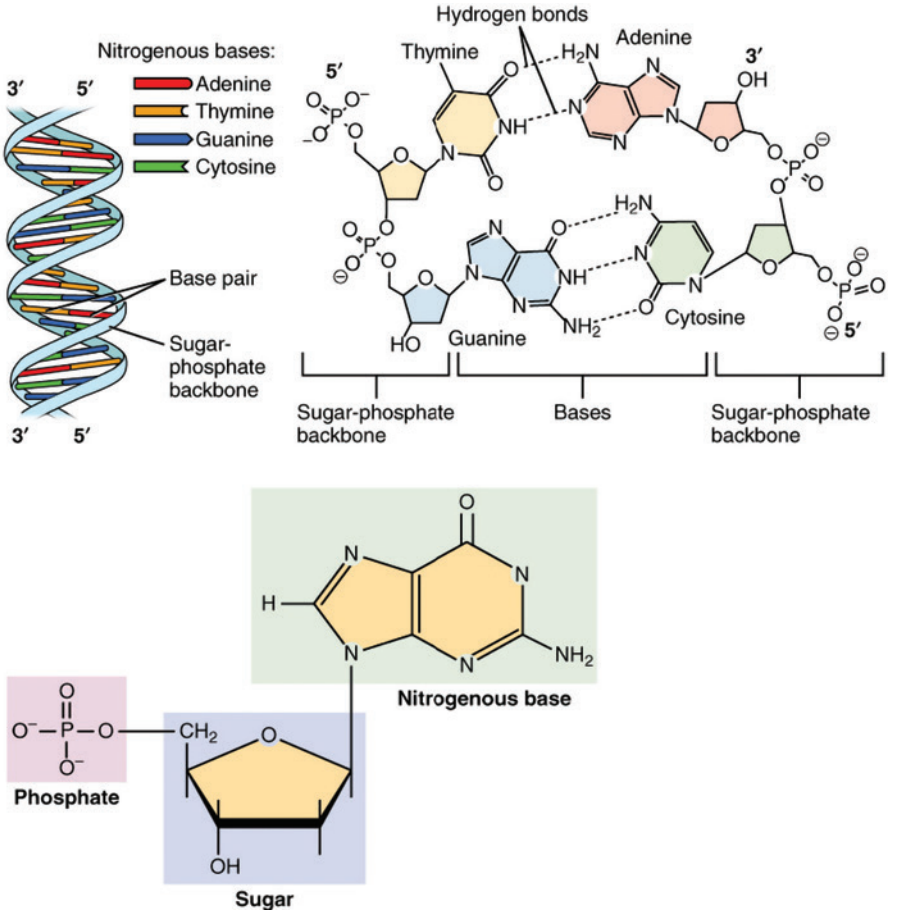


Figure 3.20 Molecular Structure of DNA. The DNA double helix is composed of two complementary strands. The strands are bonded together via their nitrogenous base pairs using hydrogen bonds.

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DNA replication is the copying of DNA that occurs before cell division can take place. After a great deal of debate and experimentation, the general method of DNA replication was deduced in 1958 by two scientists in California, Matthew Meselson and Franklin Stahl. This method is illustrated in Figure 3.21 and described here:

Stage 1: Initiation. The two complementary strands are separated, much like unzipping a zipper. Special enzymes, including helicase, untwist and separate the two strands of DNA.

Stage 2: Elongation. Each strand becomes a template along which a new complementary strand is built. **DNA polymerase** brings in the correct nucleotides to complement the template strand, synthesizing a new strand nucleotide by nucleotide. A DNA polymerase is an enzyme that adds free nucleotides to the end of a chain of DNA, making a new double strand. This growing strand continues to be built until it has fully complemented the template strand.

Stage 3: Termination. Once the two original strands are bound to their own finished, complementary strands, DNA replication is stopped and the two new identical DNA molecules are complete.

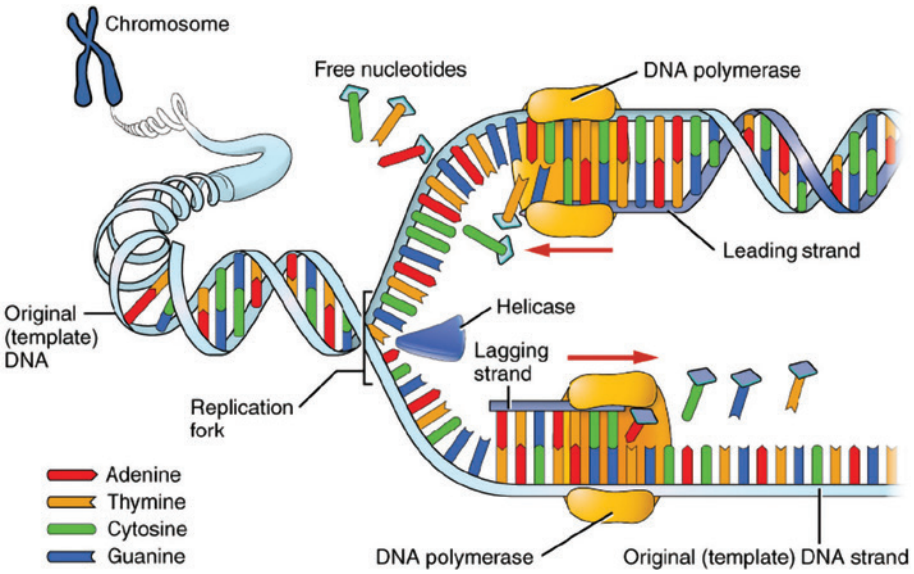


Figure 3.21 DNA Replication. DNA replication faithfully duplicates the entire genome of the cell. During DNA replication, a number of different enzymes work together to pull apart the two strands so each strand can be used as a template to synthesize new complementary strands. The two new daughter DNA molecules each contain one preexisting strand and one newly synthesized strand. Thus, DNA replication is said to be "semiconservative."

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Each new DNA molecule contains one strand from the original molecule and one newly synthesized strand. The term for this mode of replication is *semiconservative*, because half of the original DNA molecule is conserved in each new DNA molecule. This process continues until the cell's entire **genome**, the entire complement of an organism's DNA, is replicated. As you might imagine, it is very important that DNA replication takes place precisely so that new cells in the body contain the exact same genetic material as their parent cells. Mistakes made during DNA replication, such as the accidental addition of an inappropriate nucleotide, have the potential to render a gene dysfunctional or useless. Fortunately, there are mechanisms in place to minimize such mistakes. A DNA proofreading process enlists the help of special enzymes that scan the newly synthesized molecule for mistakes and correct them. Once the process of DNA replication is complete, the cell is ready to divide. You will explore the process of cell division later in the chapter.

Interactive Link 3.6

Watch this video (http://oer.aupress.ca/oer-202505/3.6) to learn about DNA replication. DNA replication proceeds simultaneously at several sites on the same molecule. What separates the base pair at the start of DNA replication?

3.4 Protein Synthesis

Learning Objectives

By the end of this section, you will be able to:

- Explain how the genetic code stored within DNA determines the protein that will form
- Describe the process of transcription
- Describe the process of translation
- Discuss the function of ribosomes

It was mentioned earlier that DNA provides a "blueprint" for the cell structure and physiology. This refers to the fact that DNA contains the information necessary for the cell to build one very important type of molecule: the protein. Most structural components of the cell are made up, at least in part, by proteins, and virtually all the functions that a cell carries out are completed with the help of

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proteins. One of the most important classes of proteins is enzymes, which help speed up necessary biochemical reactions that take place inside the cell. Some of these critical biochemical reactions include building larger molecules from smaller components (such as occurs during DNA replication or synthesis of microtubules) and breaking down larger molecules into smaller components (such as when harvesting chemical energy from nutrient molecules). Whatever the cellular process may be, it is almost sure to involve proteins. A **gene** is a functional segment of DNA that provides the genetic information necessary to build a protein. Each particular gene provides the code necessary to construct a particular protein. **Gene expression**, which transforms the information coded in a gene to a final gene product, ultimately dictates the structure and function of a cell by determining which proteins are made.

From DNA to RNA: Transcription

DNA is housed within the nucleus, and protein synthesis takes place in the cytoplasm, thus there must be some sort of intermediate messenger that leaves the nucleus and manages protein synthesis. This intermediate messenger is **messenger RNA** (**mRNA**), a single-stranded nucleic acid that carries a copy of the genetic code for a single gene out of the nucleus and into the cytoplasm, where it is used to produce proteins.

There are several different types of RNA, each having different functions in the cell.

Gene expression begins with the process called **transcription**, which is the synthesis of a strand of mRNA that is complementary to the gene of interest. This process is called transcription because the mRNA is like a transcript, or copy, of the gene's DNA code. Transcription begins in a fashion somewhat like DNA replication, in that a region of DNA unwinds and the two strands separate; however, only that small portion of the DNA will be split apart. The triplets within the gene on this section of the DNA molecule are used as the template to transcribe the complementary strand of RNA (Figure 3.22). A **codon** is a three-base sequence of mRNA, so called because it directly encodes amino acids. Like DNA replication, there are three stages to transcription: initiation, elongation, and termination.

Stage 1: Initiation. A region at the beginning of the gene called a **promoter**—a particular sequence of nucleotides—triggers the start of transcription.

Stage 2: Elongation. Transcription starts when RNA polymerase unwinds the DNA segment. One strand, referred to as the coding strand, becomes the template with the genes to be coded. The

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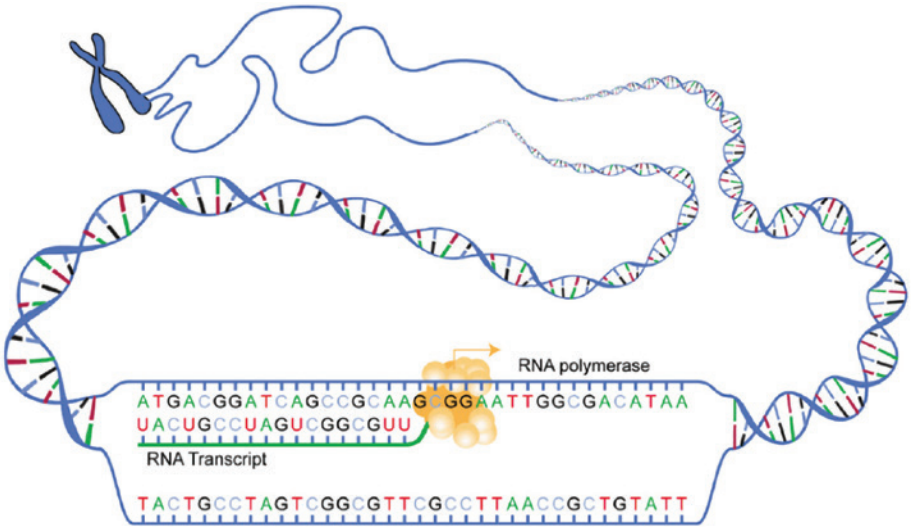


Figure 3.22 Transcription: From DNA to mRNA. In the first of the two stages of making protein from DNA, a gene on the DNA molecule is transcribed into a complementary mRNA molecule.

polymerase then aligns the correct nucleic acid (A, C, G, or U) with its complementary base on the coding strand of DNA. **RNA polymerase** is an enzyme that adds new nucleotides to a growing strand of RNA. This process builds a strand of mRNA.

Stage 3: Termination. At the end of the gene, a sequence of nucleotides called the terminator sequence causes the new RNA to fold up on itself. This fold causes the RNA to separate from the gene and from RNA polymerase, ending transcription.

From RNA to Protein: Translation

Like translating a book from one language into another, the codons on a strand of mRNA must be translated into the amino acid alphabet of proteins. **Translation** is the process of synthesizing a chain of amino acids called a **polypeptide**. **Ribosomal RNA** (**rRNA**) is a type of RNA that, together with proteins, composes the structure of the ribosome. Ribosomes exist in the cytoplasm as two distinct components, a small and a large subunit. When an mRNA molecule is ready to be translated, the two subunits come together and attach to the mRNA. The ribosome provides a substrate for translation, bringing together and aligning the mRNA molecule with the molecular "translators" that must decipher its code.

The other major requirement for protein synthesis is the translator molecules that physically "read" the mRNA codons. **Transfer RNA** (**tRNA**) is a type of RNA that ferries the appropriate corresponding amino acids to the ribosome and attaches each new amino acid to the last, building the polypeptide chain

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one by one. Thus, tRNA transfers specific amino acids from the cytoplasm to a growing polypeptide. The tRNA molecules must be able to recognize the codons on mRNA and match them with the correct amino acid. The tRNA is modified for this function. On one end of its structure is a binding site for a specific amino acid. On the other end is a base sequence that matches the codon specifying its particular amino acid. This sequence of three bases on the tRNA molecule is called an **anticodon**.

Much like the processes of DNA replication and transcription, translation consists of three main stages: initiation, elongation, and termination. The initiation stage takes place with the binding of a ribosome to an mRNA transcript. The elongation stage involves the recognition of a tRNA anticodon with the next mRNA codon in the sequence. Once the anticodon and codon sequences are bound (remember, they are complementary base pairs), the tRNA presents its amino acid cargo, and the growing polypeptide strand is attached to this next amino acid. This attachment takes place with the assistance of various enzymes and requires energy. The tRNA molecule then releases the mRNA strand, the mRNA strand shifts one codon over in the ribosome, and the next appropriate tRNA arrives with its matching anticodon. This process continues until the final codon on the mRNA is reached, which provides a "stop" message that signals termination of translation and triggers the release of the complete, newly synthesized protein. Thus, a gene within the DNA molecule is transcribed into mRNA, which is then translated into a protein product (Figure 3.23).

Commonly, an mRNA transcription will be translated simultaneously by several adjacent ribosomes. This increases the efficiency of protein synthesis. A single ribosome might translate an mRNA molecule in approximately one minute; so multiple ribosomes aboard a single transcript could produce multiple times the number of the same protein in the same minute. A **polyribosome** is a string of ribosomes translating a single mRNA strand.

Interactive Link 3.7

Watch this video (http://oer.aupress.ca/oer-202505/3.7) to learn about ribosomes. The ribosome binds to the mRNA molecule to start translation of its code into a protein. What happens to the small and large ribosomal subunits at the end of translation?

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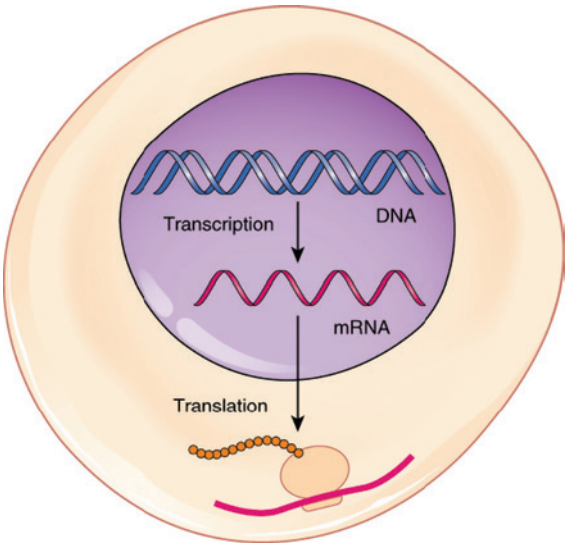


Figure 3.23 From DNA to Protein: Transcription Through Translation. Transcription within the cell nucleus produces an mRNA molecule, which is modified and then sent into the cytoplasm for translation. The transcript is decoded into a protein (red thick line in cytoplasm) with the help of a ribosome (yellow structure connected to the protein in cytoplasm) and tRNA molecules.

3.5 Cell Growth and Division

Learning Objectives

By the end of this section, you will be able to:

- Describe the stages of the cell cycle
- Discuss how the cell cycle is regulated
- Describe the stages of mitosis and cytokinesis, in order

So far in this chapter, you have read numerous times about the importance and prevalence of cell division. While there are a few cells in the body that do not undergo cell division (such as gametes, red blood cells, most neurons, and some muscle cells), most somatic cells divide regularly. A **somatic cell** is a general term for a body cell, and all human cells except for the cells that produce eggs and sperm (which are referred to as germ cells) are somatic cells. Somatic cells contain *two* copies of each of their chromosomes (one copy received from each parent). A **homologous** pair of chromosomes is the two copies of a single chromosome found in each somatic cell. The human is a **diploid** organism, having 23 homologous pairs of chromosomes in each of the somatic cells. The

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condition of having pairs of chromosomes is known as diploidy. Ova and sperm contain only half the DNA of a diploid cell and are called **haploid**.

Cells in the body replace themselves over the lifetime of a person. For example, the cells lining the gastrointestinal tract must be frequently replaced when constantly "worn off" by the movement of food through the gut. But what triggers a cell to divide, and how does it prepare for and complete cell division? The **cell cycle** is the sequence of events in the life of the cell from the moment it is created at the end of a previous cycle of cell division until it then divides itself, generating two new cells.

The Cell Cycle

One "turn" or cycle of the cell cycle consists of two general phases: interphase, followed by mitosis and cytokinesis. **Interphase** is the period of the cell cycle during which the cell is not dividing. The majority of cells are in interphase most of the time. **Mitosis** is the division of genetic material, during which the cell nucleus breaks down and two new, fully functional nuclei are formed. **Cytokinesis** divides the cytoplasm into two distinctive cells.

Interphase

A cell grows and carries out all normal metabolic functions and processes in a period called G_1 (Figure 3.24). **G_1 phase** (gap 1 phase) is the first gap, or growth phase, in the cell cycle. For cells that will divide again, G_1 is followed by replication of the DNA during the S phase. The **S phase** (synthesis phase) is the period during which a cell replicates its DNA.

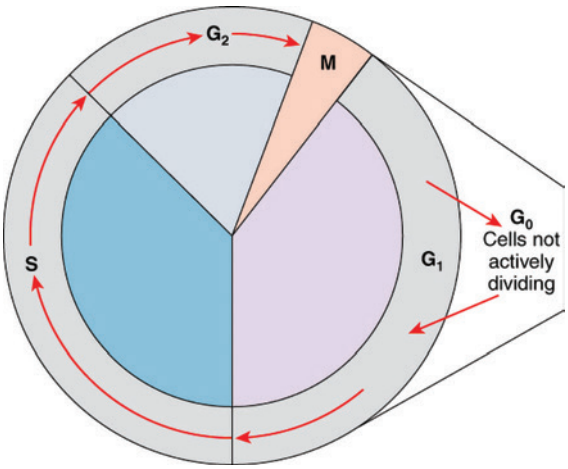


Figure 3.24 Cell Cycle. The two major phases of the cell cycle include mitosis (designated M), when the cell divides, and interphase, when the cell grows and performs all its normal functions. Interphase is further subdivided into G_1, S, and G_2 phases.

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After the synthesis phase, the cell proceeds through the G_2 phase. The **G_2 phase** is a second gap phase, during which the cell continues to grow and makes the necessary preparations for mitosis. Between the G_1, S, and G_2 phases, cells will vary the most in their duration of the G_1 phase. It is here that a cell might spend a couple of hours or many days. The S phase typically lasts between 8 and 10 hours, and the G_2 phase lasts approximately 5 hours. In contrast to these phases, the **G_0 phase** is a resting phase of the cell cycle. Cells that have temporarily stopped dividing and are resting (a common condition), and cells that have permanently ceased dividing (like nerve cells) are said to be in G_0.

The Structure of Chromosomes

DNA is in the form of chromatin during interphase but condenses to form chromosomes during cell division.

Billions of cells in the human body divide every day. During the S phase of interphase, the amount of DNA within the cell precisely doubles. Therefore, after DNA replication but before cell division, each cell actually contains *two* copies of each chromosome. Each copy of the chromosome is referred to as a **sister chromatid** and is physically bound to the other copy. (Note that the term *sister chromatid* is used regardless of the sex of the person.) The **centromere** is the structure that attaches one sister chromatid to another. Because a human cell has 46 chromosomes, during this phase, there are 92 chromatids (46 × 2) in the cell. Make sure not to confuse the concept of a pair of chromatids (one chromosome and its exact copy attached during mitosis) and a homologous pair of chromosomes (two paired chromosomes that were inherited separately, one from each parent; Figure 3.25).

Mitosis and Cytokinesis

The **mitotic phase** of the cell typically takes between 1 and 2 hours. During this phase, a cell undergoes two major processes. First, it completes mitosis, during which the contents of the nucleus are equitably pulled apart and distributed between its two halves. Cytokinesis then occurs, dividing the cytoplasm and cell body into two new cells. Mitosis is divided into four major stages that take place after interphase (Figure 3.26) and in the following order: prophase (with prometaphase), metaphase, anaphase, and telophase. The process is then followed by cytokinesis.

Prophase is the first phase of mitosis, during which the loosely packed chromatin coils and condenses into visible chromosomes. During prophase, each chromosome becomes visible with its identical partner attached, forming the familiar X shape of sister chromatids. The nucleolus disappears early during this phase, and the nuclear envelope also disintegrates.

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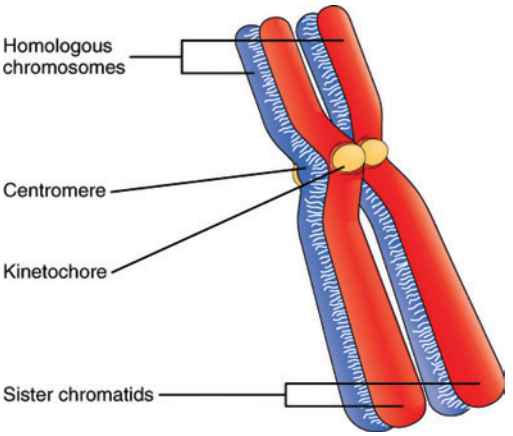


Figure 3.25 A Homologous Pair of Chromosomes with Their Attached Sister Chromatids. The red and blue colours correspond to a homologous pair of chromosomes. Each member of the pair was separately inherited from one parent. Each chromosome in the homologous pair is also bound to an identical sister chromatid, which is produced by DNA replication, and results in the familiar "X" shape.

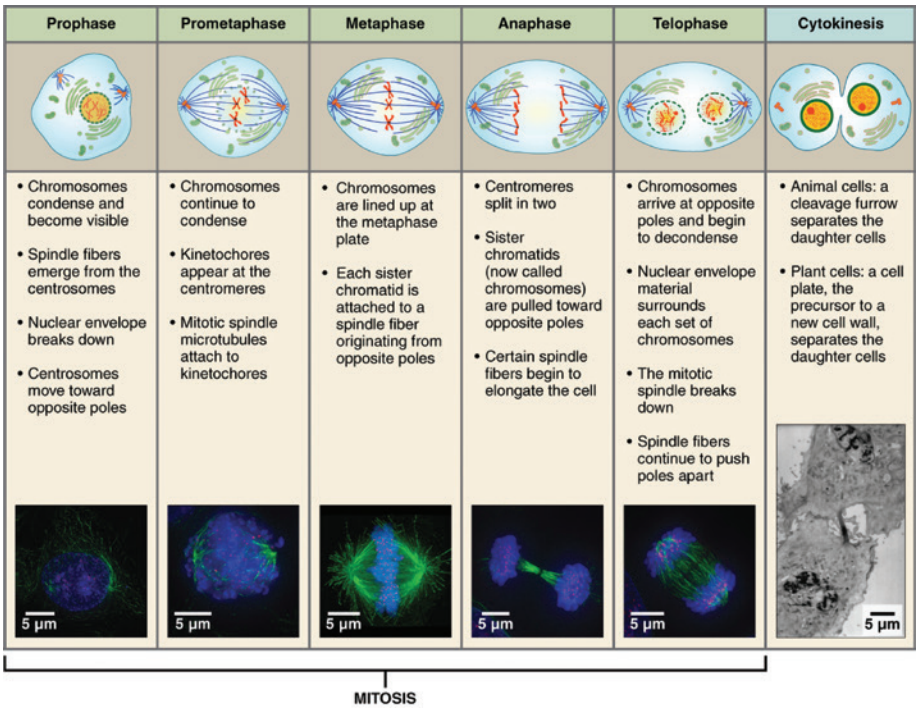


Figure 3.26 Cell Division: Mitosis Followed by Cytokinesis. The stages of cell division oversee the separation of identical genetic material into two new nuclei, followed by the division of the cytoplasm.

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A major occurrence during prophase concerns a very important structure that contains the origin site for microtubule growth. Recall the cellular structures called centrioles that serve as origin points from which microtubules extend. These tiny structures also play a very important role during mitosis. A **centrosome** is a pair of centrioles together. The cell contains two centrosomes side by side, which begin to move apart during prophase. As the centrosomes migrate to two different sides of the cell, microtubules begin to extend from each like long fingers from two hands extending toward each other. The **mitotic spindle** is a structure composed of the centrosomes and their emerging microtubules.

Near the end of prophase, there is an invasion of the nuclear area by microtubules from the mitotic spindle. The nuclear membrane has disintegrated, and the microtubules attach themselves to the centromeres that adjoin pairs of sister chromatids. The **kinetochore** is a protein structure on the centromere that is the point of attachment between the mitotic spindle and the sister chromatids. This stage is referred to as late prophase or "prometaphase" to indicate the transition between prophase and metaphase.

Metaphase is the second stage of mitosis. During this stage, the sister chromatids, with their attached microtubules, line up along a linear plane in the middle of the cell. A metaphase plate forms between the centrosomes that are now located at either end of the cell. The **metaphase plate** is the name for the plane through the centre of the spindle on which the sister chromatids are positioned. The microtubules are now poised to pull apart the sister chromatids and bring one from each pair to each side of the cell.

Anaphase is the third stage of mitosis. Anaphase takes place over a few minutes, when the pairs of sister chromatids are separated from one another, forming individual chromosomes once again. These chromosomes are pulled to opposite ends of the cell by their kinetochores as the microtubules shorten. Each end of the cell receives one partner from each pair of sister chromatids, ensuring that the two new daughter cells will contain identical genetic material.

Telophase is the final stage of mitosis. Telophase is characterized by the formation of two new daughter nuclei at either end of the dividing cell. These newly formed nuclei surround the genetic material, which uncoils such that the chromosomes return to loosely packed chromatin. Nucleoli also reappear within the new nuclei, and the mitotic spindle breaks apart, each new cell receiving its own complement of DNA, organelles, membranes, and centrioles. At this point, the cell is already beginning to split in half as cytokinesis begins.

The **cleavage furrow** is a contractile band made up of microfilaments that forms around the midline of the cell during cytokinesis. (Recall that microfilaments consist of actin.) This contractile band squeezes the two cells apart

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until they finally separate. Two new cells are now formed. One of these cells (the "stem cell") enters its own cell cycle, able to grow and divide again at some future time. The other cell transforms into the functional cell of the tissue, typically replacing an "old" cell there.

Imagine a cell that completed mitosis but never underwent cytokinesis. In some cases, a cell may divide its genetic material and grow in size but fail to undergo cytokinesis. This results in larger cells with more than one nucleus.

Usually, this is an unwanted aberration and can be a sign of cancerous cells.

Interactive Link 3.8

Visit this link (http://oer.aupress.ca/oer-202505/3.8) to learn about mitosis. Mitosis results in two identical diploid cells. What structures form during prophase?

3.6 Cellular Differentiation

Learning Objectives

By the end of this section, you will be able to:

- Discuss how the generalized cells of a developing embryo or the stem cells of an adult organism become differentiated into specialized cells
- Distinguish between the categories of stem cells

How does a complex organism such as a human develop from a single cell—a fertilized egg—into the vast array of cell types such as nerve cells, muscle cells, and epithelial cells that characterize the adult? Throughout development and adulthood, the process of cellular differentiation leads cells to assume their final morphology and physiology. Differentiation is the process by which unspecialized cells become specialized to carry out distinct functions.

Stem Cells

A **stem cell** is an unspecialized cell that can divide without limit as needed and can, under specific conditions, differentiate into specialized cells. Stem cells are divided into several categories according to their potential to differentiate.

The first embryonic cells that arise from the division of the zygote are the ultimate stem cells; these stem cells have the potential to differentiate into any of the cells needed to enable an organism to grow and develop.

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The embryonic cells that develop from totipotent stem cells and are precursors to the fundamental tissue layers of the embryo are classified as pluripotent. A **pluripotent** stem cell is one that has the potential to differentiate into any type of human tissue but cannot support the full development of an organism. These cells then become slightly more specialized and are referred to as multipotent cells.

A **multipotent** stem cell has the potential to differentiate into different types of cells within a given cell lineage or a small number of lineages, such as a red blood cell or white blood cell.

Stem cells are unique in that they can also continually divide and regenerate new stem cells instead of further specializing. There are different stem cells present at different stages of a human's life. They include the embryonic stem cells of the embryo, fetal stem cells of the fetus, and adult stem cells in the adult. One type of adult stem cell is the epithelial stem cell, which gives rise to the keratinocytes in the multiple layers of epithelial cells in the epidermis of skin. Adult bone marrow has three distinct types of stem cells: hematopoietic stem cells, which give rise to red blood cells, white blood cells, and platelets; endothelial stem cells, which give rise to the endothelial cell types that line blood and lymph vessels; and mesenchymal stem cells, which give rise to the different types of muscle cells.

Differentiation

When a cell goes through a process of **differentiation** (becomes more specialized), it may undertake major changes in its size, shape, metabolic activity, and overall function. Because all cells in the body, beginning with the fertilized egg, contain the same DNA, how do the different cell types come to be so different? The answer is analogous to a movie script. The different actors in a movie all read from the same script; however, they are each only reading their own part of the script.

Similarly, all cells contain the same full complement of DNA, but each type of cell only "reads" the portions of DNA that are relevant to its own function. In biology, this is referred to as the unique genetic expression of each cell.

Key Terms

active transport: Form of transport across the cell membrane that requires input of cellular energy.

amphipathic: Describes a molecule that exhibits a difference in polarity between its two ends, resulting in a difference in water solubility.

anaphase: Third stage of mitosis (and meiosis), during which sister chromatids separate into two new nuclear regions of a dividing cell.

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anticodon: Consecutive sequence of three nucleotides on a tRNA molecule that is complementary to a specific codon on an mRNA molecule.
antiporters: Secondary active transporters that transport substances in opposite directions.
apoptosis: Programmed cell death.
autolysis: Breakdown of cells by their own enzymatic action.
autophagy: Lysosomal breakdown of a cell's own components.
cell cycle: Life cycle of a single cell, from its birth until its division into two new daughter cells.
cell membrane: Membrane surrounding all animal cells, composed of a lipid bilayer interspersed with various molecules; also known as plasma membrane.
centriole: Small, self-replicating organelle that provides the origin for microtubule growth and moves DNA during cell division.
centromere: Region of attachment for two sister chromatids.
centrosome: Cellular structure that organizes microtubules during cell division.
channel protein: Membrane-spanning protein that has an inner pore that allows the passage of one or more substances.
chromatin: Substance consisting of DNA and associated proteins.
chromosome: Condensed version of chromatin.
cilia: Small appendage on certain cells formed by microtubules and modified for movement of materials across the cellular surface.
cleavage furrow: Contractile ring that forms around a cell during cytokinesis and pinches the cell into two halves.
codon: Consecutive sequence of three nucleotides on an mRNA molecule that corresponds to a specific amino acid.
concentration gradient: Difference in the concentration of a substance between two regions.
cytokinesis: Final stage in cell division, where the cytoplasm divides to form two separate daughter cells.
cytoplasm: Internal material between the cell membrane and nucleus of a cell, mainly consisting of a water-based fluid called cytosol, within which are all the other organelles, cellular solutes, and suspended materials.
cytoskeleton: "skeleton" of a cell; formed by rodlike proteins that support the cell's shape and provide, among other functions, locomotive abilities.
cytosol: Clear, semifluid medium of the cytoplasm, made up mostly of water.
differentiation: Process in which a cell may undertake major changes in its size, shape, metabolic activity, and overall function.

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diffusion: Movement of a substance from an area of higher concentration to one of lower concentration.

diploid: Condition marked by the presence of a double complement of genetic material (two sets of chromosomes, one set inherited from each of two parents).

DNA polymerase: Enzyme that functions in adding new nucleotides to a growing strand of DNA during DNA replication.

DNA replication: Process of duplicating a molecule of DNA.

electrical gradient: Difference in the electrical charge (potential) between two regions.

endocytosis: Import of material into the cell by formation of a membrane-bound vesicle.

endoplasmic reticulum (ER): Cellular organelle that consists of interconnected membrane-bound tubules, which may or may not be associated with ribosomes (rough type or smooth type, respectively).

exocytosis: Export of a substance out of a cell by formation of a membrane-bound vesicle.

extracellular fluid (ECF): Fluid exterior to cells; includes the interstitial fluid, blood plasma, and fluid found in other reservoirs in the body.

facilitated diffusion: Diffusion of a substance with the aid of a membrane protein.

flagellum: Appendage on certain cells formed by microtubules and modified for movement.

G_0 phase: Phase of the cell cycle usually entered from the G_1 phase; characterized by long or permanent periods where the cell does not move forward into the DNA synthesis phase.

G_1 phase: First phase of the cell cycle, after a new cell is born.

G_2 phase: Third phase of the cell cycle, after the DNA synthesis phase.

gene: Functional length of DNA that provides the genetic information necessary to build a protein.

gene expression: Active interpretation of the information coded in a gene to produce a functional gene product.

genome: Entire complement of an organism's DNA; found within virtually every cell.

glycocalyx: Coating of sugar molecules that surrounds the cell membrane.

glycoprotein: Protein that has one or more carbohydrates attached.

Golgi apparatus: Cellular organelle formed by a series of flattened, membrane-bound sacs that functions in protein modification, tagging, packaging, and transport.

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haploid: Contain only half the DNA of a diploid cell; examples are ova and sperm cells.

histone: Family of proteins that associate with DNA in the nucleus to form chromatin.

homologous: Describes two copies of the same chromosome (not identical), one inherited from each parent.

hydrophilic: Describes a substance or structure attracted to water.

hydrophobic: Describes a substance or structure repelled by water.

hypertonic: Describes a solution concentration that is higher than a reference concentration.

hypotonic: Describes a solution concentration that is lower than a reference concentration.

integral protein: Membrane-associated protein that spans the entire width of the lipid bilayer.

intermediate filament: Type of cytoskeletal filament made of keratin, characterized by an intermediate thickness, and playing a role in resisting cellular tension.

interphase: Entire life cycle of a cell, excluding mitosis.

interstitial fluid (IF): Fluid in the small spaces between cells not contained within blood vessels.

intracellular fluid (ICF): Fluid in the cytosol of cells.

isotonic: Describes a solution concentration that is the same as a reference concentration.

kinetochore: Region of a centromere where microtubules attach to a pair of sister chromatids.

ligand: Molecule that binds with specificity to a specific receptor molecule.

lysosome: Membrane-bound cellular organelle originating from the Golgi apparatus and containing digestive enzymes.

messenger RNA (mRNA): Nucleotide molecule that serves as an intermediate in the genetic code between DNA and protein.

metaphase: Second stage of mitosis (and meiosis), characterized by the linear alignment of sister chromatids in the centre of the cell.

metaphase plate: Linear alignment of sister chromatids in the centre of the cell, which takes place during metaphase.

microfilament: The thinnest of the cytoskeletal filaments; composed of actin subunits that function in muscle contraction and cellular structural support.

microtubule: The thickest of the cytoskeletal filaments, composed of tubulin subunits that function in cellular movement and structural support.

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mitochondrion: One of the cellular organelles bound by a double lipid bilayer that functions primarily in the production of cellular energy (ATP).
mitosis: Division of genetic material, during which the cell nucleus breaks down and two new, fully functional nuclei are formed.
mitotic phase: Phase of the cell cycle in which a cell undergoes mitosis.
mitotic spindle: Network of microtubules, originating from centrioles, that arranges and pulls apart chromosomes during mitosis.
multipotent: Describes the condition of being able to differentiate into different types of cells within a given cell lineage or a small number of lineages, such as a red blood cell or white blood cell.
nuclear envelope: Membrane that surrounds the nucleus, consisting of a double lipid bilayer.
nuclear pore: One of the small, protein-lined openings found scattered throughout the nuclear envelope.
nucleolus: Small region of the nucleus that functions in ribosome synthesis.
nucleus: Cell's central organelle; contains the cell's DNA.
organelle: Any of several different types of membrane-enclosed specialized structures in the cell that perform specific functions for the cell.
osmosis: Diffusion of water molecules down their concentration gradient across a selectively permeable membrane.
passive transport: Form of transport across the cell membrane that does not require input of cellular energy.
peripheral protein: Membrane-associated protein that does not span the width of the lipid bilayer, but is attached peripherally to integral proteins, membrane lipids, or other components of the membrane.
peroxisome: Membrane-bound organelle that contains enzymes primarily responsible for detoxifying harmful substances.
phagocytosis: Endocytosis of large particles.
pinocytosis: Endocytosis of fluid.
pluripotent: Describes the condition of being able to differentiate into a large variety of cell types.
polypeptide: Chain of amino acids linked by peptide bonds.
polyribosome: Simultaneous translation of a single mRNA transcript by multiple ribosomes.
promoter: Region of DNA that signals transcription to begin at that site within the gene.
prophase: First stage of mitosis (and meiosis), characterized by breakdown of the nuclear envelope and condensing of the chromatin to form chromosomes.

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receptor: Protein molecule that contains a binding site for another specific molecule (called a ligand).

receptor-mediated endocytosis: Endocytosis of ligands attached to membrane-bound receptors.

ribosomal RNA (rRNA): RNA that makes up the subunits of a ribosome.

ribosome: Cellular organelle that functions in protein synthesis.

RNA polymerase: Enzyme that unwinds DNA and then adds new nucleotides to a growing strand of RNA for the transcription phase of protein synthesis.

rough ER (RER): Organelle that function as the site for protein synthesis; many ribosomes attach to the ER giving it the studded appearance of rough ER.

secondary active transport: Process harnessing an electrochemical gradient established by primary active transport to drive the transport of a second molecule.

selective permeability: Feature of any barrier that allows certain substances to cross but excludes others.

sister chromatid: One of a pair of identical chromosomes, formed during DNA replication.

smooth ER (SER): Organelle lacking attached ribosomes that are specialized for lipid synthesis, detoxification, carbohydrate metabolism, and calcium ion storage.

sodium-potassium pump (also Na^+/K^+ ATPase): Membrane-embedded protein pump that uses ATP to move Na^+ out of a cell and K^+ into the cell.

somatic cell: All cells of the body excluding gamete cells.

S phase: Stage of the cell cycle during which DNA replication occurs.

stem cell: Cell that is oligo-, multi-, or pluripotent and has the ability to produce additional stem cells rather than becoming further specialized.

symporters: Secondary active transporters that move two substances in the same direction.

telophase: Final stage of mitosis (and meiosis), preceding cytokinesis, characterized by the formation of two new daughter nuclei.

tonicity: A measure of a solution's ability to change the volume of cells by altering their water content.

transcription: Process of producing an mRNA molecule that is complementary to a particular gene of DNA.

transfer RNA (tRNA): Molecules of RNA that serve to bring amino acids to a growing polypeptide strand and properly place them into the sequence.

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translation: Process of producing a protein from the nucleotide sequence code of an mRNA transcript.

vesicle: Membrane-bound structure that contains materials within or outside of the cell.

Chapter Review

3.1 The Cell Membrane

The cell membrane provides a barrier around the cell, separating its internal components from the extracellular environment. It is composed of a phospholipid bilayer, with hydrophobic internal lipid "tails" and hydrophilic external phosphate "heads." Various membrane proteins are scattered throughout the bilayer, both inserted within it and attached to it peripherally. The cell membrane is selectively permeable, allowing only a limited number of materials to diffuse through its lipid bilayer. All materials that cross the membrane do so using passive (non-energy-requiring) or active (energy-requiring) transport processes. During passive transport, materials move by simple diffusion or by facilitated diffusion through the membrane, down their concentration gradient. Water passes through the membrane in a diffusion process called osmosis. During active transport, energy is expended to assist materials' movement across the membrane in a direction against their concentration gradient. Active transport may take place with the help of protein pumps or through the use of vesicles.

3.2 The Cytoplasm and Cellular Organelles

The internal environment of a living cell is made up of a fluid, jellylike substance called cytosol, which consists mainly of water but also contains various dissolved nutrients and other molecules. The cell contains an array of cellular organelles, each one performing a unique function and helping maintain the health and activity of the cell. The cytosol and organelles together compose the cell's cytoplasm.

Most organelles are surrounded by a lipid membrane similar to the cell membrane of the cell. The endoplasmic reticulum (ER), Golgi apparatus, and lysosomes share a functional connectivity and are collectively referred to as the endomembrane system. There are two types of ER: smooth and rough. While the smooth ER performs many functions, including lipid synthesis and ion storage, the rough ER is mainly responsible for protein synthesis using its associated ribosomes. The rough ER sends newly made proteins to the Golgi apparatus, where they are modified and packaged for delivery to various locations within

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or outside of the cell. Some of these protein products are enzymes destined to break down unwanted material and are packaged as lysosomes for use inside the cell.

Cells also contain mitochondria and peroxisomes, which are the organelles responsible for producing the cell's energy supply and detoxifying certain chemicals, respectively. Biochemical reactions within mitochondria transform energy-carrying molecules into the usable form of cellular energy known as ATP. Peroxisomes contain enzymes that transform harmful substances such as free radicals into oxygen and water. Cells also contain a miniaturized "skeleton" of protein filaments that extends throughout their interior. Three different kinds of filaments compose this cytoskeleton (in order of increasing thickness): microfilaments, intermediate filaments, and microtubules. Each cytoskeletal component performs unique functions as well as provides a supportive framework for the cell.

3.3 The Nucleus and DNA Replication

The nucleus is the command centre of the cell, containing the genetic instructions for all the materials a cell will make (and thus all the functions it can perform). The nucleus is encased within a membrane of two interconnected lipid bilayers, side by side. This nuclear envelope is studded with protein-lined pores that allow materials to be trafficked into and out of the nucleus. The nucleus contains one or more nucleoli, which serve as sites for ribosome synthesis. The nucleus houses the genetic material of the cell: DNA. DNA is normally found as a loosely contained structure called chromatin within the nucleus, where it is wound up and associated with a variety of histone proteins. When a cell is about to divide, the chromatin coils tightly and condenses to form chromosomes.

There is a pool of cells constantly dividing within your body. The result is billions of new cells being created each day. Before any cell is ready to divide, it must replicate its DNA so that each new daughter cell will receive an exact copy of the organism's genome. A variety of enzymes are enlisted during DNA replication. These enzymes unwind the DNA molecule, separate the two strands, and assist with the building of complementary strands along each parent strand. The original DNA strands serve as templates from which the nucleotide sequences of the new strands are determined and synthesized. When replication is completed, two identical DNA molecules exist. Each one contains one original strand and one newly synthesized complementary strand.

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3.4 Protein Synthesis

DNA stores the information necessary for instructing the cell to perform all its functions. Cells use the genetic code stored within DNA to build proteins, which ultimately determine the structure and function of the cell. This genetic code lies in the particular sequence of nucleotides that make up each gene along the DNA molecule. To "read" this code, the cell must perform two sequential steps. In the first step, transcription, the DNA code is converted into an RNA code. A molecule of messenger RNA that is complementary to a specific gene is synthesized in a process similar to DNA replication. The molecule of mRNA provides the code to synthesize a protein. In the process of translation, the mRNA attaches to a ribosome. Next, tRNA molecules shuttle the appropriate amino acids to the ribosome one by one, coded by sequential triplet codons on the mRNA, until the protein is fully synthesized. When completed, the mRNA detaches from the ribosome, and the protein is released. Typically, multiple ribosomes attach to a single mRNA molecule at once, such that multiple proteins can be manufactured from the mRNA concurrently.

3.5 Cell Growth and Division

The life of a cell consists of stages that make up the cell cycle. After a cell is born, it passes through an interphase before it is ready to replicate itself and produce daughter cells. This interphase includes two gap phases (G_1 and G_2) as well as an S phase, during which its DNA is replicated in preparation for cell division. The cell cycle is under precise regulation by chemical messengers both inside and outside the cell that provide "stop" and "go" signals for movement from one phase to the next. Failures of these signals can result in cells that continue to divide uncontrollably, which can lead to cancer.

Once a cell has completed interphase and is ready for cell division, it proceeds through four separate stages of mitosis (prophase, metaphase, anaphase, and telophase). Telophase is followed by the division of the cytoplasm (cytokinesis), which generates two daughter cells. This process takes place in all normally dividing cells of the body except for the germ cells that produce eggs and sperm.

3.6 Cellular Differentiation

One of the major areas of research in biology is that of how cells specialize to assume their unique structures and functions, since all cells essentially originate from a single fertilized egg. Cell differentiation is the process of cells becoming specialized as the body develops. A stem cell is an unspecialized cell that can divide without limit as needed and can, under specific conditions, differentiate into specialized cells. Stem cells are divided into several categories

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according to their potential to differentiate. While all somatic cells contain the exact same genome, different cell types only express some of those genes at any given time.

These differences in gene expression ultimately dictate a cell's unique morphological and physiological characteristics. The use of different transcription factor proteins, which bind to DNA and promote or hinder the transcription of different genes, is the primary mechanism that determines which genes will be expressed and which ones will not. Through the action of these transcription factors, cells specialize into one of hundreds of different cell types in the human body.

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4

The Tissue Level of Organization

Chapter Objectives

After studying this chapter, you will be able to:

- Identify the main tissue types and discuss their roles in the human body
- Identify the four types of tissue membranes and the characteristics of each that make them functional
- Explain the functions of various epithelial tissues and how their forms enable their functions
- Explain the functions of various connective tissues and how their forms enable their functions
- Describe the characteristics of muscle tissue and how these enable function
- Discuss the characteristics of nervous tissue and how these enable information processing and control of muscular and glandular activities

The body contains at least 200 distinct cell types. These cells contain essentially the same internal structures, yet they vary enormously in shape and function. The different types of cells are not randomly distributed throughout the body; rather, they occur in organized layers, a level of organization referred to as tissue. The variety in shape reflects the many different roles that cells fulfil in your body. The human body starts as a single cell at fertilization. As this fertilized egg divides, it gives rise to trillions of cells, each built from the same blueprint but organizing into tissues and becoming irreversibly committed to a developmental pathway.

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4.1 Types of Tissues

Learning Objectives

By the end of this section, you will be able to:

- Identify the four main tissue types
- Discuss the functions of each tissue type
- Relate the structure of each tissue type to its function
- Discuss the embryonic origin of tissue
- Identify the three major germ layers
- Identify the main types of tissue membranes

The term **tissue** is used to describe a group of cells found together in the body. The cells within a tissue share a common embryonic origin. Microscopic observation reveals that the cells in a tissue share morphological features and are arranged in an orderly pattern that achieves the tissue's functions. From the evolutionary perspective, tissues appear in more complex organisms. For example, multicellular protists, ancient eukaryotes, do not have cells organized into tissues.

Although there are many types of cells in the human body, they are organized into four broad categories of tissues: epithelial, connective, muscle, and nervous. Each of these categories is characterized by specific functions that contribute to the overall health and maintenance of the body. A disruption of the structure is a sign of injury or disease. Such changes can be detected through histology, the microscopic study of tissue appearance, organization, and function.

The Four Types of Tissues

Epithelial tissue, also referred to as epithelium, refers to the sheets of cells that cover exterior surfaces of the body, line internal cavities and passageways, and form certain glands. **Connective tissue**, as its name implies, binds the cells and organs of the body together and functions in the protection, support, and integration of all parts of the body. **Muscle tissue** is excitable, responding to stimulation and contracting to provide movement, and occurs in three major types: skeletal (voluntary) muscle, smooth muscle, and cardiac muscle in the heart. **Nervous tissue** is also excitable, allowing the propagation of electrochemical signals in the form of nerve impulses that communicate between different regions of the body (Figure 4.1).

The next level of organization is the organ, where several types of tissues come together to form a working unit. Just as knowing the structure and

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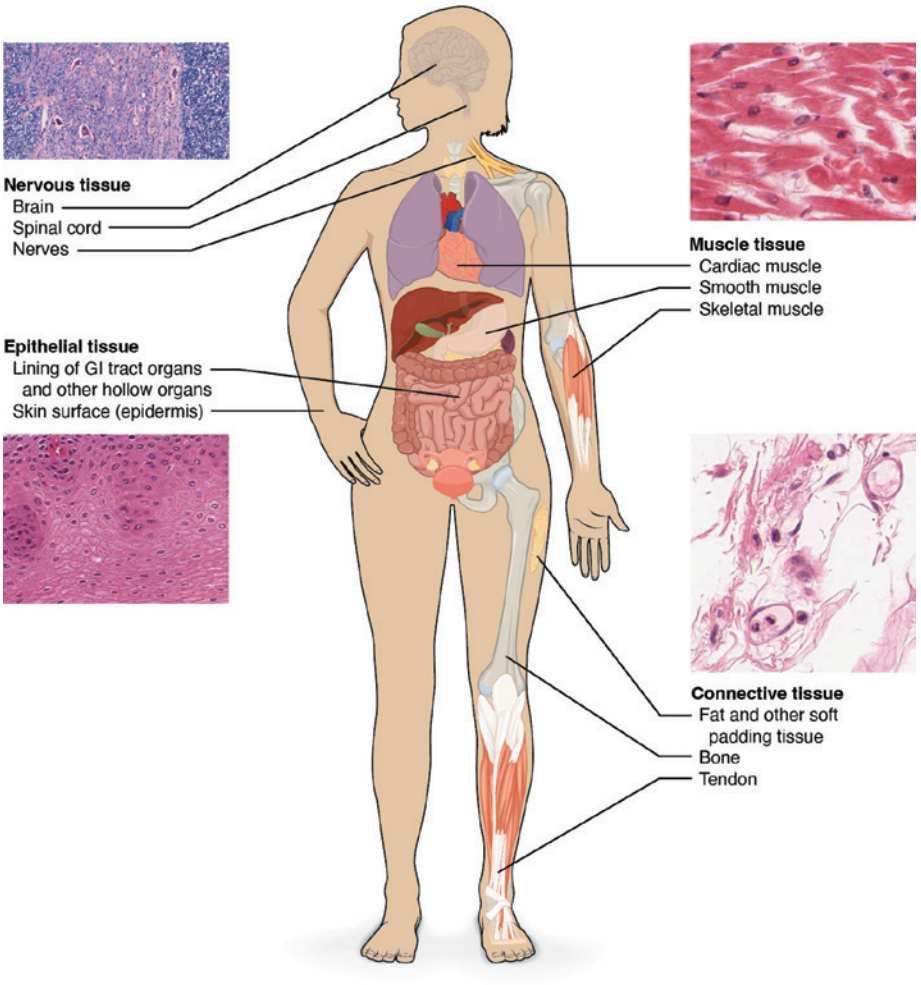


Figure 4.1 Four Types of Tissue: Body. The four types of tissues are exemplified in nervous tissue, stratified squamous epithelial tissue, cardiac muscle tissue, and connective tissue. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)

function of cells helps you in your study of tissues, knowledge of tissues will help you understand how organs function. The epithelial and connective tissues are discussed in detail in this chapter. Muscle and nervous tissues will be discussed only briefly in this chapter.

Embryonic Origin of Tissues

Each germ layer is identified by its relative position: **ectoderm** (*ecto-* = "outer"), **mesoderm** (*meso-* = "middle"), and **endoderm** (*endo-* = "inner"). The epithelial tissue originates in all three layers, whereas nervous tissue derives primarily from the ectoderm and muscle tissue from the mesoderm.

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Interactive Link 4.1

Watch this video (http://oer.aupress.ca/oer-202505/4.1) to learn more about stem cells. How do somatic stem cells differ from embryonic stem cells?

Tissue Membranes

A **tissue membrane** is a thin layer or sheet of cells that covers the outside of the body (e.g., skin), the organs (e.g., pericardium), internal passageways that lead to the exterior of the body (e.g., mucosa of the stomach), and the lining of the movable joint cavities. There are two basic types of tissue membranes: connective tissue and epithelial membranes (Figure 4.2).

Connective Tissue Membranes

The **connective tissue membrane** is formed solely from connective tissue. These membranes encapsulate organs, such as the kidneys, and line our movable joints. A **synovial membrane** is a type of connective tissue membrane that lines the cavity of a freely movable joint.

For example, synovial membranes surround the joints of the shoulder, elbow, and knee. Fibroblasts in the inner layer of the synovial membrane release hyaluronan into the joint cavity. The hyaluronan effectively traps available water to form the synovial fluid, a natural lubricant that enables the bones of a joint to move freely against one another without much friction. This synovial fluid readily exchanges water and nutrients with blood, as do all body fluids.

Epithelial Membranes

The **epithelial membrane** is composed of epithelium attached to a layer of connective tissue, for example, your skin. The **mucous membrane** (**mucosa**) is also a composite of connective and epithelial tissues. These epithelial membranes line the body cavities and hollow passageways that open to the external environment, including the digestive, respiratory, excretory, and reproductive tracts. Mucus, produced by the epithelial exocrine glands, covers the epithelial layer. The underlying connective tissue, called the **lamina propria**, helps support the fragile epithelial layer.

A **serous membrane** is an epithelial membrane that lines the cavities of the body that do not open to the outside. Serous membranes cover the organs located within those cavities. They are essentially membranous bags with mesothelium lining the inside and connective tissue on the outside. Serous

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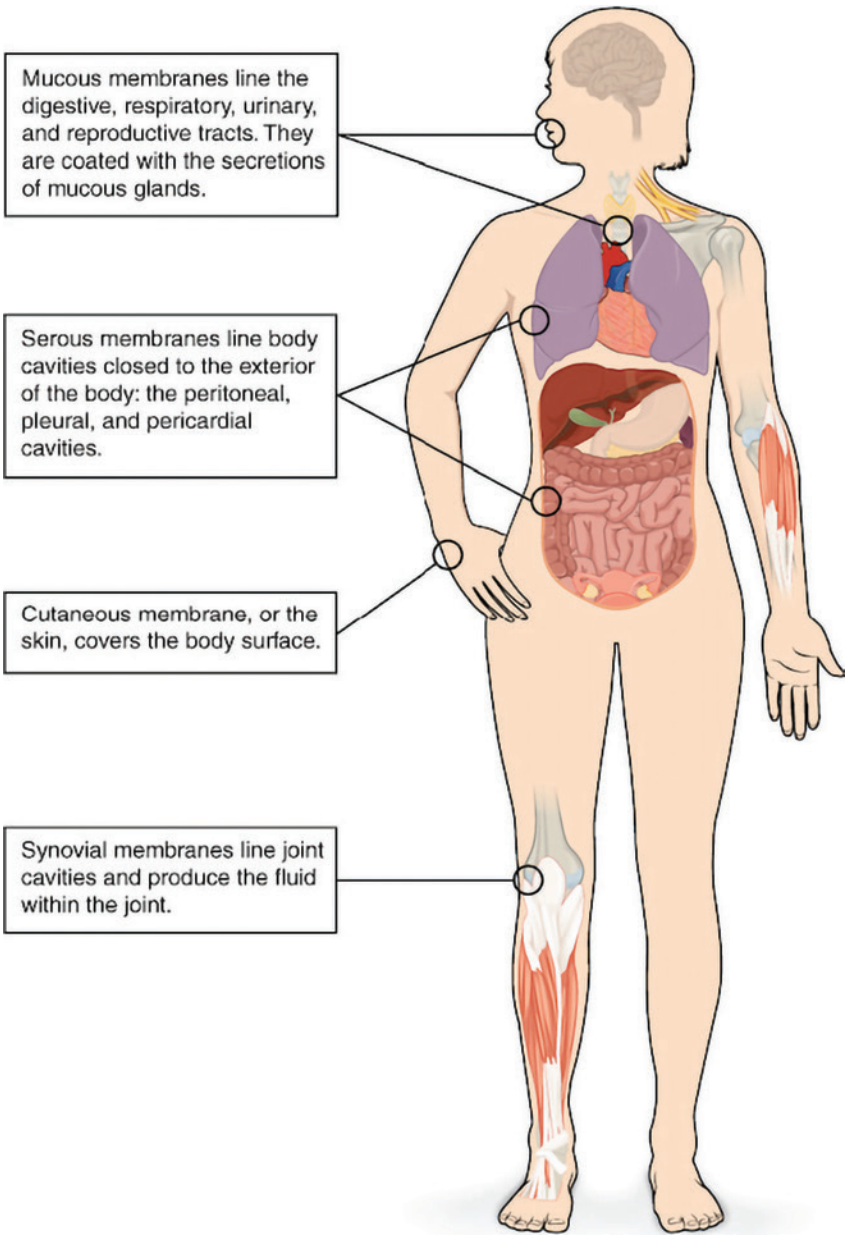


Figure 4.2 Tissue Membranes. The two broad categories of tissue membranes in the body are (1) connective tissue membranes, which include synovial membranes, and (2) epithelial membranes, which include mucous membranes, serous membranes, and the cutaneous membrane, in other words, the skin.

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fluid secreted by the cells of the thin squamous mesothelium lubricates the membrane and reduces abrasion and friction between organs. Serous membranes are identified according to location. Three serous membranes line the thoracic cavity: the two pleura that cover the lungs and the pericardium that covers the heart. A fourth, the peritoneum, is the serous membrane in the abdominal cavity that covers abdominal organs and forms double sheets of mesenteries that suspend many of the digestive organs.

The skin is an epithelial membrane also called the **cutaneous membrane**. It is a stratified squamous epithelial membrane resting on top of connective tissue. The apical surface of this membrane is exposed to the external environment and is covered with dead, keratinized cells that help protect the body from desiccation and pathogens.

4.2 Epithelial Tissue

Learning Objectives

By the end of this section, you will be able to:

- Explain the structure and function of epithelial tissue
- Distinguish between tight junctions, anchoring junctions, and gap junctions
- Distinguish between simple epithelia and stratified epithelia as well as between squamous, cuboidal, and columnar epithelia
- Describe the structure and function of endocrine and exocrine glands and their respective secretions

Most **epithelial tissues** are essentially large sheets of tightly packed cells covering all the surfaces of the body exposed to the outside world and lining the outsides of organs. Epithelium also forms much of the glandular tissue of the body. Skin is not the only area of the body exposed to the outside. Other areas include the airways, the digestive tract, and the urinary and reproductive systems, all of which are lined by an epithelium. Hollow organs and body cavities that do not connect to the exterior of the body, which include blood vessels and serous membranes, are lined by **endothelium** (plural = endothelia), which is a type of epithelium.

Epithelial cells derive from all three major embryonic layers. The epithelia lining the skin, parts of the mouth and nose, and the anus develop from the ectoderm. Cells lining the airways and most of the digestive system originate in the endoderm. The epithelium that lines vessels in the lymphatic and cardiovascular system derives from the mesoderm and is called an endothelium.

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All epithelia share some important structural and functional features. This tissue is highly cellular, with little or no extracellular material present between cells. Adjoining cells form a specialized intercellular connection between their cell membranes called a **cell junction**. The epithelial cells exhibit polarity with differences in structure and function between the exposed or apical-facing surface of the cell and the basal surface close to the underlying body structures. The **basal lamina**, a mixture of glycoproteins and collagen, provides an attachment site for epithelium, separating it from the underlying connective tissue. The basal lamina attaches to a **reticular lamina**, which is secreted by the underlying connective tissue, forming a **basement membrane** that helps hold it all together.

Epithelial tissues are nearly completely avascular—no blood vessels cross the basement membrane to enter the tissue, and nutrients must come by diffusion or absorption from underlying tissues or the surface. Many epithelial tissues are capable of rapidly replacing damaged and dead cells. Sloughing off damaged or dead cells is a characteristic of surface epithelium and allows our airways and digestive tracts to rapidly replace damaged cells with new cells.

Generalized Functions of Epithelial Tissue

Epithelial tissues provide the body's first line of protection from physical, chemical, and biological wear and tear. The cells of an epithelium act as gatekeepers of the body by controlling permeability and allowing selective transfer of materials across a physical barrier. All substances that enter the body must cross an epithelium. Some epithelia often include structural features that allow the selective transport of molecules and ions across their cell membranes. Many epithelial cells are capable of secretion and release mucous and specific chemical compounds onto their apical surfaces.

Examples: The epithelium of the small intestine releases digestive enzymes. Cells lining the respiratory tract secrete mucous that traps incoming microorganisms and particles. Glandular epithelium contains many secretory cells.

The Epithelial Cell

Epithelial cells are typically characterized by the polarized distribution of organelles and membrane-bound proteins between their basal and apical surfaces. Particular structures found in some epithelial cells are adaptations to specific functions. Certain organelles are segregated to the basal sides, whereas other organelles and extensions, such as cilia, when present, are on the apical surface.

Cilia are microscopic extensions of the apical cell membrane that are supported by microtubules. They beat in unison and move fluids as well as trapped particles across their surface. Ciliated epithelium lines the ventricles of the

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brain, where it helps circulate the cerebrospinal fluid. The ciliated epithelium of your airway forms a mucociliary escalator that sweeps particles of dust and pathogens trapped in the secreted mucous toward the throat. It is called an escalator because it continuously pushes mucous with trapped particles upward. In contrast, nasal cilia sweep mucous down toward your throat. In both cases, the transported materials are usually swallowed and end up in the acidic environment of your stomach.

Cell-to-Cell Junctions

Cells of epithelia are closely connected and are not separated by intracellular material. Three basic types of connections allow varying degrees of interaction between the cells: tight junctions, anchoring junctions, and gap junctions (Figure 4.3).

Tight junctions occur when there is no extracellular space between two adjacent epithelial cells and the movement of some substances between cells is blocked. Hydrophilic ions and molecules cannot cross through this barrier. Note that hydrophobic molecules freely move through the cells themselves and are therefore not blocked by tight junctions. This enables the epithelia to act as selective barriers. An **anchoring junction** includes several types of cell junctions that help stabilize epithelial tissues. Anchoring junctions are common on the lateral and basal surfaces of cells, where they provide strong and flexible connections. There are three types of anchoring junctions: desmosomes, hemidesmosomes, and adherens. **Desmosomes** occur in patches on the membranes of cells. The patches are structural proteins on the inner surface of the cell's membrane. The adhesion molecule is embedded in these patches and projects through the cell membrane to link with the same molecules of adjacent cells. These connections are especially important in holding cells together. **Hemidesmosomes**, which look like half a desmosome, link cells to the extracellular matrix (for example, the basal lamina). While similar in appearance to desmosomes, they include different types of adhesion proteins. **Adherens junctions** use adhesion proteins found in either desmosomes or hemidesmosomes, depending on whether they are linking to other cells or the matrix.

The junctions are characterized by the presence of the contractile protein actin, located on the cytoplasmic surface of the cell membrane. The actin can connect isolated patches or form a beltlike structure inside the cell. These junctions influence the shape and folding of the epithelial tissue.

In contrast with the tight and anchoring junctions, a **gap junction** forms an intercellular passageway between the membranes of adjacent cells to facilitate

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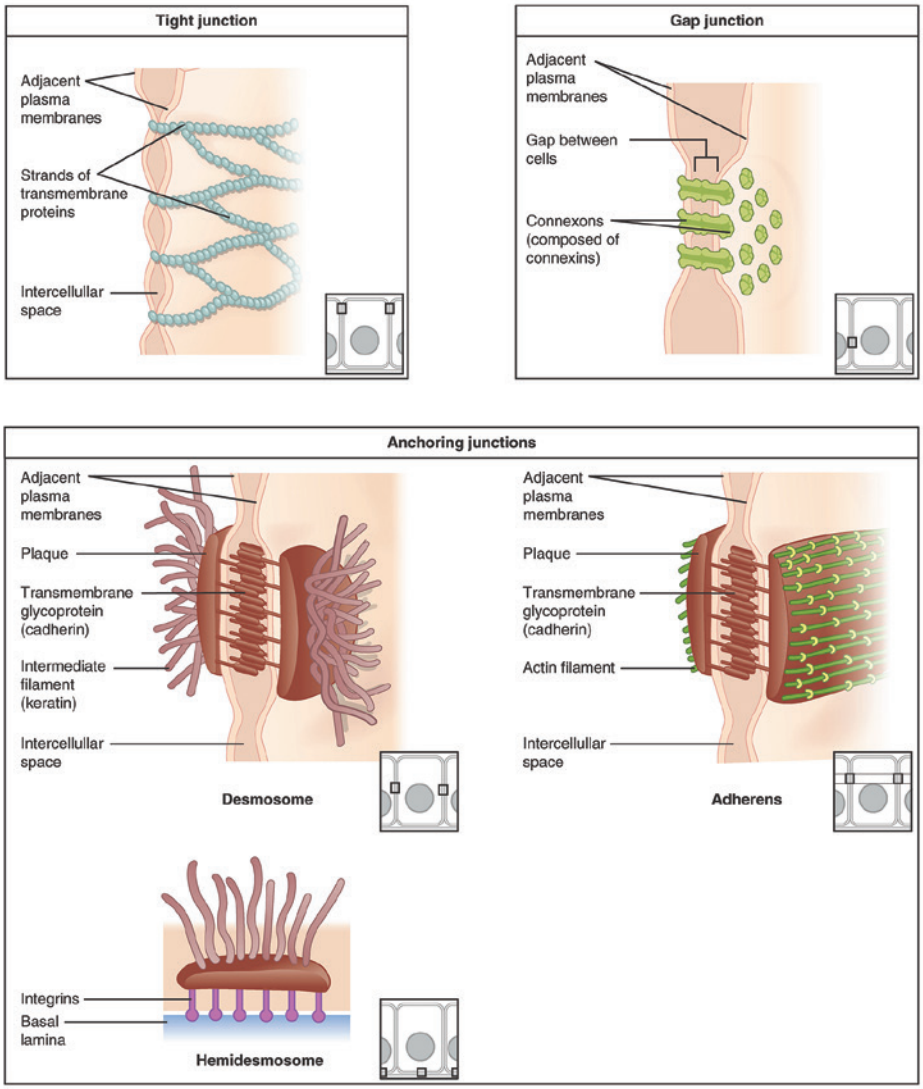


Figure 4.3 Types of Cell Junctions. The three basic types of cell-to-cell junctions are tight junctions, gap junctions, and anchoring junctions.

the movement of small molecules and ions between the cytoplasm of adjacent cells. These junctions allow electrical and metabolic coupling of adjacent cells, which coordinates function in large groups of cells.

Classification of Epithelial Tissues

Epithelial tissues are classified according to the shape of the cells and the number of cell layers formed (Figure 4.4). Cell shapes can be squamous (flattened and thin), cuboidal (boxy, as wide as it is tall), or columnar (rectangular, taller

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than it is wide). Similarly, the number of cell layers in the tissue can be one, which is a simple epithelium (where every cell rests on the basal lamina), or more than one, which is a stratified epithelium (only the basal layer of cells rests on the basal lamina). *Pseudostratified* describes tissue with a single layer of irregularly shaped cells that gives the appearance of more than one layer. *Transitional* describes a form of specialized stratified epithelium in which the shape of the cells can vary.

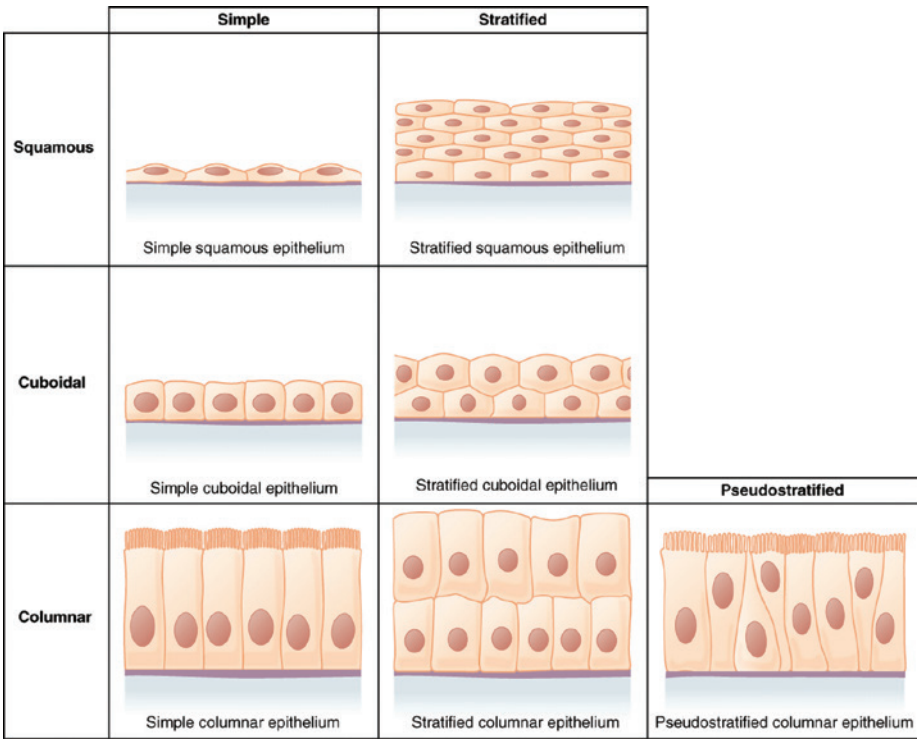


Figure 4.4 Cells of Epithelial Tissue. Simple epithelial tissue is organized as a single layer of cells, and stratified epithelial tissue is formed by several layers of cells.

Simple Epithelium

The shape of the cells in the single cell layer of simple epithelium reflects the functioning of those cells. The cells in **simple squamous epithelium** have the appearance of thin scales. Squamous cell nuclei tend to be flat, horizontal, and elliptical, mirroring the form of the cell. Endothelium is the epithelial tissue that lines vessels of the lymphatic and cardiovascular system, and it is made up of a single layer of squamous cells. Simple squamous epithelium, because of the thinness of the cell, is present where the rapid passage of chemical compounds is observed.

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Example: The alveoli of the lungs, where gases diffuse; the segments of kidney tubules; and the linings of capillaries are also made of simple squamous epithelial tissue.

The **mesothelium** is a simple squamous epithelium that forms the surface layer of the serous membrane that lines body cavities and internal organs. Its primary function is to provide a smooth and protective surface. Mesothelial cells are squamous epithelial cells that secrete a fluid that lubricates the mesothelium.

In **simple cuboidal epithelium**, the nucleus of the boxlike cells appears round and is generally located near the centre of the cell. These epithelia are active in the secretion and absorption of molecules.

Example: Simple cuboidal epithelia are observed in the lining of the kidney tubules and in the ducts of glands.

In **simple columnar epithelium**, the nucleus of the tall columnlike cells tends to be elongated and located at the basal end of the cells. Like cuboidal epithelia, this epithelium is active in the absorption and secretion of molecules.

Example: Simple columnar epithelium forms the lining of some sections of the digestive system and parts of the female reproductive tract.

Ciliated columnar epithelium is composed of simple columnar epithelial cells with cilia on their apical surfaces. These epithelial cells are found in the lining of the fallopian tubes and parts of the respiratory system, where the beating of the cilia helps remove particulate matter.

Pseudostratified columnar epithelium is a type of epithelium that appears to be stratified but instead consists of a single layer of irregularly shaped and differently sized columnar cells. In pseudostratified epithelium, nuclei of neighbouring cells appear at different levels rather than clustered in the basal end. The arrangement gives the appearance of stratification, but in fact, all the cells are in contact with the basal lamina, although some do not reach the apical surface.

Example: Pseudostratified columnar epithelium is found in the respiratory tract, where some of these cells have cilia.

Both simple and pseudostratified columnar epithelia are heterogeneous epithelia because they include additional types of cells interspersed among the epithelial cells. A **goblet cell** is a mucous-secreting unicellular "gland" interspersed between the columnar epithelial cells of mucous membranes (Figure 4.5).

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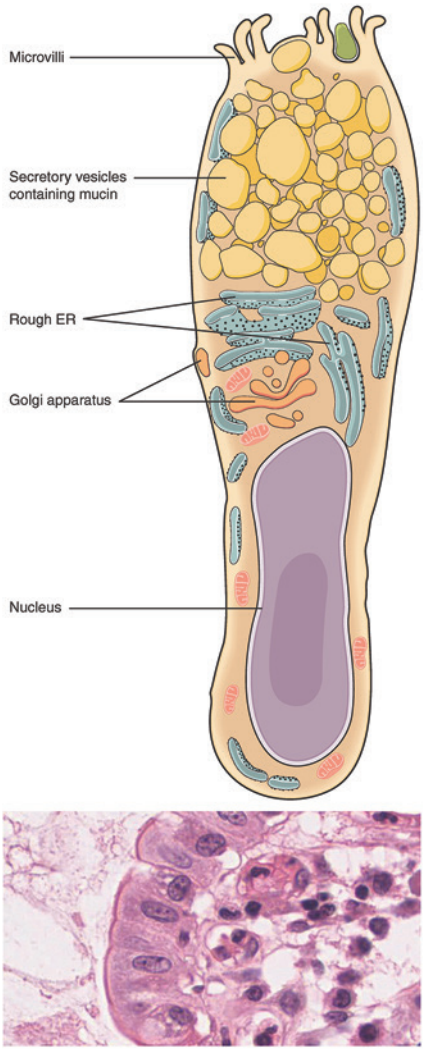


Figure 4.5 Goblet Cell. (a) In the lining of the small intestine, columnar epithelium cells are interspersed with goblet cells.

Interactive Link 4.2

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/4.2) to explore the tissue sample in greater detail.

Stratified Epithelium

A stratified epithelium consists of several stacked layers of cells. This epithelium protects against physical and chemical wear and tear. The stratified epithelium is named by the shape of the most apical layer of cells, closest to

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the free space. **Stratified squamous epithelium** is the most common type of stratified epithelium in the human body. The apical cells are squamous, whereas the basal layer contains either columnar or cuboidal cells. The top layer may be covered with dead cells filled with keratin. Mammalian skin is an example of this dry, keratinized stratified squamous epithelium. The lining of the mouth cavity is an example of an unkeratinized stratified squamous epithelium. **Stratified cuboidal epithelium** and **stratified columnar epithelium** can also be found in certain glands and ducts but are uncommon in the human body.

Another kind of stratified epithelium is **transitional epithelium**, so called because of the gradual changes in the shapes of the apical cells as the bladder fills with urine. It is found only in the urinary system, specifically the ureters and urinary bladder. When the bladder is empty, this epithelium is convoluted and has cuboidal apical cells with convex, umbrella-shaped apical surfaces. As the bladder fills with urine, this epithelium loses its convolutions, and the apical cells transition from cuboidal to squamous. It appears thicker and more multilayered when the bladder is empty but more stretched out and less stratified when the bladder is full and distended.

Figure 4.6 summarizes the different categories of epithelial cell tissue cells.

Interactive Link 4.3

Watch this video (http://oer.aupress.ca/oer-202505/4.3) to find out more about the anatomy of epithelial tissues. Where in the body would one find nonkeratinizing stratified squamous epithelium?

Glandular Epithelium

A **gland** is a structure made up of one or more cells modified to synthesize and secrete chemical substances. Most glands consist of groups of epithelial cells. A gland can be classified as an **endocrine gland**, a ductless gland that releases secretions directly into surrounding interstitial fluid and blood, or an **exocrine gland**, whose secretions leave through a duct that opens directly, or indirectly, to the external environment. These secretions move into the lumens of hollow organs or onto epithelial surfaces.

Endocrine Glands

The secretions of endocrine glands are called hormones. Hormones are released into the interstitial fluid, diffused into the bloodstream, and delivered to targets—in other words, cells that have receptors to bind the hormones.

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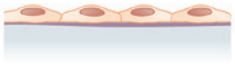
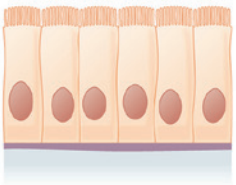
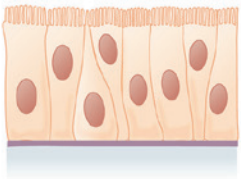
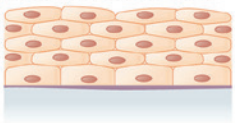
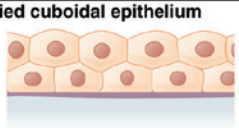
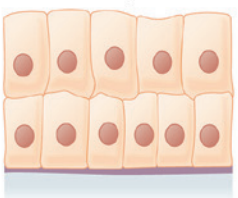
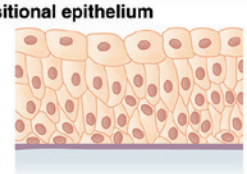
Cells	Location	Function
Simple squamous epithelium 	Air sacs of lungs and the lining of the heart, blood vessels, and lymphatic vessels	Allows materials to pass through by diffusion and filtration, and secretes lubricating substance
Simple cuboidal epithelium 	In ducts and secretory portions of small glands and in kidney tubules	Secretes and absorbs
Simple columnar epithelium 	Ciliated tissues are in larger bronchioles, uterine tubes, and uterus; smooth (nonciliated tissues) are in the digestive tract, bladder	Absorbs; it also secretes mucus and enzymes
Pseudostratified columnar epithelium 	Ciliated tissue lines the bronchi, trachea, and much of the upper respiratory tract	Secretes mucus; ciliated tissue moves mucus
Stratified squamous epithelium 	Lines the esophagus, mouth, and vagina	Protects against abrasion
Stratified cuboidal epithelium 	Sweat glands, salivary glands, and the mammary glands	Protective tissue
Stratified columnar epithelium 	The male and female urethrae and the ducts of some glands	Secretes and protects
Transitional epithelium 	Lines the bladder, urethra, and the ureters	Allows the urinary organs to expand and stretch

Figure 4.6 Summary of Epithelial Tissue Cells.

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The endocrine system is part of a major regulatory system coordinating the regulation and integration of body responses.

Example: The anterior pituitary, thymus, adrenal cortex, and gonads are all endocrine glands.

Exocrine Glands

Exocrine glands release their contents through a duct into the lumen of hollow organs or onto epithelial surfaces.

Example: Mucous, sweat, saliva, and breast milk are all examples of secretions from exocrine glands. They are all discharged through tubular ducts. Secretions into the lumen of the gastrointestinal tract, technically outside of the body, are of the exocrine category.

Glandular Structure

Exocrine glands are classified as either unicellular or multicellular. The unicellular glands are scattered single cells, such as goblet cells, found in the mucous membranes of the small and large intestine. The multicellular exocrine glands known as serous glands develop from simple epithelium to form a secretory surface that secretes directly into an inner cavity.

These glands line the internal cavities of the abdomen and chest and release their secretions directly into the cavities. Other multicellular exocrine glands release their contents through a tubular duct. The duct is single in a simple gland but in compound glands is divided into one or more branches. In tubular glands, the ducts can be straight or coiled, whereas tubes that form pockets are alveolar (acinar), such as the exocrine portion of the pancreas. Combinations of tubes and pockets are known as tubuloalveolar (tubuloacinar) compound glands. In a branched gland, a duct is connected to more than one secretory group of cells.

Methods and Types of Secretion

Exocrine glands can be classified by their mode of secretion and the nature of the substances released as well as by the structure of the glands and shape of the ducts (Figure 4.7). **Merocrine secretion** is the most common type of exocrine secretion. The secretions are enclosed in vesicles that move to the apical surface of the cell, where the contents are released by exocytosis.

Example: Watery mucous contains the glycoprotein mucin, a lubricant that offers some pathogen protection, and is a merocrine secretion. The eccrine glands that produce and secrete sweat are another example.

Apocrine secretion accumulates near the apical portion of the cell. That portion of the cell and its secretory contents pinch off from the cell and are

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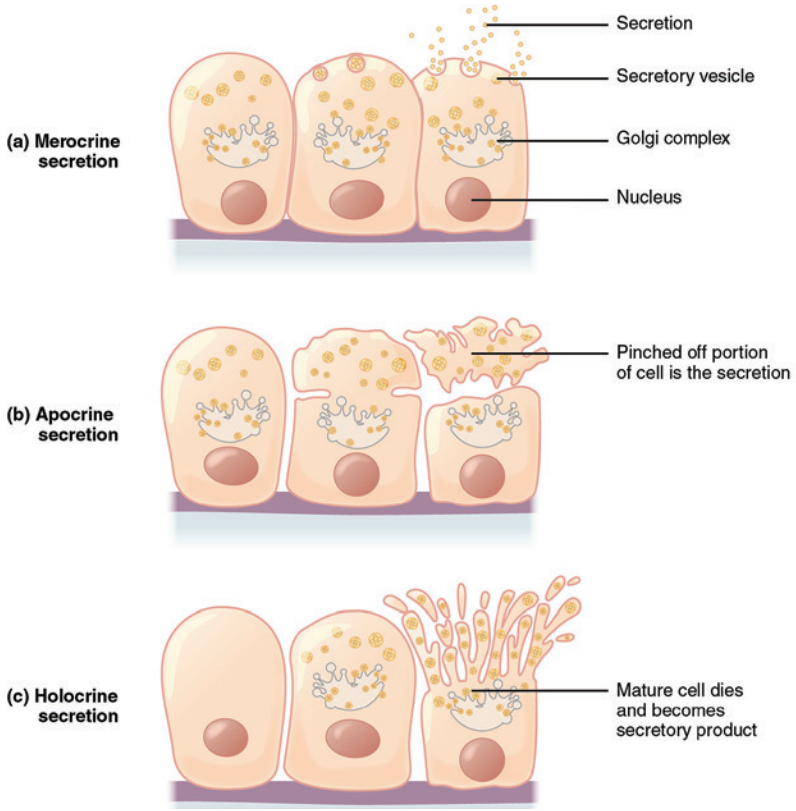


Figure 4.7 Modes of Glandular Secretion. (a) In merocrine secretion, the cell remains intact. (b) In apocrine secretion, the apical portion of the cell is released as well. (c) In holocrine secretion, the cell is destroyed as it releases its product, and the cell itself becomes part of the secretion.

released. Apocrine sweat glands in the axillary and genital areas release fatty secretions that local bacteria break down; this causes body odour. Both merocrine and apocrine glands continue to produce and secrete their contents with little damage caused to the cell because the nucleus and Golgi regions remain intact after secretion.

In contrast, the process of **holocrine secretion** involves the rupture and destruction of the entire gland cell. The cell accumulates its secretory products and releases them only when it bursts. New gland cells differentiate from cells in the surrounding tissue to replace those lost by secretion. The sebaceous glands that produce the oils on the skin and hair are holocrine glands/cells (Figure 4.8).

Glands are also named after the products they produce. The **serous gland** produces watery, blood plasma–like secretions rich in enzymes such as alpha amylase, whereas the **mucous gland** releases watery to viscous products rich

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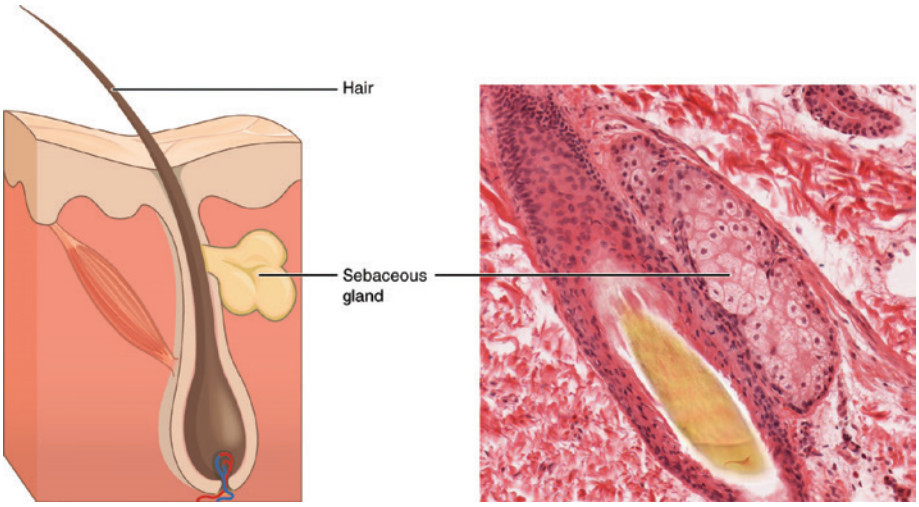


Figure 4.8 Sebaceous Glands. These glands secrete oils that lubricate and protect the skin. They are holocrine glands and are destroyed after releasing their contents. New glandular cells form to replace the cells that are lost. LM × 400. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

in the glycoprotein mucin. Both serous and mucous glands are common in the salivary glands of the mouth.

Mixed exocrine glands contain both serous and mucous glands and release both types of secretions.

4.3 Connective Tissue Supports and Protects

Learning Objectives

By the end of this section, you will be able to:

- Identify and distinguish between the types of connective tissue: proper, supportive, and fluid
- Explain the functions of connective tissues

As may be obvious from its name, one of the major functions of connective tissue is to connect tissues and organs. Unlike epithelial tissue, which is composed of cells closely packed with little or no extracellular space in between, connective tissue cells are dispersed in a **matrix**. The matrix usually includes a large amount of extracellular material produced by the connective tissue cells that are embedded within it. The matrix plays a major role in the functioning of this tissue. The major component of the matrix is a **ground substance** often

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crisscrossed by protein fibres. This ground substance is usually a fluid, but it can also be mineralized and solid, as in bones.

Connective tissues come in a vast variety of forms, yet they typically have in common three characteristic components: cells, large amounts of amorphous ground substance, and protein fibres. The amount and structure of each component correlate with the function of the tissue, from the rigid ground substance in bones supporting the body to the inclusion of specialized cells—for example, a phagocytic cell that engulfs pathogens and also rids tissue of cellular debris.

Functions of Connective Tissues

Connective tissues perform many functions in the body, but most importantly, they support and connect other tissues, from the connective tissue sheath that surrounds muscle cells to the tendons that attach muscles to bones and to the skeleton that supports the positions of the body. Protection is another major function of connective tissue, in the form of fibrous capsules and bones that protect delicate organs and, of course, the skeletal system.

Specialized cells in connective tissue defend the body from microorganisms that enter the body. Transport of fluids, nutrients, waste, and chemical messengers is ensured by specialized fluid connective tissues, such as blood and lymph. Adipose cells store surplus energy in the form of fat and contribute to the thermal insulation of the body.

Classification of Connective Tissues

The three broad categories of connective tissue are classified according to the characteristics of their ground substance and the types of fibres found within the matrix (Table 4.1).

Connective tissue proper includes **loose connective tissue** and **dense connective tissue**. Both tissues have a variety of cell types and protein fibres suspended in a viscous ground substance. Dense connective tissue is reinforced by bundles of fibres that provide tensile strength, elasticity, and protection. In loose connective tissue, the fibres are loosely organized, leaving large spaces in between. **Supportive connective tissue**—bone and cartilage—provides structure and strength to the body and protects soft tissues. A few distinct cell types and densely packed fibres in a matrix characterize these tissues. In bone, the matrix is rigid and described as calcified because of the deposited calcium salts. In **fluid connective tissue**—in other words, lymph and blood—various specialized cells circulate in a watery fluid containing salts, nutrients, and dissolved proteins.

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Table 4.1 Connective Tissue Examples

Connective tissue proper	Supportive connective tissue	Fluid connective tissue
Loose connective tissue • Areolar • Adipose • Reticular Dense connective tissue • Dense regular • Elastic • Dense irregular	Cartilage • Hyaline • Fibrocartilage • Elastic bone	Blood Lymph

Connective Tissue Proper

Fibroblasts are present in all connective tissue proper (Figure 4.9). Fibrocytes, adipocytes, and mesenchymal cells are fixed cells, which means they remain within the connective tissue. Other cells move into and out of the connective tissue in response to chemical signals. Macrophages, mast cells, lymphocytes, plasma cells, and phagocytic cells are found in connective tissue proper but are actually part of the immune system, protecting the body.

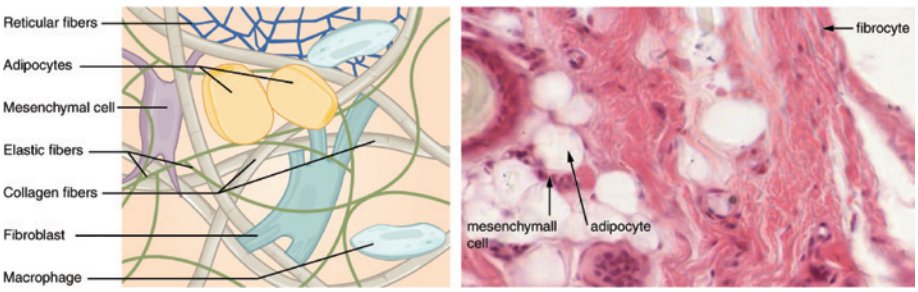


Figure 4.9 Connective Tissue Proper. Fibroblasts produce this fibrous tissue. Connective tissue proper includes the fixed cells fibrocytes, adipocytes, and mesenchymal cells. LM × 400. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Cell Types

The most abundant cell in connective tissue proper is the **fibroblast**. Polysaccharides and proteins secreted by fibroblasts combine with extracellular fluids to produce a viscous ground substance that, with embedded fibrous proteins, forms the extracellular matrix. As you might expect, a **fibrocyte**, a less active form of a fibroblast, is the second-most common cell type in connective tissue proper.

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Adipocytes are cells that store lipids as droplets that fill most of the cytoplasm. There are two basic types of adipocytes: white and brown. The brown adipocytes store lipids as many droplets and have high metabolic activity. In contrast, white fat adipocytes store lipids as a single large drop and are metabolically less active. Their effectiveness at storing large amounts of fat is witnessed in obese individuals. The number and type of adipocytes depend on the tissue and location and vary among individuals in the population.

The **mesenchymal cell** is a multipotent adult stem cell. These cells can differentiate into any type of connective tissue cell needed for the repair and healing of damaged tissue.

Connective Tissue Fibres and Ground Substance

Three main types of fibres are secreted by fibroblasts: collagen fibres, elastic fibres, and reticular fibres. **Collagen fibre** is made from fibrous protein subunits linked together to form a long and straight fibre. Collagen fibres, while flexible, have great tensile strength, resist stretching, and give ligaments and tendons their characteristic resilience and strength. These fibres hold connective tissues together, even during the movement of the body.

Elastic fibre contains the protein elastin along with lesser amounts of other proteins and glycoproteins. The main property of elastin is that after being stretched or compressed, it will return to its original shape. Elastic fibres are prominent in elastic tissues found in skin and the elastic ligaments of the vertebral column.

Reticular fibre is also formed from the same protein subunits as collagen fibres; however, these fibres remain narrow and are arrayed in a branching network. They are found throughout the body but are most abundant in the reticular tissue of soft organs, such as the liver and spleen, where they anchor and provide structural support to the **parenchyma** (the functional cells, blood vessels, and nerves of the organ).

All these fibre types are embedded in ground substance. Secreted by fibroblasts, ground substance is made of polysaccharides, specifically hyaluronic acid, and proteins. These combine to form a proteoglycan with a protein core and polysaccharide branches. The proteoglycan attracts and traps available moisture, forming the clear, viscous, colourless matrix known as ground substance.

Loose Connective Tissue

Loose connective tissue is found between many organs, where it acts to both absorb shock and bind tissues together. It allows water, salts, and various nutrients to diffuse through to adjacent or embedded cells and tissues.

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Adipose tissue consists mostly of fat storage cells, with little extracellular matrix (Figure 4.10). A large number of capillaries allows rapid storage and mobilization of lipid molecules. White adipose tissue is most abundant. It can appear yellow and owes its colour to carotene and related pigments from plant food. White fat contributes mostly to lipid storage and can serve as insulation from cold temperatures and mechanical injuries. White adipose tissue can be found protecting the kidneys and cushioning the back of the eye. Brown adipose tissue is more common in infants, hence the term *baby fat*. In adults, there is a reduced amount of brown fat, and it is found mainly in the neck and clavicular regions of the body. Brown adipose tissue is thermogenic, meaning that as it breaks down fats, it releases metabolic heat rather than producing adenosine triphosphate (ATP), a key molecule used in metabolism.

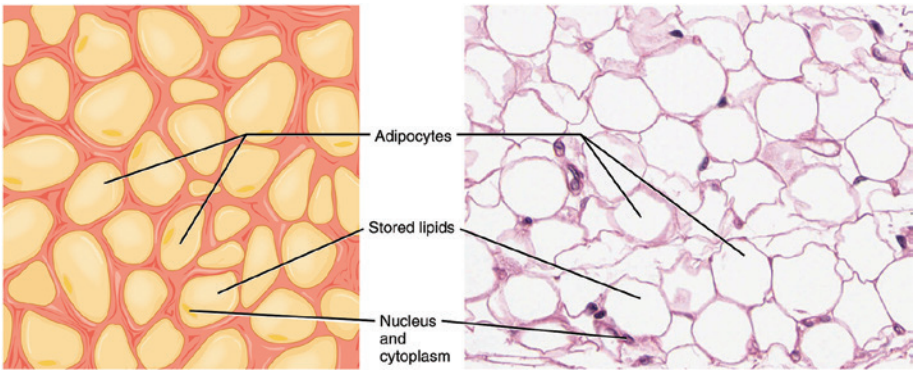


Figure 4.10 Adipose Tissue. This is a loose connective tissue that consists of fat cells with a little extracellular matrix. It stores fat for energy and provides insulation. LM × 800. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Areolar tissue shows little specialization. It contains all the cell types and fibres previously described and is distributed in a random, weblike fashion. It fills the spaces between muscle fibres, surrounds blood and lymph vessels, and supports organs in the abdominal cavity. Areolar tissue underlies most epithelia and represents the connective tissue component of epithelial membranes, which are described further in a later section.

Reticular tissue is a meshlike, supportive framework for soft organs such as lymphatic tissue, the spleen, and the liver (Figure 4.11). Reticular cells produce the reticular fibres that form the network onto which other cells attach. It derives its name from the Latin *reticulus*, which means "little net."

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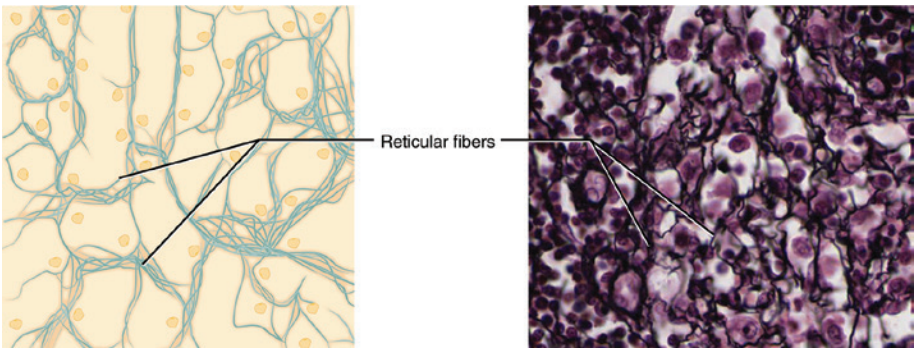


Figure 4.11 Reticular Tissue. This is a loose connective tissue made up of a network of reticular fibres that provides a supportive framework for soft organs. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Dense Connective Tissue

Dense connective tissue contains more collagen fibres than does loose connective tissue. As a consequence, it displays greater resistance to stretching. There are two major categories of dense connective tissue: regular and irregular. Dense regular connective tissue fibres are parallel to each other, enhancing tensile strength and resistance to stretching in the direction of the fibre orientations. Ligaments and tendons are made of dense regular connective tissue, but in ligaments, not all fibres are parallel. Dense regular elastic tissue contains elastin fibres in addition to collagen fibres, which allows the ligament to return to its original length after stretching. The ligaments in the vocal folds and between the vertebrae in the vertebral column are elastic.

In dense irregular connective tissue, the direction of fibres is random. This arrangement gives the tissue greater strength in all directions and less strength in one particular direction. In some tissues, fibres crisscross and form a mesh. In other tissues, stretching in several directions is achieved by alternating layers where fibres run in the same orientation in each layer, and it is the layers themselves that are stacked at an angle. The dermis of the skin is an example of dense irregular connective tissue rich in collagen fibres. Dense irregular elastic tissues give arterial walls the strength and the ability to regain their original shape after stretching (Figure 4.12).

Interactive Link 4.4

Watch this animation (http://oer.aupress.ca/oer-202505/4.4) to learn more about tendonitis, a painful condition caused by swollen or injured tendons.

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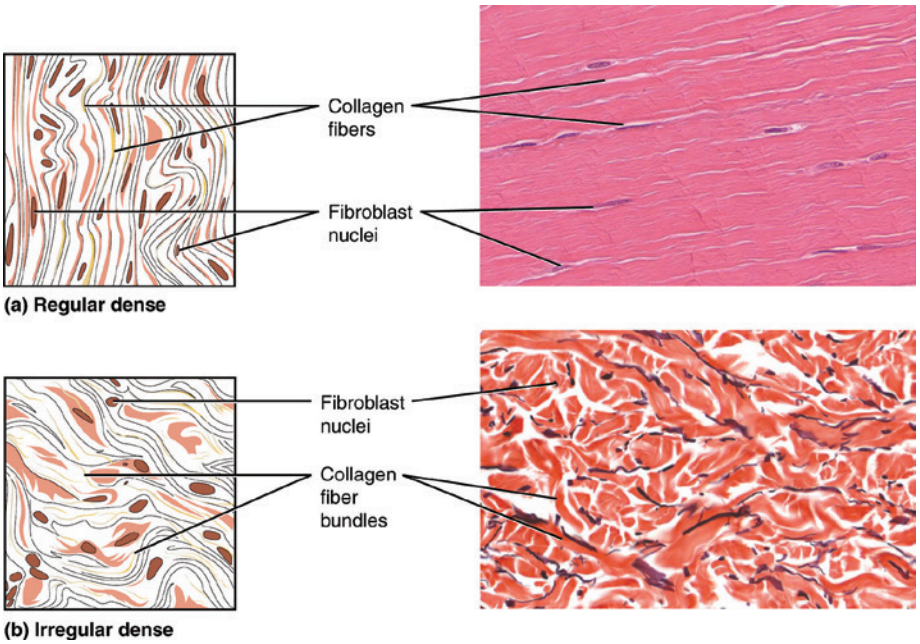


Figure 4.12 Dense Connective Tissue. (a) Dense regular connective tissue consists of collagenous fibres packed into parallel bundles. (b) Dense irregular connective tissue consists of collagenous fibres interwoven into a meshlike network. From top, LM × 1000, LM × 200. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)

Supportive Connective Tissues

Two major forms of supportive connective tissue, cartilage and bone, allow the body to maintain its posture and protect internal organs.

Cartilage

The distinctive appearance of cartilage is due to polysaccharides called chondroitin sulfates, which bind with ground substance proteins to form proteoglycans. Embedded within the cartilage matrix are **chondrocytes**, or cartilage cells, and the spaces they occupy are called **lacunae** (singular = lacuna). A layer of dense irregular connective tissue, the perichondrium, encapsulates the cartilage. Cartilaginous tissue is avascular; thus all nutrients need to diffuse through the matrix to reach the chondrocytes. This is a factor contributing to the very slow healing of cartilaginous tissues.

The three main types of cartilage tissue are hyaline cartilage, fibrocartilage, and elastic cartilage (Figure 4.13). **Hyaline cartilage**, the most common type of cartilage in the body, consists of short and dispersed collagen fibres and contains large amounts of proteoglycans. Under a microscope, tissue samples appear clear. The surface of hyaline cartilage is smooth. Both strong and flexible, it is found in the rib cage and nose and covers bones where they meet to

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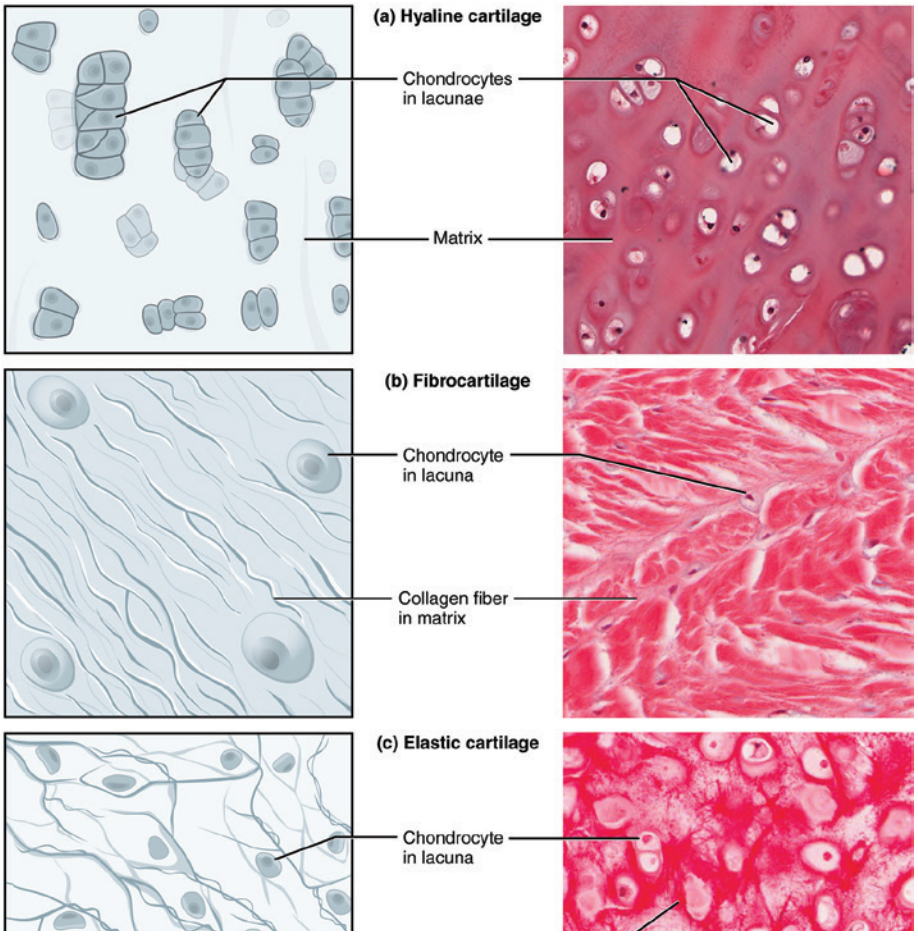


Figure 4.13 Types of Cartilage. Cartilage is a connective tissue consisting of collagenous fibres embedded in a firm matrix of chondroitin sulfates. (a) Hyaline cartilage provides support with some flexibility. The example is from dog tissue. (b) Fibrocartilage provides some compressibility and can absorb pressure. (c) Elastic cartilage provides firm but elastic support. From top, LM × 300, LM × 1200, LM × 1016. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)

form movable joints. It makes up a template of the embryonic skeleton before bone formation. Plates of hyaline cartilage at the ends of bones allow continued growth until adulthood. **Fibrocartilage** is tough because it has thick bundles of collagen fibres dispersed through its matrix. Menisci in the knee joint and the intervertebral discs are examples of fibrocartilage. **Elastic cartilage** contains elastic fibres as well as collagen and proteoglycans. This tissue gives rigid support as well as elasticity. Tug gently at your ear lobes, and notice that the lobes return to their initial shape. The external ear contains elastic cartilage.

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Bone

Bone is the hardest connective tissue. It provides protection to internal organs, works with the skeletal muscle to produce movement, and allows us to remain upright. Bone's rigid extracellular matrix contains mostly collagen fibres embedded in a mineralized ground substance containing hydroxyapatite, a form of calcium phosphate. Both components of the matrix, organic and inorganic, contribute to the unusual properties of bone. Without collagen, bones would be brittle and shatter easily. Without mineral crystals, bones would flex and provide little support. **Osteocytes**, bone cells like chondrocytes, are located within lacunae. The histology of transverse tissue from a long bone shows a typical arrangement of osteocytes in concentric circles around a central canal. Bone is a highly vascularized tissue. Unlike cartilage, bone tissue can recover from injuries in a relatively short time. (See Figure 6.12.)

Cancellous bone looks like a sponge under the microscope and contains empty spaces between trabeculae, or arches of bone proper. It is lighter than compact bone and found in the interior of some bones and at the ends of long bones. Compact bone is solid and has greater structural strength.

Fluid Connective Tissue

Blood and lymph are fluid connective tissues. Cells circulate in a liquid extracellular matrix. The formed elements circulating in blood are all derived from hematopoietic stem cells located in bone marrow (Figure 4.14). Erythrocytes, red blood cells, transport oxygen and some carbon dioxide. Leukocytes, white

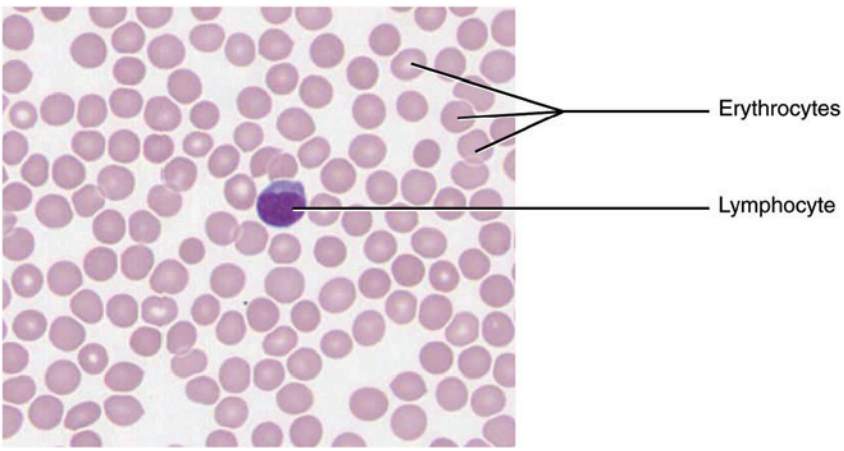


Figure 4.14 Blood: A Fluid Connective Tissue. Blood is a fluid connective tissue containing erythrocytes and various types of leukocytes that circulate in a liquid extracellular matrix. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

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blood cells, are responsible for defending against potentially harmful microorganisms or molecules. Platelets are cell fragments involved in blood clotting. Some white blood cells have the ability to cross the endothelial layer that lines blood vessels and enter adjacent tissues. Nutrients, salts, and wastes are dissolved in the liquid matrix and transported through the body.

Lymph contains a liquid matrix and white blood cells. Lymphatic capillaries are extremely permeable, allowing larger molecules and excess fluid from interstitial spaces to enter the lymphatic vessels. Lymph drains into blood vessels, delivering molecules to the blood that could not otherwise directly enter the bloodstream. In this way, specialized lymphatic capillaries transport absorbed fats away from the intestine and deliver these molecules to the blood.

Interactive Link 4.5

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/4.5) to explore the tissue sample in greater detail.

4.4 Muscle Tissue and Motion

Learning Objectives

By the end of this section, you will be able to:

- Identify the three types of muscle tissue
- Compare and contrast the functions of each muscle tissue type
- Explain how muscle tissue can enable motion

Muscle tissue is characterized by properties that allow movement. Muscle cells are excitable; they respond to stimuli. They are contractile, meaning they can shorten and generate a pulling force. When attached between two movable objects—in other words, bones—muscle contractions cause the bones to move. Some muscle movement is voluntary, which means it is under conscious control. For example, a person decides to open a book and read a chapter on anatomy. Other movements are involuntary, meaning they are not under conscious control, such as the contraction of your pupil in bright light. Muscle tissue is classified into three types according to structure and function: skeletal, cardiac, and smooth (Table 4.2).

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Table 4.2 Comparison of Structure and Properties of Muscle Tissue Types

Tissue	Histology	Function	Location
Skeletal	Long cylindrical fibre, striated, many peripherally located nuclei	Voluntary movement, produces heat, protects organs	Attached to bones and around entrance points to the body (e.g., mouth, anus)
Cardiac	Short, branched, striated, single central nucleus	Contracts to pump blood	Heart
Smooth	Short, spindle-shaped, no evident striation, single nucleus in each fibre	Involuntary movement, moves food, involuntary control of respiration, moves secretions, regulates flow of blood in arteries by contraction	Walls of major organs and passageways

Skeletal muscle is attached to bones, and its contraction makes possible locomotion, facial expressions, posture, and other voluntary movements of the body. Forty percent of your body mass is made up of skeletal muscle.

Skeletal muscles generate heat as a by-product of their contraction and thus participate in thermal homeostasis, and these functions are the result of a large number of mitochondria in each muscle cell. Shivering is an involuntary contraction of skeletal muscles in response to perceived lower-than-normal body temperature. The muscle cells, or **myocytes**, remain relatively constant in number throughout life. Skeletal muscle tissue is arranged in bundles surrounded by connective tissue. Under a light microscope, muscle cells appear striated with many nuclei squeezed along the membranes. The **striation** is due to the regular alternation of the contractile proteins actin and myosin, along with the structural proteins that couple the contractile proteins to connective tissues. The cells are multinucleated as a result of the fusion of the many myoblasts that form each long muscle fibre.

Cardiac muscle forms the contractile walls of the heart. The cells of cardiac muscle, known as cardiomyocytes, also appear striated under a microscope. Unlike skeletal muscle fibres, cardiomyocytes are single cells, typically with a single centrally located nucleus. A principal characteristic of cardiomyocytes is that they contract on their own intrinsic rhythms without any external stimulation. Cardiomyocytes attach to one another with specialized cell junctions called intercalated discs. Intercalated discs have both anchoring

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junctions and gap junctions. Attached cells form long, branching cardiac muscle fibres that are, essentially, a mechanical and electrochemical syncytium, allowing the cells to contract all at once. The cardiac muscle pumps blood through the body and is under involuntary control. The attachment junctions hold adjacent cells together across the dynamic pressure changes of the cardiac cycle.

Smooth muscle tissue contraction is responsible for involuntary movements in the internal organs. It forms the contractile component of the digestive, urinary, and reproductive systems as well as the airways and arteries. Each cell is spindle-shaped with a single nucleus and no visible striations (Figure 4.15).

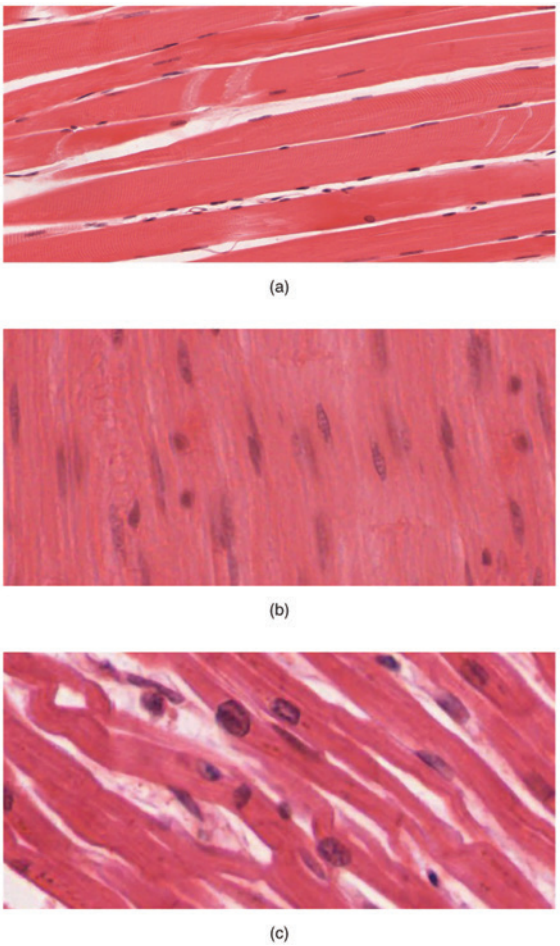


Figure 4.15 Muscle Tissue. (a) Skeletal muscle cells have prominent striation and nuclei on their periphery. (b) Smooth muscle cells have a single nucleus and no visible striations. (c) Cardiac muscle cells appear striated and have a single nucleus. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)

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Interactive Link 4.6

Watch this video (http://oer.aupress.ca/oer-202505/4.6) to learn more about muscle tissue. In looking through a microscope, how could you distinguish skeletal muscle from smooth muscle tissue?

4.5 Nervous Tissue Mediates Perception and Response

Learning Objectives

By the end of this section, you will be able to:

- Identify the classes of cells that make up nervous tissue
- Discuss how nervous tissue mediates perception and response

Nervous tissue is characterized as being excitable and capable of sending and receiving electrochemical signals that provide the body with information. Two main classes of cells make up nervous tissue: the **neuron** and **neuroglia** (Figure 4.16). Neurons propagate information via electrochemical impulses, called action potentials, which are biochemically linked to the release of chemical signals. Neuroglia play an essential role in supporting neurons and modulating their information propagation.

Interactive Link 4.7

Follow this link (http://oer.aupress.ca/oer-202505/4.7) to learn more about nervous tissue. What are the main parts of a nerve cell?

Neurons display distinctive morphology, well suited to their role as conducting cells, with three main parts. The cell body includes most of the cytoplasm, the organelles, and the nucleus. **Dendrites** branch off the cell body and appear as thin extensions. A long "tail," the **axon**, extends from the neuron body and can be wrapped in an insulating layer known as **myelin**, which is formed by accessory cells. The synapse is the gap between nerve cells or between a nerve cell and its target—for example, a muscle or a gland—across which the impulse is transmitted by chemical compounds known as neurotransmitters.

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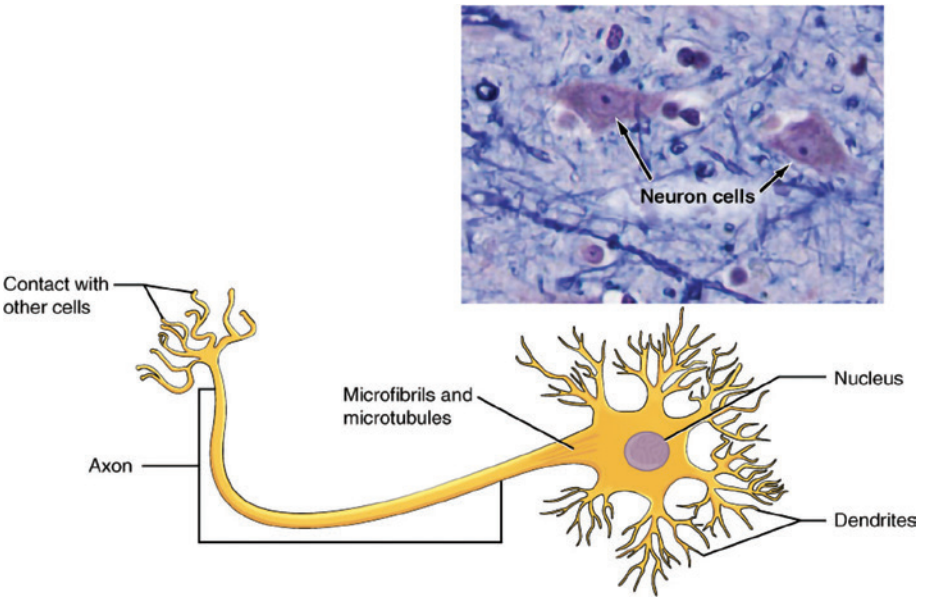


Figure 4.16 The Neuron. The cell body of a neuron, also called the soma, contains the nucleus and mitochondria. The dendrites transfer the nerve impulse to the soma. The axon carries the action potential away to another excitable cell. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

When a neuron is sufficiently stimulated, it generates an action potential that propagates down the axon toward the synapse. If enough neurotransmitters are released at the synapse to stimulate the next neuron or target, a response is generated.

The second class of neural cells comprises the **neuroglia** or **glial cells**, which have been characterized as having a simple support role. The word *glia* comes from the Greek word for glue. Recent research is shedding light on the more complex role of neuroglia in the function of the brain and nervous system. **Astrocyte** cells, named for their distinctive star shape, are abundant in the central nervous system. The astrocytes have many functions, including regulation of ion concentration in the intercellular space, uptake and/or breakdown of some neurotransmitters, and formation of the blood-brain barrier, the membrane that separates the circulatory system from the brain. **Microglia** protect the nervous system against infection but are not nervous tissue because they are related to macrophages. **Oligodendrocyte** cells produce myelin in the central nervous system (brain and spinal cord), while the **Schwann cells** produce myelin in the peripheral nervous system (Figure 4.17).

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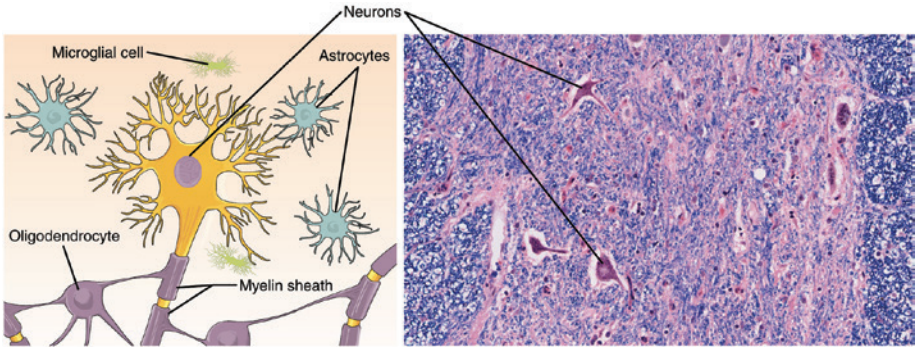


Figure 4.17 Nervous Tissue. Nervous tissue is made up of neurons and neuroglia. The cells of nervous tissue are specialized to transmit and receive impulses. LM × 872. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Key Terms

adherens junction: Type of cell junction; uses adhesion proteins found in either desmosomes or hemidesmosomes, depending on whether they are linking to other cells or the matrix.

adipocytes: Lipid storage cells.

adipose tissue: Specialized areolar tissue rich in stored fat.

anchoring junction: Mechanically attaches adjacent cells to each other or to the basement membrane.

apocrine secretion: Release of a substance along with the apical portion of the cell.

areolar tissue (also loose connective tissue): A type of connective tissue proper that shows little specialization with cells dispersed in the matrix.

astrocyte: Star-shaped cell in the central nervous system that regulates ions and uptake and/or breakdown of some neurotransmitters and contributes to the formation of the blood-brain barrier.

axon: A long "tail" that extends from the neuron body and can be wrapped in an insulating layer known as myelin.

basal lamina: Thin extracellular layer that lies underneath epithelial cells and separates them from other tissues.

basement membrane: In epithelial tissue, a thin layer of fibrous material that anchors the epithelial tissue to the underlying connective tissue; made up of the basal lamina and reticular lamina.

cardiac muscle: Heart muscle under involuntary control; composed of striated cells that attach to form fibres; each cell contains a single nucleus and contracts autonomously.

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cell junction: Point of cell-to-cell contact that connects one cell to another in a tissue.

chondrocytes: Cells of the cartilage.

ciliated columnar epithelium: Tissue composed of simple columnar epithelial cells with cilia on their apical surfaces.

collagen fibre: Flexible fibrous proteins that give connective tissue tensile strength.

connective tissue: Type of tissue that serves to hold in place, connect, and integrate the body's organs and systems.

connective tissue membrane: Connective tissue that encapsulates organs and lines movable joints.

connective tissue proper: Connective tissue containing a viscous matrix, fibres, and cells.

cutaneous membrane: Skin; epithelial tissue made up of a stratified squamous epithelial cells that cover the outside of the body.

dendrites: Branches off the neuron cell body and appear as thin extensions.

dense connective tissue: Connective tissue proper that contains many fibres that provide both elasticity and protection.

desmosomes: Type of cell junction that anchors cells together by linking adhesion molecules across their membranes.

ectoderm: Outermost embryonic germ layer from which the epidermis and the nervous tissue derive.

elastic cartilage: Type of cartilage, with elastin as the major protein, characterized by rigid support as well as elasticity.

elastic fibre: Fibrous protein within connective tissue that contains a high percentage of the protein elastin, which allows the fibres to stretch and return to their original size.

endocrine gland: Groups of cells that release chemical signals into the intercellular fluid to be picked up and transported to their target organs by blood.

endoderm: Innermost embryonic germ layer from which most of the digestive system and lower respiratory system derive.

endothelium: Tissue that lines vessels of the lymphatic and cardiovascular system, made up of a simple squamous epithelium.

epithelial membrane: Epithelium attached to a layer of connective tissue.

epithelial tissue: Type of tissue that serves primarily as a covering or lining of body parts, protecting the body; it also functions in absorption, transport, and secretion.

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exocrine gland: Group of epithelial cells that secrete substances through ducts that open to the skin or to internal body surfaces that lead to the exterior of the body.

fibroblast: Most abundant cell type in connective tissue, secretes protein fibres and matrix into the extracellular space.

fibrocartilage: Tough form of cartilage, made of thick bundles of collagen fibres embedded in chondroitin sulfate ground substance.

fibrocyte: Less active form of fibroblast.

fluid connective tissue: Specialized cells that circulate in a watery fluid containing salts, nutrients, and dissolved proteins.

gap junction: Allows cytoplasmic communication to occur between cells.

gland: Structure made up of one or more cells modified to synthesize and secrete chemical substances.

goblet cell: Unicellular gland found in columnar epithelium that secretes mucous.

ground substance: Fluid or semifluid portion of the matrix.

hemidesmosomes: Type of cell junction that links cells to the extracellular matrix.

holocrine secretion: Release of a substance caused by the rupture of a gland cell, which becomes part of the secretion.

hyaline cartilage: Most common type of cartilage, smooth and made of short collagen fibres embedded in a chondroitin sulfate ground substance.

lacunae (singular = lacuna): Small spaces in bone or cartilage tissue that cells occupy.

lamina propria: Areolar connective tissue underlying a mucous membrane.

loose connective tissue (also areolar tissue): Type of connective tissue proper that shows little specialization, with cells dispersed in the matrix.

matrix: Extracellular material that is produced by the cells embedded in it, containing ground substance and fibres.

merocrine secretion: Release of a substance from a gland via exocytosis.

mesenchymal cell: Adult stem cell from which most connective tissue cells are derived.

mesoderm: Middle embryonic germ layer from which connective tissue, muscle tissue, and some epithelial tissue derive.

mesothelium: Simple squamous epithelial tissue that covers the major body cavities and is the epithelial portion of serous membranes.

microglia: Glial cells that protect the nervous system against infection but are not nervous tissue because they are related to macrophages.

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mucous gland: Group of cells that secrete mucous, a thick, slippery substance that keeps tissues moist and acts as a lubricant.

mucous membrane (mucosa): Tissue membrane that is covered by protective mucous and lines tissue exposed to the outside environment.

muscle tissue: Type of tissue that is capable of contracting and generating tension in response to stimulation; produces movement.

myelin: Layer of lipid inside some neuroglial cells that wraps around the axons of some neurons.

myocyte: Muscle cells.

nervous tissue: Type of tissue that is capable of sending and receiving impulses through electrochemical signals.

neuroglia (glial cells): Supportive neural cells.

neuron: Excitable neural cell that transfers nerve impulses.

oligodendrocyte: Neuroglial cell that produces myelin in the brain.

osteocyte: Bone cell located within lacunae typically arranged in concentric circles around a central canal.

parenchyma: Functional cells of a gland or organ, in contrast with the supportive or connective tissue of a gland or organ.

pseudostratified columnar epithelium: Tissue that consists of a single layer of irregularly shaped and sized cells that give the appearance of multiple layers; found in ducts of certain glands and the upper respiratory tract.

reticular fibre: Fine fibrous protein, made of collagen subunits, which cross-link to form supporting "nets" within connective tissue.

reticular lamina: Matrix containing collagen and elastin secreted by connective tissue; a component of the basement membrane.

reticular tissue: Type of loose connective tissue that provides a supportive framework to soft organs, such as the lymphatic tissue, spleen, and liver.

Schwann cell: Neuroglial cell that produces myelin in the peripheral nervous system.

serous gland: Group of cells within the serous membrane that secrete a lubricating substance onto the surface.

serous membrane: Type of tissue membrane that lines body cavities and lubricates them with serous fluid.

simple columnar epithelium: Tissue that consists of a single layer of columnlike cells; promotes secretion and absorption in tissues and organs.

simple cuboidal epithelium: Tissue that consists of a single layer of cube-shaped cells; promotes secretion and absorption in ducts and tubules.

simple squamous epithelium: Tissue that consists of a single layer of flat, scalelike cells; promotes diffusion and filtration across surfaces.

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skeletal muscle: Usually attached to bone, under voluntary control, each cell is a fibre that is multinucleated and striated.

smooth muscle: Under involuntary control, moves internal organs; cells contain a single nucleus, are spindle-shaped, and do not appear striated; each cell is a fibre.

stratified columnar epithelium: Tissue that consists of two or more layers of columnlike cells, contains glands, and is found in some ducts.

stratified cuboidal epithelium: Tissue that consists of two or more layers of cube-shaped cells, found in some ducts.

stratified squamous epithelium: Tissue that consists of multiple layers of cells, with the most apical being flat scalelike cells; protects surfaces from abrasion.

striation: Alignment of parallel actin and myosin filaments, which form a banded pattern.

supportive connective tissue: Type of connective tissue that provides strength to the body and protects soft tissue.

synovial membrane: Connective tissue membrane that lines the cavities of freely movable joints, producing synovial fluid for lubrication.

tight junction: Forms an impermeable barrier between cells that blocks hydrophilic ions or molecules.

tissue: Group of cells that are similar in form and perform related functions.

tissue membrane: Thin layer or sheet of cells that covers the outside of the body, organs, internal passageways, and the lining of joint cavities.

transitional epithelium: Form of stratified epithelium found in the urinary tract, characterized by an apical layer of cells that change shape in response to the presence of urine.

Chapter Review

4.1 Types of Tissues

The human body contains more than 200 types of cells that can all be classified into four types of tissues: epithelial, connective, muscle, and nervous. Epithelial tissues act as coverings controlling the movement of materials across the surface. Connective tissue integrates the various parts of the body and provides support and protection to organs. Muscle tissue allows the body to move. Nervous tissues propagate information.

The study of the shape and arrangement of cells in tissue is called histology. All cells and tissues in the body derive from three germ layers in the embryo: the ectoderm, mesoderm, and endoderm.

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Different types of tissues form membranes that enclose organs, provide a friction-free interaction between organs, and keep organs together. Synovial membranes are connective tissue membranes that protect and line the joints. Epithelial membranes are formed from epithelial tissue attached to a layer of connective tissue. There are three types of epithelial membranes: mucous, which contain glands; serous, which secrete fluid; and cutaneous, which make up the skin.

4.2 Epithelial Tissue

In epithelial tissue, cells are closely packed with little or no extracellular matrix except for the basal lamina that separates the epithelium from the underlying tissue. The main functions of epithelia are protection from the environment, coverage, secretion and excretion, absorption, and filtration. Cells are bound together by tight junctions that form an impermeable barrier. They can also be connected by gap junctions, which allow free exchange of soluble molecules between cells, and anchoring junctions, which attach from cell to cell or from cell to matrix. The different types of epithelial tissues cover the outside of the body, organs, and internal cavities and are characterized by their cellular shapes and arrangements: squamous, cuboidal, or columnar epithelia. Single-cell layers form simple epithelia, whereas stacked cells form stratified epithelia. Very few capillaries penetrate these tissues.

Glands are secretory tissues and organs that are derived from epithelial tissues. Exocrine glands release their products through ducts. Endocrine glands secrete hormones directly into the interstitial fluid and bloodstream. Glands are classified both according to the type of secretion and by their structure. Merocrine glands secrete products as they are synthesized.

Apocrine glands release secretions by pinching off the apical portion of the cell, whereas holocrine gland cells store their secretions until they rupture and release their contents. In this case, the cell becomes part of the secretion.

4.3 Connective Tissue Supports and Protects

Connective tissue is a heterogeneous tissue with many cell shapes and tissue architectures. Structurally, all connective tissues contain cells that are embedded in an extracellular matrix stabilized by proteins. The chemical nature and physical layout of the extracellular matrix and proteins vary enormously among tissues, reflecting the variety of functions that connective tissue fulfils in the body. Connective tissues separate and cushion organs, protecting them from shifting or traumatic injury. Connective tissues provide support and assist movement, store and transport energy molecules, protect against infections, and contribute to temperature homeostasis.

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Many different cells contribute to the formation of connective tissues. They originate in the mesodermal germ layer and differentiate from mesenchyme and hematopoietic tissue in the bone marrow. Fibroblasts are the most abundant and secrete many protein fibres, adipocytes specialize in fat storage, hematopoietic cells from the bone marrow give rise to all the blood cells, chondrocytes form cartilage, and osteocytes form bone. The extracellular matrix contains fluid, proteins, polysaccharide derivatives, and in the case of bone, mineral crystals. Protein fibres fall into three major groups: collagen fibres that are thick, strong, flexible, and resist stretch; reticular fibres that are thin and form a supportive mesh; and elastin fibres that are thin and elastic.

The major types of connective tissue are connective tissue proper, supportive tissue, and fluid tissue. Loose connective tissue proper includes adipose tissue, areolar tissue, and reticular tissue. These serve to hold organs and other tissues in place and, in the case of adipose tissue, isolate and store energy reserves. The matrix is the most abundant feature for loose tissue, although adipose tissue does not have much extracellular matrix. Dense connective tissue proper is richer in fibres and may be regular, with fibres oriented in parallel, as in ligaments and tendons, or irregular, with fibres oriented in several directions. Organ capsules (collagenous type) and walls of arteries (elastic type) contain dense irregular connective tissue. Cartilage and bone are supportive tissue. Cartilage contains chondrocytes and is somewhat flexible.

Hyaline cartilage is smooth and clear, covers joints, and is found in the growing portion of bones. Fibrocartilage is tough because of extra collagen fibres and forms, among other things, the intervertebral discs. Elastic cartilage can stretch and recoil to its original shape because of its high content of elastic fibres. The matrix contains very few blood vessels. Bones are made of a rigid, mineralized matrix containing calcium salts, crystals, and osteocytes lodged in lacunae. Bone tissue is highly vascularized. Cancellous bone is spongy and less solid than compact bone. Fluid tissue, such as blood and lymph, is characterized by a liquid matrix and no supporting fibres.

4.4 Muscle Tissue and Motion

The three types of muscle cells are skeletal, cardiac, and smooth. Their morphologies match their specific functions in the body. Skeletal muscle is voluntary and responds to conscious stimuli. The cells are striated and multinucleated, appearing as long, unbranched cylinders. Cardiac muscle is involuntary and found only in the heart. Each cell is striated with a single nucleus, and they attach to one another to form long fibres. Cells are attached to one another at intercalated disks. The cells are interconnected physically and electrochemically to act as a syncytium. Cardiac muscle cells contract

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autonomously and involuntarily. Smooth muscle is involuntary. Each cell is a spindle-shaped fibre and contains a single nucleus. No striations are evident because the actin and myosin filaments do not align in the cytoplasm.

4.5 Nervous Tissue Mediates Perception and Response

The most prominent cell of the nervous tissue, the neuron, is characterized mainly by its ability to receive stimuli and respond by generating an electrical signal, known as an action potential, which can travel rapidly over great distances in the body. A typical neuron displays a distinctive morphology: A large cell body branches out into short extensions called dendrites, which receive chemical signals from other neurons, and a long tail called an axon relays signals away from the cell to other neurons, muscles, or glands. Many axons are wrapped in a myelin sheath, a lipid derivative that acts as an insulator and speeds up the transmission of the action potential. Other cells in the nervous tissue, the neuroglia, include the astrocytes, microglia, oligodendrocytes, and Schwann cells.

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PART 2

Support and Movement

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5

The Integumentary System

Chapter Objectives

After studying this chapter, you will be able to:

- Describe the integumentary system and the role it plays in homeostasis
- Describe the layers of the skin and the functions of each layer
- Describe the accessory structures of the skin and the functions of each

What do you think when you look at your skin in the mirror? Do you think about covering it with makeup, adding a tattoo, or maybe a body piercing? Or do you think about the fact that the skin belongs to one of the body's most essential and dynamic systems: the integumentary system? The integumentary system refers to the skin and its accessory structures, and it is responsible for much more than simply lending to your outward appearance. In the adult human body, the skin makes up about 16 percent of body weight and covers an area of 1.5 to 2 m^2. In fact, the skin and accessory structures are the largest organ system in the human body. As such, the skin protects your inner organs, and it needs daily care and protection to maintain its health. This chapter will introduce the structure and functions of the integumentary system as well as some of the diseases, disorders, and injuries that can affect this system.

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5.1 Layers of the Skin

Learning Objectives

By the end of this section, you will be able to:

- Identify the components of the integumentary system
- Describe the layers of the skin and the functions of each layer
- Identify and describe the hypodermis and deep fascia
- Describe the role of keratinocytes and their life cycle
- Describe the role of melanocytes in skin pigmentation

Although you may not typically think of the skin as an organ, it is in fact made of tissues that work together as a single structure to perform unique and critical functions. The skin and its accessory structures make up the **integumentary system**, which provides the body with overall protection. The skin is made of multiple layers of cells and tissues, which are held to underlying structures by connective tissue (Figure 5.1). The deeper layer of skin is well vascularized (has numerous blood vessels). It also has numerous sensory, autonomic, and sympathetic nerve fibres, ensuring communication to and from the brain.

Interactive Link 5.1

The skin consists of two main layers and a closely associated layer. View this animation (http://oer.aupress.ca/oer-202505/5.1) to learn more about layers of the skin. What are the basic functions of each of these layers?

The Epidermis

The **epidermis** is composed of keratinized stratified squamous epithelium. It is made of four or five layers of epithelial cells, depending on its location in the body. It does not have any blood vessels within it (i.e., it is avascular). Skin that has four layers of cells is referred to as "thin skin." From deep to superficial, these layers are the stratum basale, stratum spinosum, stratum granulosum, and stratum corneum. Most of the skin can be classified as thin skin. "Thick skin" is found only on the palms of the hands and the soles of the feet. It has a fifth layer, called the stratum lucidum, located between the stratum corneum and the stratum granulosum (Figure 5.2).

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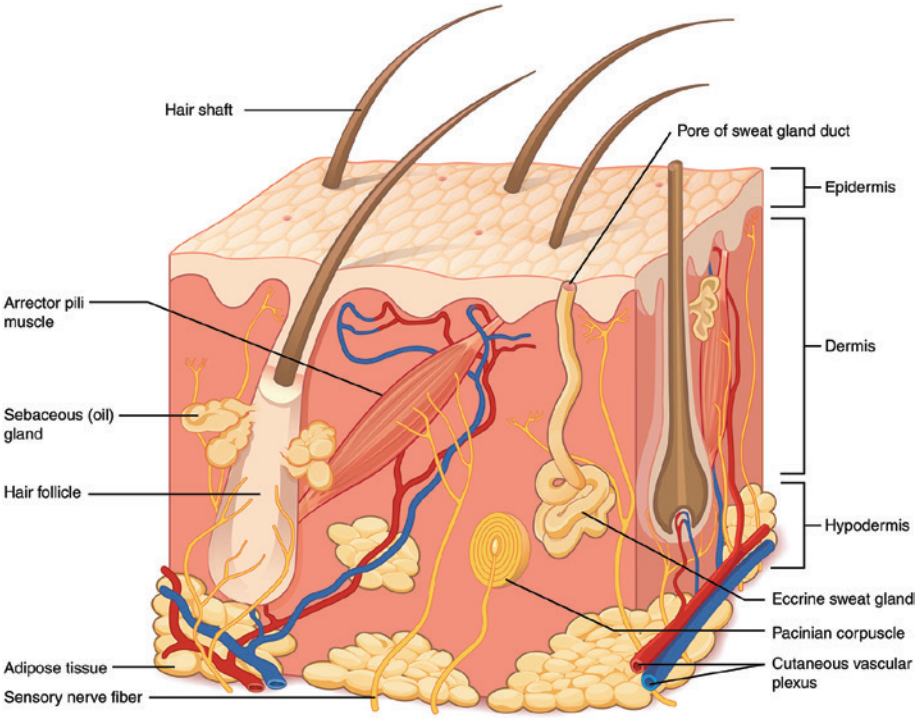


Figure 5.1 Layers of Skin. The skin is composed of two main layers: the epidermis, made of closely packed epithelial cells, and the dermis, made of dense irregular connective tissue that houses blood vessels, hair follicles, sweat glands, and other structures. Beneath the dermis lies the hypodermis, which is composed mainly of loose connective and fatty tissues.

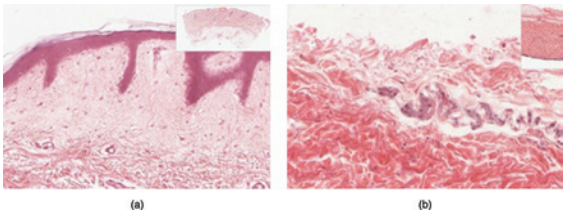


Figure 5.2 Thin Skin Versus Thick Skin. These slides show cross-sections of the epidermis and dermis of (a) thin and (b) thick skin. Note the significant difference in the thickness of the epithelial layer of the thick skin. From top, LM × 40, LM × 40. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)

The cells in all the layers except the stratum basale are called keratinocytes. A **keratinocyte** is a cell that manufactures and stores the protein keratin. **Keratin** is an intracellular fibrous protein that gives hair, nails, and skin their hardness and water-resistant properties. The keratinocytes in the stratum corneum are dead and regularly slough away, being replaced by cells from the deeper layers (Figure 5.3).

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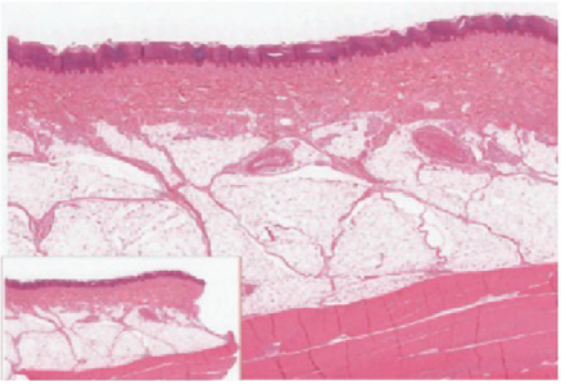


Figure 5.3 Epidermis. The epidermis is epithelium composed of multiple layers of cells. The basal layer consists of cuboidal cells, whereas the outer layers are squamous, keratinized cells, so the whole epithelium is often described as being keratinized stratified squamous epithelium. LM × 40. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Interactive Link 5.2

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/5.2) to explore the tissue sample in greater detail. If you zoom in on the cells at the outermost layer of this section of skin, what do you notice about the cells?

Stratum Basale

The **stratum basale** is the deepest epidermal layer and attaches the epidermis to the basal lamina, below which lie the layers of the dermis. The cells in the stratum basale bond to the dermis via intertwining collagen fibres, referred to as the basement membrane. A finger-like projection, or fold, known as the **dermal papilla** (plural = dermal papillae) is found in the superficial portion of the dermis. Dermal papillae increase the strength of the connection between the epidermis and dermis: the greater the folding, the stronger the connections made (Figure 5.4).

The stratum basale is a single layer of cells primarily made of basal cells. A **basal cell** is a cuboidal-shaped stem cell that is a precursor of the keratinocytes of the epidermis. All the keratinocytes are produced from this single layer of cells, which are constantly going through mitosis to produce new cells. As new cells are formed, the existing cells are pushed superficially away from the stratum basale, eventually up to the stratum corneum.

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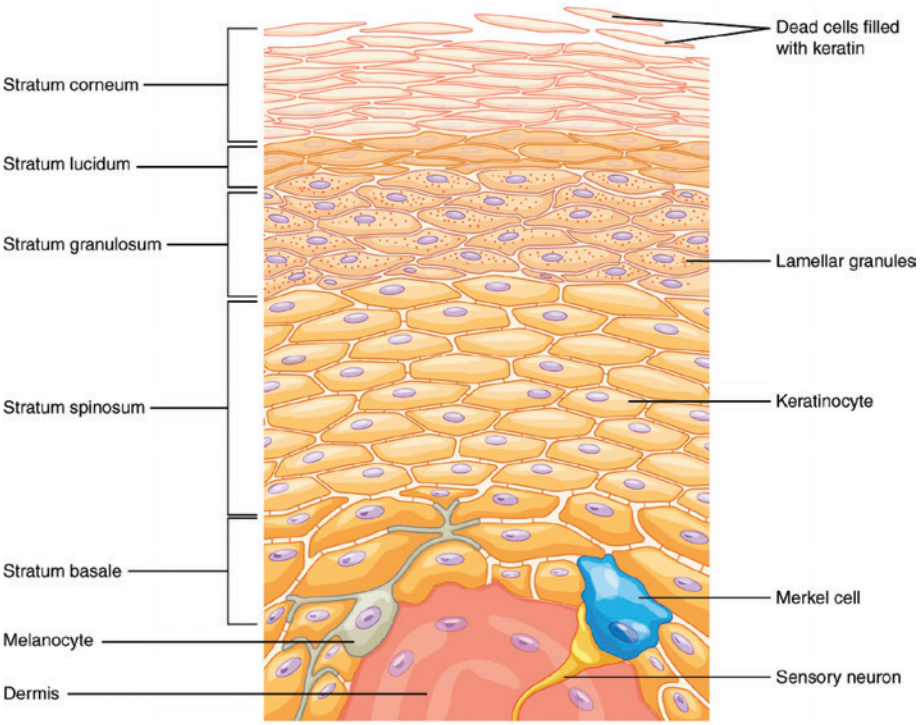


Figure 5.4 Layers of the Epidermis. The epidermis of thick skin has five layers: stratum basale, stratum spinosum, stratum granulosum, stratum lucidum, and stratum corneum.

Two other cell types are found dispersed among the basal cells in the stratum basale. The first is a **Merkel cell**, which functions as a receptor and is responsible for stimulating sensory nerves that the brain perceives as touch. These cells are especially abundant on the surfaces of the hands and feet. The second is a **melanocyte**, a cell that produces the pigment melanin. **Melanin** gives hair and skin its colour and also helps protect the living cells of the epidermis from ultraviolet (UV) radiation damage.

In a growing fetus, fingerprints form where the cells of the stratum basale meet the papillae of the underlying dermal layer (papillary layer), resulting in the formation of the ridges on your fingers that you recognize as fingerprints. Fingerprints are unique to each individual and are used for forensic analyses because the patterns do not change with the growth and aging processes.

Stratum Spinosum

As the name suggests, the **stratum spinosum** is spiny in appearance due to the protruding cell processes that join the cells via a structure called a **desmosome**. The desmosomes interlock with each other and strengthen the bond between

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the cells. It is interesting to note that the "spiny" nature of this layer is an artifact of the staining process. Unstained epidermis samples do not exhibit this characteristic appearance. The stratum spinosum is composed of 8 to 10 layers of keratinocytes, formed as a result of cell division in the stratum basale (Figure 5.5). Interspersed among the keratinocytes of this layer is a type of dendritic cell called the **Langerhans cell**, which functions as a macrophage by engulfing bacteria, foreign particles, and damaged cells that occur in this layer.

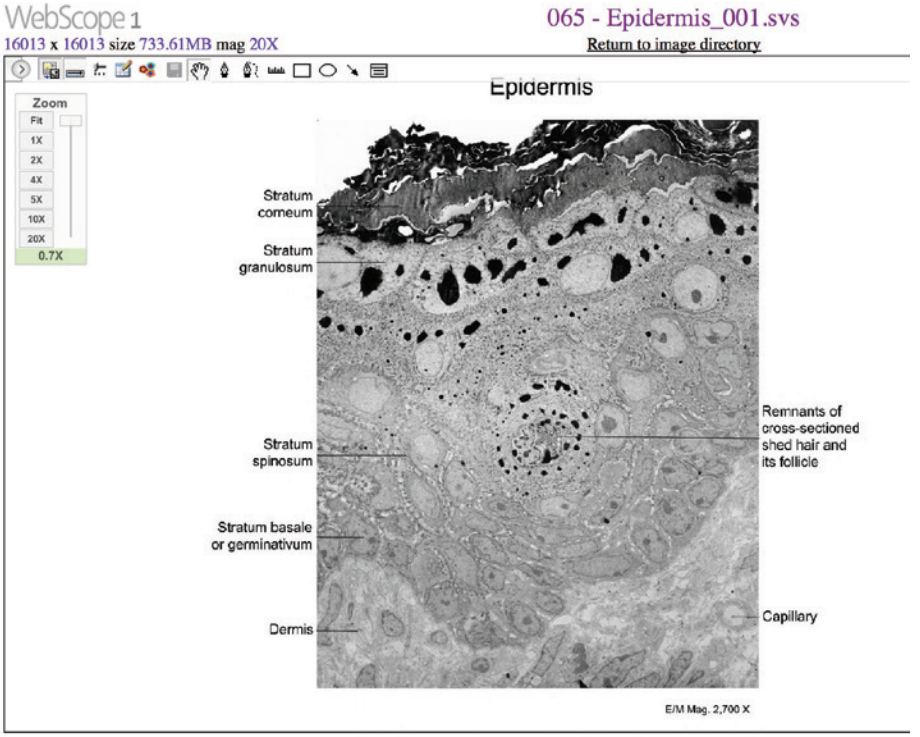


Figure 5.5 Cells of the Epidermis. The cells in the different layers of the epidermis originate from basal cells located in the stratum basale, yet the cells of each layer are distinctively different. EM × 2700. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Interactive Link 5.3

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/5.3) to explore the tissue sample in greater detail. If you zoom on the cells at the outermost layer of this section of skin, what do you notice about the cells?

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The keratinocytes in the stratum spinosum begin the synthesis of keratin and release a water-repelling glycolipid that helps prevent water loss from the body, making the skin relatively waterproof. As new keratinocytes are produced atop the stratum basale, the keratinocytes of the stratum spinosum are pushed into the stratum granulosum.

Stratum Granulosum

The **stratum granulosum** has a grainy appearance due to further changes to the keratinocytes as they are pushed from the stratum spinosum. The cells (three to five layers deep) become flatter, their cell membranes thicken, and they generate large amounts of keratin and **keratohyalin**, which accumulates as lamellar granules within the cells (see Figure 5.4). These two proteins make up the bulk of the keratinocyte mass in the stratum granulosum and give the layer its grainy appearance. The nuclei and other cell organelles disintegrate as the cells die, leaving behind the keratin, keratohyalin, and cell membranes that will form the stratum lucidum, the stratum corneum, and the accessory structures of hair and nails.

Stratum Lucidum

The **stratum lucidum** is a smooth, seemingly translucent layer of the epidermis located just above the stratum granulosum and below the stratum corneum. This thin layer of cells is found only in the thick skin of the palms, soles, and digits. The keratinocytes that compose the stratum lucidum are dead and flattened (see Figure 5.4). These cells are densely packed with a clear protein, derived from keratohyalin, which gives these cells their transparent (i.e., lucid) appearance.

Stratum Corneum

The **stratum corneum** is the most superficial layer of the epidermis and is the layer exposed to the outside environment (see Figure 5.4). The increased keratinization (also called cornification) of the cells in this layer gives it its name. There are usually 15 to 30 layers of cells in the stratum corneum. This dry, dead layer helps prevent the penetration of microbes and the dehydration of underlying tissues and provides mechanical protection against abrasion for the more delicate, underlying layers. Cells in this layer are shed periodically and are replaced by cells pushed up from the stratum granulosum (or stratum lucidum in the case of the palms and soles of feet). The entire layer is replaced during a period of about four weeks.

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Dermis

The **dermis** might be considered the "core" of the integumentary system, as distinct from the epidermis and hypodermis. It contains blood and lymph vessels, nerves, and other structures, such as hair follicles and sweat glands. The dermis is made of two layers of connective tissue that compose an interconnected mesh of elastin and collagenous fibres, produced by fibroblasts (Figure 5.6).



Figure 5.6 Layers of the Dermis. This stained slide shows the two components of the dermis—the papillary layer and the reticular layer. Both are made of connective tissue with fibres of collagen extending from one to the other, making the border between the two somewhat indistinct. The dermal papillae extending into the epidermis belong to the papillary layer, whereas the dense collagen fibre bundles below belong to the reticular layer. LM × 10. (credit: modification of work by "kilbad"/Wikimedia Commons)

Papillary Layer

The **papillary layer** is made of loose, areolar connective tissue, which means the collagen and elastin fibres of this layer form a loose mesh. This superficial layer

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of the dermis projects into the stratum basale of the epidermis to form finger-like dermal papillae (see Figure 5.6). Within the papillary layer are fibroblasts, a small number of fat cells (adipocytes), and an abundance of small blood vessels. In addition, the papillary layer contains phagocytes, defensive cells that help fight bacteria or other infections that have breached the skin. This layer also contains lymphatic capillaries, nerve fibres, and touch receptors called the Meissner corpuscles.

Reticular Layer

Underlying the papillary layer is the much thicker **reticular layer**, composed of dense irregular connective tissue. This layer is well vascularized and has a rich sensory and sympathetic nerve supply. The reticular layer appears reticulated (net-like) due to a tight meshwork of fibres. **Elastic fibres** provide some elasticity to the skin, enabling movement. Collagen fibres provide structure and tensile strength, with strands of collagen extending into both the papillary layer and the hypodermis. In addition, collagen binds water to keep the skin hydrated.

Hypodermis

The **hypodermis** (also called the subcutaneous layer or superficial fascia) is a layer directly below the dermis and serves to connect the skin to the underlying fascia (fibrous tissue) of the bones and muscles. It is not strictly a part of the skin, although the border between the hypodermis and dermis can be difficult to distinguish. The hypodermis consists of well-vascularized, loose, areolar connective tissue and adipose tissue, which functions as a mode of fat storage and provides insulation and cushioning for the integument.

Pigmentation

The colour of skin is influenced by a number of pigments, including melanin, carotene, and hemoglobin. Recall that melanin is produced by cells called melanocytes, which are found scattered throughout the stratum basale of the epidermis. The melanin is transferred into the keratinocytes via a cellular vesicle called a **melanosome** (Figure 5.7).

Melanin occurs in two primary forms. Exposure to the UV rays of the sun or a tanning bed causes melanin to be manufactured and built up in keratinocytes, as UV exposure stimulates keratinocytes to secrete chemicals that stimulate melanocytes. The accumulation of melanin in keratinocytes results in the darkening of the skin, or a tan. This increased melanin accumulation protects the DNA of epidermal cells from UV-ray damage and the breakdown of folic

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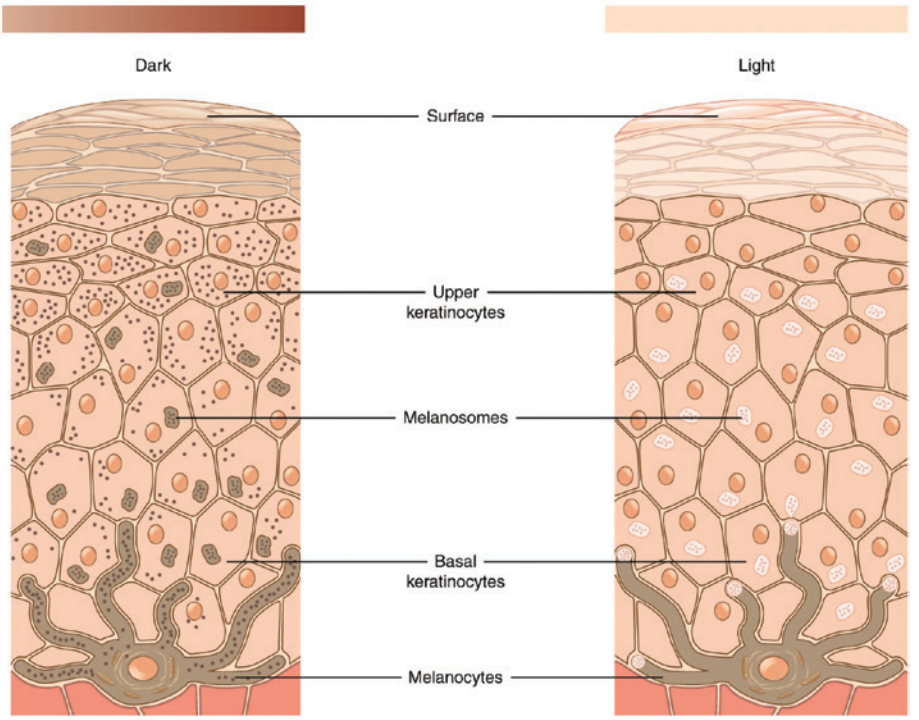


Figure 5.7 Skin Pigmentation. The relative colouration of the skin depends on the amount of melanin produced by melanocytes in the stratum basale and taken up by keratinocytes.

acid, a nutrient necessary for our health and well-being. In contrast, too much melanin can interfere with the production of vitamin D, an important nutrient involved in calcium absorption. Thus, the amount of melanin present in our skin is dependent on genetics and balances between available sunlight and folic acid destruction and between protection from UV radiation and vitamin D production.

Too much sun exposure can eventually lead to wrinkling due to the destruction of the cellular structure of the skin and, in severe cases, can cause sufficient DNA damage to result in skin cancer. When there is an irregular accumulation of melanocytes in the skin, freckles appear. Moles are larger masses of melanocytes, and although most are benign, they should be monitored for changes that might indicate the presence of cancer.

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5.2 Accessory Structures of the Skin

Learning Objectives

By the end of this section, you will be able to:

- Identify the accessory structures of the skin
- Describe the structure and function of hair and nails
- Describe the structure and function of sweat glands and sebaceous glands

Accessory structures of the skin include hair, nails, sweat glands, and sebaceous glands. These structures embryologically originate from the epidermis and can extend down through the dermis into the hypodermis.

Hair

Hair is a keratinous filament growing out of the epidermis. It is primarily made of dead, keratinized cells. Strands of hair originate in an epidermal penetration of the dermis called the **hair follicle**. The **hair shaft** is the part of the hair not anchored to the follicle, and much of this is exposed at the skin's surface. The rest of the hair, which is anchored in the follicle, lies below the surface of the skin and is referred to as the **hair root**. The hair root ends deep in the dermis at the **hair bulb** and includes a layer of mitotically active basal cells called the **hair matrix**. The hair bulb surrounds the **hair papilla**, which is made of connective tissue and contains blood capillaries and nerve endings from the dermis (Figure 5.8).

Just as the basal layer of the epidermis forms the layers of epidermis that get pushed to the surface as the dead skin on the surface sheds, the basal cells of the hair bulb divide and push cells outward in the hair root and shaft as the hair grows. The **medulla** forms the central core of the hair, which is surrounded by the **cortex**, a layer of compressed, keratinized cells that is covered by an outer layer of very hard, keratinized cells known as the **cuticle**. These layers are depicted in a longitudinal cross-section of the hair follicle (Figure 5.9), although not all hair has a medullary layer. Hair texture (straight, curly) is determined by the shape and structure of the cortex and, to the extent that it is present, the medulla. The shape and structure of these layers are, in turn, determined by the shape of the hair follicle. Hair growth begins with the production of keratinocytes by the basal cells of the hair bulb. As new cells are deposited at the hair bulb, the hair shaft is pushed through the follicle toward the surface. Keratinization is completed as the cells are pushed to the skin surface to form the shaft of hair that is externally visible.

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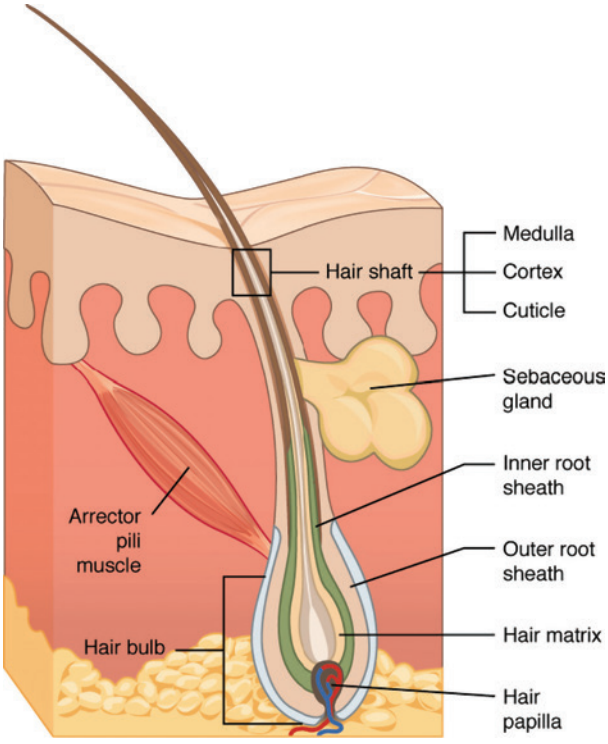


Figure 5.8 Hair. Hair follicles originate in the epidermis and have many different parts.

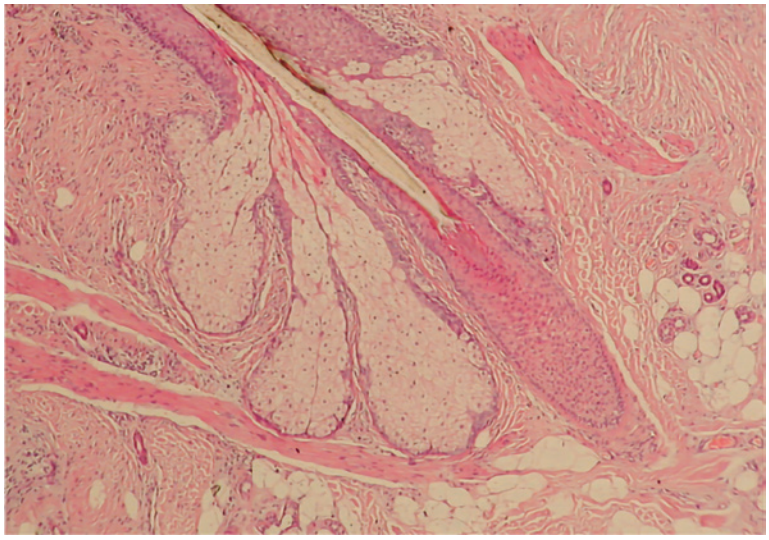


Figure 5.9 Hair Follicle. The slide shows a cross-section of a hair follicle. Basal cells of the hair matrix in the centre differentiate into cells of the inner root sheath. Basal cells at the base of the hair root form the outer root sheath. LM × 4. (credit: modification of work by "kilbad"/ Wikimedia Commons)

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The external hair is completely dead and composed entirely of keratin. For this reason, our hair does not have sensation.

Furthermore, you can cut your hair or shave it without damaging the hair structure because the cut is superficial. Most chemical hair removers also act superficially; however, electrolysis and yanking both attempt to destroy the hair bulb so hair cannot grow.

The wall of the hair follicle is made of three concentric layers of cells. The cells of the **internal root sheath** surround the root of the growing hair and extend just up to the hair shaft. They are derived from the basal cells of the hair matrix. The **external root sheath**, which is an extension of the epidermis, encloses the hair root. It is made of basal cells at the base of the hair root and tends to be more keratinous in the upper regions. The **glassy membrane** is a thick, clear connective tissue sheath covering the hair root, connecting it to the tissue of the dermis.

Interactive Link 5.4

The hair follicle is made of multiple layers of cells that form from basal cells in the hair matrix and the hair root. Cells of the hair matrix divide and differentiate to form the layers of the hair. Watch this video (https://oer.aupress.ca/oer-202505/5.4) to learn more about hair follicles.

Hair serves a variety of functions in humans, including protection, sensory input, and thermoregulation.

Example: Hair on the head protects the skull from the sun; the hair in the nose and ears and around the eyes (eyelashes) defends the body by trapping and excluding dust particles that may contain allergens and microbes; hair of the eyebrows prevents sweat and other particles from dripping into and bothering the eyes.

Hair also has a sensory function due to sensory innervation by a hair root plexus surrounding the base of each hair follicle. Hair is extremely sensitive to air movement or other disturbances in the environment, much more so than the skin surface. This feature is also useful for the detection of the presence of insects or other potentially damaging substances on the skin surface.

Each hair root is connected to a smooth muscle called the **arrector pili** that contracts in response to nerve signals from the sympathetic nervous system, making the external hair shaft "stand up." The primary purpose for this in other species is to trap a layer of air to add insulation. Humans do not have enough "fur" for this, but it is visible as goose bumps.

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Hair Growth

Hair grows and is eventually shed and replaced by new hair. This occurs in three phases. The first is the anagen phase, during which cells divide rapidly at the root of the hair, pushing the hair shaft up and out. The length of this phase is measured in years, typically from 2 to 7 years. The catagen phase lasts only 2 to 3 weeks and marks a transition from the hair follicle's active growth. Finally, during the telogen phase, the hair follicle is at rest, and no new growth occurs. At the end of this phase, which lasts about 2 to 4 months, another anagen phase begins. The basal cells in the hair matrix then produce a new hair follicle, which pushes the old hair out as the growth cycle repeats itself. Hair typically grows at the rate of 0.3 mm per day during the anagen phase. On average, 50 hairs are lost and replaced per day. Hair loss occurs if there is more hair shed than what is replaced and can happen due to hormonal or dietary changes. Hair loss can also result from the aging process.

Hair Colour

Similar to the skin, hair gets its colour from the pigment melanin, produced by melanocytes in the hair papilla. Different hair colour results from differences in the type of melanin, which is genetically determined. As a person ages, the melanin production decreases, and hair tends to lose its colour and become white.

Nails

The nail bed is a specialized structure of the epidermis that is found at the tips of our fingers and toes. The **nail body** is formed on the **nail bed** and protects the tips of our fingers and toes, as they are the farthest extremities and the parts of the body that experience the maximum mechanical stress (Figure 5.10). In addition, the nail body forms a back support for picking up small objects with the fingers. The nail body is composed of densely packed dead keratinocytes. The epidermis in this part of the body has evolved a specialized structure upon which nails can form. The nail body forms at the **nail root**, which has a matrix of proliferating cells from the stratum basale that enables the nail to grow continuously. The lateral **nail fold** overlaps the nail on the sides, helping anchor the nail body. The nail fold that meets the proximal end of the nail body forms the **nail cuticle**, also called the **eponychium**. The nail bed is rich in blood vessels, making it appear pink, except at the base, where a thick layer of epithelium over the nail matrix forms a crescent-shaped region called the **lunula**. The area beneath the free edge of the nail, farthest from the cuticle, is called the **hyponychium**. It consists of a thickened layer of stratum corneum.

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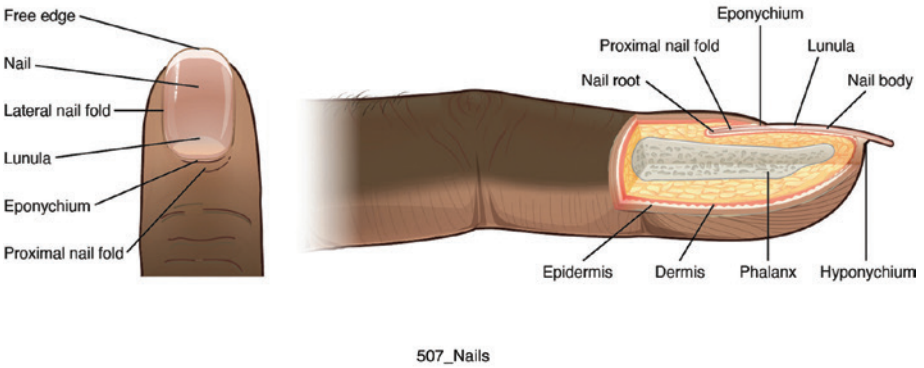


Figure 5.10 Nails. The nail is an accessory structure of the integumentary system.

Interactive Link 5.5

Nails are accessory structures of the integumentary system. Visit this link (http://oer.aupress.ca/oer-202505/5.5) to learn more about the origin and growth of fingernails.

Sweat Glands

When the body becomes warm, **sweat glands**, also called **sudoriferous glands**, produce sweat to cool the body. Sweat glands develop from epidermal projections into the dermis and are classified as merocrine glands; that is, the secretions are excreted by exocytosis through a duct without affecting the cells of the gland. There are two types of sweat glands, each secreting slightly different products.

An **eccrine sweat gland** is a type of gland that produces a hypotonic sweat for thermoregulation. These glands are found all over the skin's surface but are especially abundant on the palms of the hand, the soles of the feet, and the forehead (Figure 5.11). They are coiled glands lying deep in the dermis, with the duct rising up to a pore on the skin surface, where the sweat is released. This type of sweat, released by exocytosis, is hypotonic and composed mostly of water, with some salt, antibodies, traces of metabolic waste, and dermicidin, an antimicrobial peptide. Eccrine glands are a primary component of thermoregulation in humans and thus help maintain homeostasis.

An **apocrine sweat gland** is usually associated with hair follicles in densely hairy areas, such as armpits and genital regions. Apocrine sweat glands are larger than eccrine sweat glands and lie deeper in the dermis, sometimes even reaching the hypodermis, with the duct normally emptying into the hair follicle. In addition to water and salts, apocrine sweat includes organic compounds that

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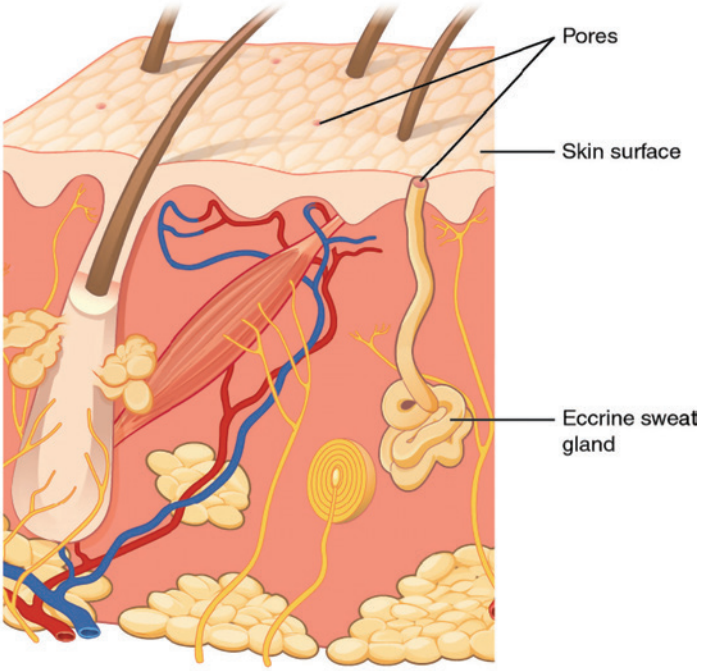


Figure 5.11 Eccrine Gland. Eccrine glands are coiled glands in the dermis that release sweat that is mostly water.

make the sweat thicker and subject to bacterial decomposition and subsequent smell. The release of this sweat is under both nervous and hormonal control and plays a role in the poorly understood human pheromone response. Some commercial antiperspirants use an aluminum-based compound as their primary active ingredient to stop sweat. When the antiperspirant enters the sweat gland duct, the aluminum-based compounds precipitate due to a change in pH and form a physical block in the duct, which prevents sweat from coming out of the pore.

Interactive Link 5.6

Sweating regulates body temperature. The composition of sweat determines whether body odour is a by-product of sweating. Visit this link (http://oer.aupress.ca/oer-202505/5.6) to learn more about sweating and body odour.

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Sebaceous Glands

A **sebaceous gland** is a type of oil gland that is found all over the body and helps lubricate and waterproof the skin and hair. Most sebaceous glands are associated with hair follicles. They generate and excrete **sebum**, a mixture of lipids, onto the skin surface, thereby naturally lubricating the dry and dead layer of keratinized cells of the stratum corneum, keeping it pliable. The fatty acids of sebum also have antibacterial properties and prevent water loss from the skin in low-humidity environments. The secretion of sebum is stimulated by hormones, many of which do not become active until puberty. Thus, sebaceous glands are relatively inactive during childhood.

5.3 Functions of the Integumentary System

Learning Objectives

By the end of this section, you will be able to:

- Describe the different functions of the skin and the structures that enable them
- Explain how the skin helps maintain body temperature

The skin and accessory structures perform a variety of essential functions, such as protecting the body from invasion by microorganisms, chemicals, and other environmental factors; preventing dehydration; acting as a sensory organ; modulating body temperature and electrolyte balance; and synthesizing vitamin D. The underlying hypodermis has important roles in storing fats, forming a "cushion" over underlying structures, and providing insulation from cold temperatures.

Protective Barrier

The skin protects the rest of the body from the basic elements of nature such as wind, water, and ultraviolet (UV) sunlight. It acts as a protective barrier against water loss due to the presence of layers of keratin and glycolipids in the stratum corneum. It is also the first line of defence against abrasive activity due to contact with grit, microbes, or harmful chemicals. Sweat excreted from sweat glands deters microbes from overcolonizing the skin surface by generating dermicidin, which has antibiotic properties.

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Sensory Function

The fact that you can feel an ant crawling on your skin, allowing you to flick it off before it bites, is because the skin, and especially the hairs projecting from hair follicles in the skin, can sense changes in the environment. The hair root plexus surrounding the base of the hair follicle senses a disturbance and then transmits the information to the central nervous system (brain and spinal cord), which can then respond by activating the skeletal muscles of your eyes to see the ant and the skeletal muscles of the body to act against the ant.

The skin acts as a sense organ because the epidermis, dermis, and hypodermis contain specialized sensory nerve structures that detect touch, surface temperature, and pain. These receptors are more concentrated on the tips of the fingers, which are most sensitive to touch, especially the **Meissner corpuscle** (tactile corpuscle; Figure 5.12), which responds to light touch, and the **Pacinian corpuscle** (lamellated corpuscle), which responds to vibration. **Merkel cells**, seen scattered in the stratum basale, are also touch receptors. In addition to these specialized receptors, there are sensory nerves connected to each hair follicle, pain and temperature receptors are scattered throughout the skin, and motor nerves innervate the arrector pili muscles and glands. This rich innervation helps us sense our environment and react accordingly.

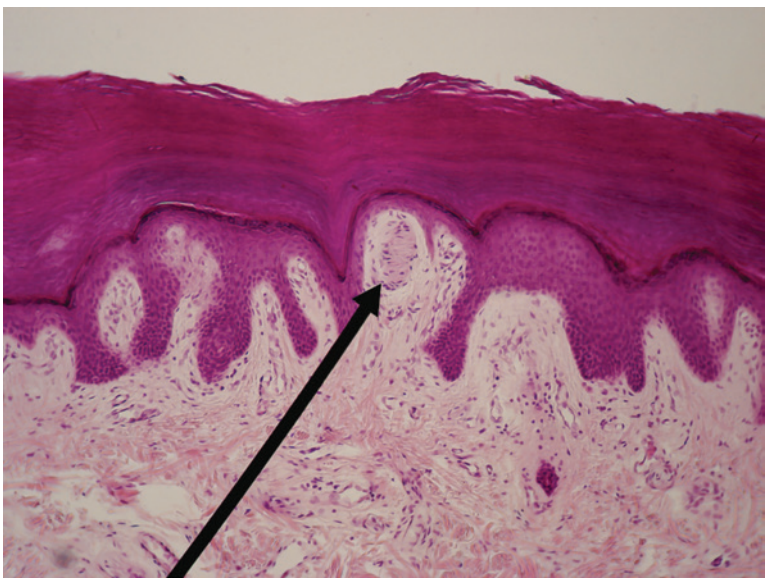


Figure 5.12 Light Micrograph of a Meissner Corpuscle. In this micrograph of a skin cross-section, you can see a Meissner corpuscle (arrow), a type of touch receptor located in a dermal papilla adjacent to the basement membrane and stratum basale of the overlying epidermis. LM × 100. (credit: "Wbensmith"/Wikimedia Commons)

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Thermoregulation

The integumentary system helps regulate body temperature through its tight association with the sympathetic nervous system, the division of the nervous system involved in our fight-or-flight responses. The sympathetic nervous system is continuously monitoring body temperature and initiating appropriate motor responses. Recall that sweat glands, accessory structures to the skin, secrete water, salt, and other substances to cool the body when it becomes warm. Even when the body does not appear to be noticeably sweating, approximately 500 mL of sweat (insensible perspiration) is secreted a day. If the body becomes excessively warm due to high temperatures, vigorous activity (Figure 5.13a and c), or a combination of the two, sweat glands will be stimulated by the sympathetic nervous system to produce large amounts of sweat, as much as 0.7 to 1.5 L per hour for an active person. When the sweat evaporates from the skin surface, the body is cooled as body heat is dissipated.

In addition to sweating, arterioles in the dermis dilate so that excess heat carried by the blood can dissipate through the skin and into the surrounding environment (Figure 5.13b). This accounts for the skin redness that many people experience when exercising.

When body temperatures drop, the peripheral arterioles constrict to minimize heat loss, particularly in the ends of the digits and tip of the nose. This reduced circulation can result in the skin taking on a whitish hue. Although the temperature of the skin drops as a result, passive heat loss is prevented, and internal organs and structures remain warm. If the temperature of the

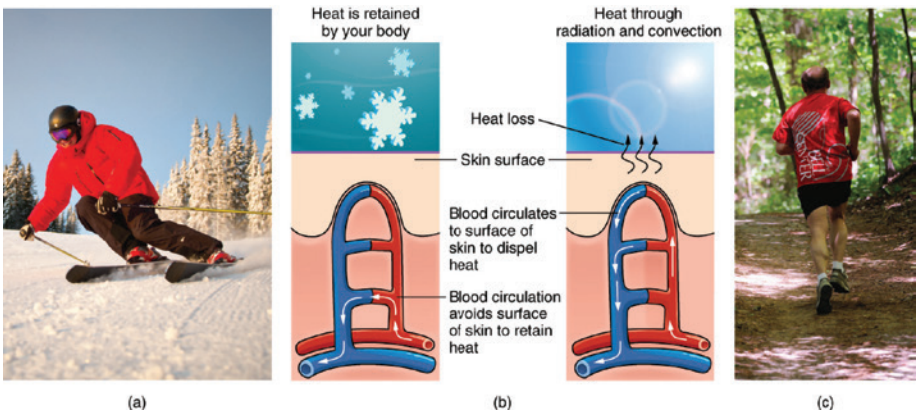


Figure 5.13 Thermoregulation. During strenuous physical activities, such as skiing (a) or running (c), the dermal blood vessels dilate and sweat secretion increases (b). These mechanisms prevent the body from overheating. In contrast, the dermal blood vessels constrict to minimize heat loss in response to low temperatures (b). (credit a: "Trysil"/flickr; credit c: Ralph Daily)

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skin drops too much (such as in environmental temperatures below freezing), the conservation of body core heat can result in the skin actually freezing, a condition called frostbite.

Vitamin D Synthesis

The epidermal layer of human skin synthesizes **vitamin D** when exposed to UV radiation. Vitamin D is essential for normal absorption of calcium and phosphorus, which are required for healthy bones. In addition to its essential role in bone health, vitamin D is essential for general immunity against bacterial, viral, and fungal infections. Recent studies are also finding a link between insufficient vitamin D and cancer.

Key Terms

apocrine sweat gland: Type of sweat gland that is associated with hair follicles in the armpits and genital regions.

arrector pili: Smooth muscle that is activated in response to external stimuli that pull on hair follicles and make the hair "stand up."

basal cell: Type of stem cell found in the stratum basale and in the hair matrix that continually undergoes cell division, producing the keratinocytes of the epidermis.

cortex: In hair, the second or middle layer of keratinocytes originating from the hair matrix, as seen in a cross-section of the hair bulb.

cuticle: In hair, the outermost layer of keratinocytes originating from the hair matrix, as seen in a cross-section of the hair bulb.

dermal papilla (plural = dermal papillae): Extension of the papillary layer of the dermis that increases surface contact between the epidermis and dermis.

dermis: Layer of skin between the epidermis and hypodermis, composed mainly of connective tissue and containing blood vessels, hair follicles, sweat glands, and other structures.

desmosome: Structure that forms an impermeable junction between cells.

eccrine sweat gland: Type of sweat gland that is common throughout the skin surface; it produces a hypotonic sweat for thermoregulation.

elastic fibres: Fibres made of the protein elastin that increase the elasticity of the dermis.

epidermis: Outermost tissue layer of the skin.

external root sheath: Outer layer of the hair follicle that is an extension of the epidermis, which encloses the hair root.

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glassy membrane: Layer of connective tissue that surrounds the base of the hair follicle, connecting it to the dermis.
hair: Keratinous filament growing out of the epidermis.
hair bulb: Structure at the base of the hair root that surrounds the dermal papilla.
hair follicle: Cavity or sac from which hair originates.
hair matrix: Layer of basal cells from which a strand of hair grows.
hair papilla: Mass of connective tissue, blood capillaries, and nerve endings at the base of the hair follicle.
hair root: Part of hair that is below the epidermis anchored to the follicle.
hair shaft: Part of hair that is above the epidermis but is not anchored to the follicle.
hypodermis: Connective tissue connecting the integument to the underlying bone and muscle.
hyponychium: Thickened layer of stratum corneum that lies below the free edge of the nail.
integumentary system: Skin and its accessory structures.
internal root sheath: Innermost layer of keratinocytes in the hair follicle that surround the hair root up to the hair shaft.
keratin: Type of structural protein that gives skin, hair, and nails its hard, water-resistant properties.
keratinocyte: Cell that produces keratin and is the most predominant type of cell found in the epidermis.
keratohyalin: Granulated protein found in the stratum granulosum.
Langerhans cell: Specialized dendritic cell found in the stratum spinosum that functions as a macrophage.
lunula: Basal part of the nail body that consists of a crescent-shaped layer of thick epithelium.
medulla: In hair, the innermost layer of keratinocytes originating from the hair matrix.
Meissner corpuscle (also tactile corpuscle): Receptor in the skin that responds to light touch.
melanin: Pigment that determines the colour of hair and skin.
melanocyte: Cell found in the stratum basale of the epidermis that produces the pigment melanin.
melanosome: Intercellular vesicle that transfers melanin from melanocytes into keratinocytes of the epidermis.
Merkel cell: Receptor cell in the stratum basale of the epidermis that responds to the sense of touch.

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nail bed: Layer of epidermis upon which the nail body forms.
nail body: Main keratinous plate that forms the nail.
nail cuticle (eponychium): Fold of epithelium that extends over the nail bed, also called the eponychium.
nail fold: Fold of epithelium that extends over the sides of the nail body, holding it in place.
nail root: Part of the nail that is lodged deep in the epidermis from which the nail grows.
Pacinian corpuscle (also lamellated corpuscle): Receptor in the skin that responds to vibration.
papillary layer: Superficial layer of the dermis, made of loose, areolar connective tissue.
reticular layer: Deeper layer of the dermis; it has a reticulated appearance due to the presence of abundant collagen and elastin fibres.
sebaceous gland: Type of oil gland found in the dermis all over the body and helps lubricate and waterproof the skin and hair by secreting sebum.
sebum: Oily substance that is composed of a mixture of lipids that lubricates the skin and hair.
stratum basale: Deepest layer of the epidermis, made of epidermal stem cells.
stratum corneum: Most superficial layer of the epidermis.
stratum granulosum: Layer of the epidermis superficial to the stratum spinosum.
stratum lucidum: Layer of the epidermis between the stratum granulosum and stratum corneum, found only in thick skin covering the palms, soles of the feet, and digits.
stratum spinosum: Layer of the epidermis superficial to the stratum basale, characterized by the presence of desmosomes.
sudoriferous gland: Sweat gland.
sweat gland: Type of gland found in the dermis that secretes sweat through a duct to cool the body.
vitamin D: Compound that aids absorption of calcium and phosphates in the intestine to improve bone health.

Chapter Review

5.1 Layers of the Skin

The skin is composed of two major layers: a superficial epidermis and a deeper dermis. The epidermis consists of several layers beginning with the innermost (deepest) stratum basale (germinatum), followed by the stratum

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spinosum, stratum granulosum, stratum lucidum (when present), and ending with the outermost layer, the stratum corneum. The topmost layer, the stratum corneum, consists of dead cells that shed periodically and is progressively replaced by cells formed from the basal layer. The stratum basale also contains melanocytes, cells that produce melanin, the pigment primarily responsible for giving skin its colour. Melanin is transferred to keratinocytes in the stratum spinosum to protect cells from UV rays.

The dermis connects the epidermis to the hypodermis and provides strength and elasticity due to the presence of collagen and elastin fibres. It has only two layers: the papillary layer with papillae that extend into the epidermis and the lower, reticular layer composed of loose connective tissue. The hypodermis, deep to the dermis of skin, is the connective tissue that connects the dermis to underlying structures; it also harbors adipose tissue for fat storage and protection.

5.2 Accessory Structures of the Skin

Accessory structures of the skin include hair, nails, sweat glands, and sebaceous glands. Hair is made of dead keratinized cells and gets its colour from melanin pigments. Nails, also made of dead keratinized cells, protect the extremities of our fingers and toes from mechanical damage. Sweat glands and sebaceous glands produce sweat and sebum, respectively. Each of these fluids has a role to play in maintaining homeostasis. Sweat cools the body surface when it gets overheated and helps excrete small amounts of metabolic waste. Sebum acts as a natural moisturizer and keeps the dead, flaky, outer keratin layer healthy.

5.3 Functions of the Integumentary System

The skin plays important roles in protection, sensing stimuli, thermoregulation, and vitamin D synthesis. It is the first layer of defence to prevent dehydration, infection, and injury to the rest of the body. Sweat glands in the skin allow the skin surface to cool when the body gets overheated. Thermoregulation is also accomplished by the dilation or constriction of heat-carrying blood vessels in the skin. Immune cells present among the skin layers patrol the areas to keep them free of foreign materials. Fat stores in the hypodermis aid in both thermoregulation and protection. Finally, the skin plays a role in the synthesis of vitamin D, which is necessary for our well-being but not easily available in natural foods.

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6

Bone Tissue and the Skeletal System

Chapter Objectives

After studying this chapter, you will be able to:

- List and describe the functions of bones
- Describe the classes of bones
- Discuss the process of bone formation and development
- Explain how bone repairs itself after a fracture
- Discuss the effect of exercise, nutrition, and hormones on bone tissue
- Describe how an imbalance of calcium can affect bone tissue

Bones make good fossils. While the soft tissue of a once-living organism will decay and fall away over time, bone tissue will, under the right conditions, undergo a process of mineralization, effectively turning the bone to stone. A well-preserved fossil skeleton can give us a good sense of the size and shape of an organism, just as your skeleton helps define your size and shape. Unlike a fossil skeleton, however, your skeleton is a structure of living tissue that grows, repairs, and renews itself. The bones within it are dynamic and complex organs that serve a number of important functions, including some necessary to maintain homeostasis.

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6.1 The Functions of the Skeletal System

Learning Objectives

By the end of this section, you will be able to:

- Define bone, cartilage, and the skeletal system
- List and describe the functions of the skeletal system

Bone, or **osseous tissue**, is a hard, dense connective tissue that forms most of the adult skeleton, the support structure of the body. In the areas of the skeleton where bones move (for example, the ribcage and joints), **cartilage**, a semirigid form of connective tissue, provides flexibility and smooth surfaces for movement. The **skeletal system** is the body system composed of bones and cartilage and performs the following critical functions for the human body:

- supports the body
- facilitates movement
- protects internal organs
- produces blood cells
- stores and releases minerals and fat

Support, Movement, and Protection

The most apparent functions of the skeletal system are the gross functions—those visible by observation. Simply by looking at a person, you can see how the bones support, facilitate movement, and protect the human body.

Just as the steel beams of a building provide a scaffold to support its weight, the bones and cartilage of your skeletal system compose the scaffold that supports the rest of your body. Without the skeletal system, you would be a limp mass of organs, muscle, and skin.

Bones also facilitate movement by serving as points of attachment for your muscles. While some bones only serve as a support for the muscles, others also transmit the forces produced when your muscles contract. From a mechanical point of view, bones act as levers and joints serve as fulcrums. Unless a muscle spans a joint and contracts, a bone is not going to move.

Bones also protect internal organs from injury by covering or surrounding them. For example, your ribs protect your lungs and heart, the bones of your vertebral column (spine) protect your spinal cord, and the bones of your cranium (skull) protect your brain.

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Mineral Storage, Energy Storage, and Hematopoiesis

On a metabolic level, bone tissue performs several critical functions. For one, the bone matrix acts as a reservoir for a number of minerals important to the functioning of the body, especially calcium, and phosphorus. These minerals, incorporated into bone tissue, can be released back into the bloodstream to maintain levels needed to support physiological processes. Calcium ions, for example, are essential for muscle contractions and controlling the flow of other ions involved in the transmission of nerve impulses.

Bone also serves as a site for fat storage and blood cell production. The softer connective tissue that fills the interior of most bone is referred to as bone marrow (Figure 6.1). There are two types of bone marrow: yellow marrow and red marrow. **Yellow marrow** contains adipose tissue; the triglycerides stored in the adipocytes of the tissue can serve as a source of energy. **Red marrow** is where **hematopoiesis**—the production of blood cells—takes place. Red blood cells, white blood cells, and platelets are all produced in the red marrow.

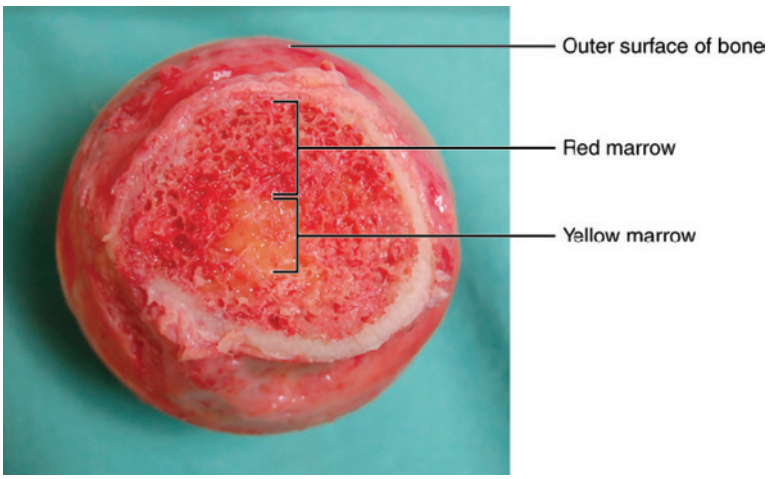


Figure 6.1 Head of Femur Showing Red and Yellow Marrow. The head of the femur contains both yellow and red marrow. Yellow marrow stores fat. Red marrow is responsible for hematopoiesis. (credit: modification of work by "stevenfruitsmaak"/Wikimedia Commons)

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6.2 Bone Classification

Learning Objectives

By the end of this section, you will be able to:

- Classify bones according to their shapes
- Describe the function of each category of bones

The 206 bones that compose the adult skeleton are divided into five categories based on their shapes (Figure 6.2). Their shapes and their functions are related such that each categorical shape of bone has a distinct function.

Long Bones

A **long bone** is one that is cylindrical in shape, being longer than it is wide. Keep in mind, however, that the term describes the shape of a bone, not its size. Long bones are found in the arms (humerus, ulna, radius) and legs (femur, tibia, fibula) as well as in the fingers (metacarpals, phalanges) and toes (metatarsals, phalanges). Long bones function as levers; they move when muscles contract.

Short Bones

A **short bone** is one that is cube-like in shape, being approximately equal in length, width, and thickness. The only short bones in the human skeleton are in the carpals of the wrists and the tarsals of the ankles. Short bones provide stability and support as well as some limited motion.

Flat Bones

The term **flat bone** is somewhat of a misnomer because although a flat bone is typically thin, it is also often curved. Examples include the cranial (skull) bones, the scapulae (shoulder blades), the sternum (breastbone), and the ribs. Flat bones serve as points of attachment for muscles and often protect internal organs.

Irregular Bones

An **irregular bone** is one that does not have any easily characterized shape and therefore does not fit any other classification. These bones tend to have more complex shapes, like the vertebrae that support the spinal cord and protect it from compressive forces. Many facial bones, particularly the ones containing sinuses, are classified as irregular bones.

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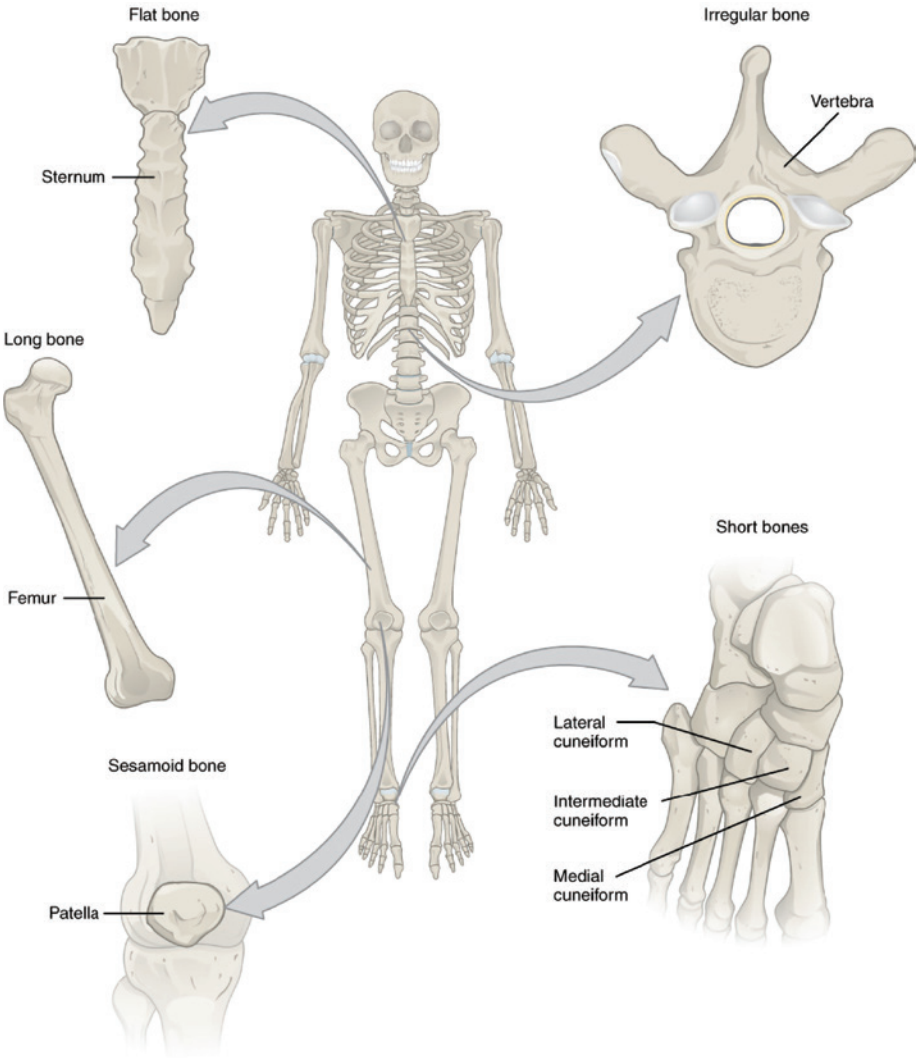


Figure 6.2 Classifications of Bones. Bones are classified according to their shape.

Sesamoid Bones

A **sesamoid bone** is a small, round bone that, as the name suggests, is shaped like a sesame seed. These bones form in tendons (the sheaths of tissue that connect bones to muscles) where a great deal of pressure is generated in a joint. The sesamoid bones protect tendons by helping them overcome compressive forces. Sesamoid bones vary in number and placement from person to person but are typically found in tendons associated with the feet, hands, and knees. The patellae (singular = patella) are the only sesamoid bones found in common with every person. Table 6.1 reviews bone classifications with their associated features, functions, and examples.

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Table 6.1 Bone Classifications

Bone classification	Features	Function(s)	Examples
Long	Cylinder-like shape, longer than it is wide	Leverage	Femur, tibia, fibula, metatarsals, humerus, ulna, radius, metacarpals, phalanges
Short	Cube-like shape, approximately equal in length, width, and thickness	Provide stability, support, while allowing for some motion	Carpals, tarsals
Flat	Thin and curved	Points of attachment for muscles; protectors of internal organs	Sternum, ribs, scapulae, cranial bones
Irregular	Complex shape	Protect internal organs	Vertebrae, facial bones
Sesamoid	Small and round; embedded in tendons	Protect tendons from compressive forces	Patellae

6.3 Bone Structure

Learning Objectives

By the end of this section, you will be able to:

- Identify the anatomical features of a bone
- Define and list examples of bone markings
- Describe the histology of bone tissue
- Compare and contrast compact and spongy bone
- Identify the structures that compose compact and spongy bone
- Describe how bones are nourished and innervated

Bone tissue (osseous tissue) differs greatly from other tissues in the body. Bone is hard, and many of its functions depend on that characteristic hardness. Later discussions in this chapter will show that bone is also dynamic in that its shape adjusts to accommodate stresses. This section will examine the gross anatomy of bone first and then move on to its histology.

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Gross Anatomy of Bone

The structure of a long bone allows for the best visualization of all the parts of a bone (Figure 6.3). A long bone has two parts: the **diaphysis** and the **epiphysis**. The diaphysis is the tubular shaft that runs between the proximal and distal ends of the bone. The hollow region in the diaphysis is called the **medullary cavity**, which is filled with yellow marrow. The walls of the diaphysis are composed of dense and hard **compact bone**.

The wider section at each end of the bone is called the **epiphysis** (plural = epiphyses), which is filled with spongy bone. Red marrow fills the spaces in

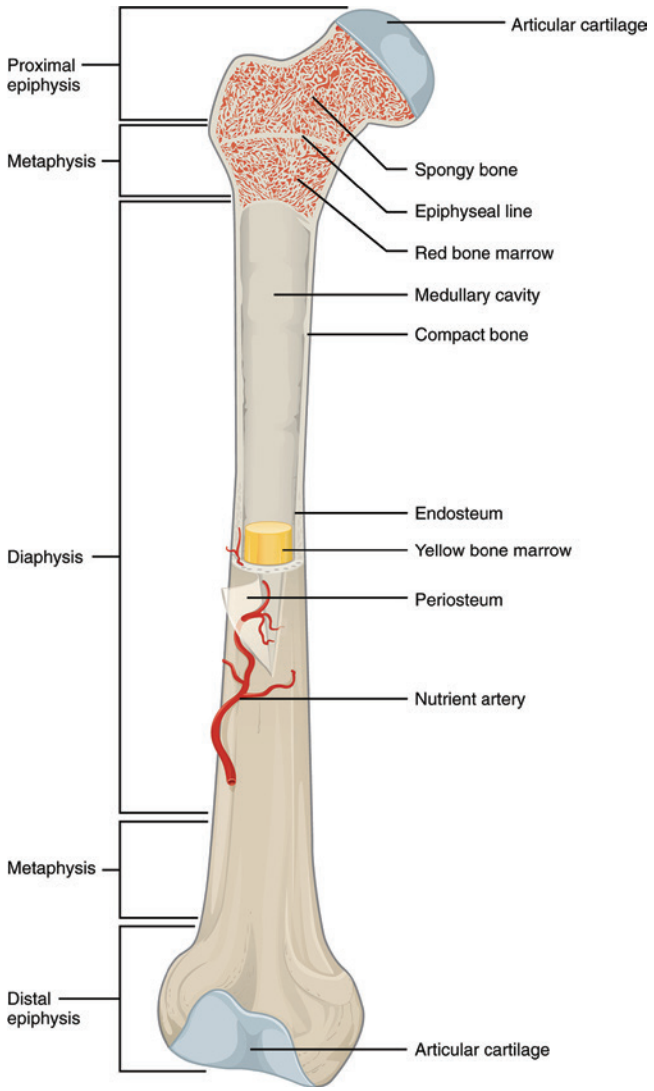


Figure 6.3 Anatomy of a Long Bone. A typical long bone shows the gross anatomical characteristics of bone.

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the spongy bone. Each epiphysis meets the diaphysis at the metaphysis, the narrow area that contains the **epiphyseal plate** (growth plate), a layer of hyaline (transparent) cartilage in a growing bone. When the bone stops growing in early adulthood (approximately 18–21 years), the cartilage is replaced by osseous tissue and the epiphyseal plate becomes an **epiphyseal line**.

The medullary cavity has a delicate membranous lining called the **endosteum**, where bone growth, repair, and remodelling occur. The outer surface of the bone is covered with a fibrous membrane called the **periosteum**. The periosteum contains blood vessels, nerves, and lymphatic vessels that nourish compact bone. Tendons and ligaments also attach to bones at the periosteum. The periosteum covers the entire outer surface except where the epiphyses meet other bones to form joints (Figure 6.4). In this region, the epiphyses are covered with **articular cartilage**, a thin layer of cartilage that reduces friction and acts as a shock absorber.

Flat bones, like those of the cranium, consist of a layer of **spongy bone** (diploë) lined on either side by a layer of compact bone (Figure 6.5). The two layers of compact bone and the interior spongy bone work together to protect the internal organs. If the outer layer of a cranial bone fractures, the brain is still protected by the intact inner layer.

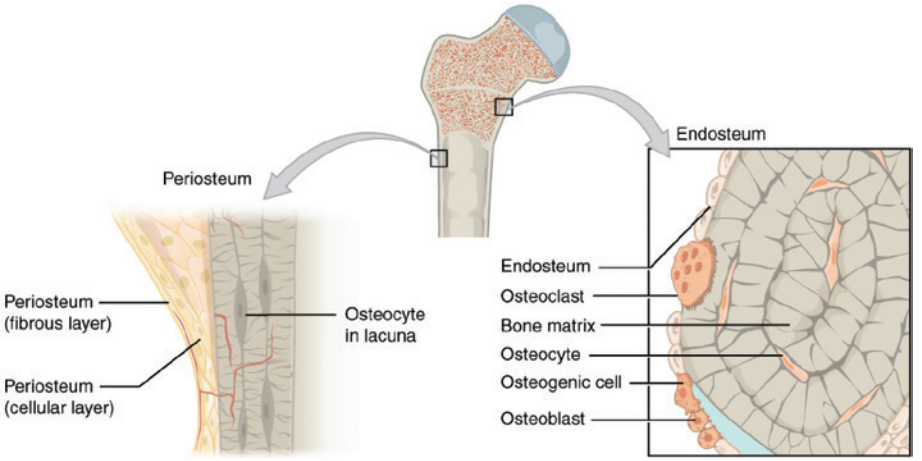


Figure 6.4 Periosteum and Endosteum. The periosteum forms the outer surface of bone, and the endosteum lines the medullary cavity.

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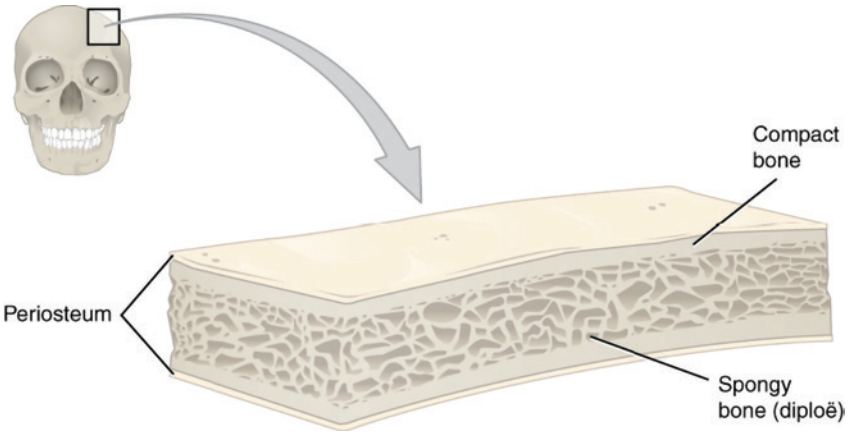


Figure 6.5 Anatomy of a Flat Bone. This cross-section of a flat bone shows the spongy bone (diploë) lined on either side by a layer of compact bone.

Bone Markings

The surface features of bones vary considerably, depending on the function and location in the body. Table 6.2 describes the bone markings, which are illustrated in Figure 6.6. There are three general classes of bone markings: (1) articulations, (2) projections, and (3) holes. As the name implies, an **articulation** is where two bone surfaces come together. These surfaces tend to conform to one another, such as one being rounded and the other cupped, to facilitate the function of the articulation. A **projection** is an area of a bone that projects above the surface of the bone. These are the attachment points for tendons and ligaments. In general, their size and shape are indications of the forces exerted through the attachment to the bone. A **hole** is an opening or groove in the bone that allows blood vessels and nerves to enter the bone. As with the other markings, their size and shape reflect the size of the vessels and nerves that penetrate the bone at these points.

Bone Cells and Tissue

Bone contains a relatively small number of cells entrenched in a matrix of collagen fibres that provide a surface for inorganic salt crystals to adhere. These salt crystals form when calcium phosphate and calcium carbonate combine to create hydroxyapatite, which incorporates other inorganic salts like magnesium hydroxide, fluoride, and sulfate as it crystallizes, or calcifies, on the collagen fibres. The hydroxyapatite crystals give bones their hardness and strength, while the collagen fibres give them flexibility so that they are not brittle.

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Table 6.2 Bone Markings

Marking	Description	Example
Articulations	Where two bones meet	Knee joint
Head	Prominent rounded surface	Head of femur
Facet	Flat surface	Vertebrae
Condyle	Rounded surface	Occipital condyles
Projections	Raised markings	Spinous process of the vertebrae
Protuberance	Protruding	Chin
Process	Prominence feature	Transverse process of vertebra
Spine	Sharp process	Ischial spine
Tubercle	Small, rounded process	Tubercle of humerus
Tuberosity	Rough surface	Deltoid tuberosity
Line	Slight, elongated ridge	Temporal lines of the parietal bones
Crest	Ridge	Iliac crest
Holes	Holes and depressions	Foramen (holes that blood vessels can pass through)
Fossa	Elongated basin	Mandibular fossa
Fovea	Small pit	Fovea capitis on the head of the femur
Sulcus	Groove	Sigmoid sulcus of the temporal bones
Canal	Passage in bone	Auditory canal
Fissure	Slit through bone	Auricular fissure
Foramen	Hole through bone	Foramen magnum in the occipital bone
Meatus	Opening into canal	External auditory meatus
Sinus	Air-filled space in bone	Nasal sinus

Although bone cells compose a small amount of the bone volume, they are crucial to the function of bones. Four types of cells are found within bone tissue: osteoblasts, osteocytes, osteogenic cells, and osteoclasts (Figure 6.7).

The **osteoblast** is the bone cell responsible for forming new bone and is found in the growing portions of bone, including the periosteum and endosteum.

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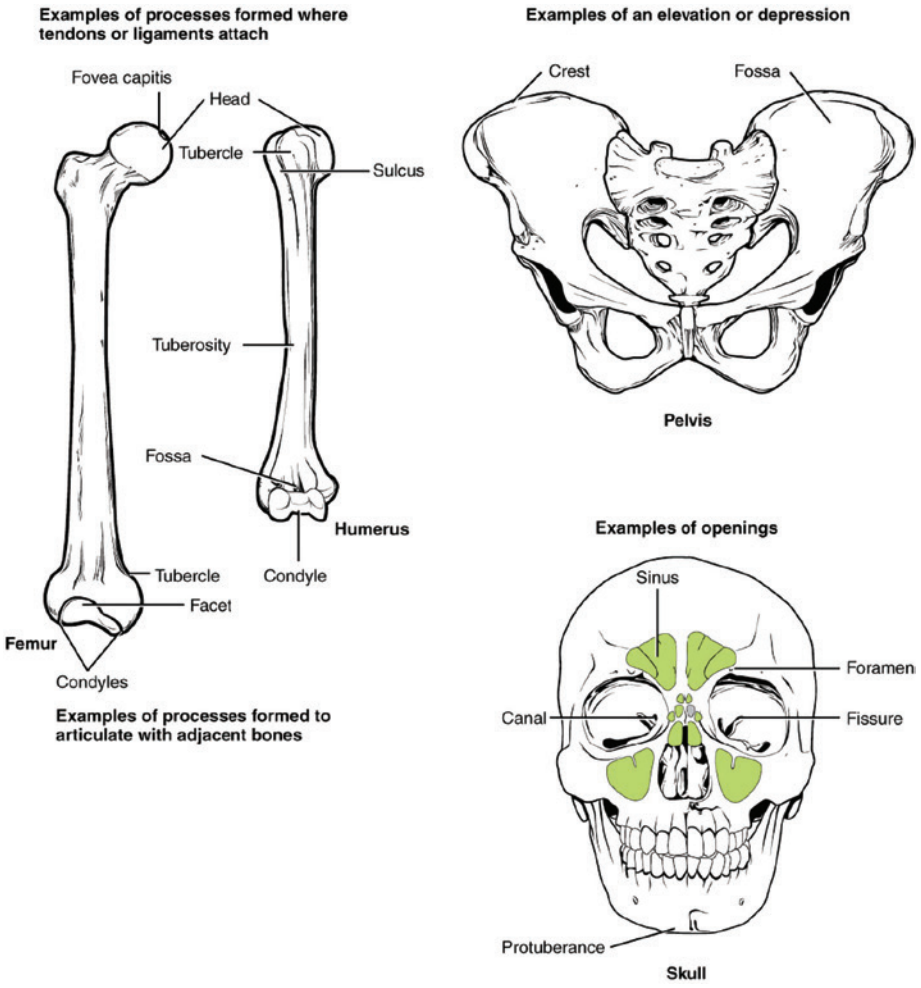


Figure 6.6 Bone Features. The surface features of bones depend on their function, their location, the attachment of ligaments and tendons, and the penetration of blood vessels and nerves.

Osteoblasts, which do not divide, synthesize and secrete the collagen matrix and calcium salts. As the secreted matrix surrounding the osteoblast calcifies, the osteoblast becomes trapped within it; as a result, it changes in structure and becomes an **osteocyte**, the primary cell of mature bone and the most common type of bone cell. Each osteocyte is located in a space called a **lacuna** surrounded by bone tissue. Osteocytes maintain the mineral concentration of the matrix via the secretion of enzymes. Like osteoblasts, osteocytes lack mitotic activity. They can communicate with each other and receive nutrients via long cytoplasmic processes that extend through **canaliculi** (singular = canaliculus), channels within the bone matrix.

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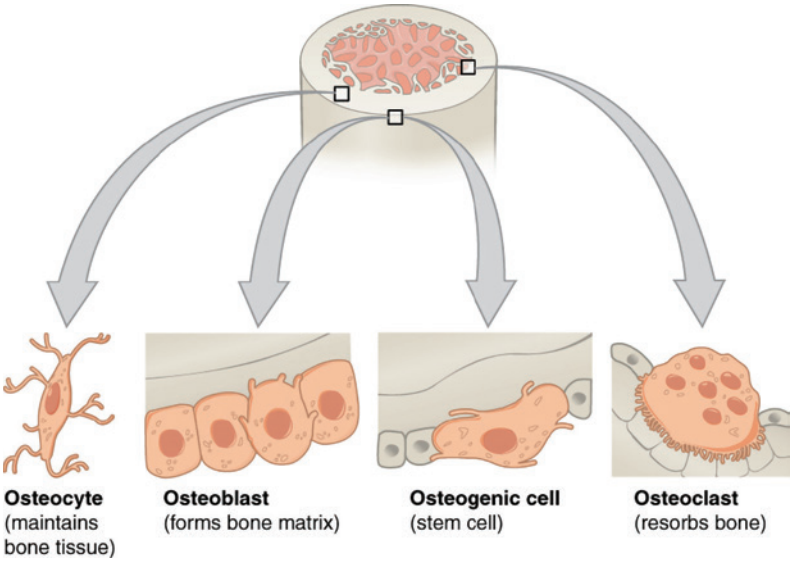


Figure 6.7 Bone Cells. Four types of cells are found within bone tissue. Osteogenic cells are undifferentiated and develop into osteoblasts. When osteoblasts get trapped within the calcified matrix, their structure and function change, and they become osteocytes. Osteoclasts develop from monocytes and macrophages and differ in appearance from other bone cells.

If osteoblasts and osteocytes are incapable of mitosis, then how are they replenished when old ones die? The answer lies in the properties of a third category of bone cells—the **osteogenic cell**. These osteogenic cells are undifferentiated with high mitotic activity, and they are the only bone cells that divide. Immature osteogenic cells are found in the deep layers of the periosteum and the marrow. They differentiate and develop into osteoblasts.

The dynamic nature of bone means that new tissue is constantly formed, and old, injured, or unnecessary bone is dissolved for repair or for calcium release. The cells responsible for bone resorption, or breakdown, are **osteoclasts**. They are found on bone surfaces, are multinucleated, and originate from monocytes and macrophages, two types of white blood cells, not from osteogenic cells. Osteoclasts are continually breaking down old bone while osteoblasts are continually forming new bone. The ongoing balance between osteoblasts and osteoclasts is responsible for the constant but subtle reshaping of bone. Table 6.3 reviews the bone cells, their functions, and their locations.

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Table 6.3 Bone Cells

Cell type	Function	Location
Osteogenic cells	Develop into osteoblasts	Deep layers of the periosteum and the marrow
Osteoblasts	Bone formation	Growing portions of bone, including periosteum and endosteum
Osteocytes	Maintain mineral concentration of matrix	Entrapped in matrix
Osteoclasts	Bone resorption	Bone surfaces and at sites of old, injured, or unneeded bone

Compact and Spongy Bone

The differences between compact and spongy bone are best explored via their histology. Most bones contain compact and spongy osseous tissue, but their distribution and concentration vary based on the bone's overall function. Compact bone is dense so that it can withstand compressive forces, while spongy (cancellous) bone has open spaces and supports shifts in weight distribution.

Compact Bone

Compact bone is the denser, stronger of the two types of bone tissue (Figure 6.8). It can be found under the periosteum and in the diaphyses of long bones, where it provides support and protection.

The microscopic structural unit of compact bone is called an **osteon**, or **Haversian system**. Each osteon is composed of concentric rings of calcified matrix called **lamellae** (singular = lamella). Running down the centre of each osteon is the **central canal**, or **Haversian canal**, which contains blood vessels, nerves, and lymphatic vessels. These vessels and nerves branch off at right angles through a **perforating canal**, also known as **Volkmann's canals**, to extend to the periosteum and endosteum.

The osteocytes are located inside spaces called **lacunae** (singular = lacuna), found at the borders of adjacent lamellae. As described earlier, canaliculi connect with the canaliculi of other lacunae and eventually with the central canal. This system allows nutrients to be transported to the osteocytes and wastes to be removed from them.

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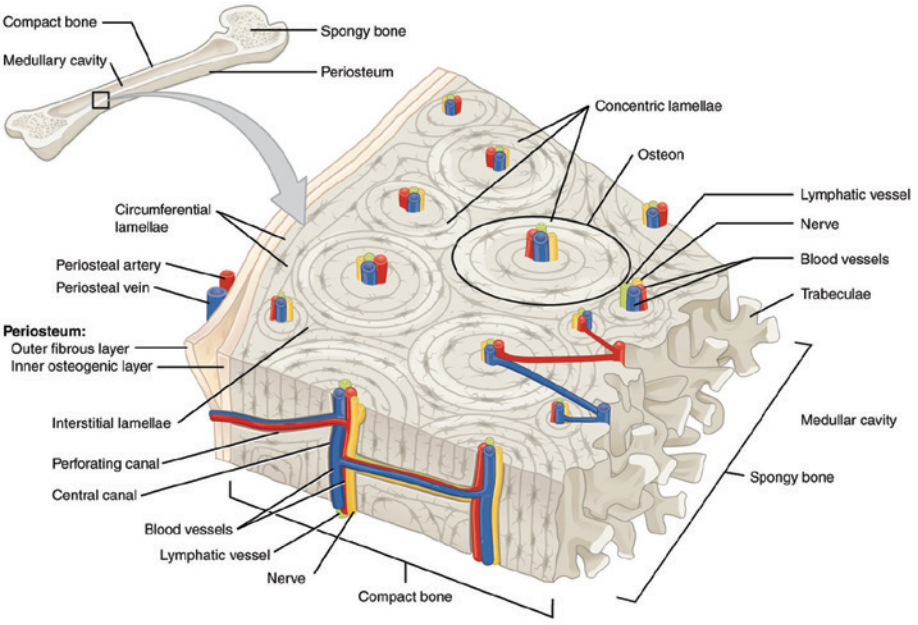


Figure 6.8 Diagram of Compact Bone. (a) This cross-sectional view of compact bone shows the basic structural unit, the osteon. (b) In this micrograph of the osteon, you can clearly see the concentric lamellae and central canals. LM × 40. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Spongy (Cancellous) Bone

Like compact bone, spongy bone, also known as cancellous bone, contains osteocytes housed in lacunae, but they are not arranged in concentric circles. Instead, the lacunae and osteocytes are found in a latticelike network of matrix spikes called **trabeculae** (singular = trabecula; Figure 6.9). The trabeculae may appear to be a random network, but each trabecula forms along lines of stress to provide strength to the bone. The spaces of the trabeculated network provide

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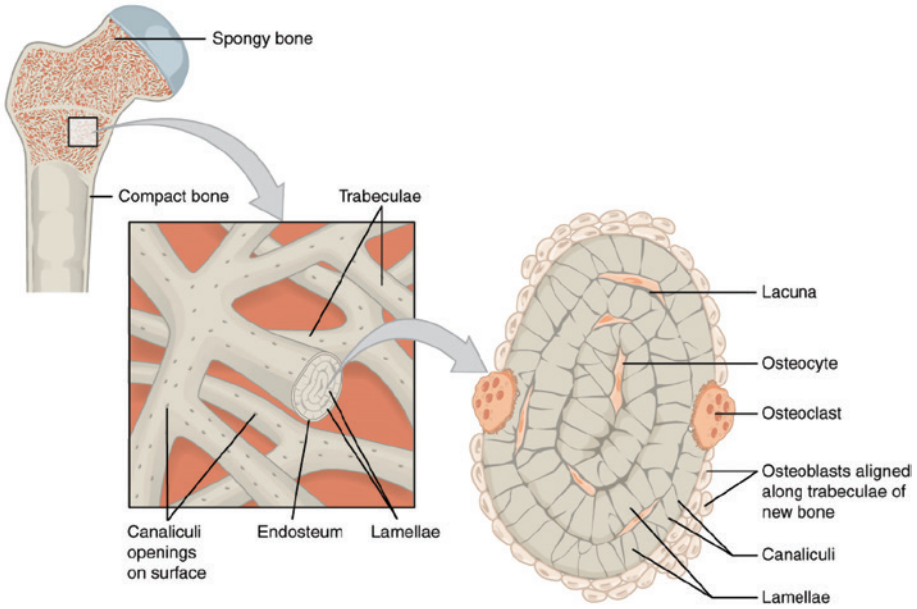


Figure 6.9 Diagram of Spongy Bone. Spongy bone is composed of trabeculae that contain the osteocytes. Red marrow fills the spaces in some bones.

balance to the dense and heavy compact bone by making bones lighter so that muscles can move them more easily. In addition, the spaces in some spongy bones contain red marrow, protected by the trabeculae, where hematopoiesis occurs.

Blood and Nerve Supply

The spongy bone and medullary cavity receive nourishment from arteries that pass through the compact bone. The arteries enter through the **nutrient foramina** (singular = foramen), small openings in the diaphysis (Figure 6.10). The osteocytes in spongy bone are nourished by blood vessels of the periosteum that penetrate spongy bone and blood that circulates in the marrow cavities. As the blood passes through the marrow cavities, it is collected by veins, which then pass out of the bone through the foramina.

In addition to the blood vessels, **nerves** follow the same paths into the bone, where they tend to concentrate in the more metabolically active regions of the bone. The nerves sense pain, and it appears the nerves also play roles in regulating blood supplies and in bone growth, hence their concentrations in metabolically active sites of the bone.

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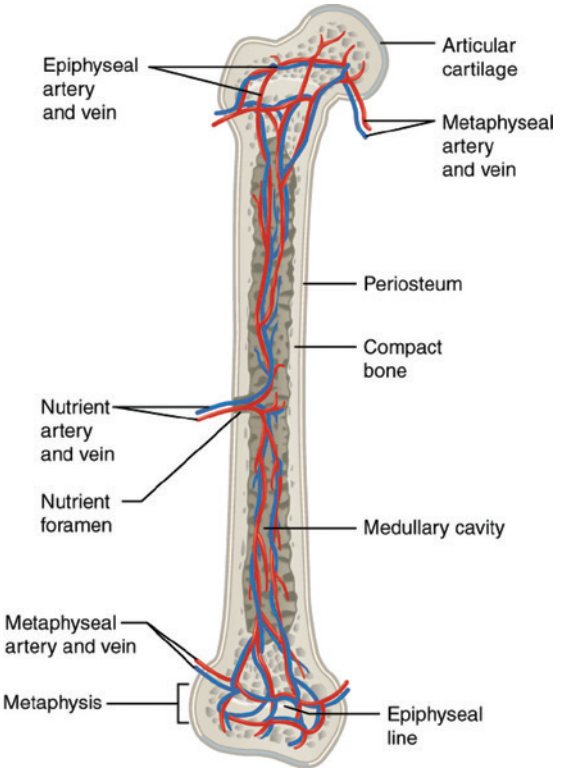


Figure 6.10 Diagram of Blood and Nerve Supply to Bone. Blood vessels and nerves enter the bone through the nutrient foramen.

Interactive Link 6.1

Watch this video (http://oer.aupress.ca/oer-202505/6.1) to see the microscopic features of a bone.

6.4 Bone Formation and Development

Learning Objectives

By the end of this section, you will be able to:

- Explain the function of cartilage
- List the steps of intramembranous ossification
- List the steps of endochondral ossification
- Explain the growth activity at the epiphyseal plate
- Compare and contrast the processes of modelling and remodelling

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In the early stages of embryonic development, the embryo's skeleton consists of fibrous membranes and hyaline cartilage. By the sixth or seventh week of embryonic life, the actual process of bone development, **ossification** (osteogenesis), begins. There are two osteogenic pathways—intramembranous ossification and endochondral ossification—but bone is the same regardless of the pathway that produces it.

Cartilage Templates

Bone is a replacement tissue; that is, it uses a model tissue on which to lay down its mineral matrix. For skeletal development, the most common template is cartilage. During fetal development, a framework is laid down that determines where bones will form. This framework is a flexible, semisolid matrix produced by chondroblasts and consists of hyaluronic acid, chondroitin sulfate, collagen fibres, and water. As the matrix surrounds and isolates chondroblasts, they are called chondrocytes. Unlike most connective tissues, cartilage is avascular, meaning that it has no blood vessels supplying nutrients and removing metabolic wastes. All these functions are carried on by diffusion through the matrix. This is why damaged cartilage does not repair itself as readily as most tissues do.

Throughout fetal development and into childhood growth and development, bone forms on the cartilaginous matrix. By the time a fetus is born, most of the cartilage has been replaced with bone. Some additional cartilage will be replaced throughout childhood, and some cartilage remains in the adult skeleton.

Intramembranous Ossification

During **intramembranous ossification**, compact and spongy bone develop directly from sheets of mesenchymal (undifferentiated) connective tissue. The flat bones of the face, most of the cranial bones, and the clavicles (collarbones) are formed via intramembranous ossification.

The process begins when mesenchymal cells in the embryonic skeleton gather together and begin to differentiate into specialized cells (Figure 6.11a). Some of these cells will differentiate into capillaries, while others will become osteogenic cells and then osteoblasts. Although they will ultimately be spread out by the formation of bone tissue, early osteoblasts appear in a cluster called an **ossification centre**.

The osteoblasts secrete **osteoid**, uncalcified matrix, which calcifies (hardens) within a few days as mineral salts are deposited on it, thereby entrapping the osteoblasts within. Once entrapped, the osteoblasts become osteocytes (Figure 6.11b). As osteoblasts transform into osteocytes, osteogenic cells in the surrounding connective tissue differentiate into new osteoblasts.

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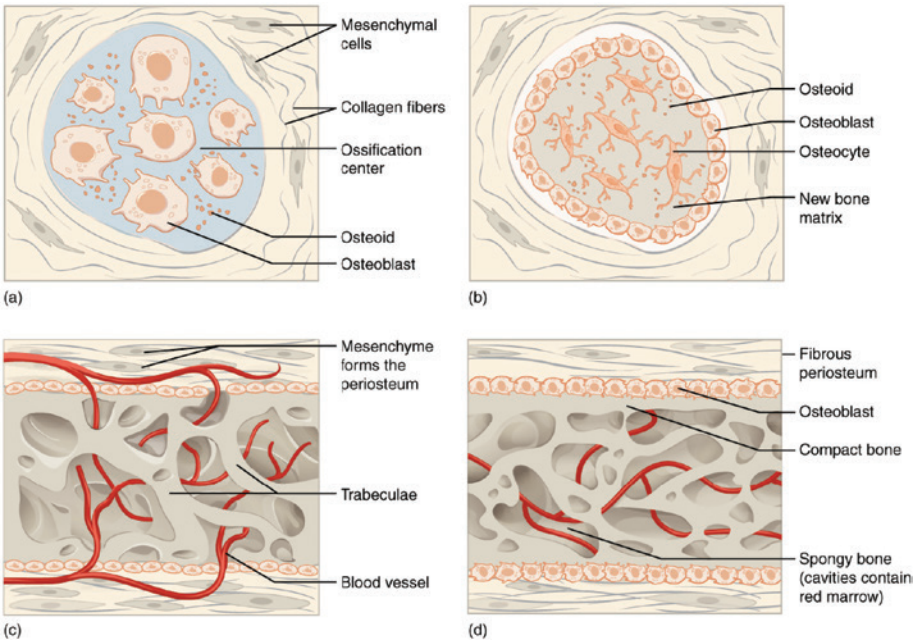


Figure 6.11 Intramembranous Ossification. Intramembranous ossification follows four steps. (a) Mesenchymal cells group into clusters, and ossification centres form. (b) Secreted osteoid traps osteoblasts, which then become osteocytes. (c) Trabecular matrix and periosteum form. (d) Compact bone develops superficial to the trabecular bone, and crowded blood vessels condense into red marrow.

Osteoid (unmineralized bone matrix) secreted around the capillaries results in a trabecular matrix, while osteoblasts on the surface of the spongy bone become the periosteum (Figure 6.11c). The periosteum then creates a protective layer of compact bone superficial to the trabecular bone. The trabecular bone crowds nearby blood vessels, which eventually condense into red marrow (Figure 6.11d).

Intramembranous ossification begins in utero during fetal development and continues on into adolescence. At birth, the skull and clavicles are not fully ossified, nor are the sutures of the skull closed. This allows the skull and shoulders to deform during passage through the birth canal. The last bones to ossify via intramembranous ossification are the flat bones of the face, which reach their adult size at the end of the adolescent growth spurt.

Endochondral Ossification

In **endochondral ossification**, bone develops by *replacing* hyaline cartilage. Cartilage does not become bone. Instead, cartilage serves as a template to be completely replaced by new bone. Endochondral ossification takes much

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longer than intramembranous ossification. Bones at the base of the skull and long bones form via endochondral ossification.

In a long bone, for example, at about 6 to 8 weeks after conception, some of the mesenchymal cells differentiate into chondrocytes (cartilage cells) that form the cartilaginous skeletal precursor of the bones (Figure 6.12a). Soon after, the **perichondrium**, a membrane that covers the cartilage, appears (Figure 6.12b).

As more matrix is produced, the chondrocytes in the centre of the cartilaginous model grow in size. As the matrix calcifies, nutrients can no longer reach the chondrocytes. This results in their death and the disintegration of the surrounding cartilage. Blood vessels invade the resulting spaces, not only enlarging the cavities but also carrying osteogenic cells with them, many of which will become osteoblasts. These enlarging spaces eventually combine to become the medullary cavity.

As the cartilage grows, capillaries penetrate it. This penetration initiates the transformation of the perichondrium into the bone-producing periosteum. Here, the osteoblasts form a periosteal collar of compact bone around the cartilage of the diaphysis. By the second or third month of fetal life, bone cell development and ossification ramp up and create the **primary ossification centre**, a region deep in the periosteal collar where ossification begins (Figure 6.12c).

While these deep changes are occurring, chondrocytes and cartilage continue to grow at the ends of the bone (the future epiphyses), which increases the bone's length at the same time bone is replacing cartilage in the diaphyses (Figure 6.12d). By the time the fetal skeleton is fully formed, cartilage only remains at the joint surface as articular cartilage and between the diaphysis and epiphysis as the epiphyseal plate, the latter of which is responsible for the longitudinal growth of bones. After birth, this same sequence of events (matrix mineralization, death of chondrocytes, invasion of blood vessels from the periosteum, and seeding with osteogenic cells that become osteoblasts) occurs in the epiphyseal regions, and each of these centres of activity is referred to as a **secondary ossification centre** (Figure 6.12e).

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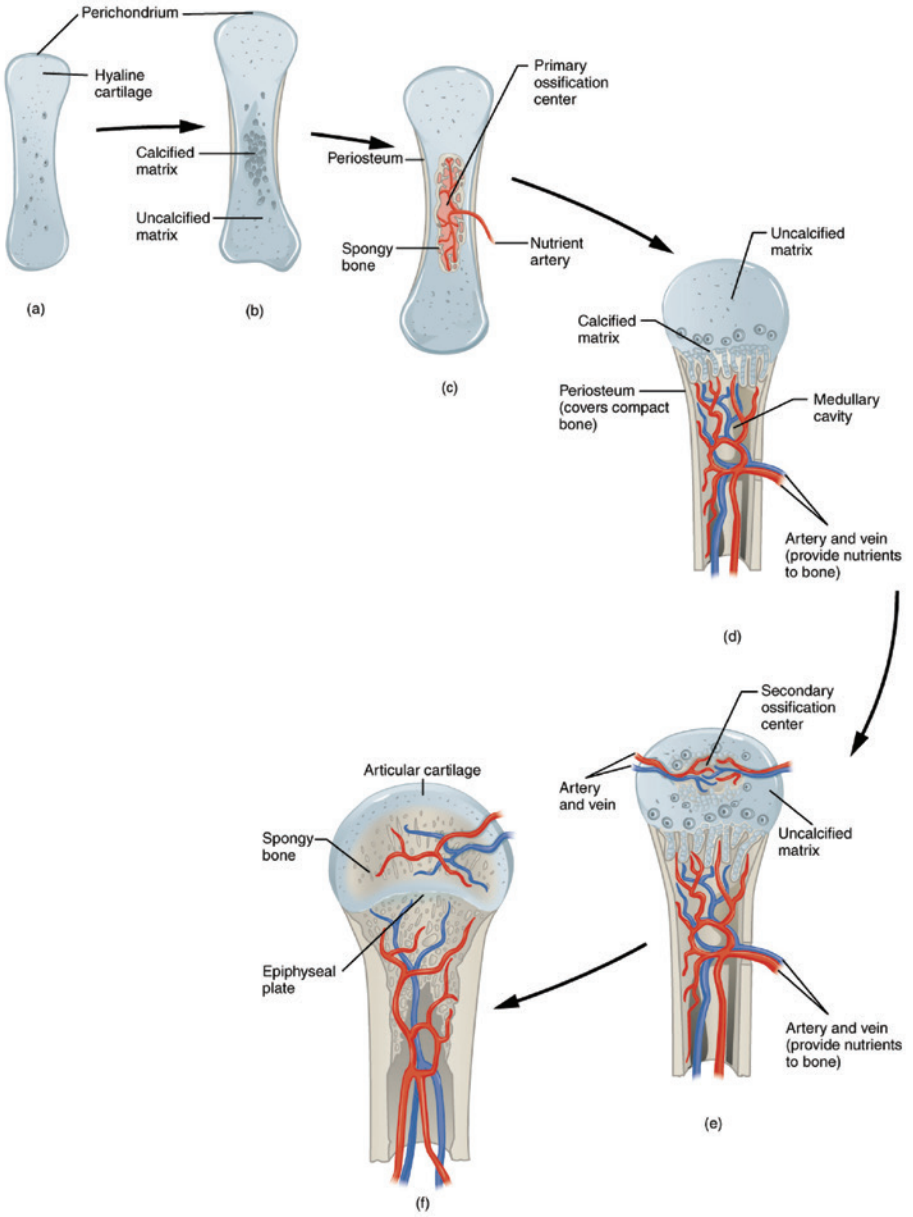


Figure 6.12 Endochondral Ossification. Endochondral ossification follows five steps. (a) Mesenchymal cells differentiate into chondrocytes. (b) The cartilage model of the future bony skeleton and the perichondrium form. (c) Capillaries penetrate cartilage. Perichondrium transforms into periosteum. Periosteal collar develops. Primary ossification centre develops. (d) Cartilage and chondrocytes continue to grow at ends of the bone. (e) Secondary ossification centres develop. Cartilage remains at epiphyseal (growth) plate and at joint surface as articular cartilage.

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How Bones Grow in Length

The epiphyseal plate is the area of growth in a long bone. It is a layer of hyaline cartilage where ossification occurs in immature bones. On the epiphyseal side of the epiphyseal plate, cartilage is formed. On the diaphyseal side, cartilage is ossified, and the diaphysis grows in length. Bones continue to grow in length until early adulthood. The rate of growth is controlled by hormones, which will be discussed later. When the chondrocytes in the epiphyseal plate cease their proliferation and bone replaces the cartilage, longitudinal growth stops. All that remains of the epiphyseal plate is the **epiphyseal line**.

How Bones Grow in Diameter

While bones are increasing in length, they are also increasing in diameter; growth in diameter can continue even after longitudinal growth ceases. This is called appositional growth. Osteoclasts resorb old bone that lines the medullary cavity, while osteoblasts, via intramembranous ossification, produce new bone tissue beneath the periosteum. The erosion of old bone along the medullary cavity and the deposition of new bone beneath the periosteum not only increase the diameter of the diaphysis but also increase the diameter of the medullary cavity. This process is called **modelling**.

Bone Remodelling

The process in which matrix is resorbed on one surface of a bone and deposited on another is known as bone modelling. Modelling primarily takes place during a bone's growth. However, in adult life, bone undergoes **remodelling**, in which resorption of old or damaged bone takes place on the same surface where osteoblasts lay new bone to replace that which is resorbed. Injury, exercise, and other activities lead to remodelling. Those influences are discussed later in the chapter, but even without injury or exercise, about 5 to 10 percent of the skeleton is remodelled annually just by destroying old bone and renewing it with fresh bone.

Interactive Link 6.2

Watch this video (http://oer.aupress.ca/oer-202505/6.2) to see how a bone grows.

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6.5 Fractures: Bone Repair

Learning Objectives

By the end of this section, you will be able to:

- Differentiate among the closed and open reductions
- Describe the steps involved in bone repair

A **fracture** is a broken bone. It will heal whether or not a physician resets it in its anatomical position. If the bone is not reset correctly, the healing process will keep the bone in its deformed position.

When a broken bone is manipulated and set into its natural position without surgery, the procedure is called a **closed reduction**. **Open reduction** requires surgery to expose the fracture and reset the bone. While some fractures can be minor, others are quite severe and result in grave complications. For example, a fractured diaphysis of the femur has the potential to release fat globules into the bloodstream. These can become lodged in the capillary beds of the lungs, leading to respiratory distress and, if not treated quickly, death.

Bone Repair

When a bone breaks, blood flows from any vessel torn by the fracture. These vessels could be in the periosteum, osteons, and medullary cavity. The blood begins to clot, and about six to eight hours after the fracture, the clotting blood has formed a **fracture hematoma** (Figure 6.13a). The disruption of blood flow to the bone results in the death of bone cells around the fracture.

Within about 48 hours after the fracture, chondrocytes from the endosteum have created an **internal callus** (plural = calli) by secreting a fibrocartilaginous matrix between the two ends of the broken bone, while the periosteal chondrocytes and osteoblasts create an **external callus** of hyaline cartilage and bone, respectively, around the outside of the break (Figure 6.13b). This stabilizes the fracture.

Over the next several weeks, osteoclasts resorb the dead bone; osteogenic cells become active, divide, and differentiate into osteoblasts. The cartilage in the calli is replaced by trabecular bone via endochondral ossification (Figure 6.13c).

Eventually, the internal and external calli unite, compact bone replaces spongy bone at the outer margins of the fracture, and healing is complete. A slight swelling may remain on the outer surface of the bone, but quite often, that region undergoes remodelling (Figure 6.13d), and no external evidence of the fracture remains.

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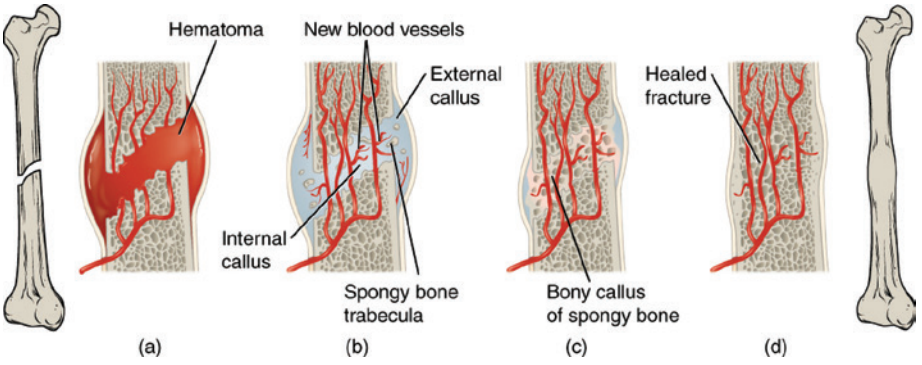


Figure 6.13 Stages in Fracture Repair. The healing of a bone fracture follows a series of progressive steps: (a) A fracture hematoma forms. (b) Internal and external calli form. (c) Cartilage of the calli is replaced by trabecular bone. (d) Remodelling occurs.

Interactive Link 6.3

Visit this website (http://oer.aupress.ca/oer-202505/6.3) to review different types of fractures and then take a short self-assessment quiz.

6.6 Nutrition, Hormones, and Bone Tissue

Learning Objectives

By the end of this section, you will be able to:

- List the nutrients that affect bone health
- Discuss the roles those nutrients play in bone health
- Describe the effects of hormones on bone tissue

All the organ systems of your body are interdependent, and the skeletal system is no exception. The food you take in via your digestive system and the hormones secreted by your endocrine system affect your bones. Even using your muscles to engage in exercise has an impact on your bones.

Nutrition and Bone Tissue

The vitamins and minerals contained in all the food we consume are important for all our organ systems. However, there are certain nutrients that affect bone health.

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Calcium and Vitamin D

You already know that calcium is a critical component of bone, especially in the form of calcium phosphate and calcium carbonate. Since the body cannot make calcium, it must be obtained from the diet. However, calcium cannot be absorbed from the small intestine without vitamin D. Therefore, intake of vitamin D is also critical to bone health. In addition to vitamin D's role in calcium absorption, it also plays a role, though not as clearly understood, in bone remodelling.

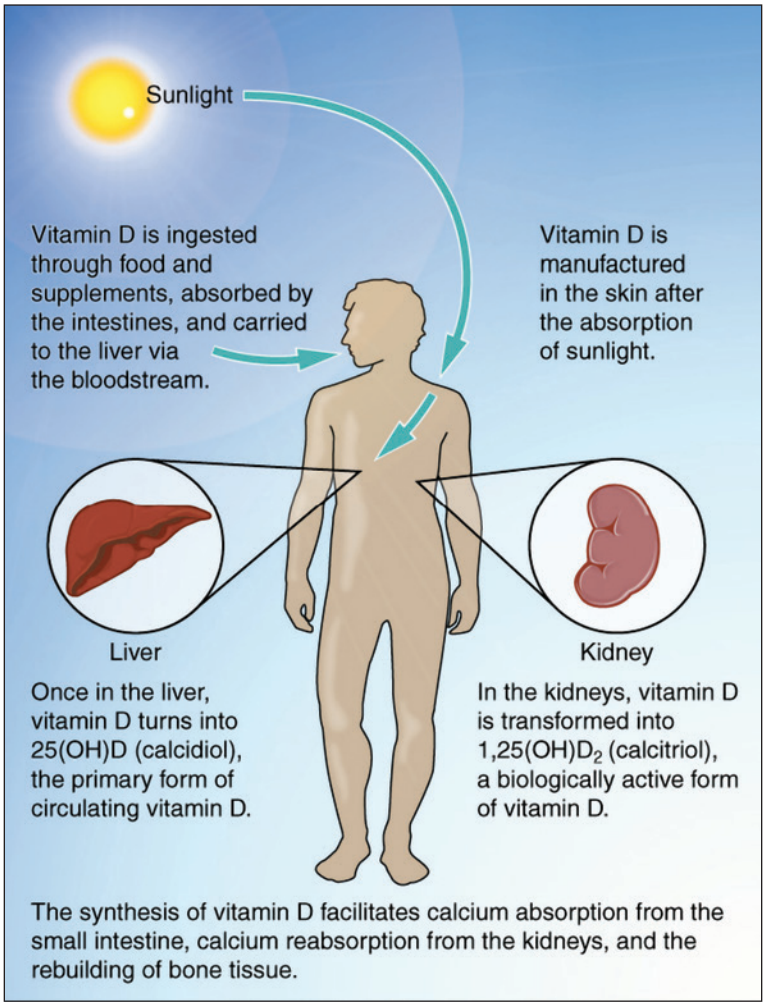


Figure 6.14 Synthesis of Vitamin D. Sunlight is one source of vitamin D.

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Other Nutrients

Vitamin K also supports bone mineralization and may have a synergistic role with vitamin D in the regulation of bone growth. Green leafy vegetables are a good source of vitamin K.

The minerals magnesium and fluoride may also play a role in supporting bone health.

Omega-3 fatty acids have long been known to reduce inflammation in various parts of the body. Inflammation can interfere with the function of osteoblasts, so consuming omega-3 fatty acids, in the diet or in supplements, may also help enhance production of new osseous tissue. Table 6.4 summarizes the role of nutrients in bone health.

Table 6.4 Nutrients and Bone Health

Nutrient	Role in bone health
Calcium	Needed to make calcium phosphate and calcium carbonate, which form the hydroxyapatite crystals that give bone its hardness
Vitamin D	Needed for calcium absorption
Vitamin K	Supports bone mineralization; may have synergistic effect with vitamin D
Magnesium	Structural component of bone
Fluoride	Structural component of bone
Omega-3 fatty acids	Reduces inflammation that may interfere with osteoblast function

Hormones and Bone Tissue

The endocrine system produces and secretes hormones, many of which interact with the skeletal system. These hormones are involved in controlling bone growth, maintaining bone once it is formed, and remodelling it.

Hormones That Influence Osteoblasts and/or Maintain the Matrix

Several hormones are necessary for controlling bone growth and maintaining the bone matrix. The pituitary gland secretes growth hormone (GH), which, as its name implies, controls bone growth in several ways. It triggers chondrocyte proliferation in epiphyseal plates, resulting in the increasing length of long bones. GH also increases calcium retention, which enhances mineralization, and stimulates osteoblastic activity, which improves bone density.

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Thyroxine, a hormone secreted by the thyroid gland, promotes osteoblastic activity and the synthesis of bone matrix.

During puberty, the sex hormones (estrogen and testosterone) also come into play. They too promote osteoblastic activity and production of bone matrix, and they are responsible for the growth spurt that often occurs during adolescence. They also promote the conversion of the epiphyseal plate to the epiphyseal line (i.e., cartilage to its bony remnant), thus bringing an end to the longitudinal growth of bones.

Calcitriol, the active form of vitamin D, is produced by the kidneys and stimulates the absorption of calcium and phosphate from the digestive tract.

Hormones That Influence Osteoclasts

Bone modelling and remodelling require osteoclasts to resorb unneeded, damaged, or old bone and osteoblasts to lay down new bone. Two hormones that affect the osteoclasts are parathyroid hormone (PTH) and calcitonin.

PTH stimulates osteoclast proliferation and activity. As a result, calcium is released from the bones into the circulation, thus increasing the calcium ion concentration in the blood. PTH also promotes the reabsorption of calcium by the kidney tubules, which can affect calcium homeostasis (see 6.7 Calcium Homeostasis).

The small intestine is also affected by PTH, albeit indirectly. Because another function of PTH is to stimulate the synthesis of vitamin D, and because vitamin D promotes intestinal absorption of calcium, PTH indirectly increases calcium uptake by the small intestine. Calcitonin, a hormone secreted by the thyroid gland, has some effects that counteract those of PTH.

Calcitonin inhibits osteoclast activity and stimulates calcium uptake by the bones, thus reducing the concentration of calcium ions in the blood. As evidenced by their opposing functions in maintaining calcium homeostasis, PTH and calcitonin are generally *not* secreted at the same time. Table 6.5 summarizes the hormones that influence the skeletal system.

6.7 Calcium Homeostasis: Interactions of the Skeletal System and Other Organ Systems

Learning Objectives

By the end of this section, you will be able to:

- Describe the effect of too much or too little calcium on the body
- Explain the process of calcium homeostasis

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Table 6.5 Hormones That Affect the Skeletal System

Hormone	Role
Growth hormone	Increases length of long bones, enhances mineralization, and improves bone density
Thyroxine	Stimulates bone growth and promotes synthesis of bone matrix
Sex hormones	Promote osteoblastic activity and production of bone matrix; responsible for adolescent growth spurt; promote conversion of epiphyseal plate to epiphyseal line
Calcitriol	Stimulates absorption of calcium and phosphate from digestive tract
Parathyroid hormone	Stimulates osteoclast proliferation and resorption of bone by osteoclasts; promotes reabsorption of calcium by kidney tubules; indirectly increases calcium absorption by small intestine
Calcitonin	Inhibits osteoclast activity and stimulates calcium uptake by bones

Calcium is not only the most abundant mineral in bone; it is also the most abundant mineral in the human body. Calcium ions are needed not only for bone mineralization but for tooth health, regulation of the heart rate and strength of contraction, blood coagulation, contraction of smooth and skeletal muscle cells, and regulation of nerve impulse conduction. The normal level of calcium in the blood is about 10 mg/dL (milligrams per decilitre). When the body cannot maintain this level, a person will experience hypo- or hypercalcemia.

Hypocalcemia, a condition characterized by abnormally low levels of calcium, can have adverse effects on a number of different body systems, including circulation, muscles, nerves, and bone. Without adequate calcium, blood has difficulty coagulating, the heart may skip beats or stop beating altogether, muscles may have difficulty contracting, nerves may have difficulty functioning, and bones may become brittle. The causes of hypocalcemia can range from hormonal imbalances to an improper diet. Treatments vary according to the cause, but prognoses are generally good.

Conversely, in **hypercalcemia**, a condition characterized by abnormally high levels of calcium, the nervous system is underactive, which results in lethargy, sluggish reflexes, constipation and loss of appetite, confusion, and in severe cases, coma.

Calcium homeostasis is critical. The skeletal, endocrine, and digestive systems play a role in this, but the kidneys do, too. These body systems work together to maintain a normal calcium level in the blood.

Calcium is a chemical element that cannot be produced by any biological processes. The only way it can enter the body is through the diet. The bones

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act as a storage site for calcium: The body deposits calcium in the bones when blood levels get too high, and it releases calcium when blood levels drop too low. This process is regulated by PTH, vitamin D, and calcitonin.

Cells of the parathyroid gland have plasma membrane receptors for calcium. When calcium is not binding to these receptors, the cells release PTH, which stimulates osteoclast proliferation and resorption of bone by osteoclasts. This demineralization process releases calcium into the blood. PTH promotes reabsorption of calcium from the urine by the kidneys, so that the calcium returns to the blood. Finally, PTH stimulates the synthesis of vitamin D, which in turn stimulates calcium absorption from any digested food in the small intestine.

When all these processes return blood calcium levels to normal, there is enough calcium to bind with the receptors on the surface of the cells of the parathyroid glands, and this cycle of events is turned off.

When blood levels of calcium get too high, the thyroid gland is stimulated to release calcitonin, which inhibits osteoclast activity and stimulates calcium uptake by the bones but also decreases reabsorption of calcium by the kidneys. All these actions lower blood levels of calcium. When blood calcium levels return to normal, the thyroid gland stops secreting calcitonin.

Key Terms

articular cartilage: Thin layer of cartilage covering an epiphysis; reduces friction and acts as a shock absorber.

articulation: Where two bone surfaces meet.

bone (osseous tissue): Hard, dense connective tissue that forms the structural elements of the skeleton.

canaliculi (singular = canaliculus): Channels within the bone matrix that house one of an osteocyte's many cytoplasmic extensions that it uses to communicate and receive nutrients.

cartilage: Semirigid connective tissue found on the skeleton in areas where flexibility and smooth surfaces support movement.

central canal (Haversian canal): Longitudinal channel in the centre of each osteon; contains blood vessels, nerves, and lymphatic vessels.

closed reduction: Manual manipulation of a broken bone to set it into its natural position without surgery.

compact bone: Dense osseous tissue that can withstand compressive forces.

diaphysis: Tubular shaft that runs between the proximal and distal ends of a long bone.

endochondral ossification: Process in which bone forms by replacing hyaline cartilage.

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endosteum: Delicate membranous lining of a bone's medullary cavity.
epiphyseal line: Completely ossified remnant of the epiphyseal plate.
epiphyseal plate (also growth plate): Sheet of hyaline cartilage in the metaphysis of an immature bone; replaced by bone tissue as the organ grows in length.
epiphysis: Wide section at each end of a long bone; filled with spongy bone and red marrow.
external callus: Collar of hyaline cartilage and bone that forms around the outside of a fracture.
flat bone: Thin and curved bone; serves as a point of attachment for muscles and protects internal organs.
fracture: Broken bone.
fracture hematoma: Blood clot that forms at the site of a broken bone.
hematopoiesis: Production of blood cells, which occurs in the red marrow of the bones.
hole: Opening or depression in a bone.
hypercalcemia: Condition characterized by abnormally high levels of calcium.
hypocalcemia: Condition characterized by abnormally low levels of calcium.
internal callus: Fibrocartilaginous matrix, in the endosteal region, between the two ends of a broken bone.
intramembranous ossification: Process by which bone forms directly from mesenchymal tissue.
irregular bone: Bone of complex shape; protects internal organs from compressive forces.
lacunae (singular = lacuna): Spaces in a bone that house an osteocyte.
lamellae: Concentric rings of calcified matrix in the centre of each osteon.
long bone: Cylinder-shaped bone that is longer than it is wide; functions as a lever.
medullary cavity: Hollow region of the diaphysis; filled with yellow marrow.
modelling: Process, during bone growth, by which bone is resorbed on one surface of a bone and deposited on another.
nutrient foramen: Small opening in the middle of the external surface of the diaphysis, through which an artery enters the bone to provide nourishment.
open reduction: Surgical exposure of a bone to reset a fracture.
ossification (also osteogenesis): Bone formation.
ossification centre: Cluster of osteoblasts found in the early stages of intramembranous ossification.
osteoblast: Cell responsible for forming new bone.

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osteoclast: Cell responsible for resorbing bone.
osteocyte: Primary cell in mature bone; responsible for maintaining the matrix.
osteogenic cell: Undifferentiated cell with high mitotic activity; the only bone cells that divide; they differentiate and develop into osteoblasts.
osteoid: Uncalcified bone matrix secreted by osteoblasts.
osteon (also Haversian system): Basic structural unit of compact bone; made of concentric layers of calcified matrix.
perforating canal (also Volkmann's canal): Channel that branches off from the central canal and houses vessels and nerves that extend to the periosteum and endosteum.
perichondrium: Membrane that covers cartilage.
periosteum: Fibrous membrane covering the outer surface of bone and continuous with ligaments.
primary ossification centre: Region, deep in the periosteal collar, where bone development starts during endochondral ossification.
projection: Bone markings where part of the surface sticks out above the rest of the surface, where tendons and ligaments attach.
red marrow: Connective tissue in the interior cavity of a bone where hematopoiesis takes place.
remodelling: Process by which osteoclasts resorb old or damaged bone at the same time as and on the same surface where osteoblasts form new bone to replace that which is resorbed.
secondary ossification centre: Region of bone development in the epiphyses.
sesamoid bone: Small, round bone embedded in a tendon; protects the tendon from compressive forces.
short bone: Cube-shaped bone that is approximately equal in length, width, and thickness; provides limited motion.
skeletal system: Organ system composed of bones and cartilage that provides for movement, support, and protection.
spongy bone (also cancellous bone): Trabeculated osseous tissue that supports shifts in weight distribution.
trabeculae (singular = trabecula): Spikes or sections of the latticelike matrix in spongy bone.
yellow marrow: Connective tissue in the interior cavity of a bone where fat is stored.

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Chapter Review

6.1 The Functions of the Skeletal System

The major functions of the bones are body support, facilitation of movement, protection of internal organs, storage of minerals and fat, and hematopoiesis. Together, the muscular system and skeletal system are known as the musculoskeletal system.

6.2 Bone Classification

Bones can be classified according to their shapes. Long bones, such as the femur, are longer than they are wide. Short bones, such as the carpals, are approximately equal in length, width, and thickness. Flat bones are thin, but are often curved, such as the ribs. Irregular bones such as those of the face have no characteristic shape. Sesamoid bones, such as the patellae, are small, round, and located in tendons.

6.3 Bone Structure

A hollow medullary cavity filled with yellow marrow runs the length of the diaphysis of a long bone. The walls of the diaphysis are compact bone. The epiphyses, which are wider sections at each end of a long bone, are filled with spongy bone and red marrow. The epiphyseal plate, a layer of hyaline cartilage, is replaced by osseous tissue as the organ grows in length. The medullary cavity has a delicate membranous lining called the endosteum. The outer surface of bone, except in regions covered with articular cartilage, is covered with a fibrous membrane called the periosteum. Flat bones consist of two layers of compact bone surrounding a layer of spongy bone. Bone markings depend on the function and location of bones. Articulations are places where two bones meet. Projections stick out from the surface of the bone and provide attachment points for tendons and ligaments. Holes are openings or depressions in the bones.

Bone matrix consists of collagen fibres and organic ground substance, primarily hydroxyapatite formed from calcium salts. Osteogenic cells develop into osteoblasts. Osteoblasts are cells that make new bone. They become osteocytes, the cells of mature bone, when they get trapped in the matrix. Osteoclasts engage in bone resorption. Compact bone is dense and composed of osteons, while spongy bone is less dense and made up of trabeculae. Blood vessels and nerves enter the bone through the nutrient foramina to nourish and innervate bones.

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6.4 Bone Formation and Development

All bone formation is a replacement process. Embryos develop a cartilaginous skeleton and various membranes. During development, these are replaced by bone through the ossification process. In intramembranous ossification, bone develops directly from sheets of mesenchymal connective tissue. In endochondral ossification, bone develops by replacing hyaline cartilage. Activity in the epiphyseal plate enables bones to grow in length. Modelling allows bones to grow in diameter. Remodelling occurs as bone is resorbed and replaced by new bone. Osteogenesis imperfecta is a genetic disease in which collagen production is altered, resulting in fragile, brittle bones.

6.5 Fractures: Bone Repair

Fractured bones may be repaired by closed reduction or open reduction. Healing of fractures begins with the formation of a hematoma, followed by internal and external calli. Osteoclasts resorb dead bone, while osteoblasts create new bone that replaces the cartilage in the calli. The calli eventually unite, remodelling occurs, and healing is complete.

6.6 Nutrition, Hormones, and Bone Tissue

Mechanical stress stimulates the deposition of mineral salts and collagen fibres within bones. Calcium, the predominant mineral in bone, cannot be absorbed from the small intestine if vitamin D is lacking. Vitamin K supports bone mineralization and may have a synergistic role with vitamin D. Magnesium and fluoride, as structural elements, play a supporting role in bone health. Omega-3 fatty acids reduce inflammation and may promote production of new osseous tissue. Growth hormone increases the length of long bones, enhances mineralization, and improves bone density. Thyroxine stimulates bone growth and promotes the synthesis of bone matrix. The sex hormones (estrogen and testosterone) promote osteoblastic activity and the production of bone matrix, are responsible for the adolescent growth spurt, and promote closure of the epiphyseal plates. Parathyroid hormone (PTH) stimulates osteoclast proliferation and resorption of bone by osteoclasts. Vitamin D plays a synergistic role with PTH in stimulating the osteoclasts. Additional functions of PTH include promoting reabsorption of calcium by kidney tubules and indirectly increasing calcium absorption from the small intestine. Calcitonin inhibits osteoclast activity and stimulates calcium uptake by bones.

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6.7 Calcium Homeostasis: Interactions of the Skeletal System and Other Organ Systems

Calcium is the most abundant mineral in the human body and is essential for bone and tooth health, muscle contraction, heart regulation, nerve transmission, and blood clotting. Normal blood calcium levels are about 10 mg/dL. Low calcium levels (hypocalcemia) can cause problems with circulation, muscle and nerve function, and bone strength, leading to symptoms such as irregular heartbeat, poor muscle contraction, and brittle bones. It can result from hormonal issues or dietary deficiencies but is usually treatable. High calcium levels (hypercalcemia) depress nervous system activity, causing fatigue, constipation, confusion, and potentially coma. Calcium balance, or homeostasis, involves the skeletal, endocrine, digestive, and renal systems. Calcium enters the body only through diet, and bones store excess calcium or release it when needed. Parathyroid hormone (PTH), vitamin D, and calcitonin regulate this balance: PTH raises calcium levels by stimulating bone resorption, kidney reabsorption, and intestinal absorption, while calcitonin lowers calcium levels by inhibiting bone breakdown and increasing kidney excretion. These feedback mechanisms maintain calcium within a narrow, healthy range essential for proper physiological function.

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7

Axial Skeleton

Chapter Objectives

After studying this chapter, you will be able to:

- Describe the functions of the skeletal system and define its two major subdivisions
- Identify the bones and bony structures of the skull, the cranial suture lines, the cranial fossae, and the openings in the skull
- Discuss the vertebral column and regional variations in its bony components and curvatures
- Describe the components of the thoracic cage
- Discuss the embryonic development of the axial skeleton

The skeletal system forms the rigid internal framework of the body. It consists of the bones, cartilages, and ligaments. Bones support the weight of the body, allow for body movements, and protect internal organs. Cartilage provides flexible strength and support for body structures such as the thoracic cage, the external ear, and the trachea and larynx. At joints of the body, cartilage can also unite adjacent bones or provide cushioning between them. Ligaments are the strong connective tissue bands that hold the bones at a movable joint together and serve to prevent excessive movements of the joint that would result in injury. Providing movement of the skeleton are the muscles of the body, which are firmly attached to the skeleton via connective tissue structures called tendons. As muscles contract, they pull on the bones to produce movements of the body.

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7.1 Divisions of the Skeletal System

Learning Objectives

By the end of this section, you will be able to:

- Discuss the functions of the skeletal system
- Distinguish between the axial skeleton and appendicular skeleton
- Define the axial skeleton and its components
- Define the appendicular skeleton and its components

The skeletal system includes all the bones, cartilages, and ligaments of the body that support and give shape to the body and body structures. The **skeleton** consists of the bones of the body. For adults, there are 206 bones in the skeleton. Younger individuals have higher numbers of bones because some bones fuse together during childhood and adolescence to form an adult bone. The primary functions of the skeleton are to provide a rigid, internal structure that can support the weight of the body against the force of gravity and to provide a structure upon which muscles can act to produce movements of the body. The lower portion of the skeleton is specialized for stability during walking or running. In contrast, the upper skeleton has greater mobility and ranges of motion, including the features that allow you to lift and carry objects or turn your head and trunk.

In addition to providing for support and movements of the body, the skeleton has protective and storage functions. It protects the internal organs, including the brain, spinal cord, heart, lungs, and pelvic organs. The bones of the skeleton serve as the primary storage site for important minerals such as calcium and phosphate. The bone marrow found within bones stores triglycerides and houses the blood-cell producing tissue of the body.

The skeleton is subdivided into two major divisions—axial and appendicular.

The Axial Skeleton

The **axial skeleton** forms the vertical, central axis of the body and includes all bones of the head, neck, chest, and back (Figure 7.1). It serves to protect the brain, spinal cord, heart, and lungs. It also serves as the attachment site for muscles that move the head, neck, and back, and for muscles that act across the shoulder and hip joints to move their corresponding limbs.

The axial skeleton of the adult consists of 80 bones, including the **skull**, the **vertebral column**, and the **thoracic cage**. The skull is formed by 22 bones. Also associated with the head are an additional seven bones, including the **hyoid**

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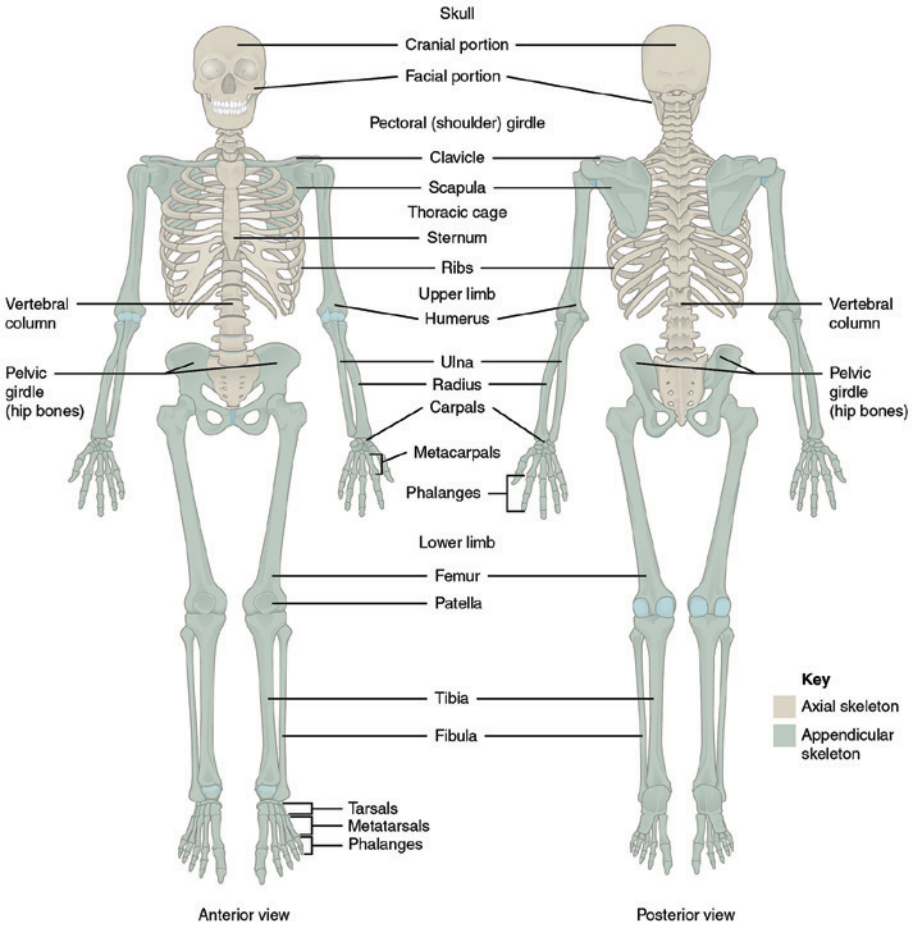


Figure 7.1 Axial and Appendicular Skeleton. The axial skeleton supports the head, neck, back, and chest and thus forms the vertical axis of the body. It consists of the skull, vertebral column (including the sacrum and coccyx), and thoracic cage, formed by the ribs and sternum. The appendicular skeleton is made up of all bones of the upper and lower limbs.

bone and the **ear ossicles** (three small bones found in each middle ear). The vertebral column consists of 24 bones, each called a **vertebra**, plus the **sacrum** and **coccyx**. The thoracic cage includes the 12 pairs of **ribs**, and the **sternum**, the flattened bone of the anterior chest.

The Appendicular Skeleton

The **appendicular skeleton** includes all bones of the upper and lower limbs, plus the bones that attach each limb to the axial skeleton. There are 126 bones in the appendicular skeleton of an adult. The bones of the appendicular skeleton are covered in a separate chapter.

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7.2 The Skull

Learning Objectives

By the end of this section, you will be able to:

- List and identify the bones of the brain case and face
- Locate the major suture lines of the skull and name the bones associated with each
- Define the paranasal sinuses and identify the location of each
- Name the bones that make up the walls of the orbit
- Identify the bones and structures that form the nasal septum and nasal conchae and locate the hyoid bone

The **cranium** (skull) is the skeletal structure of the head that supports the face and protects the brain. It is subdivided into the **facial bones** and the **brain case**, or cranial vault (Figure 7.2). The facial bones underlie the facial structures, form the nasal cavity, enclose the eyeballs, and support the teeth of the upper and lower jaws. The rounded brain case surrounds and protects the brain and houses the middle and inner ear structures.

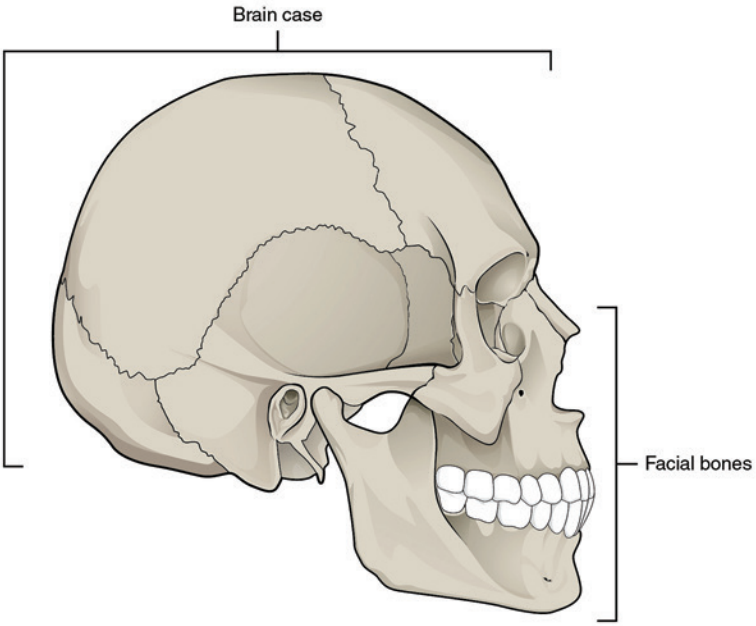


Figure 7.2 Parts of the Skull. The skull consists of the rounded brain case that houses the brain and the facial bones that form the upper and lower jaws, nose, orbits, and other facial structures.

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In the adult, the skull consists of 22 individual bones, 21 of which are immobile and united into a single unit. The 22nd bone is the **mandible** (lower jaw), which is the only movable bone of the skull.

Interactive Link 7.1

Watch this video (http://oer.aupress.ca/oer-202505/7.1) to view a rotating and exploded skull with colour-coded bones. Which bone (yellow) is centrally located and joins with most of the other bones of the skull?

Anterior View of the Skull

The anterior skull consists of the facial bones and provides the bony support for the eyes and structures of the face. This view of the skull is dominated by the openings of the orbits and the nasal cavity. Also seen are the upper and lower jaws, with their respective teeth (Figure 7.3).

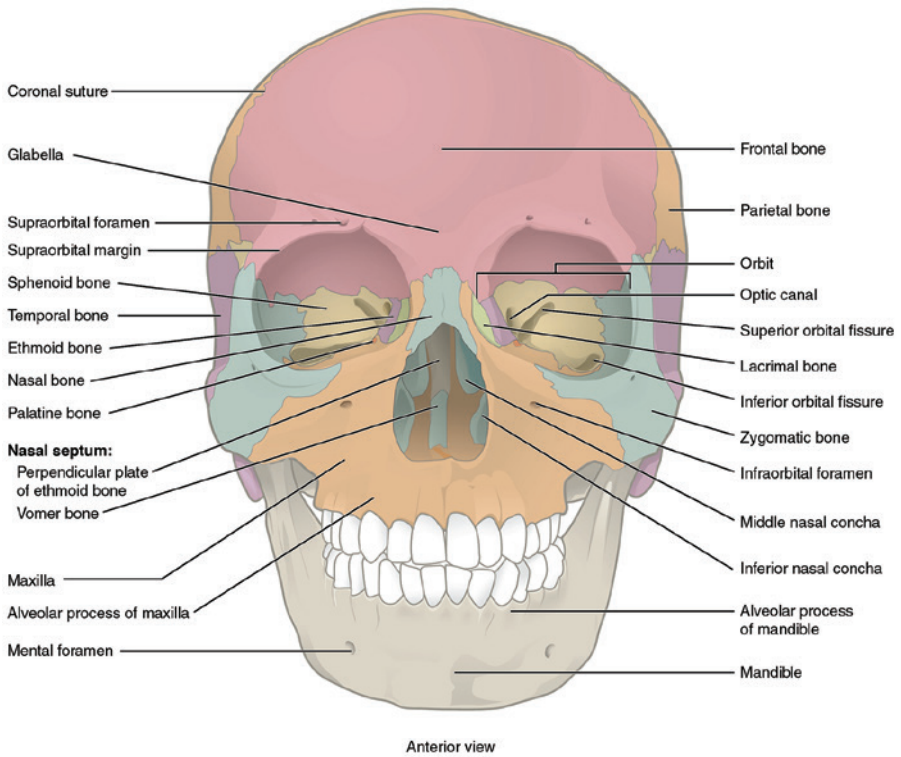


Figure 7.3 Anterior View of Skull. An anterior view of the skull shows the bones that form the forehead, orbits (eye sockets), nasal cavity, nasal septum, and upper and lower jaws.

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The **orbit** is the bony socket that houses the eyeball and muscles that move the eyeball or open the upper eyelid.

Inside the nasal area of the skull, the **nasal cavity** is divided into halves by the **nasal septum**. The upper portion of the nasal septum is formed by the **perpendicular plate of the ethmoid bone** and the lower portion is the **vomer bone**. Each side of the nasal cavity is triangular in shape, with a broad inferior space that narrows superiorly. When looking into the nasal cavity from the front of the skull, two bony plates are seen projecting from each lateral wall: **inferior nasal concha** and **middle nasal concha**. A third bony plate, also part of the ethmoid bone, is the **superior nasal concha**. It is much smaller and out of sight, above the middle concha. The superior nasal concha is located just lateral to the perpendicular plate, in the upper nasal cavity.

Lateral View of the Skull

A lateral view of the skull is dominated by the large, rounded brain case above and the upper and lower jaws with their teeth below (Figure 7.4). Separating these areas is the bridge of bone called the **zygomatic arch**. One of the major muscles that pulls the mandible upward during biting and chewing arises from the zygomatic arch.

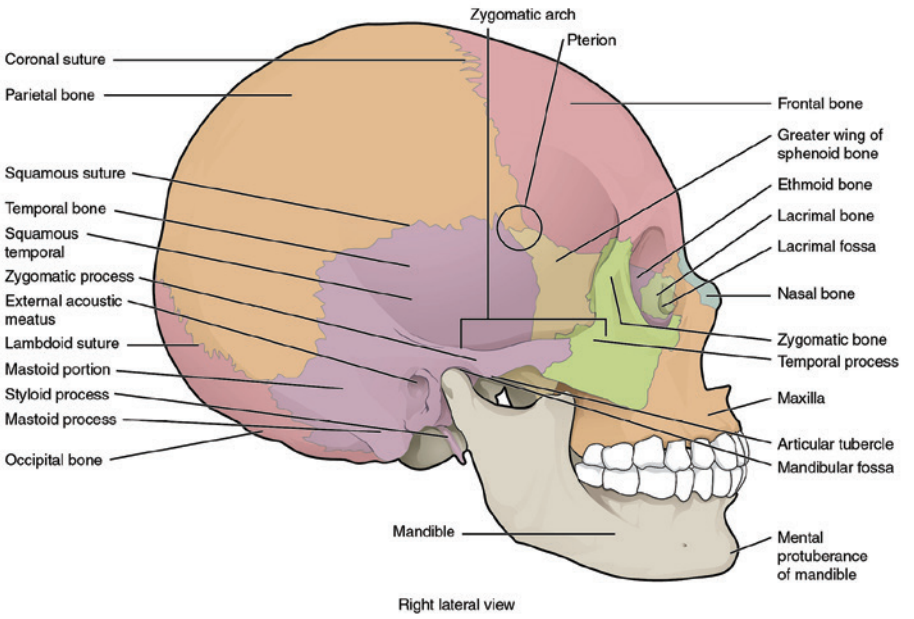


Figure 7.4 Lateral View of Skull. The lateral skull shows the large, rounded brain case, zygomatic arch, and upper and lower jaws. The zygomatic arch is formed jointly by the zygomatic process of the temporal bone and the temporal process of the zygomatic bone. The shallow space above the zygomatic arch is the temporal fossa. The space inferior to the zygomatic arch and deep to the posterior mandible is the infratemporal fossa.

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On the lateral side of the brain case, above the level of the zygomatic arch, is a shallow space called the **temporal fossa** (plural = fossae). It contains muscles that act on the mandible during chewing.

Bones of the Brain Case

The brain case contains and protects the brain. The interior space that is almost completely occupied by the brain is called the **cranial cavity** (Figure 7.5). This cavity is bounded by the lateral and posterior sides of the skull and, superiorly, the rounded top of the skull, which is called the **calvaria** (skullcap). The bones that form the top and sides of the brain case are usually referred to as the "flat" bones of the skull.

The brain case consists of eight bones. These include the paired parietal and temporal bones and the unpaired frontal, occipital, sphenoid, and ethmoid bones.

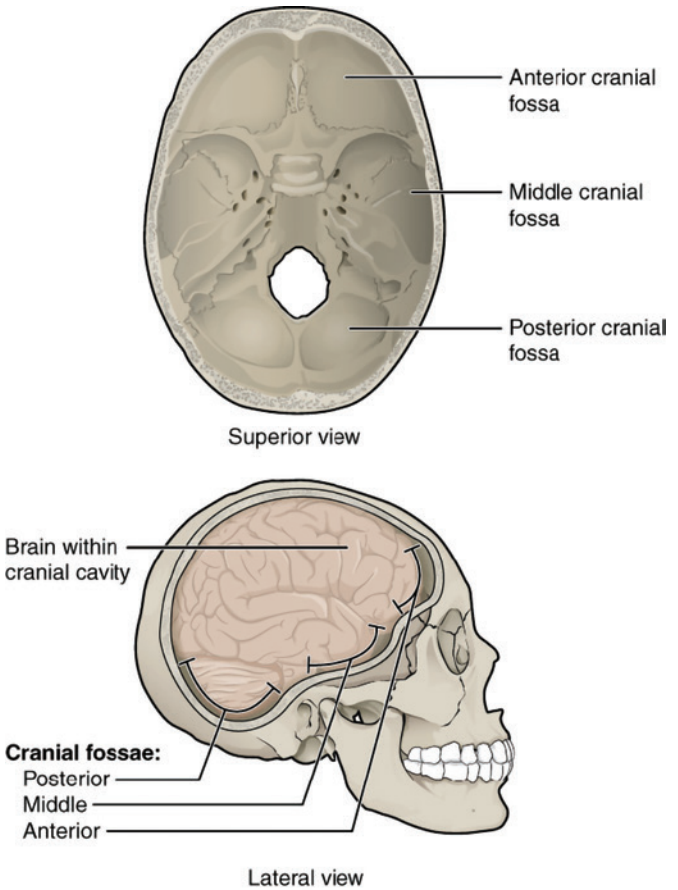


Figure 7.5 Cranial Fossae. The bones of the brain case surround and protect the brain, which occupies the cranial cavity. The base of the brain case, which forms the floor of cranial cavity, is subdivided into the shallow anterior cranial fossa, the middle cranial fossa, and the deep posterior cranial fossa.

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Parietal Bone

The **parietal bones** form most of the upper lateral sides of the skull (see Figure 7.4). These are paired bones, with the right and left parietal bones joining together at the top of the skull. Each parietal bone is also bounded anteriorly by the frontal bone, inferiorly by the temporal bone, and posteriorly by the occipital bone.

Temporal Bone

The **temporal bone** forms the lower lateral side of the skull (see Figure 7.4). The temporal bone is subdivided into several regions (Figure 7.6). The flattened, upper portion is the squamous portion of the temporal bone. Below this area and projecting anteriorly is the zygomatic process of the temporal bone, which forms the posterior portion of the zygomatic arch. Posteriorly is the mastoid portion of the temporal bone. Projecting inferiorly from this region is a large prominence, the **mastoid process**, which serves as a muscle attachment site. The mastoid process can easily be felt on the side of the head just behind your earlobe.

Important landmarks of the temporal bone, as shown in Figure 7.7, include the following:

- **External acoustic meatus** (ear canal)—This is the large opening on the lateral side of the skull that is associated with the ear.
- **Internal acoustic meatus**—This opening is located inside the cranial cavity, on the medial side of the petrous ridge. It connects to the middle and inner ear cavities of the temporal bone.
- **Mandibular fossa**—This is the deep, oval-shaped depression located on the external base of the skull, just in front of the external acoustic meatus. The mandible (lower jaw) joins with the skull at this site as part of the temporomandibular joint, which allows for movements of the mandible during opening and closing of the mouth.
- **Styloid process**—Posterior to the mandibular fossa on the external base of the skull is an elongated, downward bony projection called the styloid process, so named because of its resemblance to a stylus (a pen or writing tool). This structure serves as an attachment site for several small muscles and for a ligament that supports the hyoid bone of the neck. (See also Figure 7.6.)

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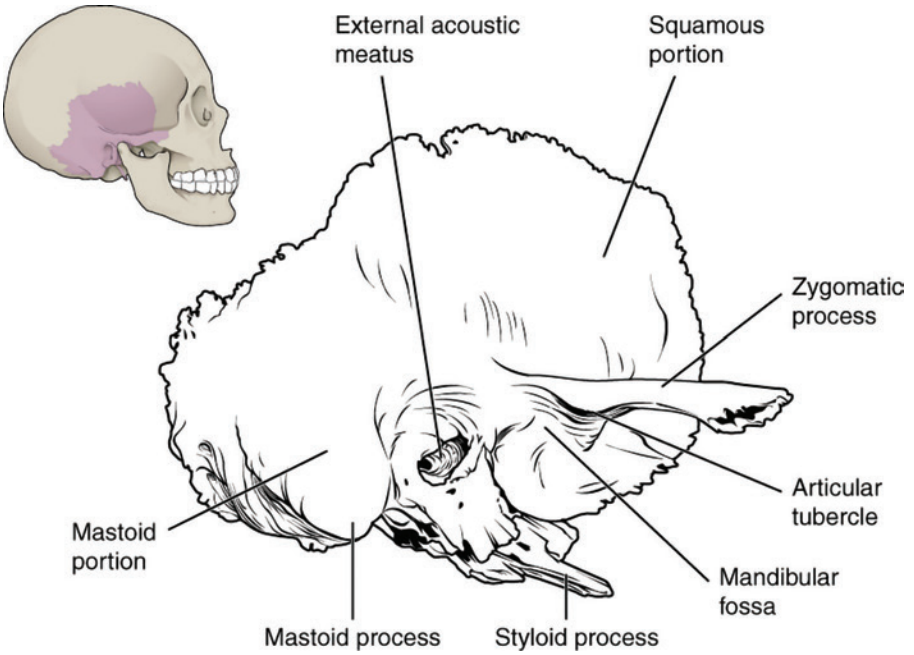


Figure 7.6 Temporal Bone. A lateral view of the isolated temporal bone shows the squamous, mastoid, and zygomatic portions of the temporal bone.

Frontal Bone

The **frontal bone** is the single bone that forms the forehead. At its anterior midline, between the eyebrows, there is a slight depression called the **glabella** (see Figure 7.3). The frontal bone also forms the supraorbital margin of the orbit. Near the middle of this margin is the **supraorbital foramen**, the opening that provides passage for a sensory nerve to the forehead. The frontal bone is thickened just above each supraorbital margin, forming rounded brow ridges. These are located just behind your eyebrows and vary in size among individuals, although they are generally larger in males. Inside the cranial cavity, the frontal bone extends posteriorly. This flattened region forms both the roof of the orbit below and the floor of the anterior cranial cavity above (see Figure 7.7b).

Occipital Bone

The **occipital bone** is the single bone that forms the posterior skull and posterior base of the cranial cavity (Figure 7.8; see also Figure 7.7). On its outside surface, at the posterior midline, is a small protrusion called the **external occipital protuberance**, which serves as an attachment site for a ligament of the posterior neck. On the base of the skull, the occipital bone contains the

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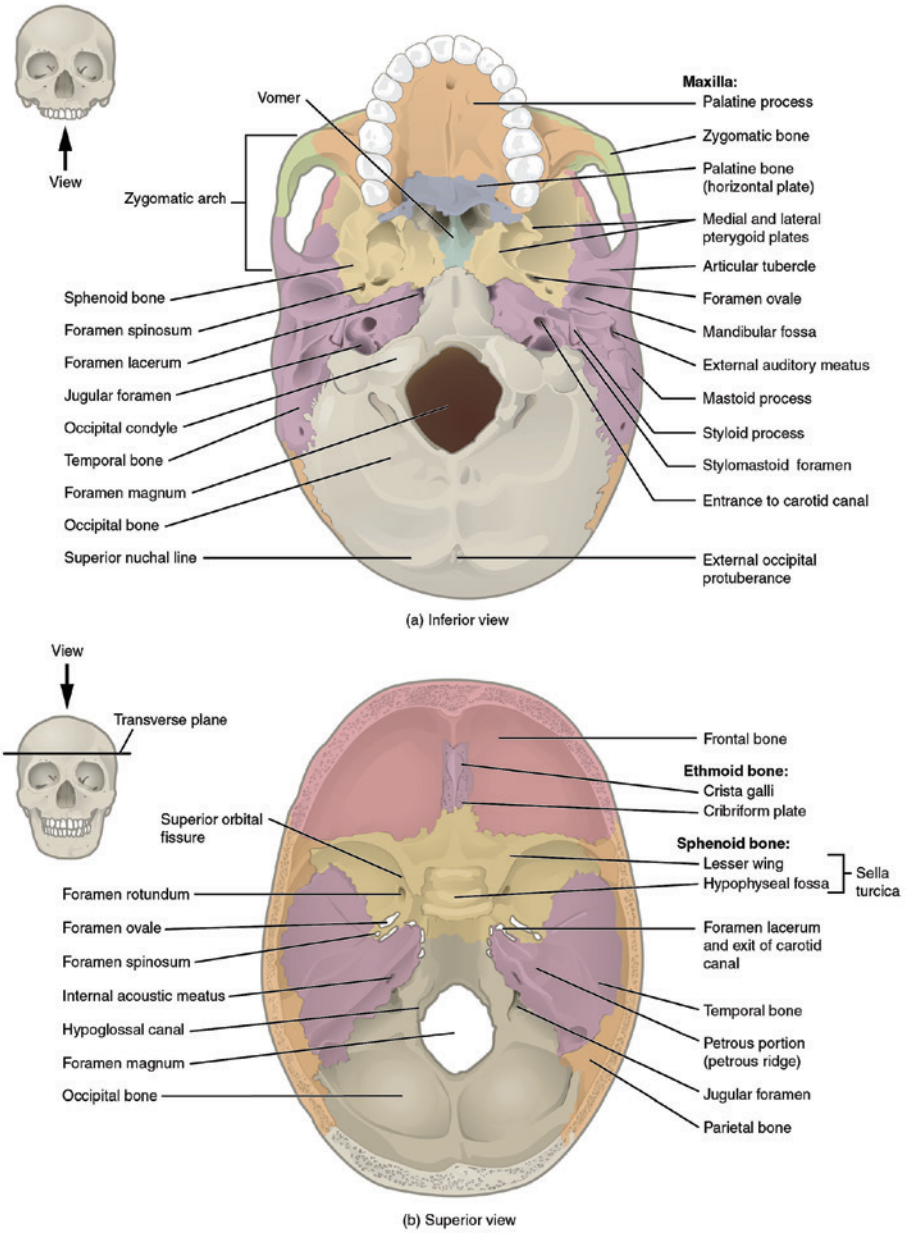


Figure 7.7 External and Internal Views of Base of Skull. (a) The hard palate is formed anteriorly by the palatine processes of the maxilla bones and posteriorly by the horizontal plate of the palatine bones. (b) The complex floor of the cranial cavity is formed by the frontal, ethmoid, sphenoid, temporal, and occipital bones. The lesser wing of the sphenoid bone separates the anterior and middle cranial fossae. The petrous ridge (petrous portion of temporal bone) separates the middle and posterior cranial fossae.

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large opening of the **foramen magnum**, which allows for passage of the spinal cord as it exits the skull. On either side of the foramen magnum is an oval-shaped **occipital condyle**. These condyles form joints with the first cervical vertebra and thus support the skull on top of the vertebral column. The **jugular foramina** are formed anteriorly by the petrous part of the temporal bone and posteriorly by the occipital bone, allowing the internal jugular vein and three cranial nerves to pass through.

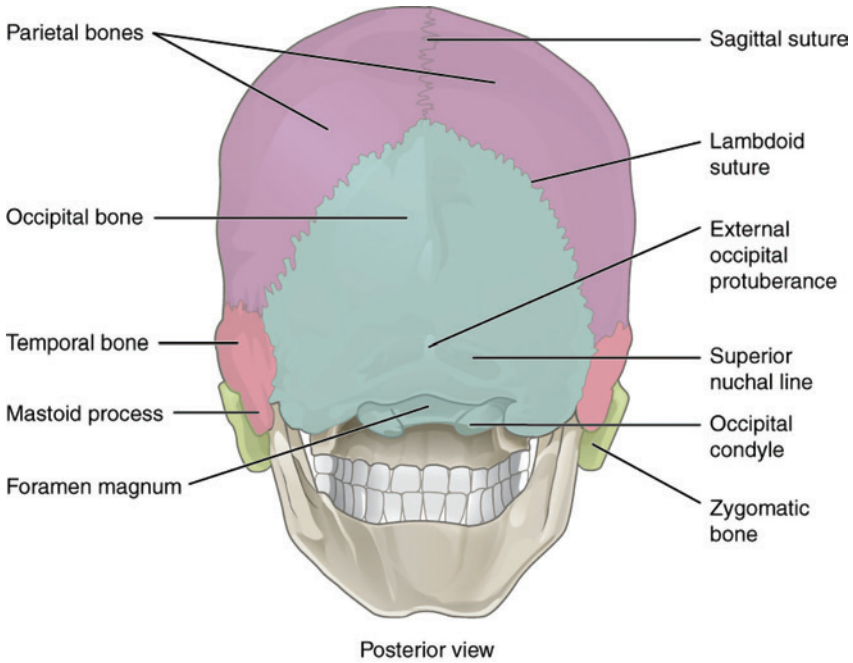


Figure 7.8 Posterior View of Skull. This view of the posterior skull shows attachment sites for muscles and joints that support the skull.

Sphenoid Bone

The **sphenoid bone** is a single, complex bone of the central skull (Figure 7.9). It serves as a "keystone" bone because it joins with almost every other bone of the skull. The sphenoid forms much of the base of the central skull (see Figure 7.7) and also extends laterally to contribute to the sides of the skull (see Figure 7.4). The **sella turcica** is located at the midline of the middle cranial fossa. The rounded depression in the floor of the sella turcica is the **hypophyseal** (**pituitary**) **fossa**, which houses the pea-sized pituitary (hypophyseal) gland.

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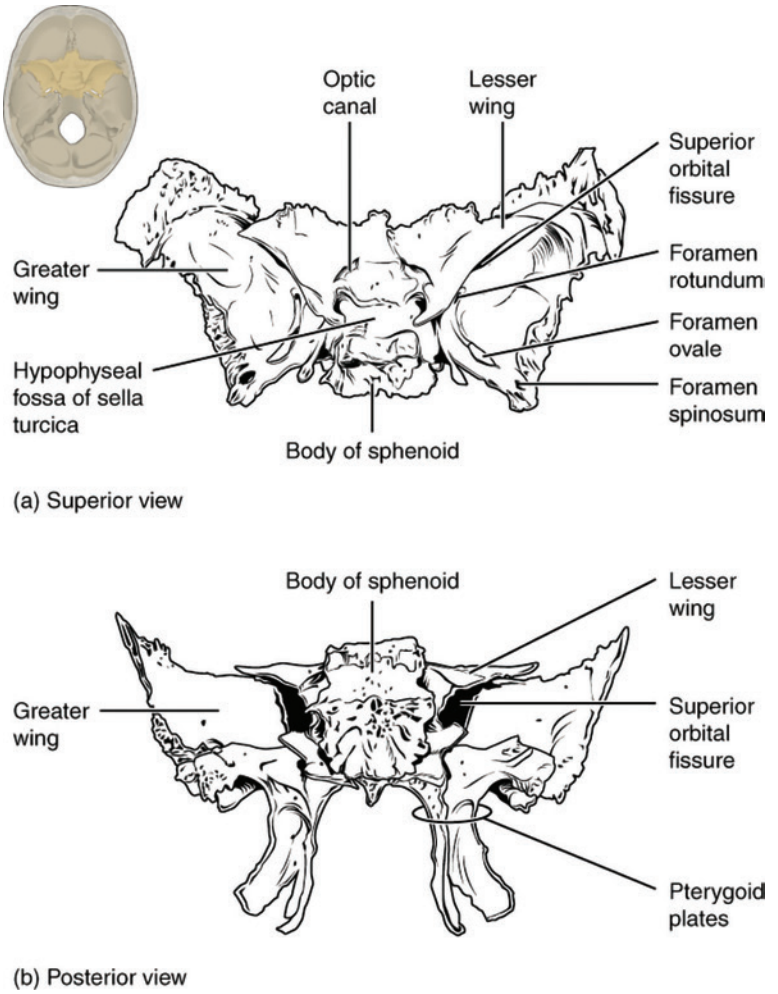


Figure 7.9 Sphenoid Bone. Shown in isolation in (a) superior and (b) posterior views, the sphenoid bone is a single midline bone that forms the anterior walls and floor of the middle cranial fossa. It has a pair of lesser wings and a pair of greater wings. The sella turcica surrounds the hypophyseal fossa. Projecting downward are the medial and lateral pterygoid plates. The sphenoid has multiple openings for the passage of nerves and blood vessels, including the optic canal, superior orbital fissure, foramen rotundum, foramen ovale, and foramen spinosum.

Ethmoid Bone

The **ethmoid bone** is a single midline bone that forms the roof and lateral walls of the upper nasal cavity, the upper portion of the nasal septum, and contributes to the medial wall of the orbit (Figure 7.10 and Figure 7.11). On the interior of the skull, the ethmoid also forms a portion of the floor of the anterior cranial cavity (see Figure 7.7b).

Within the nasal cavity, the perpendicular plate of the ethmoid bone forms the upper portion of the nasal septum. The ethmoid bone also forms the lateral

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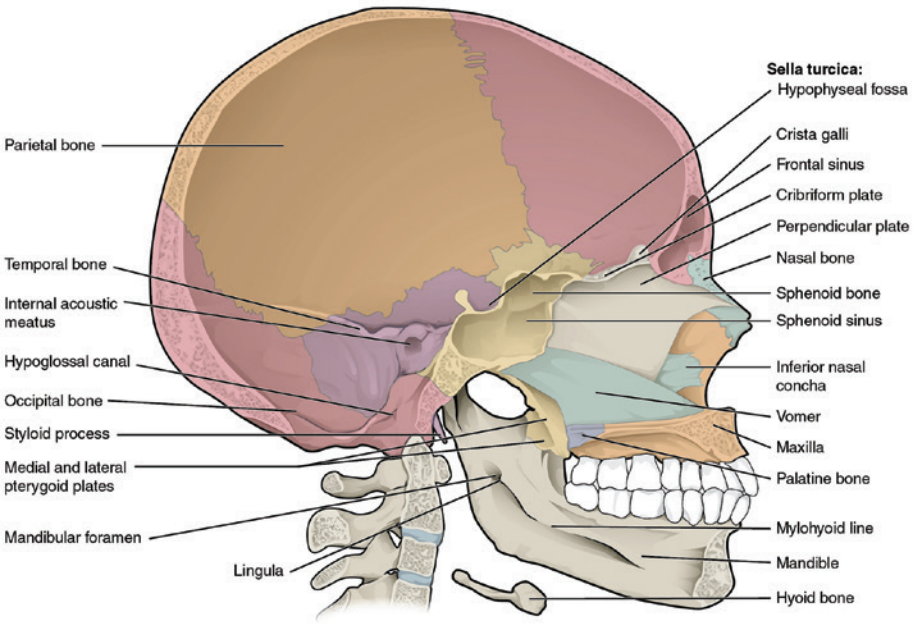


Figure 7.10 Sagittal Section of Skull. This midline view of the sagittally sectioned skull shows the nasal septum.

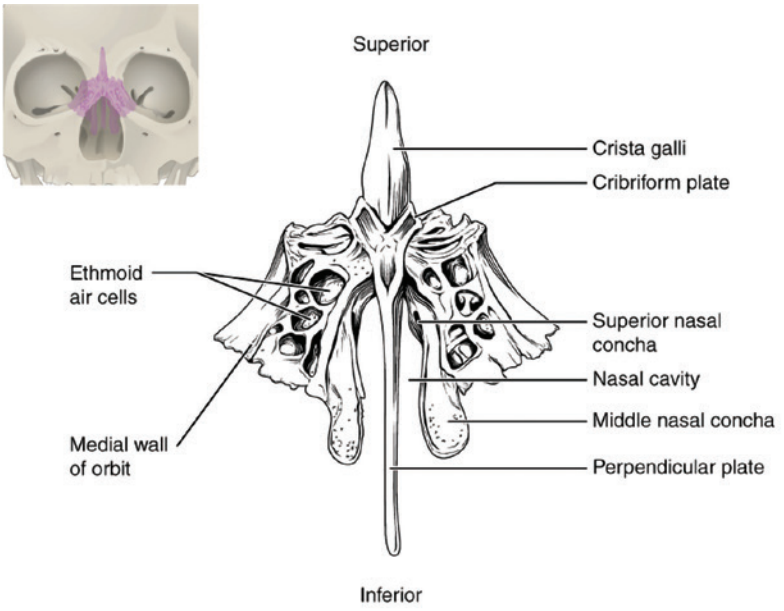


Figure 7.11 Ethmoid Bone. The unpaired ethmoid bone is located at the midline within the central skull. It has an upward projection, the crista galli, and a downward projection, the perpendicular plate, which forms the upper nasal septum. The cribriform plates form both the roof of the nasal cavity and a portion of the anterior cranial fossa floor. The lateral sides of the ethmoid bone form the lateral walls of the upper nasal cavity, make up part of the medial orbit wall, and give rise to the superior and middle nasal conchae. The ethmoid bone also contains the ethmoid air cells.

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walls of the upper nasal cavity. Extending from each lateral wall are the superior nasal concha and middle nasal concha, which are thin, curved projections that extend into the nasal cavity (Figure 7.12).

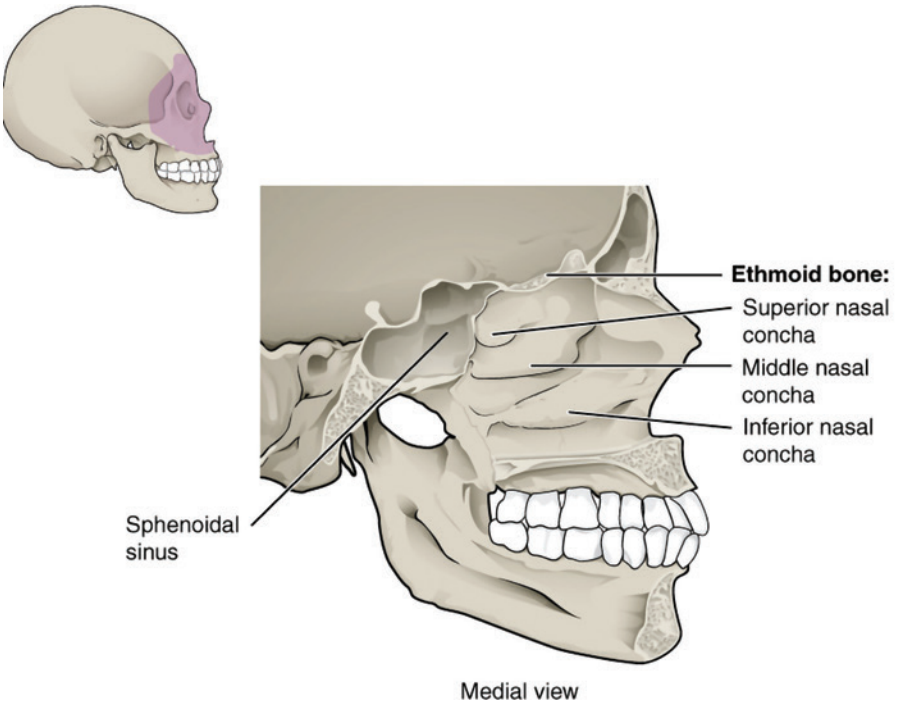


Figure 7.12 Lateral Wall of Nasal Cavity. The three nasal conchae are curved bones that project from the lateral walls of the nasal cavity. The superior nasal concha and middle nasal concha are parts of the ethmoid bone. The inferior nasal concha is an independent bone of the skull.

Sutures of the Skull

A **suture** is an immobile joint between adjacent bones of the skull. The narrow gap between the bones is filled with dense, fibrous connective tissue that unites the bones. The long sutures located between the bones of the brain case are not straight but instead follow irregular, tightly twisting paths. These twisting lines serve to tightly interlock the adjacent bones, thus adding strength to the skull for brain protection.

The two suture lines seen on the top of the skull are the coronal and sagittal sutures. The **coronal suture** runs from side to side across the skull, within the coronal plane of section (see Figure 7.4). It joins the frontal bone to the right and left parietal bones. The **sagittal suture** extends posteriorly from the coronal suture, running along the midline at the top of the skull in the sagittal plane of

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the section (see Figure 7.8). It unites the right and left parietal bones. On the posterior skull, the sagittal suture terminates by joining the lambdoid suture. The **lambdoid suture** extends downward and laterally to either side away from its junction with the sagittal suture. The lambdoid suture joins the occipital bone to the right and left parietal and temporal bones. This suture is named for its upside-down "V" shape, which resembles the capital Greek letter lambda (Λ). The **squamous suture** is located on the lateral skull. It unites the squamous portion of the temporal bone with the parietal bone (see Figure 7.4).

Interactive Link 7.2

View this animation (http://oer.aupress.ca/oer-202505/7.2) to see how a blow to the head may produce a contrecoup (counterblow) fracture of the basilar portion of the occipital bone on the base of the skull. Why may a basilar fracture be life threatening?

Facial Bones of the Skull

The facial bones of the skull form the upper and lower jaws; the nose, nasal cavity, and nasal septum; and the orbit. The facial bones include 14 bones, with six paired bones and two unpaired bones. The paired bones are the maxilla, palatine, zygomatic, nasal, lacrimal, and inferior nasal conchae bones. The unpaired bones are the vomer and mandible bones. Although classified with the brain-case bones, the ethmoid bone also contributes to the nasal septum and the walls of the nasal cavity and orbit.

Maxillary Bone

The maxillary bone, often referred to simply as the **maxilla** (plural = maxillae; see Figure 7.13), is one of a pair that together form the upper jaw, much of the hard palate, the medial floor of the orbit, and the lateral base of the nose (see Figure 7.3).

On the inferior skull, the **palatine process** from each maxillary bone can be seen joining together at the midline to form the anterior three-quarters of the hard palate (see Figure 7.7a). The **hard palate** is the bony plate that forms the roof of the mouth and floor of the nasal cavity, separating the oral and nasal cavities.

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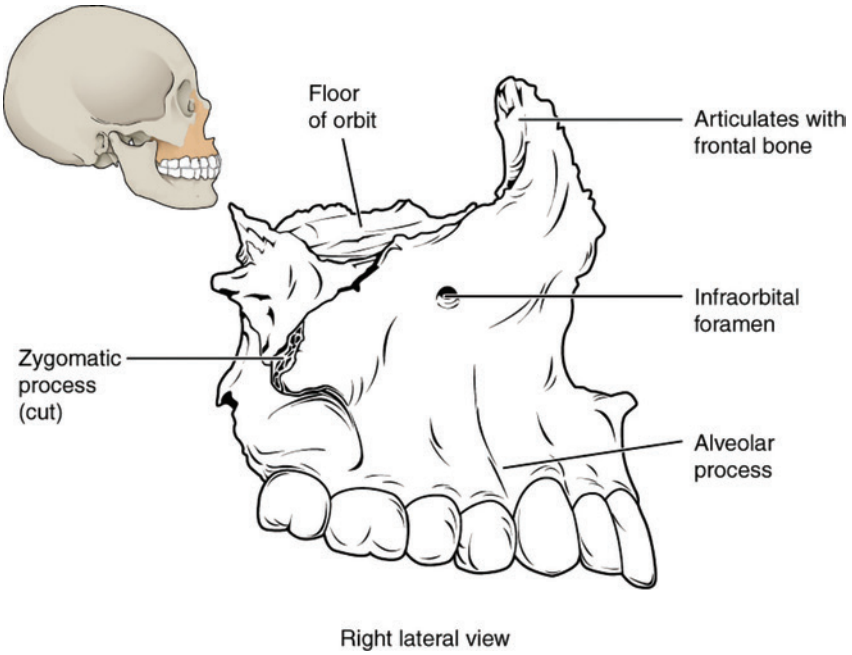


Figure 7.13 Maxillary Bone. The maxillary bone forms the upper jaw and supports the upper teeth. Each maxilla also forms the lateral floor of each orbit and the majority of the hard palate.

Palatine Bone

The **palatine bone** is one of a pair of irregularly shaped bones that contribute small areas to the lateral walls of the nasal cavity and the medial wall of each orbit (see Figure 7.7a). The palatine bones are best seen in an inferior view of the skull and hard palate.

Zygomatic Bone

The **zygomatic bone** is also known as the cheekbone. Each of the paired zygomatic bones forms much of the lateral wall of the orbit and the lateral-inferior margins of the anterior orbital opening (see Figure 7.3 and Figure 7.4).

Nasal Bone

The **nasal bone** is one of two small bones that articulate (join) with each other to form the bony base (bridge) of the nose (see Figure 7.10).

Lacrimal Bone

Each **lacrimal bone** is a small, rectangular bone that forms the anterior medial wall of the orbit (see Figure 7.3 and Figure 7.4). The anterior portion of the lacrimal bone forms a shallow depression (lacrimal fossa), and extending inferiorly

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from this is the **nasolacrimal canal**. The lacrimal fluid (tears of the eye), which serves to maintain the moist surface of the eye, drains at the medial corner of the eye into the nasolacrimal canal. This duct then extends downward to open into the nasal cavity, behind the inferior nasal concha. In the nasal cavity, the lacrimal fluid normally drains in the posterior portion of the cavity, but with an increased flow of tears due to crying or eye irritation, some fluid will also drain anteriorly, thus causing a runny nose.

Inferior Nasal Conchae

The **right and left inferior nasal conchae** form a curved bony plate that projects into the nasal cavity space from the lower lateral wall (see Figure 7.12).

Vomer Bone

The unpaired **vomer bone**, often referred to simply as the vomer, is triangular and forms the posterior-inferior part of the nasal septum (see Figure 7.10).

Mandible

The **mandible** forms the lower jaw and is the only movable bone of the skull. At the time of birth, the mandible consists of paired right and left bones, but these fuse together during the first year to form the single U-shaped mandible of the adult skull. Each side of the mandible consists of a horizontal body and, posteriorly, a vertically oriented **ramus of the mandible** (Figure 7.14). The posterior projection is the **condylar process of the mandible**, which is topped by the oval-shaped **condyle**. The condyle of the mandible articulates (joins) with the mandibular fossa and articular tubercle of the temporal bone. Together, these articulations form the temporomandibular joint, which allows for opening and closing of the mouth (see Figure 7.4). The **alveolar process of the mandible** is the upper border of the mandibular body and serves to anchor the lower teeth.

The Orbit

The orbit is the bony socket that houses the eyeball and contains the muscles that move the eyeball or open the upper eyelid. Each orbit is cone-shaped, with a narrow posterior region that widens toward the large anterior opening. The walls of each orbit include contributions from seven skull bones (Figure 7.15). The frontal bone forms the roof, and the zygomatic bone forms the lateral wall and lateral floor. The medial floor is primarily formed by the maxilla, with a small contribution from the palatine bone. The ethmoid bone and lacrimal bone make up much of the medial wall, and the sphenoid bone forms the posterior orbit.

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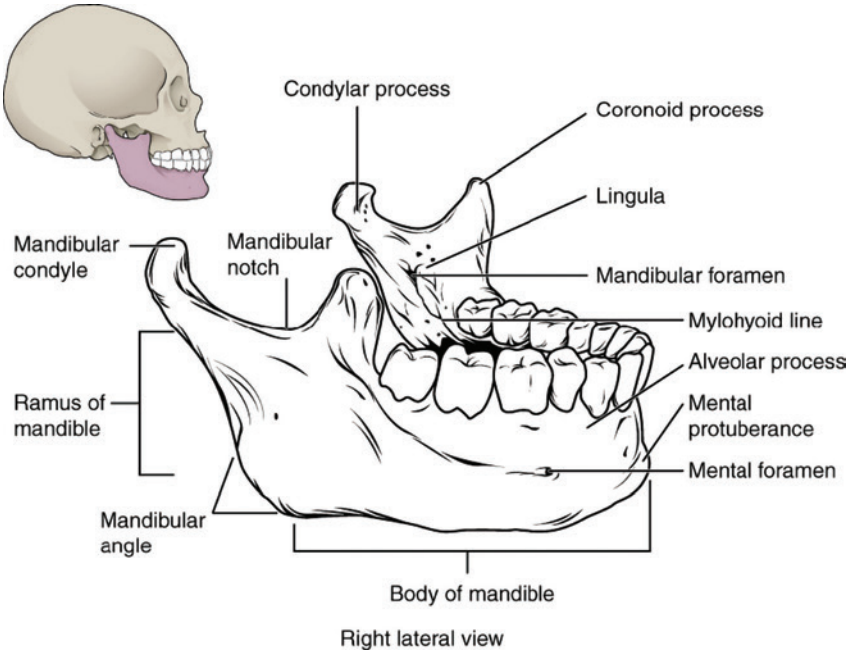


Figure 7.14 Isolated Mandible. The mandible is the only movable bone of the skull.

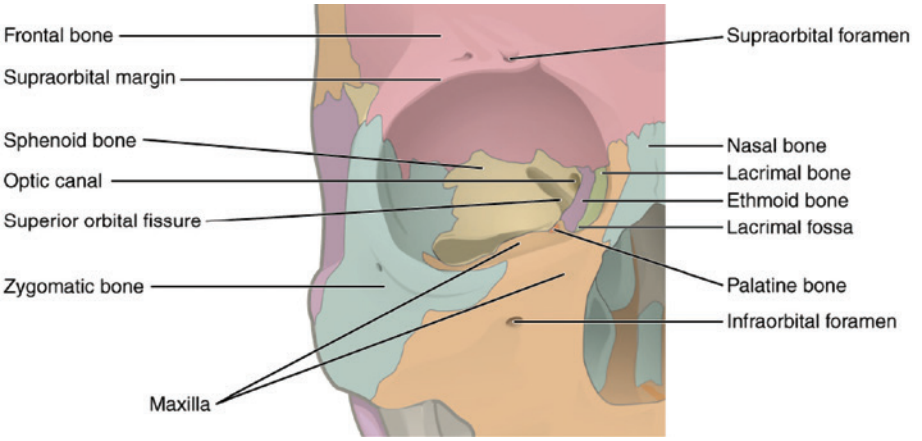


Figure 7.15 Bones of the Orbit. Seven skull bones contribute to the walls of the orbit. Opening into the posterior orbit from the cranial cavity are the optic canal and superior orbital fissure.

At the posterior apex of the orbit is the opening of the **optic canal**, which allows for the passage of the optic nerve from the retina to the brain. Lateral to this is the elongated and irregularly shaped **superior orbital fissure**, which provides passage for the artery that supplies the eyeball, sensory nerves, and the nerves that supply the muscles involved in eye movements.

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The Nasal Septum and Nasal Conchae

The **nasal septum** consists of both bone and cartilage components (Figure 7.16; see also Figure 7.10). The anterior nasal septum is formed by the **septal cartilage**, a flexible plate that fills in the gap between the perpendicular plate of the ethmoid and vomer bones. Attached to the lateral wall on each side of the nasal cavity are the superior, middle, and inferior **nasal conchae** (singular = concha), which are named for their positions (see Figure 7.12). These are bony plates that curve downward as they project into the space of the nasal cavity. They serve to swirl the incoming air, which helps warm and moisturize it before the air moves into the delicate air sacs of the lungs. This also allows mucus, secreted by the tissue lining the nasal cavity, to trap incoming dust, pollen, bacteria, and viruses.

Paranasal Sinuses

The **paranasal sinuses** are hollow, air-filled spaces located within certain bones of the skull (Figure 7.17). All the sinuses communicate with the nasal cavity and are lined with nasal mucosa. They serve to reduce bone mass and thus lighten the skull, and they also add resonance to the voice. The paranasal sinuses are named for the skull bone that each occupies. All paranasal sinuses

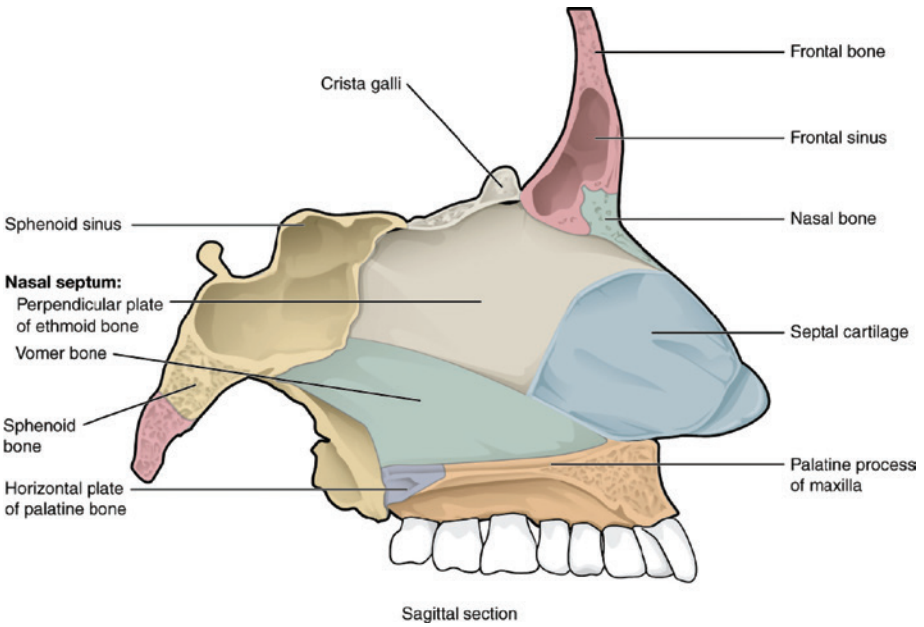


Figure 7.16 Nasal Septum. The nasal septum is formed by the perpendicular plate of the ethmoid bone and the vomer bone. The septal cartilage fills the gap between these bones and extends into the nose.

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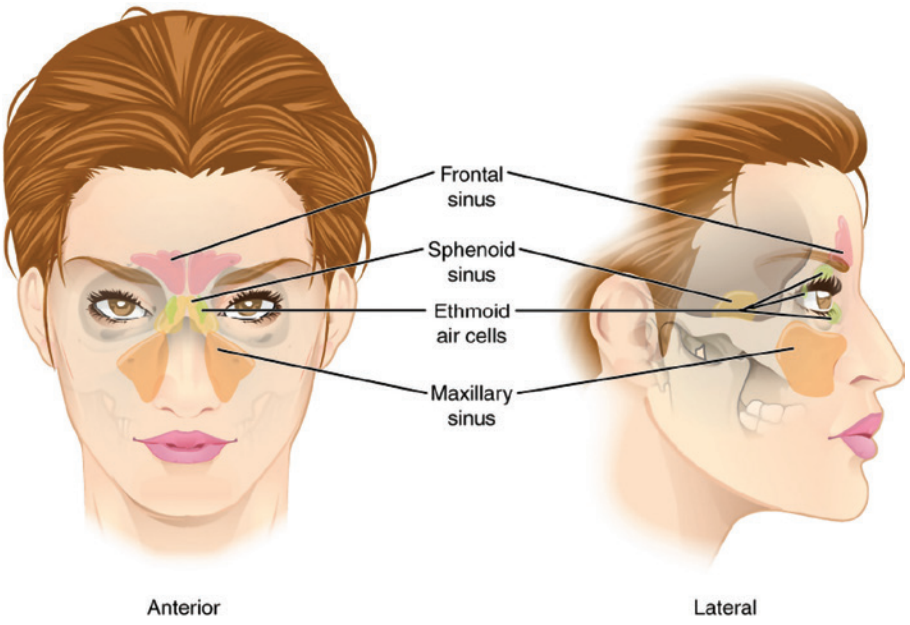


Figure 7.17 Paranasal Sinuses. The paranasal sinuses are hollow, air-filled spaces named for the skull bones that they occupy. The most anterior is the frontal sinus, located in the frontal bone above the eyebrows. The largest are the maxillary sinuses, located in the right and left maxillary bones below the orbits. The most posterior is the sphenoid sinus, located in the body of the sphenoid bone, under the sella turcica. The ethmoid air cells are multiple small spaces located in the right and left sides of the ethmoid bone, between the medial wall of the orbit and the lateral wall of the upper nasal cavity.

should be seen as pairs. So for each side of the cranium, the **frontal sinus** is located just above the eyebrows, within the frontal bone (see Figure 7.16); the largest sinus is the **maxillary sinus** located within maxillary bone, where it occupies the area just below the orbit; the **sphenoid sinus**, midline sinus, is located within the body of the sphenoid bone (some sources consider this sinus as being singular), just anterior and inferior to the sella turcica, thus making it the most posterior of the paranasal sinuses; and the **ethmoid air cells** sinus consists of multiple small spaces located in the right and left sides of the ethmoid bone, between the medial wall of the orbit and lateral wall of the upper nasal cavity.

Hyoid Bone

The **hyoid bone** is an independent bone that does not share a joint with any other bone and thus is not part of the skull (Figure 7.18). It is a small U-shaped bone located in the upper neck near the level of the inferior mandible, with the tips of the U pointing posteriorly. The hyoid serves as the base for the tongue above

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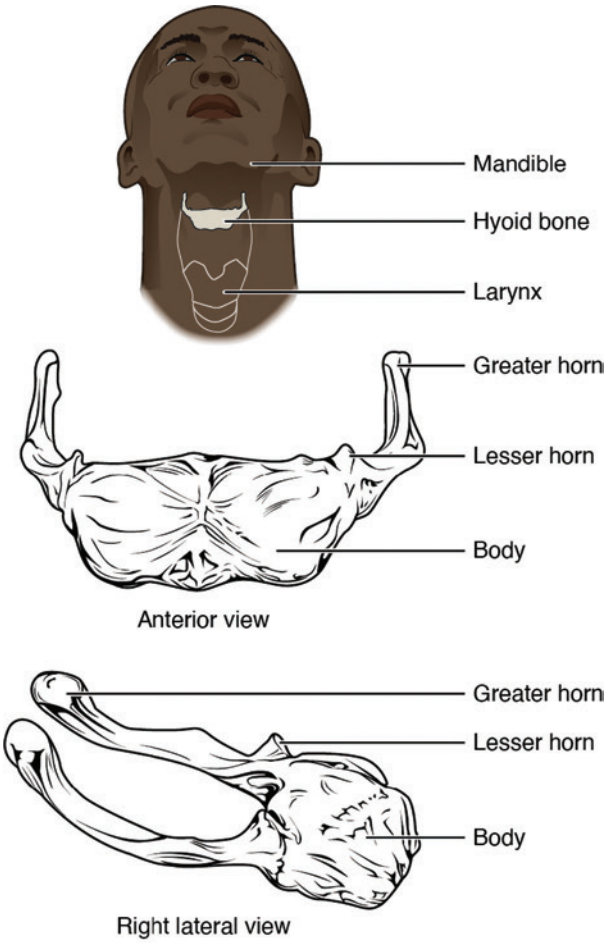


Figure 7.18 Hyoid Bone. The hyoid bone is located in the upper neck and does not join with any other bone. It provides attachments for muscles that act on the tongue, larynx, and pharynx.

and is attached to the larynx below and the pharynx posteriorly. The hyoid is held in position by a series of small muscles that attach to it from either above or below. These muscles act to move the hyoid up and down or forward and back. Movements of the hyoid are coordinated with movements of the tongue, larynx, and pharynx during swallowing and speaking.

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7.3 The Vertebral Column

Learning Objectives

By the end of this section, you will be able to:

- Describe each region of the vertebral column and the number of bones in each region
- Discuss the curves of the vertebral column and how these change after birth
- Describe a typical vertebra and determine the distinguishing characteristics for vertebrae in each vertebral region and features of the sacrum and the coccyx
- Define the structure of an intervertebral disc

The vertebral column is also known as the spinal column or spine (Figure 7.19). It consists of a sequence of **vertebrae** (singular = vertebra), each of which is separated and united by an **intervertebral disc**. Together, the vertebrae and intervertebral discs form the vertebral column. It is a flexible column that supports the head, neck, and body and allows for their movements. It also protects the spinal cord, which passes down the back through openings in the vertebrae.

Regions of the Vertebral Column

The vertebral column originally develops as a series of 33 vertebrae, but this number is eventually reduced to 24 vertebrae, plus the sacrum and coccyx. The vertebral column is subdivided into 5 regions, with the vertebrae in each area named for that region and numbered in descending order. In the neck, there are 7 cervical vertebrae, each designated with the letter "C" followed by its number. Superiorly, the C1 vertebra articulates (forms a joint) with the occipital condyles of the skull. Inferiorly, C1 articulates with the C2 vertebra, and so on. Below these are the 12 thoracic vertebrae, designated T1–T12. The lower back contains 5 lumbar vertebrae, designated L1–L5. The single sacrum, which is also part of the pelvis, is formed by the fusion of 5 sacral vertebrae. Similarly, the coccyx, or tailbone, results from the fusion of 4 small coccygeal vertebrae. However, the sacral and coccygeal fusions do not start until age 20 and are not completed until middle age.

Curvatures of the Vertebral Column

The adult vertebral column does not form a straight line but instead has four curvatures along its length (see Figure 7.19). These curves increase the vertebral

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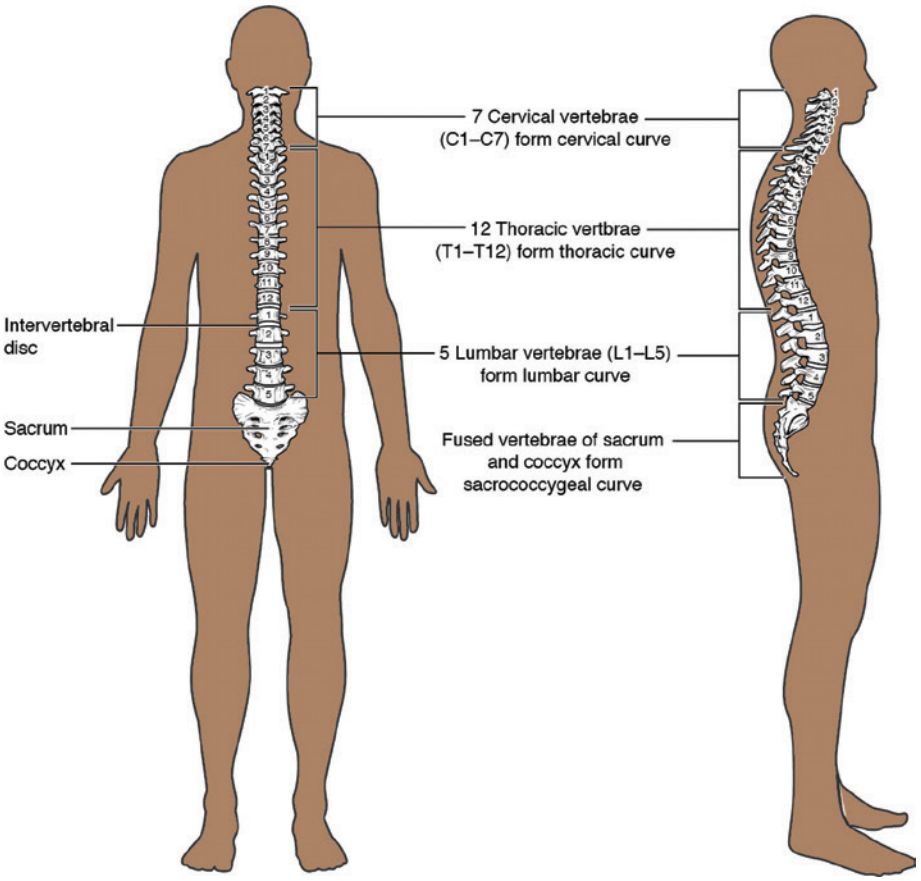


Figure 7.19 Vertebral Column. The adult vertebral column consists of 24 vertebrae, plus the sacrum and coccyx. The vertebrae are divided into three regions: cervical C1–C7 vertebrae, thoracic T1–T12 vertebrae, and lumbar L1–L5 vertebrae. The vertebral column is curved, with two primary curvatures (thoracic and sacrococcygeal curves) and two secondary curvatures (cervical and lumbar curves).

column's strength, flexibility, and ability to absorb shock. When the load on the spine is increased—by carrying a heavy backpack, for example—the curvatures increase in depth (become more curved) to accommodate the extra weight. They then spring back when the weight is removed. The four adult curvatures are classified as either primary or secondary curvatures. Primary curves are retained from the original fetal curvature, while secondary curvatures develop after birth.

During fetal development, the body is flexed anteriorly into the fetal position, giving the entire vertebral column a single curvature that is concave anteriorly. In the adult, this fetal curvature is retained in two regions of the vertebral column as the **thoracic curve**, which involves the thoracic vertebrae, and the **sacrococcygeal curve**, formed by the sacrum and coccyx. Each of these

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is thus called a **primary curve** because they are retained from the original fetal curvature of the vertebral column.

A **secondary curve** develops gradually after birth as the child learns to sit upright, stand, and walk. Secondary curves are concave posteriorly, opposite in direction to the original fetal curvature. The **cervical curve** of the neck region develops as the infant begins to hold their head upright when sitting. Later, as the child begins to stand and then to walk, the **lumbar curve** of the lower back develops. In adults, the lumbar curve is generally deeper in females.

Interactive Link 7.3

Osteoporosis is a common age-related bone disease in which bone density and strength are decreased. Watch this video (http://oer.aupress.ca/oer-202505/7.3) to get a better understanding of how thoracic vertebrae may become weakened and may fracture due to this disease.

General Structure of a Vertebra

Within the different regions of the vertebral column, vertebrae vary in size and shape, but they all follow a similar structural pattern. A typical vertebra will consist of a body, a vertebral arch, and seven processes (Figure 7.20).

The **vertebral body** is the anterior portion of each vertebra and is the part that supports the body weight. Because of this, the vertebral bodies progressively

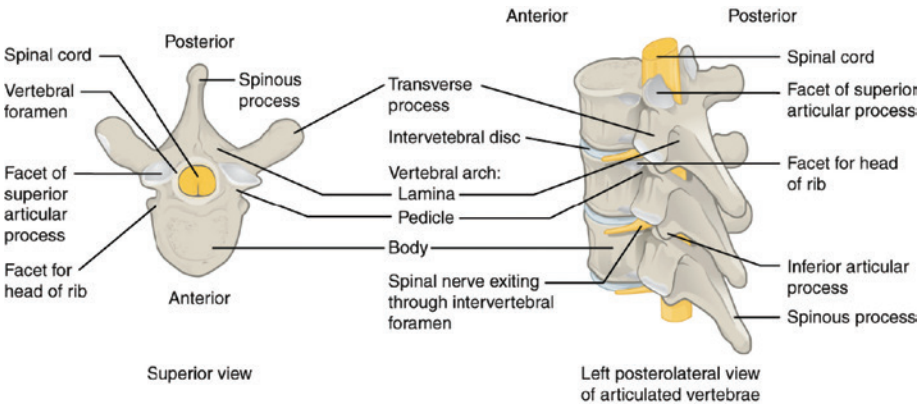


Figure 7.20 Parts of a Typical Vertebra. A typical vertebra consists of a body and a vertebral arch. The arch is formed by the paired pedicles and paired laminae. Arising from the vertebral arch are the transverse, spinous, superior articular, and inferior articular processes. The vertebral foramen provides for the passage of the spinal cord. Each spinal nerve exits through an intervertebral foramen, located between adjacent vertebrae. Intervertebral discs unite the bodies of adjacent vertebrae.

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increase in size and thickness going down the vertebral column. The bodies of adjacent vertebrae are separated and strongly united by an intervertebral disc.

The **vertebral arch** forms the posterior portion of each vertebra. It consists of four parts: the right and left pedicles and the right and left laminae. Each **pedicle** forms one of the lateral sides of the vertebral arch. The pedicles are anchored to the posterior side of the vertebral body. Each **lamina** forms part of the posterior roof of the vertebral arch. The large opening between the vertebral arch and body is the **vertebral foramen**, which contains the spinal cord. In the intact vertebral column, the vertebral foramina of all the vertebrae align to form the **vertebral** (**spinal**) **canal**, which serves as the bony protection and passageway for the spinal cord down the back. When the vertebrae are aligned in the vertebral column, notches in the margins of the pedicles of adjacent vertebrae together form an **intervertebral foramen**, the opening through which a spinal nerve exits from the vertebral column (Figure 7.21).

Seven processes arise from the vertebral arch. Each paired **transverse process** projects laterally and arises from the junction point between the pedicle and lamina. The single **spinous process** (vertebral spine) projects posteriorly at the midline of the back. The vertebral spines can easily be felt as a series of bumps just under the skin down the middle of the back. The transverse and spinous processes serve as important muscle attachment sites. A **superior articular process** extends or faces upward, and an **inferior articular process** faces or projects downward on each side of a vertebra. The paired superior articular processes of one vertebra join with the corresponding paired

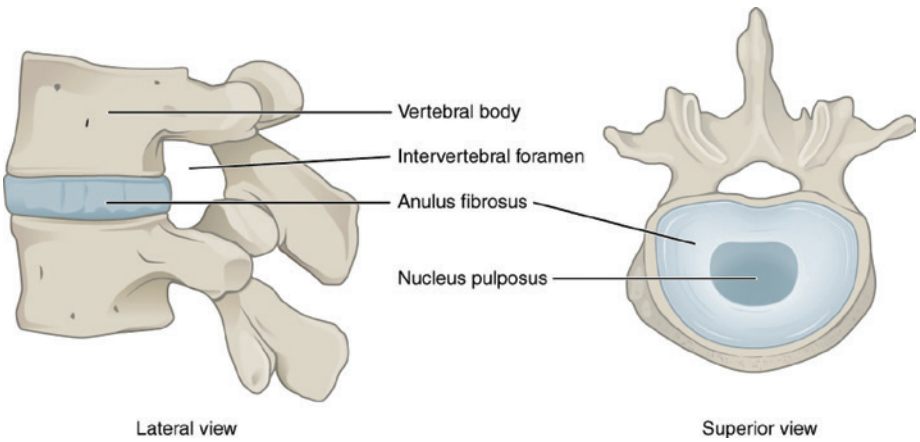


Figure 7.21 Intervertebral Disc. The bodies of adjacent vertebrae are separated and united by an intervertebral disc, which provides padding and allows for movements between adjacent vertebrae. The disc consists of a fibrous outer layer called the anulus fibrosus and a gel-like centre called the nucleus pulposus. The intervertebral foramen is the opening formed between adjacent vertebrae for the exit of a spinal nerve.

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inferior articular processes from the next higher vertebra. These junctions form slightly movable joints between the adjacent vertebrae.

Regional Modifications of Vertebrae

In addition to the general characteristics of a typical vertebra described previously, vertebrae also display characteristic size and structural features that vary between the different vertebral column regions. For example, cervical vertebrae are smaller than lumbar vertebrae due to differences in the proportion of body weight that each supports. Thoracic vertebrae have sites for rib attachment, and the vertebrae that give rise to the sacrum and coccyx have fused together into single bones.

Cervical Vertebrae

Typical **cervical vertebrae**, such as C4 or C5, have several characteristic features that differentiate them from thoracic or lumbar vertebrae (Figure 7.22). Cervical vertebrae have a small body, reflecting the fact that they carry the least amount of body weight. Cervical vertebrae usually have a bifid (Y-shaped) spinous process. The spinous processes of the C3–C6 vertebrae are short, but the spine of C7 is much longer. The transverse processes of the cervical vertebrae are sharply curved (U-shaped) to allow for the passage of the cervical spinal nerves. Each transverse process also has an opening called the **transverse foramen**. An important artery that supplies the brain ascends the neck by passing through these openings.

The first and second cervical vertebrae are further modified, giving each a distinctive appearance. The first cervical (C1) vertebra is also called the **atlas**, because this is the vertebra that supports the skull on top of the vertebral column. The C1 vertebra does not have a body or spinous process. Instead, it is ring-shaped, consisting of an **anterior arch** and a **posterior arch**. The transverse processes of the atlas are longer and extend more laterally than do the transverse processes of any other cervical vertebrae. The superior articular processes face upward and are deeply curved for articulation with the occipital condyles on the base of the skull. The inferior articular processes are flat and face downward to join with the superior articular processes of the C2 vertebra.

The second cervical (C2) vertebra is called the **axis** because it serves as the axis for rotation when turning the head toward the right or left. The axis resembles typical cervical vertebrae in most respects, but is easily distinguished by the **dens**, a bony projection (odontoid process) that extends upward from the vertebral body. The dens joins with the inner aspect of the anterior arch of the atlas, where it is held in place by the transverse ligament.

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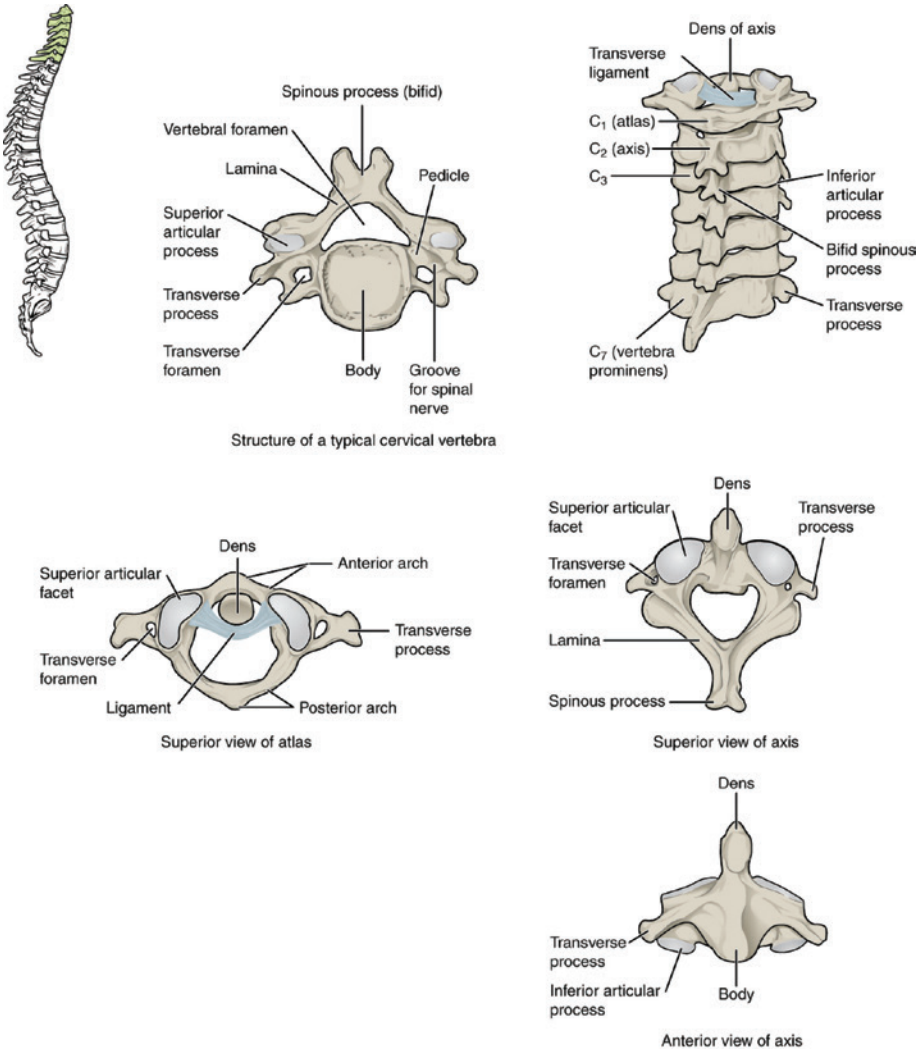


Figure 7.22 Cervical Vertebrae. A typical cervical vertebra has a small body, a bifid spinous process, and transverse processes that have a transverse foramen, and they are curved for spinal nerve passage. The atlas (C1 vertebra) does not have a body or spinous process. It consists of an anterior and a posterior arch and elongated transverse processes. The axis (C2 vertebra) has the upward projecting dens, which articulates with the anterior arch of the atlas.

Thoracic Vertebrae

The bodies of the **thoracic vertebrae** are larger than those of cervical vertebrae (Figure 7.23). The characteristic feature of a typical midthoracic vertebra is the spinous process, which is long and has a pronounced downward angle that causes it to overlap the next inferior vertebra. The superior articular processes of thoracic vertebrae face anteriorly, and the inferior processes face posteriorly. Thoracic vertebrae have several additional articulation sites, each of which is called a **facet**, where a rib is attached (Figure 7.24). Most thoracic vertebrae have

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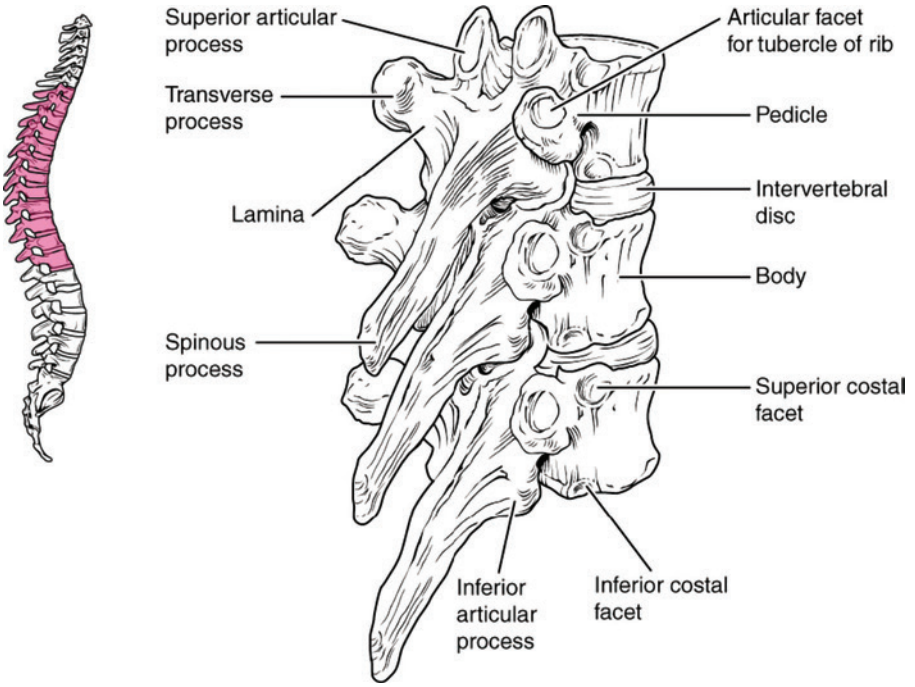


Figure 7.23 Thoracic Vertebrae. A typical thoracic vertebra is distinguished by the spinous process, which is long and projects downward to overlap the next inferior vertebra. It also has articulation sites (facets) on the vertebral body and a transverse process for rib attachment.

two facets located on the lateral sides of the body, each of which is called a **costal facet**. These are for articulation with the head (end) of a rib. An additional facet is located on the transverse process for articulation with the tubercle of a rib.

Lumbar Vertebrae

Lumbar vertebrae carry the greatest amount of body weight and are thus characterized by the large size and thickness of the vertebral body (Figure 7.25). They have short transverse processes and a short, blunt spinous process that projects posteriorly. The articular processes are large, with the superior process facing backward and the inferior process facing forward.

Sacrum and Coccyx

The sacrum is a triangular bone that is thick and wide across its superior base, where it is weight-bearing, and then tapers down to an inferior, non-weight-bearing apex (Figure 7.26). It is formed by the fusion of five sacral vertebrae, a process that does not begin until after the age of 20. On the anterior surface of the older adult sacrum, the lines of vertebral fusion can be seen as four

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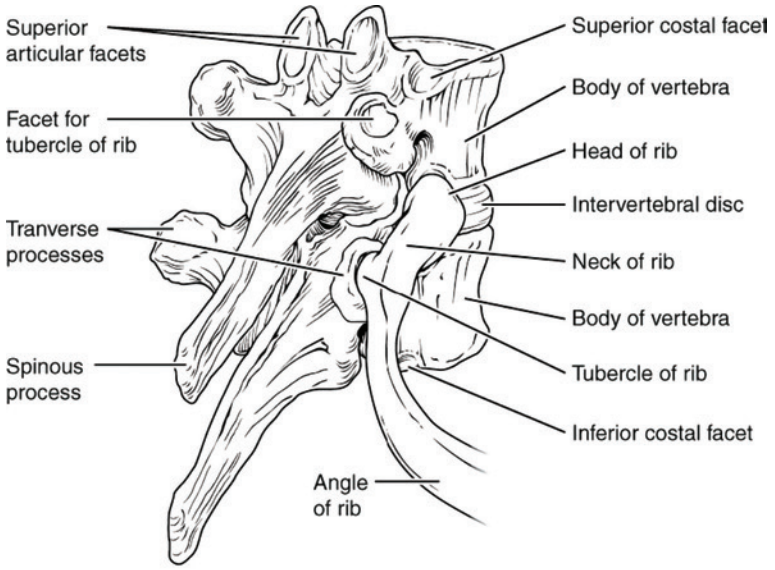


Figure 7.24 Rib Articulation in Thoracic Vertebrae. Thoracic vertebrae have superior and inferior articular facets on the vertebral body for articulation with the head of a rib and a transverse process facet for articulation with the rib tubercle.

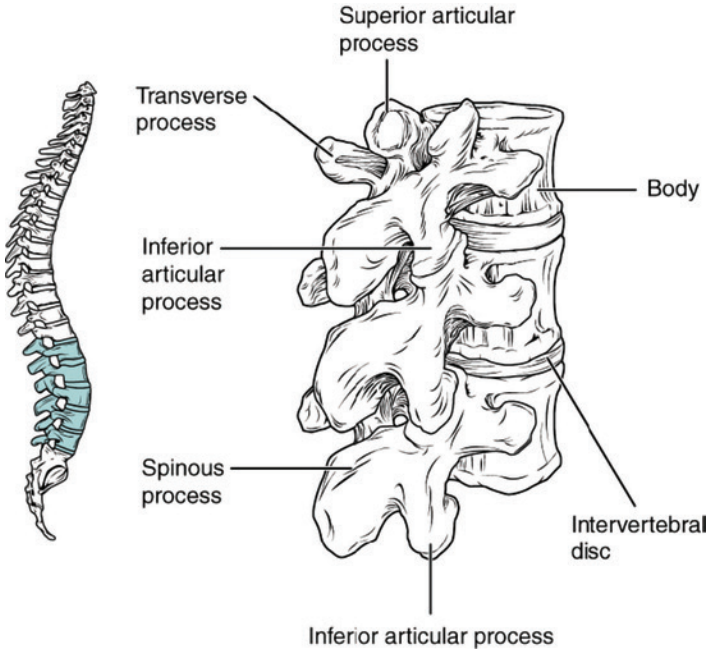


Figure 7.25 Lumbar Vertebrae. Lumbar vertebrae are characterized by having a large, thick body and a short, rounded spinous process.

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transverse ridges. The **sacral promontory** is the anterior lip of the superior base of the sacrum. Lateral to this is the roughened auricular surface, which joins with the ilium portion of the hip bone to form the immobile sacroiliac joints of the pelvis. Passing inferiorly through the sacrum is a bony tunnel called the **sacral canal**, which terminates at the **sacral hiatus** near the inferior tip of the sacrum called the **apex**. The anterior and posterior surfaces of the sacrum have a series of paired openings called **sacral foramina** that connect to the sacral canal. The **superior articular process of the sacrum**, one of which is found on either side of the superior opening of the sacral canal, articulates with the inferior articular processes from the L5 vertebra.

The **coccyx**, or tailbone, is derived from the fusion of four very small coccygeal vertebrae (see Figure 7.26). It articulates with the inferior tip of the sacrum. It is not weight-bearing in the standing position but may receive some body weight when sitting.

Intervertebral Discs and Ligaments of the Vertebral Column

The bodies of adjacent vertebrae are strongly anchored to each other by an intervertebral disc. This structure provides padding between the bones during weight-bearing and, because it can change shape, allows for movement between the vertebrae. Although the total amount of movement available between any two adjacent vertebrae is small, when these movements are summed together along the entire length of the vertebral column, large body movements can be produced. Ligaments that extend along the length of the vertebral column also contribute to its overall support and stability.

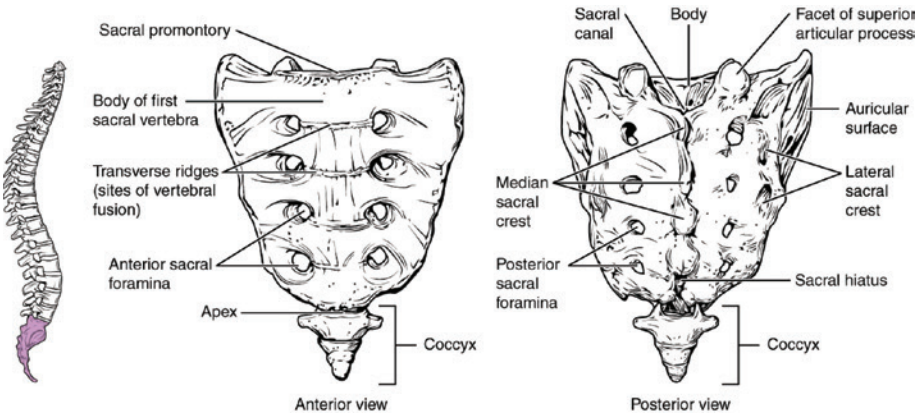


Figure 7.26 Sacrum and Coccyx. The sacrum is formed from the fusion of five sacral vertebrae, whose lines of fusion are indicated by the transverse ridges. The fused spinous processes form the median sacral crest, while the lateral sacral crest arises from the fused transverse processes. The coccyx is formed by the fusion of four small coccygeal vertebrae.

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Intervertebral Disc

An **intervertebral disc** is a fibrocartilaginous pad that fills the gap between adjacent vertebral bodies (see Figure 7.21). Each disc is anchored to the bodies of its adjacent vertebrae, thus strongly uniting these. The discs also provide padding between vertebrae during weight-bearing. Intervertebral discs are also flexible and can change shape to allow for movements of the vertebral column.

Each intervertebral disc consists of two parts. The **anulus fibrosus** is the tough, fibrous outer layer of the disc. It forms a circle and is firmly anchored to the outer margins of the adjacent vertebral bodies. Inside is the **nucleus pulposus**, consisting of a softer, more gel-like material. It has a high water content that serves to resist compression and thus is important for weight-bearing.

Interactive Link 7.4

Use this tool (http://oer.aupress.ca/oer-202505/7.4) to identify the bones, intervertebral discs, and ligaments of the vertebral column. The thickest portions of the anterior longitudinal ligament and the supraspinous ligament are found in which regions of the vertebral column?

7.4 The Thoracic Cage

Learning Objectives

By the end of this section, you will be able to:

- Discuss the components that make up the thoracic cage
- Identify the parts of the sternum and define the sternal angle
- Discuss the parts of a rib and rib classifications

The **thoracic cage** (rib cage) forms the thorax (chest) portion of the body. It consists of the 12 pairs of ribs with their costal cartilages and the sternum (Figure 7.27). The ribs are anchored posteriorly to the 12 thoracic vertebrae (T1–T12). The thoracic cage protects the heart and lungs.

Sternum

The sternum is the elongated bony structure that anchors the anterior thoracic cage. It consists of three parts: the manubrium, body, and xiphoid process. The **manubrium** is the wider, superior portion of the sternum. The top of the

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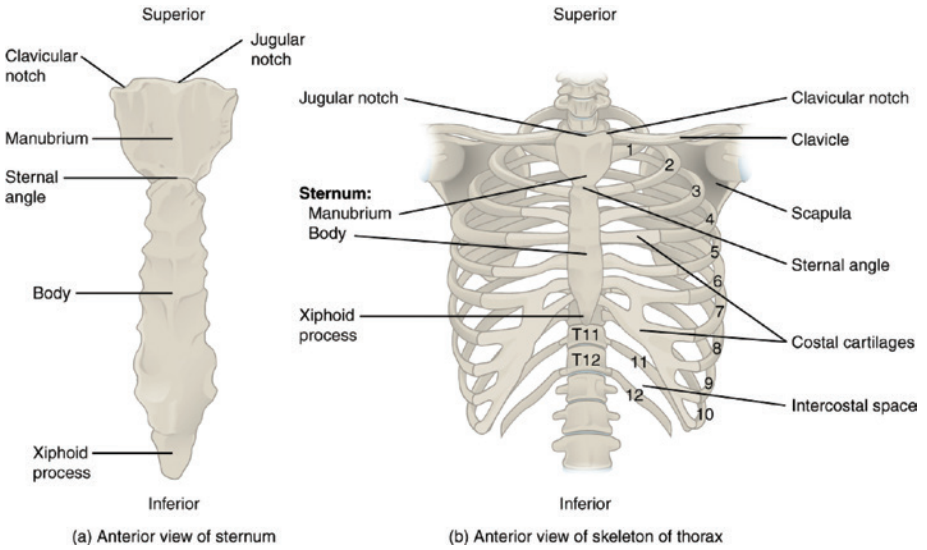


Figure 7.27 Thoracic Cage. The thoracic cage is formed by (a) the sternum and (b) 12 pairs of ribs with their costal cartilages. The ribs are anchored posteriorly to the 12 thoracic vertebrae. The sternum consists of the manubrium, body, and xiphoid process. The ribs are classified as true ribs (1–7) and false ribs (8–12). The last two pairs of false ribs are also known as floating ribs (11–12).

manubrium has a shallow, U-shaped border called the **jugular** (**suprasternal**) **notch**. This can be easily felt at the anterior base of the neck, between the medial ends of the clavicles. The **clavicular notch** is the shallow depression located on either side at the superior-lateral margins of the manubrium. This is the site of the sternoclavicular joint, between the sternum and clavicle. The first ribs also attach to the manubrium.

The elongated, central portion of the sternum is the **sternal body**. The manubrium and body join together at the **sternal angle**, so called because the junction between these two components is not flat but forms a slight bend. The second rib attaches to the sternum at the sternal angle. Since the first rib is hidden behind the clavicle, the second rib is the highest rib that can be identified by palpation. Thus, the sternal angle and second rib are important landmarks for the identification and counting of the lower ribs. Ribs 3–7 attach to the sternal body.

The inferior tip of the sternum is the **xiphoid process**. This small structure is cartilaginous early in life but gradually becomes ossified starting during middle age.

Ribs

Each rib is a curved, flattened bone that contributes to the wall of the thorax. The ribs articulate posteriorly with the T1–T12 thoracic vertebrae, and most

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attach anteriorly via their costal cartilages to the sternum. There are 12 pairs of ribs. The ribs are numbered 1–12 in accordance with the thoracic vertebrae.

Parts of a Typical Rib

The posterior end of a typical rib is called the **head of the rib** (see Figure 7.24). This region articulates primarily with the costal facet located on the body of the same numbered thoracic vertebra and, to a lesser degree, with the costal facet located on the body of the next higher vertebra. Lateral to the head is the narrowed **neck of the rib**. A small bump on the posterior rib surface is the **tubercle of the rib**, which articulates with the facet located on the transverse process of the same numbered vertebra. The remainder of the rib is the **body of the rib** (shaft). Just lateral to the tubercle is the **angle of the rib**, the point at which the rib has its greatest degree of curvature. The angles of the ribs form the most posterior extent of the thoracic cage. In the anatomical position, the angles align with the medial border of the scapula. A shallow **costal groove** for the passage of blood vessels and a nerve is found along the inferior margin of each rib.

Rib Classifications

The bony ribs do not extend anteriorly completely around to the sternum. Instead, each rib ends in a **costal cartilage**. These cartilages are made of hyaline cartilage and can extend for several centimetres. Most ribs are then attached, either directly or indirectly, to the sternum via their costal cartilage (see Figure 7.27). The ribs are classified into three groups based on their relationship to the sternum.

Ribs 1–7 are classified as **true ribs** (vertebrosternal ribs). The costal cartilage from each of these ribs attaches directly to the sternum. Ribs 8–12 are called **false ribs** (vertebrochondral ribs). The costal cartilages from these ribs do not attach directly to the sternum. For ribs 8–10, the costal cartilages are attached to the cartilage of the next higher rib. Thus, the cartilage of rib 10 attaches to the cartilage of rib 9, rib 9 then attaches to rib 8, and rib 8 is attached to rib 7. The last two false ribs (11–12) are also called **floating ribs** (vertebral ribs). These are short ribs that do not attach to the sternum at all. Instead, their small costal cartilages terminate within the musculature of the lateral abdominal wall.

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7.5 Embryonic Development of the Axial Skeleton

Learning Objectives

By the end of this section, you will be able to:

- Discuss the two types of embryonic bone development within the skull
- Describe the development of the vertebral column and thoracic cage

The axial skeleton begins to form during early embryonic development. However, growth, remodelling, and ossification (bone formation) continue for several decades after birth before the adult skeleton is fully formed. Knowledge of the developmental processes that give rise to the skeleton is important for understanding the abnormalities that may arise in skeletal structures.

Development of the Skull

The bones of the skull arise from mesenchyme during embryonic development in two different ways.

The first mechanism produces the bones that form the top and sides of the brain case. As the brain case bones grow in the fetal skull, they remain separated from one another by large areas of dense connective tissue, each of which is called a **fontanelle** (Figure 7.28). The fontanelles are the soft spots on an infant's head. They are important during birth because these areas allow the skull to change shape as it squeezes through the birth canal. After birth, the fontanelles allow for continued growth and expansion of the skull as the brain enlarges.

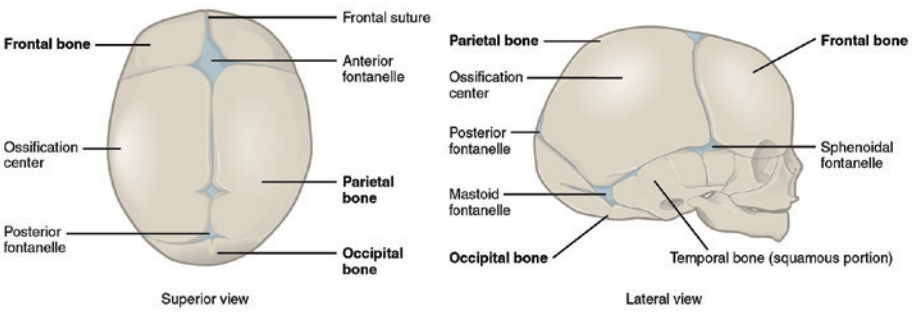


Figure 7.28 Newborn Skull. The bones of the newborn skull are not fully ossified and are separated by large areas called fontanelles, which are filled with fibrous connective tissue. The fontanelles allow for continued growth of the skull after birth. At the time of birth, the facial bones are small and underdeveloped and the mastoid process has not yet formed.

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The fontanelles decrease in size and disappear by age two. However, the skull bones remained separated from one another at the sutures, which contain dense fibrous connective tissue that unites the adjacent bones. The connective tissue of the sutures allows for continued growth of the skull bones as the brain enlarges during childhood growth.

The second mechanism for bone development in the skull produces the facial bones and floor of the brain case. This also begins with the localized accumulation of mesenchymal cells. However, these cells differentiate into cartilage cells, which produce a hyaline cartilage model of the future bone. As this cartilage model grows, it is gradually converted into bone through the process of endochondral ossification. This is a slow process, and the cartilage is not completely converted to bone until the skull achieves its full adult size.

Development of the Vertebral Column and Thoracic Cage

Development of the vertebrae begins with the accumulation of mesenchyme cells from each sclerotome around the notochord. These cells differentiate into a hyaline cartilage model for each vertebra, which then grow and eventually ossify into bone through the process of endochondral ossification. As the developing vertebrae grow, the notochord largely disappears. However, small areas of notochord tissue persist between the adjacent vertebrae, and this contributes to the formation of each intervertebral disc.

The **ribs and sternum** also develop from mesenchyme. The ribs initially develop as part of the cartilage model (endochondral ossification) for each vertebra, but in the thorax region, the rib portion separates from the vertebra by the eighth week. The cartilage model of the rib then ossifies, except for the anterior portion, which remains as the costal cartilage. The sternum initially forms as paired hyaline cartilage models (endochondral ossification), which are attached to the lateral sides of the developing sternum. The manubrium and body of the sternum are converted into bone first, with the xiphoid process remaining as cartilage until late in life.

Interactive Link 7.5

View this video (http://oer.aupress.ca/oer-202505/7.5) to review the two processes that give rise to the bones of the skull and body. What are the two mechanisms by which the bones of the body are formed, and which bones are formed by each mechanism?

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Key Terms

alveolar process of the mandible: Upper border of the mandibular body that contains the lower teeth.

angle of the rib: Portion of a rib with the greatest curvature; together, the rib angles form the most posterior extent of the thoracic cage.

anterior arch: Anterior portion of the ringlike C1 (atlas) vertebra.

anulus fibrosus: Tough, fibrous outer portion of an intervertebral disc, which is strongly anchored to the bodies of the adjacent vertebrae.

apex: The inferior tip of the sacrum.

appendicular skeleton: All bones of the upper and lower limbs, plus the girdle bones that attach each limb to the axial skeleton.

atlas: First cervical (C1) vertebra.

axial skeleton: Central, vertical axis of the body, including the skull, vertebral column, and thoracic cage.

axis: Second cervical (C2) vertebra.

body of the rib: Shaft portion of a rib.

brain case: Portion of the skull that contains and protects the brain, consisting of the eight bones that form the cranial base and rounded upper skull.

calvaria (also skullcap): Rounded top of the skull.

cervical curve: Posteriorly concave curvature of the cervical vertebral column region; a secondary curve of the vertebral column.

cervical vertebrae: Seven vertebrae numbered C1–C7 that are located in the neck region of the vertebral column.

clavicular notch: Paired notches located on the superior-lateral sides of the sternal manubrium, for articulation with the clavicle.

coccyx: Small bone located at the inferior end of the adult vertebral column that is formed by the fusion of four coccygeal vertebrae; also referred to as the tailbone.

condylar process of the mandible: Thickened upward projection from the posterior margin of the mandibular ramus.

condyle: Oval-shaped process located at the top of the condylar process of the mandible.

coronal suture: Joint that unites the frontal bone to the right and left parietal bones across the top of the skull.

costal cartilage: Hyaline cartilage structure attached to the anterior end of each rib that provides for either direct or indirect attachment of most ribs to the sternum.

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costal facet: Site on the lateral sides of a thoracic vertebra for articulation with the head of a rib.

costal groove: Shallow groove along the inferior margin of a rib that provides passage for blood vessels and a nerve.

cranial cavity: Interior space of the skull that houses the brain.

cranium: Skull.

dens: Bony projection (odontoid process) that extends upward from the body of the C2 (axis) vertebra.

ear ossicles: Three small bones located in the middle ear cavity that serve to transmit sound vibrations to the inner ear.

ethmoid air cell: One of several small, air-filled spaces located within the lateral sides of the ethmoid bone, between the orbit and upper nasal cavity.

ethmoid bone: Unpaired bone that forms the roof and upper lateral walls of the nasal cavity, portions of the floor of the anterior cranial fossa and the medial wall of the orbit, and the upper portion of the nasal septum.

external acoustic meatus: Ear canal opening located on the lateral side of the skull.

external occipital protuberance: Small bump located at the midline on the posterior skull.

facet: Small, flattened area on a bone for an articulation (joint) with another bone, or for muscle attachment.

facial bones: 14 bones that support the facial structures and form the upper and lower jaws and the hard palate.

false ribs: Vertebrochondral ribs 8–12 whose costal cartilage either attaches indirectly to the sternum via the costal cartilage of the next higher rib or does not attach to the sternum at all.

floating ribs: Vertebral ribs 11–12 that do not attach to the sternum or to the costal cartilage of another rib.

fontanelle: Expanded area of fibrous connective tissue that separates the brain case bones of the skull prior to birth and during the first year after birth.

foramen magnum: Large opening in the occipital bone of the skull through which the spinal cord emerges and the vertebral arteries enter the cranium.

frontal bone: Unpaired bone that forms the forehead, roof of the orbit, and floor of the anterior cranial fossa.

frontal sinus: Air-filled space within the frontal bone; most anterior of the paranasal sinuses.

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glabella: Slight depression of frontal bone, located at the midline between the eyebrows.

hard palate: Bony structure that forms the roof of the mouth and floor of the nasal cavity, formed by the palatine process of the maxillary bones and the horizontal plate of the palatine bones.

head of the rib: Posterior end of a rib that articulates with the bodies of thoracic vertebrae.

hyoid bone: Small, U-shaped bone located in the upper neck that does not contact any other bone.

hypophyseal (pituitary) fossa: Shallow depression on top of the sella turcica that houses the pituitary (hypophyseal) gland.

inferior articular process: Bony process that extends downward from the vertebral arch of a vertebra that articulates with the superior articular process of the next lower vertebra.

inferior nasal concha: One of the paired bones that project from the lateral walls of the nasal cavity to form the largest and most inferior of the nasal conchae.

internal acoustic meatus: Opening into the petrous ridge, located on the lateral wall of the posterior cranial fossa.

intervertebral disc: Structure located between the bodies of adjacent vertebrae that strongly joins the vertebrae; provides padding, weight-bearing ability, and enables vertebral column movements.

intervertebral foramen: Opening located between adjacent vertebrae for exit of a spinal nerve.

jugular foramina: Openings located between the temporal bone and occipital bone that allow the internal jugular vein and three cranial nerves to pass through.

jugular (suprasternal) notch: Shallow notch located on the superior surface of the sternal manubrium.

lacrimal bone: Paired bones that contribute to the anterior-medial wall of each orbit.

lambdoid suture: Inverted V-shaped joint that unites the occipital bone to the right and left parietal bones on the posterior skull.

lamina: Portion of the vertebral arch on each vertebra that extends between the transverse and spinous process.

lumbar curve: Posteriorly concave curvature of the lumbar vertebral column region; a secondary curve of the vertebral column.

lumbar vertebrae: Five vertebrae numbered L1–L5 that are located in the lumbar region (lower back) of the vertebral column.

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mandible: Unpaired bone that forms the lower jawbone; the only movable bone of the skull.

mandibular fossa: Oval depression located on the inferior surface of the skull.

manubrium: Expanded, superior portion of the sternum.

mastoid process: Large bony prominence on the inferior, lateral skull, just behind the earlobe.

maxilla (also maxillary bone): Paired bones that form the upper jaw and anterior portion of the hard palate.

maxillary sinus: Air-filled space located within each maxillary bone; largest of the paranasal sinuses.

middle nasal concha: Nasal concha formed by the ethmoid bone that is located between the superior and inferior conchae.

nasal bone: Paired bones that form the base of the nose.

nasal cavity: Opening through the skull for passage of air.

nasal conchae (singular = concha): Serve to swirl the incoming air, which helps warm and moisturize it before the air moves into the delicate air sacs of the lungs.

nasal septum: Flat, midline structure that divides the nasal cavity into halves, formed by the perpendicular plate of the ethmoid bone, vomer bone, and septal cartilage.

nasolacrimal canal: Passage for drainage of tears that extends downward from the medial-anterior orbit to the nasal cavity, terminating behind the inferior nasal conchae.

neck of the rib: Narrowed region of a rib, next to the rib head.

nucleus pulposus: Gel-like central region of an intervertebral disc; provides for padding, weight-bearing, and movement between adjacent vertebrae.

occipital bone: Unpaired bone that forms the posterior portions of the brain case and base of the skull.

occipital condyle: Paired, oval-shaped bony knobs located on the inferior skull, to either side of the foramen magnum.

optic canal: Opening spanning between middle cranial fossa and posterior orbit.

orbit: Bony socket that contains the eyeball and associated muscles.

palatine bone: Paired bones that form the posterior quarter of the hard palate and a small area in floor of the orbit.

palatine process: Medial projection from the maxilla bone that forms the anterior three-quarters of the hard palate.

paranasal sinuses: Cavities within the skull that are connected to the conchae that serve to warm and humidify incoming air, produce

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mucus, and lighten the weight of the skull; consist of frontal, maxillary, sphenoidal, and ethmoidal sinuses.

parietal bone: Paired bones that form the upper, lateral sides of the skull.

pedicle: Portion of the vertebral arch that extends from the vertebral body to the transverse process.

perpendicular plate of the ethmoid bone: Downward, midline extension of the ethmoid bone that forms the superior portion of the nasal septum.

posterior arch: Posterior portion of the ringlike C1 (atlas) vertebra.

primary curve: Anteriorly concave curvatures of the thoracic and sacrococcygeal regions that are retained from the original fetal curvature of the vertebral column.

ramus of the mandible: Vertical portion of the mandible.

ribs: Thin, curved bones of the chest wall.

sacral canal: Bony tunnel that runs through the sacrum.

sacral foramina: Series of paired openings for nerve exit located on both the anterior (ventral) and posterior (dorsal) aspects of the sacrum.

sacral hiatus: Inferior opening and termination of the sacral canal.

sacral promontory: Anterior lip of the base (superior end) of the sacrum.

sacrococcygeal curve: Anteriorly concave curvature formed by the sacrum and coccyx; a primary curve of the vertebral column.

sacrum: Single bone located near the inferior end of the adult vertebral column that is formed by the fusion of five sacral vertebrae; forms the posterior portion of the pelvis.

sagittal suture: Joint that unites the right and left parietal bones at the midline along the top of the skull.

secondary curve: Posteriorly concave curvatures of the cervical and lumbar regions of the vertebral column that develop after the time of birth.

sella turcica: Elevated area of sphenoid bone located at the midline of the middle cranial fossa.

septal cartilage: Flat cartilage structure that forms the anterior portion of the nasal septum.

skeleton: Bones of the body.

skull: Bony structure that forms the head, face, and jaws, and protects the brain; consists of 22 bones.

sphenoid bone: Unpaired bone that forms the central base of the skull.

sphenoid sinus: Air-filled space located within the sphenoid bone; most posterior of the paranasal sinuses.

spinous process: Unpaired bony process that extends posteriorly from the vertebral arch of a vertebra.

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squamous suture: Joint that unites the parietal bone to the squamous portion of the temporal bone on the lateral side of the skull.

sternal angle: Junction line between manubrium and body of the sternum; the site for attachment of the second rib to the sternum.

sternal body: The elongated, central portion of the sternum.

sternum: Flattened bone located at the centre of the anterior chest.

styloid process: Downward projecting, elongated bony process located on the inferior aspect of the skull.

superior articular process: Bony process that extends upward from the vertebral arch of a vertebra and articulates with the inferior articular process of the next higher vertebra.

superior articular process of the sacrum: Paired processes that extend upward from the sacrum to articulate (join) with the inferior articular processes from the L5 vertebra.

superior nasal concha: Smallest and most superiorly located of the nasal conchae; formed by the ethmoid bone.

superior orbital fissure: Irregularly shaped opening between the middle cranial fossa and the posterior orbit.

supraorbital foramen: Opening located on the anterior skull, at the superior margin of the orbit.

suture: Junction line at which adjacent bones of the skull are united by fibrous connective tissue.

temporal bone: Paired bones that form the lateral, inferior portions of the skull, with squamous, mastoid, and petrous portions.

temporal fossa: Shallow space on the lateral side of the skull, above the level of the zygomatic arch.

thoracic cage: Consists of 12 pairs of ribs and the sternum.

thoracic curve: Anteriorly concave curvature of the thoracic vertebral column region; a primary curve of the vertebral column.

thoracic vertebrae: 12 vertebrae numbered T1–T12 that are located in the thoracic region (upper back) of the vertebral column.

transverse foramen: Opening found only in the transverse processes of cervical vertebrae.

transverse process: Paired bony process that extends laterally from the vertebral arch of a vertebra.

true ribs: Vertebrosternal ribs 1–7, which attach via their costal cartilage directly to the sternum.

tubercle of the rib: Small bump on the posterior side of a rib for articulation with the transverse process of a thoracic vertebra.

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vertebra: Individual bone in the neck and back regions of the vertebral column.

vertebral (spinal) canal: Bony passageway within the vertebral column for the spinal cord that is formed by a series of individual vertebral foramina.

vertebral arch: Bony arch formed by the posterior portion of each vertebra that surrounds and protects the spinal cord.

vertebral body: The anterior portion of each vertebra; the part that supports body weight.

vertebral column: Entire sequence of bones that extend from the skull to the tailbone.

vertebral foramen: Opening associated with each vertebra, defined by the vertebral arch that provides passage for the spinal cord.

vomer bone: Unpaired bone that forms the inferior and posterior portions of the nasal septum.

xiphoid process: Small process that forms the inferior tip of the sternum.

zygomatic arch: Elongated, freestanding arch on the lateral skull, formed anteriorly by the temporal process of the zygomatic bone.

zygomatic bone: Cheekbone; paired bones that contribute to the lateral orbit and anterior zygomatic arch.

Chapter Review

7.1 Divisions of the Skeletal System

The skeletal system includes all the bones, cartilages, and ligaments of the body. It serves to support the body, protect the brain and other internal organs, and provides a rigid structure upon which muscles can pull to generate body movements. It also stores fat and the tissue responsible for the production of blood cells. The skeleton is subdivided into two parts. The axial skeleton forms a vertical axis that includes the head, neck, back, and chest. It has 80 bones and consists of the skull, vertebral column, and thoracic cage. The adult vertebral column consists of 24 vertebrae plus the sacrum and coccyx. The thoracic cage is formed by 12 pairs of ribs and the sternum. The appendicular skeleton consists of 126 bones in the adult and includes all the bones of the upper and lower limbs, plus the bones that anchor each limb to the axial skeleton.

7.2 The Skull

The skull consists of the brain case and the facial bones. The brain case surrounds and protects the brain, which occupies the cranial cavity inside the skull. It consists of the rounded calvaria and a complex base. The brain case is formed by

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eight bones, the paired parietal and temporal bones, plus the unpaired frontal, occipital, sphenoid, and ethmoid bones. The narrow gap between the bones is filled with dense, fibrous connective tissue that unites the bones. The sagittal suture joins the right and left parietal bones. The coronal suture joins the parietal bones to the frontal bone, the lambdoid suture joins them to the occipital bone, and the squamous suture joins them to the temporal bone.

The facial bones support the facial structures and form the upper and lower jaws. These consist of 14 bones: the paired maxillary, palatine, zygomatic, nasal, lacrimal, and inferior conchae bones and the unpaired vomer and mandible bones. The ethmoid bone also contributes to the formation of facial structures. The maxilla forms the upper jaw, and the mandible forms the lower jaw. The maxilla also forms the larger anterior portion of the hard palate, which is completed by the smaller palatine bones that form the posterior portion of the hard palate.

The floor of the cranial cavity increases in depth from front to back and is divided into three cranial fossae. The right and left sides are separated at the midline by the sella turcica, which surrounds the shallow hypophyseal fossa.

Openings through the skull in the floor of the middle fossa include the optic canal and superior orbital fissure (which open into the posterior orbit), the foramen ovale, and the exit of the carotid canal. Openings through the posterior cranial fossa include the large foramen magnum, the internal acoustic meatus, and the jugular foramina.

The anterior skull has the orbits that house the eyeballs and associated muscles. The walls of the orbit are formed by contributions from seven bones: the frontal, zygomatic, maxillary, palatine, ethmoid, lacrimal, and sphenoid. Located at the superior margin of the orbit is the supraorbital foramen. The nasal conchae are bony projections from the lateral walls of the nasal cavity. The large inferior nasal concha is an independent bone, while the middle and superior conchae are parts of the ethmoid bone.

The nasal septum is formed by the perpendicular plate of the ethmoid bone, the vomer bone, and the septal cartilage. The paranasal sinuses are air-filled spaces located within the frontal, maxillary, sphenoid, and ethmoid bones.

The temporal fossa is the shallow space located on the lateral skull above the level of the zygomatic arch.

The hyoid bone is located in the upper neck and does not join with any other bone. It is held in position by muscles and serves to support the tongue above, the larynx below, and the pharynx posteriorly.

7.3 The Vertebral Column

The vertebral column forms the neck and back. The vertebral column originally develops as 33 vertebrae but is eventually reduced to 24 vertebrae, plus the sacrum

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and coccyx. The vertebrae are divided into the cervical region (C1–C7 vertebrae), the thoracic region (T1–T12 vertebrae), and the lumbar region (L1–L5 vertebrae). The sacrum arises from the fusion of five sacral vertebrae and the coccyx from the fusion of four small coccygeal vertebrae. The vertebral column has four curvatures: the cervical, thoracic, lumbar, and sacrococcygeal curves. The thoracic and sacrococcygeal curves are primary curves retained from the original fetal curvature. The cervical and lumbar curves develop after birth and thus are secondary curves. The cervical curve develops as the infant begins to hold up the head, and the lumbar curve appears with standing and walking.

A typical vertebra consists of an enlarged anterior portion called the body, which provides weight-bearing support. Attached posteriorly to the body is a vertebral arch, which surrounds and defines the vertebral foramen for passage of the spinal cord. The vertebral arch consists of the pedicles, which attach to the vertebral body, and the laminae, which come together to form the roof of the arch. Arising from the vertebral arch are the laterally projecting transverse processes and the posteriorly oriented spinous process. The superior articular processes project upward, where they articulate with the downward-projecting inferior articular processes of the next higher vertebrae.

A typical cervical vertebra has a small body, a bifid (Y-shaped) spinous process, and U-shaped transverse processes with a transverse foramen. In addition to these characteristics, the axis (C2 vertebra) also has the dens projecting upward from the vertebral body. The atlas (C1 vertebra) differs from the other cervical vertebrae in that it does not have a body but instead consists of a bony ring formed by the anterior and posterior arches. The atlas articulates with the dens from the axis. A typical thoracic vertebra is distinguished by its long, downward-projecting spinous process. Thoracic vertebrae also have articulation facets on the body and transverse processes for attachment of the ribs. Lumbar vertebrae support the greatest amount of body weight and thus have a large, thick body. They also have a short, blunt spinous process. The sacrum is triangular in shape. Anterior (ventral) and posterior (dorsal) sacral foramina allow branches of the sacral spinal nerves to exit the sacrum. The auricular surfaces are articulation sites on the lateral sacrum that anchor the sacrum to the hip bones to form the pelvis. The coccyx is small and derived from the fusion of four small vertebrae.

The intervertebral discs fill in the gaps between the bodies of adjacent vertebrae. They provide strong attachments and padding between the vertebrae. The outer, fibrous layer of a disc is called the anulus fibrosus. The gel-like interior is called the nucleus pulposus. The disc can change shape to allow for movement between vertebrae. If the anulus fibrosus is weakened or damaged, the nucleus pulposus can protrude outward, resulting in a herniated disc.

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7.4 The Thoracic Cage

The thoracic cage protects the heart and lungs. It is composed of 12 pairs of ribs with their costal cartilages and the sternum. The ribs are anchored posteriorly to the 12 thoracic vertebrae. The sternum consists of the manubrium, body, and xiphoid process. The manubrium and body are joined at the sternal angle, which is also the site for attachment of the second ribs.

Ribs are flattened, curved bones and are numbered 1–12. Posteriorly, the head of the rib articulates with the costal facets located on the bodies of thoracic vertebrae and the rib tubercle articulates with the facet located on the vertebral transverse process. The angle of the ribs forms the most posterior portion of the thoracic cage. The costal groove in the inferior margin of each rib carries blood vessels and a nerve.

Anteriorly, each rib ends in a costal cartilage. True ribs (1–7) attach directly to the sternum via their costal cartilage. The false ribs (8–12) attach to the sternum either indirectly or not at all. Ribs 8–10 have their costal cartilages attached to the cartilage of the next higher rib. The floating ribs (11–12) are short and do not attach to the sternum or to another rib.

7.5 Embryonic Development of the Axial Skeleton

Formation of the axial skeleton begins during early embryonic development with the appearance of the rodlike notochord along the dorsal length of the early embryo. Repeating, paired blocks of tissue called somites then appear along either side of the notochord. As the somites grow, they split into parts. This consists of mesenchyme, the embryonic tissue that will become the bones, cartilages, and connective tissues of the body.

Mesenchyme in the head region will produce the bones of the skull via two different mechanisms. The bones of the brain case arise via intramembranous ossification, in which embryonic mesenchyme tissue converts directly into bone. At the time of birth, these bones are separated by fontanelles, wide areas of fibrous connective tissue. As the bones grow, the fontanelles are reduced to sutures, which allow for continued growth of the skull throughout childhood. In contrast, the cranial base and facial bones are produced by the process of endochondral ossification, in which mesenchyme tissue initially produces a hyaline cartilage model of the future bone. The cartilage model allows for the growth of the bone and is gradually converted into bone over a period of many years.

The vertebrae, ribs, and sternum also develop via endochondral ossification. Mesenchyme accumulates around the notochord and produces hyaline cartilage models of the vertebrae. The notochord largely disappears,

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but remnants of the notochord contribute to formation of the intervertebral discs. In the thorax region, a portion of the vertebral cartilage model splits off to form the ribs. These then become attached anteriorly to the developing cartilage model of the sternum. Growth of the cartilage models for the vertebrae, ribs, and sternum allows for enlargement of the thoracic cage during childhood and adolescence. The cartilage models gradually undergo ossification and are converted into bone.

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8

The Appendicular Skeleton

Chapter Objectives

After studying this chapter, you will be able to:

- Discuss the bones of the pectoral and pelvic girdles and describe how these unite the limbs with the axial skeleton
- Describe the bones of the upper limb, including the bones of the arm, forearm, wrist, and hand
- Identify the features of the pelvis and explain how these differ between the adult male and female pelvis
- Describe the bones of the lower limb, including the bones of the thigh, leg, ankle, and foot

Your skeleton provides the internal supporting structure of the body. The adult axial skeleton consists of 80 bones that form the head and trunk. Attached to this are the limbs, whose 126 bones constitute the appendicular skeleton. These bones are divided into two groups: the bones that are located within the limbs themselves and the girdle bones that attach the limbs to the axial skeleton. The bones of the shoulder region form the pectoral girdle, which anchors the upper limbs to the thoracic cage of the axial skeleton. The lower limbs are attached to the vertebral column by the pelvic girdle.

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8.1 The Pectoral Girdles

Learning Objectives

By the end of this section, you will be able to:

- Describe the bones that form the right and left pectoral girdles
- List the functions of the pectoral girdles

The appendicular skeleton includes all the limb bones, plus the bones that unite each limb with the axial skeleton (Figure 8.1). The bones that attach each upper limb to the axial skeleton form the **pectoral girdle** (shoulder girdle). This consists of two bones, the scapula and clavicle (Figure 8.2). The clavicle (collarbone) is an S-shaped bone located on the anterior side of the shoulder. It is attached on its medial end to the sternum of the thoracic cage, which is part of the axial skeleton. The lateral end of the clavicle articulates (joins) with the scapula just above the shoulder joint. You can easily palpate, or feel with your fingers, the entire length of your clavicle.

The **scapula** (shoulder blade) lies on the posterior aspect of the shoulder. It is supported by the **clavicle** and articulates with the humerus (arm bone) to form the shoulder joint. The scapula is a flat, triangular bone with a prominent ridge running across its posterior surface. This ridge extends out laterally, where it forms the bony tip of the shoulder and joins with the lateral end of the clavicle. By following along the clavicle, you can palpate out to the bony tip of the shoulder, and from there, you can move back across your posterior shoulder to follow the ridge of the scapula. Move your shoulder around and feel how the clavicle and scapula move together as a unit. Both of these bones serve as important attachment sites for muscles that aid movements of the shoulder and arm.

The right and left pectoral girdles are not joined to each other, allowing each to operate independently. In addition, the clavicle of each pectoral girdle is anchored to the axial skeleton by a single, highly mobile joint. This allows for the extensive mobility of the entire pectoral girdle, which in turn enhances movements of the shoulder and upper limb.

Clavicle

The clavicle is the only long bone that lies in a horizontal position in the body (see Figure 8.2). The clavicle has several important functions. First, anchored by muscles from above, it serves as a strut that extends laterally to support the scapula. This in turn holds the shoulder joint superiorly and laterally from

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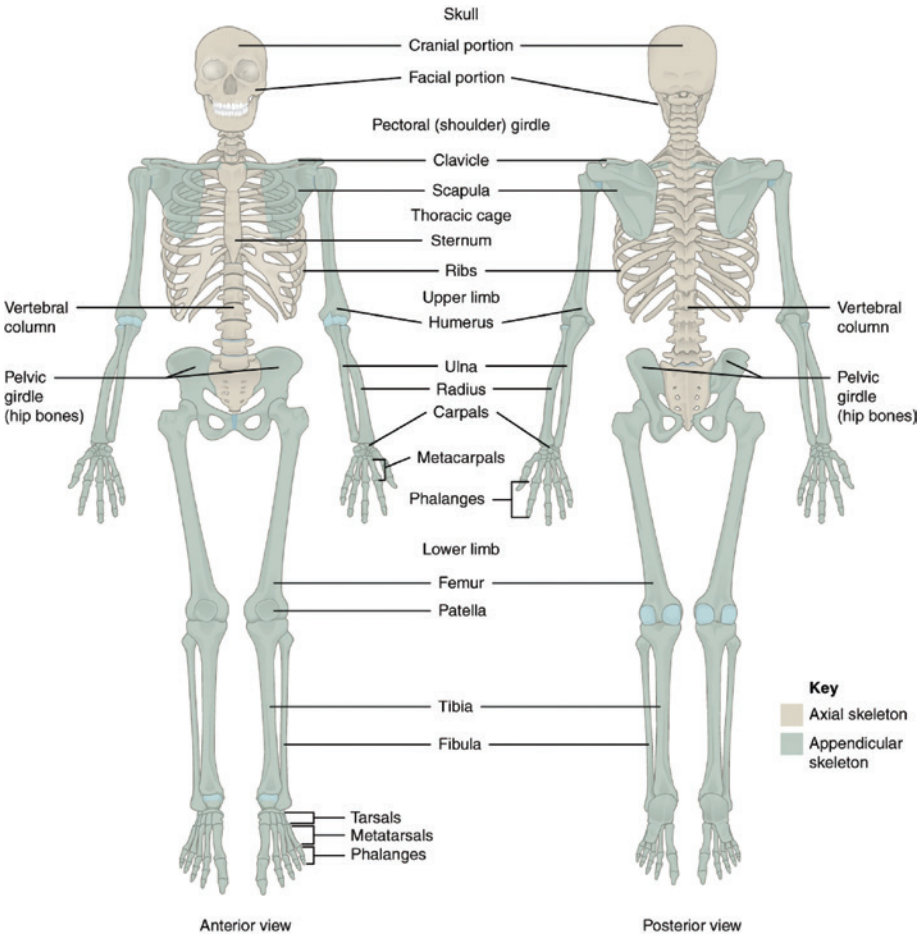


Figure 8.1 Axial and Appendicular Skeletons. The axial skeleton forms the central axis of the body and consists of the skull, vertebral column, and thoracic cage. The appendicular skeleton consists of the pectoral and pelvic girdles, the limb bones, and the bones of the hands and feet.

the trunk, allowing for maximal freedom of motion for the upper limb. The clavicle also transmits forces acting on the upper limb to the sternum and axial skeleton. Finally, it serves to protect the underlying nerves and blood vessels as they pass between the trunk of the body and the upper limb.

The clavicle has three regions: the medial end, the lateral end, and the shaft. The **sternal** (**medial**) **end** of the clavicle has a triangular shape and articulates with the manubrium portion of the sternum. This forms the **sternoclavicular joint**, which is the only bony articulation between the pectoral girdle of the upper limb and the axial skeleton. This joint allows considerable mobility, enabling the clavicle and scapula to move in upward/downward and anterior/posterior directions during shoulder movements. The **acromial** (**lateral**) **end**

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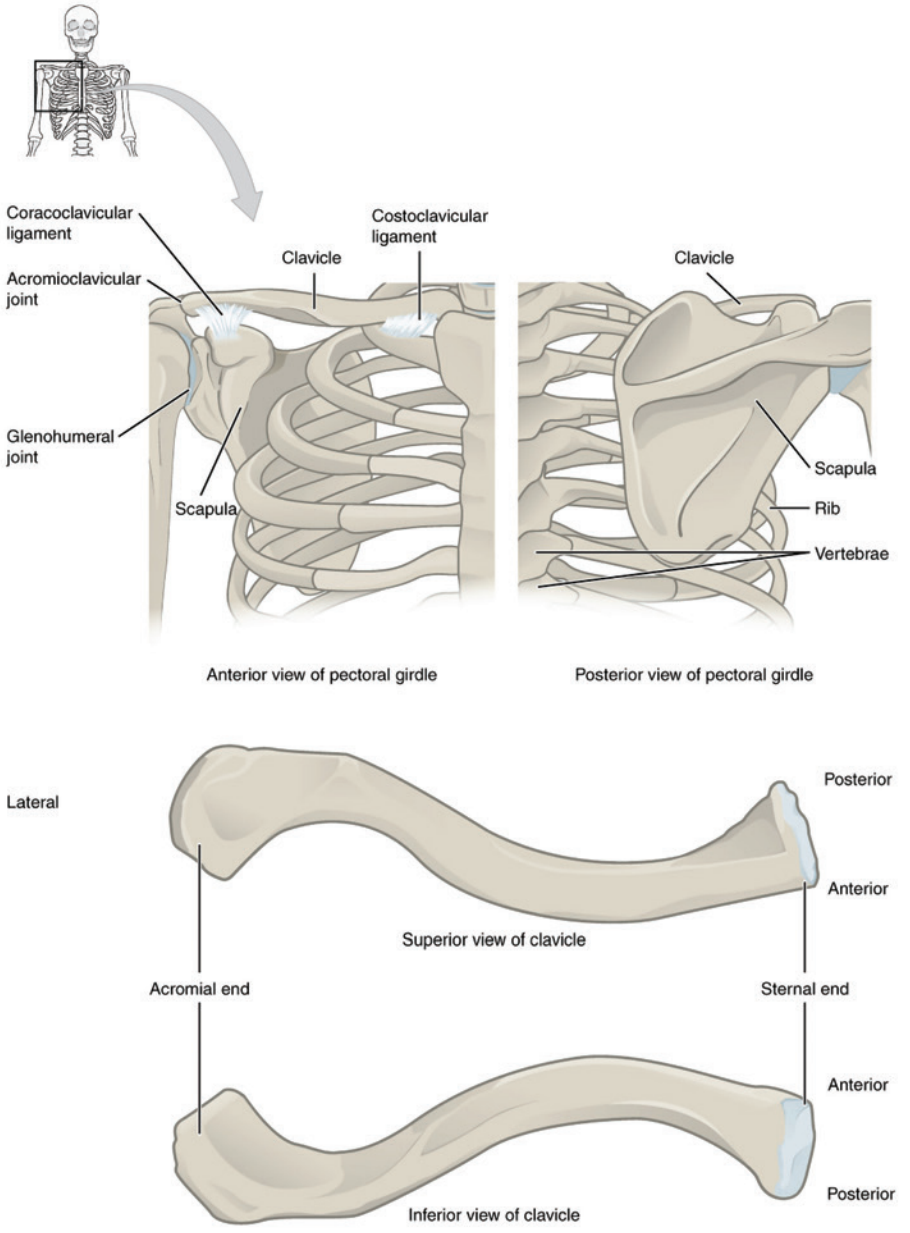


Figure 8.2 Pectoral Girdle. The pectoral girdle consists of the clavicle and the scapula, which serve to attach the upper limb to the sternum of the axial skeleton.

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of the clavicle articulates with the acromion of the scapula, the portion of the scapula that forms the bony tip of the shoulder. For the **shaft of the clavicle**, there are some sex differences in its morphology: in females, the clavicle tends to be shorter, thinner, and less curved; in males, the clavicle is heavier and longer, and it has a greater curvature and rougher surfaces where muscles attach, features that are more pronounced in manual workers.

Scapula

The scapula is also part of the pectoral girdle and thus plays an important role in anchoring the upper limb to the body. The scapula is located on the posterior side of the shoulder. It is surrounded by muscles on both its anterior (deep) and posterior (superficial) sides and thus does not articulate with the ribs of the thoracic cage.

The scapula has several important landmarks (Figure 8.3). The three margins or borders (superior, medial, and inferior) of the scapula are named for their positions within the body. The **suprascapular notch** is located lateral to the midpoint of the superior border. There are two corners of the triangular scapula at either end of the medial border—superior and inferior angles. The **inferior angle** is the most inferior portion of the scapula and is particularly important because it serves as the attachment point for several powerful muscles involved in shoulder and upper limb movements. The remaining corner of the scapula, between the superior and lateral borders, is the location of the **glenoid cavity** (glenoid fossa).

The scapula also has two prominent projections. Toward the lateral end of the superior border, between the suprascapular notch and glenoid cavity, is the hooklike **coracoid process**. This process projects anteriorly and curves laterally. At the shoulder, the coracoid process is located inferior to the lateral end of the clavicle. It is anchored to the clavicle by a strong ligament and serves as the attachment site for muscles of the anterior chest and arm. On the posterior aspect, the **spine of the scapula** is a long and prominent ridge that runs across its upper portion. Extending laterally from the spine is a flattened and expanded region called the **acromion** or **acromial process**.

The scapula has three depressions, each of which is called a **fossa** (plural = fossae). Two of these are found on the posterior scapula, above and below the scapular spine. Superior to the spine is the narrow **supraspinous fossa**, and inferior to the spine is the broad **infraspinous fossa**. The anterior (deep) surface of the scapula forms the broad **subscapular fossa**. All these fossae provide large surface areas for the attachment of muscles that cross the shoulder joint to act on the humerus.

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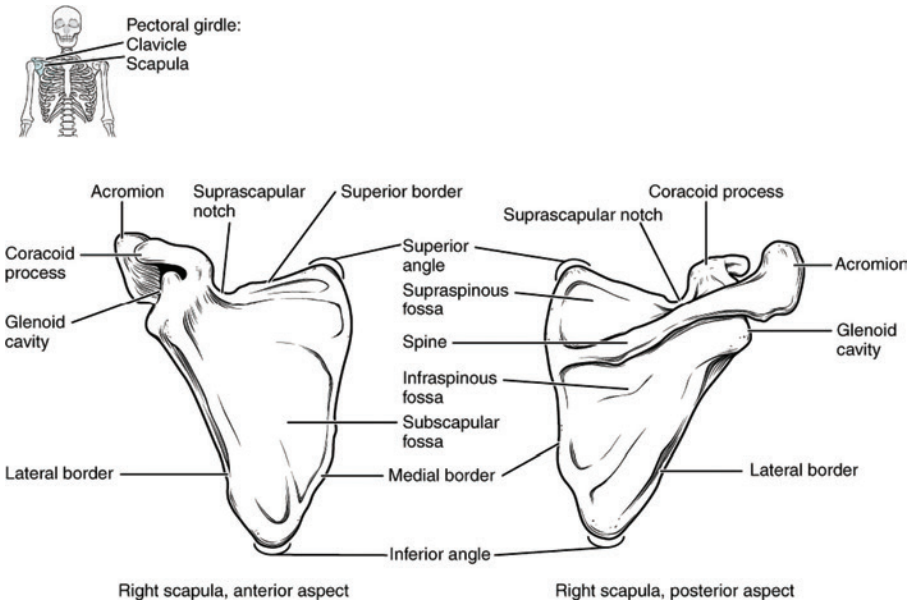


Figure 8.3 Scapula. The isolated scapula is shown here from its anterior (deep) side and its posterior (superficial) side.

8.2 Bones of the Upper Limb

Learning Objectives

By the end of this section, you will be able to:

- Identify the divisions of the upper limb and describe the bones in each region
- List the bones and bony landmarks that articulate at each joint of the upper limb

The upper limb is divided into three regions. These consist of the **arm**, located between the shoulder and elbow joints; the **forearm**, which is between the elbow and wrist joints; and the **hand**, which is located distal to the wrist. There are 30 bones in each upper limb (see Figure 8.1). The humerus is the single bone of the upper arm, and the ulna (medially) and the radius (laterally) are the paired bones of the forearm. The base of the hand contains eight bones, each called a carpal bone, and the palm of the hand is formed by five bones, each called a **metacarpal bone**. The fingers and thumb contain a total of 14 bones, each of which is a phalanx bone of the hand.

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Humerus

The **humerus** is the single bone of the upper arm region (Figure 8.4). At its proximal end is the **head of the humerus**. This is the large, round, smooth region that faces medially. The head articulates with the glenoid cavity of the scapula to form the glenohumeral (shoulder) joint. The margin of the smooth area of the head is the **anatomical neck** of the humerus. Located on the lateral side of the proximal humerus is an expanded bony area called the **greater tubercle**. The smaller **lesser tubercle** of the humerus is found on the anterior aspect of the humerus. Both the greater and lesser tubercles serve as attachment sites for muscles that act across the shoulder joint. The **surgical neck** is located at the base of the expanded, proximal end of the humerus, where it joins the narrow **shaft of the humerus**. The surgical neck is a common site of arm fractures. The **deltoid tuberosity** is a roughened, V-shaped region located

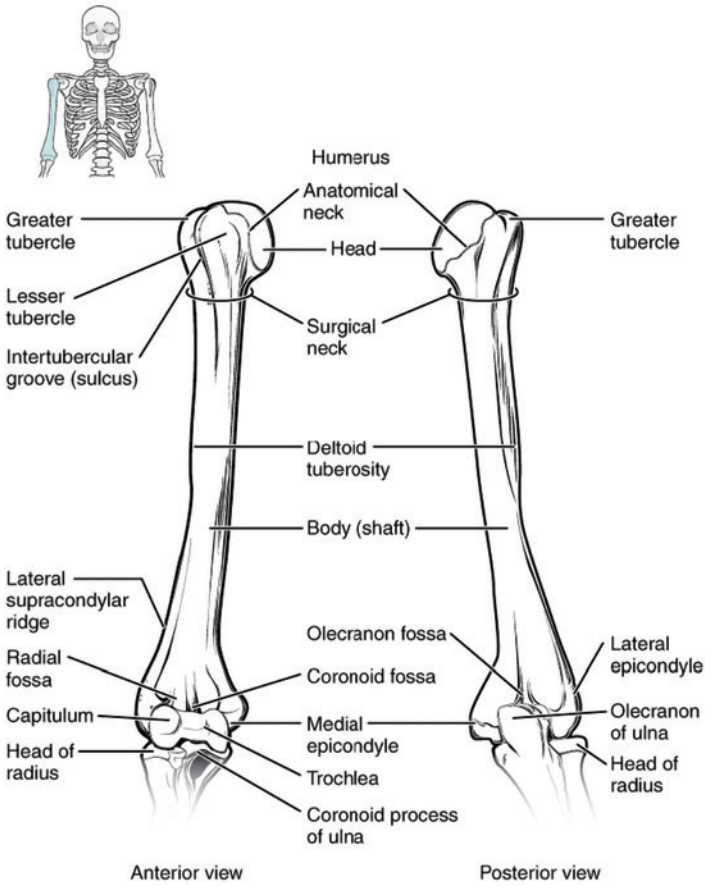


Figure 8.4 Humerus and Elbow Joint. The humerus is the single bone of the upper arm region. It articulates with the radius and ulna bones of the forearm to form the elbow joint.

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on the lateral side in the middle of the humerus shaft. As its name indicates, it is the site of attachment for the deltoid muscle.

The distal end of the humerus has two articulation areas, which join the ulna and radius bones of the forearm to form the **elbow joint**. The more medial of these areas is the **trochlea**, a spindle- or pulley-shaped region that articulates with the ulna bone. Immediately lateral to the trochlea is the **capitulum**, a knoblike structure located on the anterior surface of the distal humerus. The capitulum articulates with the radius bone of the forearm. Just above these bony areas are two small depressions. These spaces accommodate the forearm bones when the elbow is fully bent (flexed).

Ulna

The **ulna** is the medial bone of the forearm. It runs parallel to the radius, which is the lateral bone of the forearm (Figure 8.5). The proximal end of the ulna resembles a crescent wrench with its large, C-shaped **trochlear notch**. This region articulates with the trochlea of the humerus as part of the elbow joint. The inferior margin of the trochlear notch is formed by a prominent lip of bone called the **coronoid process of the ulna**. Just below this on the anterior ulna is a roughened area called the **ulnar tuberosity**. The posterior and superior portions of the proximal ulna make up the **olecranon process**, which forms the bony tip of the elbow.

More distal is the **shaft of the ulna**. The small, rounded area that forms the distal end is the **head of the ulna**. Projecting from the posterior side of the ulnar head is the **styloid process of the ulna**, a short bony projection. This serves as an attachment point for a connective tissue structure that unites the distal ends of the ulna and radius.

Radius

The **radius** runs parallel to the ulna, on the lateral (thumb) side of the forearm (see Figure 8.5). The **head of the radius** is a disc-shaped structure that forms the proximal end. The small depression on the surface of the head articulates with the capitulum of the humerus as part of the elbow joint, whereas the smooth, outer margin of the head articulates with the radial notch of the ulna at the proximal radioulnar joint. The **neck of the radius** is the narrowed region immediately below the expanded head. Inferior to this point on the medial side is the **radial tuberosity**, an oval-shaped, bony protuberance that serves as a muscle attachment point. The **shaft of the radius** is slightly curved and has a small ridge along its medial side. The lateral end of the radius has a pointed projection called the **styloid process of the radius**. This provides attachment for ligaments that support the lateral side of the wrist joint. Compared to the

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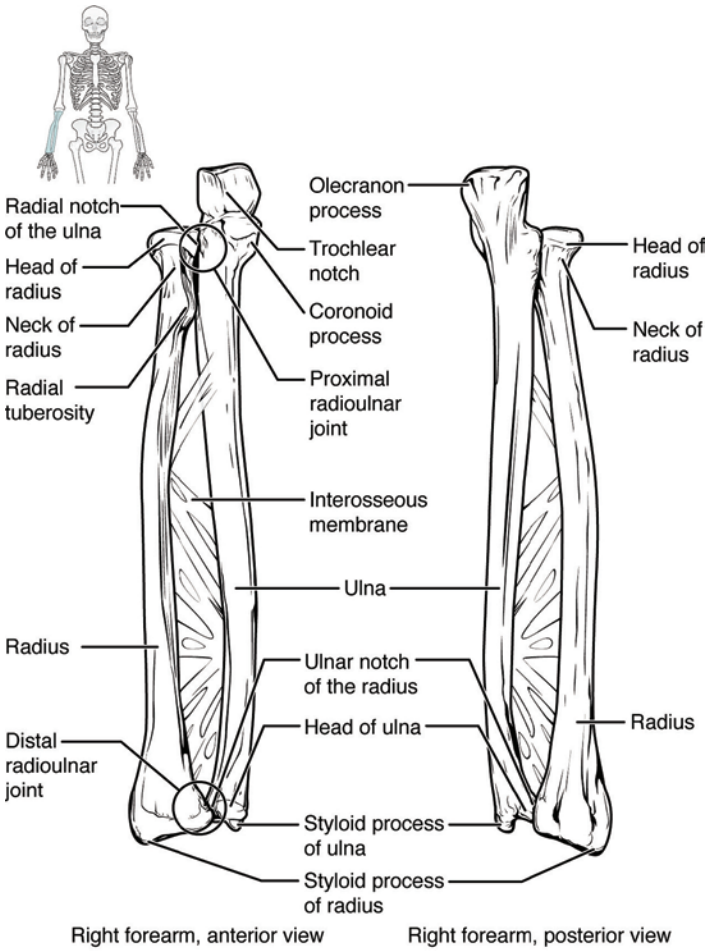


Figure 8.5 Ulna and Radius. The ulna is located on the medial side of the forearm, and the radius is on the lateral side. These bones are attached to each other by an interosseous membrane.

styloid process of the ulna, the styloid process of the radius projects more distally, thereby limiting the range of movement for lateral deviations of the hand at the wrist joint.

Interactive Link 8.1

Watch this video (http://oer.aupress.ca/oer-202505/8.1) to see how fractures of the distal radius bone can affect the wrist joint. Explain the problems that may occur if a fracture of the distal radius involves the joint surface of the radiocarpal joint of the wrist.

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Carpal Bones

The wrist and base of the hand are formed by a series of eight small **carpal bones** (see Figure 8.6). The carpal bones are arranged in two rows, forming a proximal row of four carpal bones and a distal row of four carpal bones.

The carpal bones form the base of the hand. Within the carpal bones, the four proximal bones are united to each other by ligaments to form a unit. Only three of these bones (the scaphoid, lunate, and triquetrum) contribute to the **radiocarpal joint**. The scaphoid and lunate bones articulate directly with the distal end of the radius, whereas the triquetrum bone articulates with a fibrocartilaginous pad that spans the radius and styloid process of the ulna. The distal end of the ulna thus does not directly articulate with any of the carpal bones.

The four distal carpal bones are also held together as a group by ligaments. The proximal and distal rows of carpal bones articulate with each other. Together, the radiocarpal and midcarpal joints are responsible for all movements of the hand at the wrist. The distal carpal bones also articulate with the metacarpal bones of the hand.

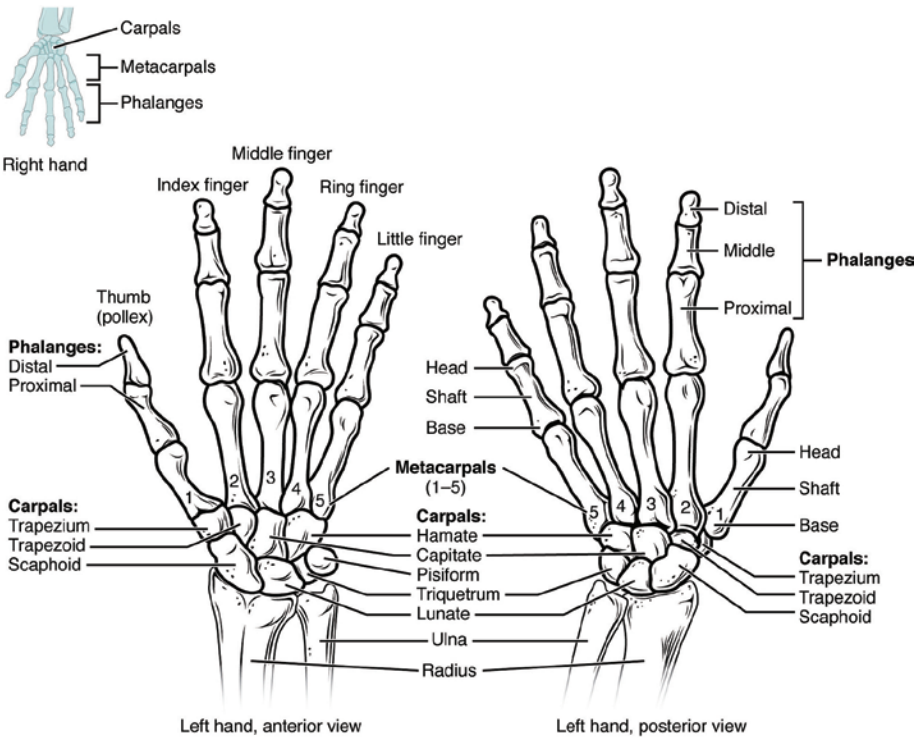


Figure 8.6 Bones of the Wrist and Hand. The eight carpal bones form the base of the hand. These are arranged into proximal and distal rows of four bones each. The metacarpal bones form the palm of the hand. The thumb and fingers consist of the phalanx bones.

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In the articulated hand, the carpal bones form a U-shaped grouping. A strong ligament called the **flexor retinaculum** spans the top of this U-shaped area to maintain this grouping of the carpal bones. Together, the carpal bones and the flexor retinaculum form a passageway called the **carpal tunnel**, with the carpal bones forming the walls and floor and the flexor retinaculum forming the roof of this space.

Metacarpal Bones

The palm of the hand contains five elongated metacarpal bones. These bones lie between the carpal bones of the wrist and the bones of the fingers and thumb (see Figure 8.6). The proximal end of each metacarpal bone articulates with one of the distal carpal bones. The metacarpal bones are numbered 1–5, beginning at the thumb.

The first metacarpal bone, at the base of the thumb, is separated from the other metacarpal bones. This allows it a freedom of motion that is independent of the other metacarpal bones, which is very important for thumb mobility. The remaining metacarpal bones are united to form the palm of the hand. The second and third metacarpal bones are firmly anchored in place and are immobile. However, the fourth and fifth metacarpal bones have limited anterior-posterior mobility, a motion that is greater for the fifth bone. This mobility is important during power gripping with the hand (Figure 8.7). The anterior movement of these bones, particularly the fifth metacarpal bone, increases the strength of contact for the medial hand during gripping actions.



Figure 8.7 Hand During Gripping. During tight gripping—compare (b) to (a)—the fourth and, particularly, the fifth metatarsal bones are pulled anteriorly. This increases the contact between the object and the medial side of the hand, thus improving the firmness of the grip.

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Phalanx Bones

The fingers and thumb contain 14 bones, each of which is called a **phalanx bone** (plural = phalanges), named after the ancient Greek phalanx (a rectangular block of soldiers). The **pollex** (thumb) is digit number 1 and has two phalanges, a proximal phalanx, and a distal phalanx bone (see Figure 8.6). Digits 2 (index finger) through 5 (little finger) have three phalanges each, called the proximal, middle, and distal phalanx bones.

Interactive Link 8.2

Visit this site (http://oer.aupress.ca/oer-202505/8.2) to explore the bones and joints of the hand.

8.3 The Pelvic Girdle and Pelvis

Learning Objectives

By the end of this section, you will be able to:

- Define the pelvic girdle and describe the bones and ligaments of the pelvis
- Explain the three regions of the hip bone and identify their bony landmarks
- Describe the openings of the pelvis and the boundaries of the greater and lesser pelvis

The **pelvic girdle** (hip girdle) is formed by two bones: the right and left **hip bones** or **coxal bones** (*coxal* = "hip"), which serve as the attachment points for each lower limb. Each hip bone, in turn, is firmly joined to the axial skeleton via its attachment to the sacrum of the vertebral column. The right and left hip bones also converge anteriorly to attach to each other. The **bony pelvis** is the entire structure formed by the two hip bones, the sacrum, and, attached inferiorly to the sacrum, the coccyx (Figure 8.8).

Unlike the bones of the pectoral girdle, which are highly mobile to enhance the range of upper limb movements, the bones of the **pelvis** are strongly united to one another to form a largely immobile, weight-bearing structure. This is important for stability because it enables the weight of the body to be easily transferred laterally from the vertebral column, through the pelvic girdle and

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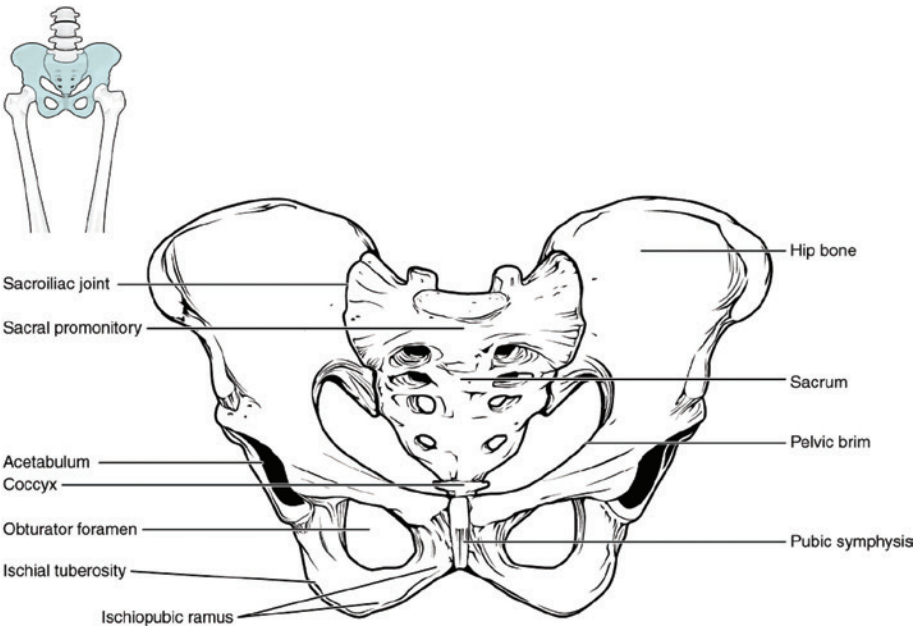


Figure 8.8 Pelvis. The pelvic girdle is formed by two hip bones. The hip bones attach the lower limb to the axial skeleton through their articulation with the sacrum. The right and left hip bones, plus the sacrum and the coccyx, together form the pelvis.

hip joints, and into either lower limb whenever the other limb is not bearing weight. Thus, the immobility of the pelvis provides a strong foundation for the upper body as it rests on top of the mobile lower limbs.

Hip Bone

The hip bone, or coxal bone, forms the pelvic girdle portion of the pelvis. The paired hip bones are the large, curved bones that form the lateral and anterior aspects of the pelvis. Each adult hip bone is formed by three separate bones that fuse together during the late teenage years. These bony components are the ilium, ischium, and pubis (Figure 8.9). These names are retained and used to define the three regions of the adult hip bone.

The **ilium** is the fanlike, superior region that forms the largest part of the hip bone. It is firmly united to the sacrum at the largely immobile **sacroiliac joint** (see Figure 8.8). The **ischium** forms the posteroinferior region of each hip bone. It supports the body when sitting. The **pubis** forms the anterior portion of the hip bone. The pubis curves medially, where it joins to the pubis of the opposite hip bone at a specialized joint called the **pubic symphysis**.

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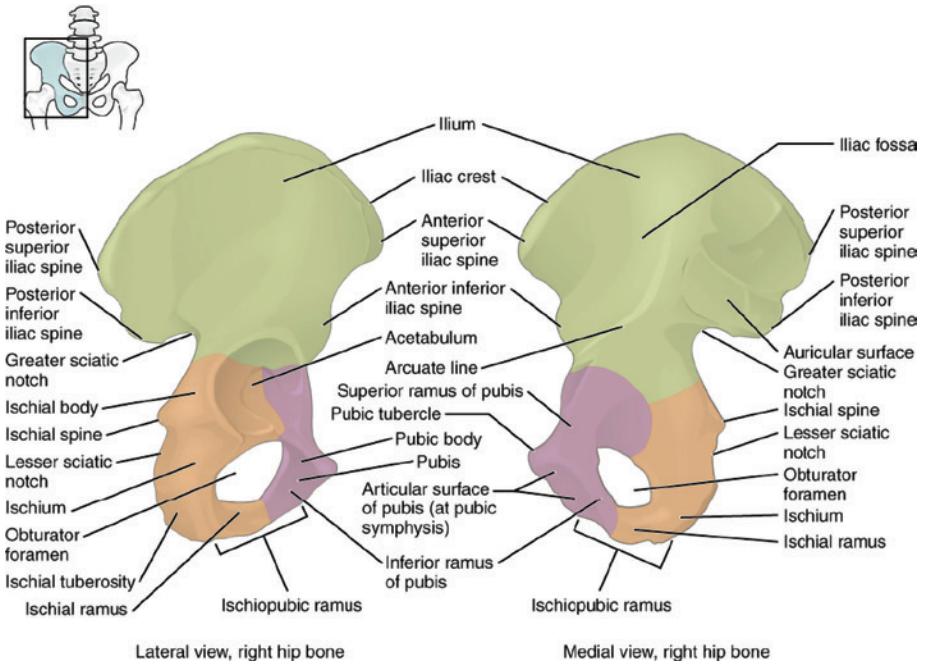


Figure 8.9 The Hip Bone. The adult hip bone consists of three regions. The ilium forms the large, fan-shaped superior portion, the ischium forms the posteroinferior portion, and the pubis forms the anteromedial portion.

Ilium

When you place your hands on your waist, you can feel the arching, superior margin of the ilium along your waistline (see Figure 8.9). This curved, superior margin of the ilium is the **iliac crest**. The shallow depression located on the anteromedial (internal) surface of the upper ilium is called the **iliac fossa**. The large, inverted U-shaped indentation located on the posterior margin of the lower ilium is called the **greater sciatic notch**.

Ischium

The ischium forms the posterolateral portion of the hip bone (see Figure 8.9). The large, roughened area of the inferior ischium is the **ischial tuberosity**. This serves as the attachment for the posterior thigh muscles and also carries the weight of the body when sitting. You can feel the ischial tuberosity if you wiggle your pelvis against the seat of a chair. Projecting superiorly and anteriorly from the ischial tuberosity is a narrow segment of bone called the **ischial ramus**. The slightly curved posterior margin of the ischium above the ischial tuberosity is the **lesser sciatic notch**. The bony projection separating the lesser sciatic notch and greater sciatic notch is the **ischial spine**.

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Pubis

The pubis forms the anterior portion of the hip bone (see Figure 8.9). The enlarged medial portion of the pubis is the **pubic body**. The **superior pubic ramus** is the segment of bone that passes laterally from the pubic body to join the ilium.

The pubic body is joined to the pubic body of the opposite hip bone by the pubic symphysis. Extending downward and laterally from the body is the **inferior pubic ramus**. The **pubic arch** is the bony structure formed by the pubic symphysis and the bodies and inferior pubic rami of the adjacent pubic bones. The inferior pubic ramus extends downward to join the ischial ramus.

Pelvis

The pelvis consists of four bones: the right and left hip bones, the sacrum, and the coccyx (see Figure 8.8). The pelvis has several important functions. Its primary role is to support the weight of the upper body when sitting and to transfer this weight to the lower limbs when standing. It serves as an attachment point for trunk and lower limb muscles and also protects the internal pelvic organs. When standing in the anatomical position, the pelvis is tilted anteriorly. In this position, the anterior superior iliac spines and the pubic tubercles lie in the same vertical plane, and the anterior (internal) surface of the sacrum faces forward and downward.

The three areas of each hip bone (the ilium, pubis, and ischium) converge centrally to form a deep, cup-shaped cavity called the **acetabulum**. This is located on the lateral side of the hip bone and is part of the hip joint. The large opening in the anteroinferior hip bone between the ischium and pubis is the **obturator foramen**. This space is largely filled in by a layer of connective tissue and serves for the attachment of muscles on both its internal and external surfaces.

Several ligaments unite the bones of the pelvis (Figure 8.10). The largely immobile sacroiliac joint is supported by a pair of strong ligaments that are attached between the sacrum and ilium portions of the hip bone. These ligaments help support and immobilize the sacrum as it carries the weight of the body (only a few will be listed here).

Interactive Link 8.3

Watch this video (http://oer.aupress.ca/oer-202505/8.3) for a 3-D view of the pelvis and its associated ligaments. What is the large opening in the bony pelvis, located between the ischium and pubic regions, and what two parts of the pubis contribute to the formation of this opening?

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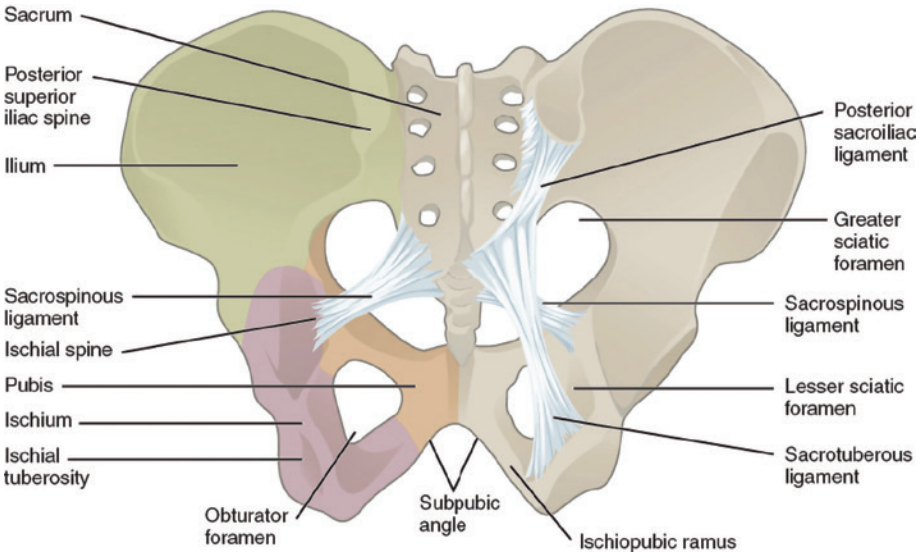


Figure 8.10 Ligaments of the Pelvis. The posterior sacroiliac ligament supports the sacroiliac joint. The sacrospinous ligament spans the sacrum to the ischial spine, and the sacrotuberous ligament spans the sacrum to the ischial tuberosity. The sacrospinous and sacrotuberous ligaments contribute to the formation of the greater and lesser sciatic foramina.

The space enclosed by the bony pelvis is divided into two regions (Figure 8.11). The broad superior region, defined laterally by the large, fanlike portion of the upper hip bone, is called the **greater pelvis** (greater pelvic cavity). This broad area is occupied by portions of the small and large intestines, and because it is more closely associated with the abdominal cavity, it is sometimes referred to as the false pelvis. More inferiorly, the narrow, rounded space of the **lesser pelvis** (lesser pelvic cavity) contains the bladder and other pelvic organs and thus is also known as the true pelvis. The **pelvic brim** (also known as the **pelvic inlet**) forms the superior margin of the lesser pelvis, separating it from the greater pelvis. The pelvic brim is defined by a line formed by the upper margin of the pubic symphysis anteriorly and the pectineal line of the pubis, the arcuate line of the ilium, and the sacral promontory (the anterior margin of the superior sacrum) posteriorly. The inferior limit of the lesser pelvic cavity is called the **pelvic outlet**. This large opening is defined by the inferior margin of the pubic symphysis anteriorly and the **ischiopubic ramus**, the ischial tuberosity, the ligament, and the inferior tip of the coccyx posteriorly. Because of the anterior tilt of the pelvis, the lesser pelvis is also angled, giving it an anterosuperior (pelvic inlet) to posteroinferior (pelvic outlet) orientation.

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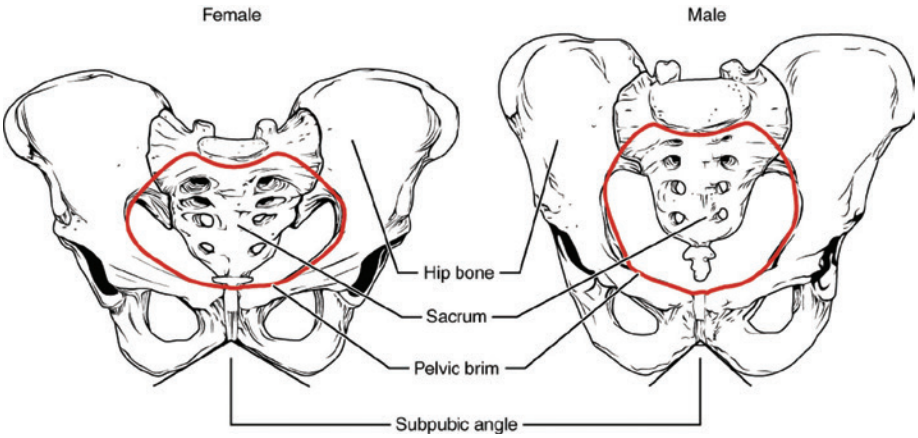


Figure 8.11 Male and Female Pelvis. The female pelvis is adapted for childbirth and is broader, with a larger subpubic angle, a rounder pelvic brim, and a wider and shallower lesser pelvic cavity than the male pelvis.

Comparison of the Female and Male Pelvis

The differences between the adult female and male pelvis relate to function and body size. In general, the bones of the male pelvis are thicker and heavier, adapted for support of the male's heavier physical build and stronger muscles. The greater sciatic notch of the male hip bone is narrower and deeper than the broader notch of females. Because the female pelvis is adapted for childbirth, it is wider than the male pelvis, as evidenced by the distance between the anterior superior iliac spines (see Figure 8.11). The ischial tuberosities of females are also farther apart, which increases the size of the pelvic outlet. Because of this increased pelvic width, the **subpubic angle** is larger in females (greater than 80 degrees) than it is in males (less than 70 degrees). The female sacrum is wider, shorter, and less curved, and the sacral promontory projects less into the pelvic cavity, thus giving the female pelvic inlet (pelvic brim) a more rounded or oval shape compared to males. The lesser pelvic cavity of females is also wider and shallower than the narrower, deeper, and tapering lesser pelvis of males. Because of the obvious differences between female and male hip bones, this is the one bone of the body that allows for the most accurate sex determination. Table 8.1 provides an overview of the general differences between the female and male pelvis.

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Table 8.1 Overview of Differences Between the Female and Male Pelvis

	Female pelvis	Male pelvis
Pelvic weight	Bones of the pelvis are lighter and thinner	Bones of the pelvis are thicker and heavier
Pelvic inlet shape	Pelvic inlet has a round or oval shape	Pelvic inlet is heart-shaped
Lesser pelvic cavity shape	Lesser pelvic cavity is shorter and wider	Lesser pelvic cavity is longer and narrower
Subpubic angle	Subpubic angle is greater than 80 degrees	Subpubic angle is less than 70 degrees
Pelvic outlet shape	Pelvic outlet is rounded and larger	Pelvic outlet is smaller

8.4 Bones of the Lower Limb

Learning Objectives

By the end of this section, you will be able to:

- Identify the divisions of the lower limb and describe the bones of each region
- Describe the bones and bony landmarks that articulate at each joint of the lower limb

Like the upper limb, the lower limb is divided into three regions. The **thigh** is that portion of the lower limb located between the hip joint and knee joint. The **leg** is specifically the region between the knee joint and the ankle joint. Distal to the ankle is the **foot**. The lower limb contains 30 bones. These are the femur, patella, tibia, fibula, tarsal bones, metatarsal bones, and phalanges (see Figure 8.1). The **femur** is the single bone of the thigh. The **patella** is the kneecap and articulates with the distal femur. The **tibia** is the larger, weight-bearing bone located on the medial side of the leg, and the **fibula** is the thin bone of the lateral leg. The bones of the foot are divided into three groups. The posterior portion of the foot is formed by a group of seven bones, each of which is known as a **tarsal bone**, whereas the midfoot contains five elongated bones, each of which is a **metatarsal bone**. The toes contain 14 small bones, each of which is a **phalanx bone of the foot**.

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Femur

The femur, or thigh bone, is the single bone of the thigh region (Figure 8.12). It is the longest and strongest bone of the body and accounts for approximately one-quarter of a person's total height. The rounded, proximal end is the **head of the femur**, which articulates with the acetabulum of the hip bone to form

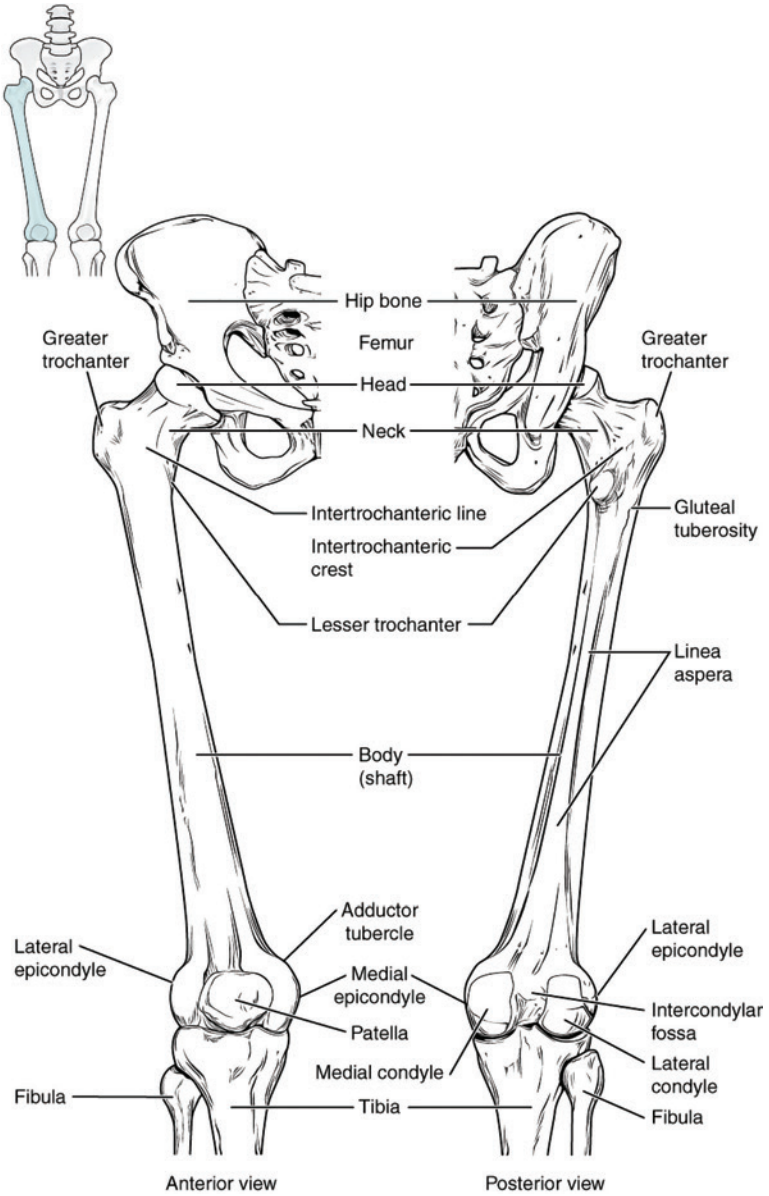


Figure 8.12 Femur and Patella. The femur is the single bone of the thigh region. It articulates superiorly with the hip bone at the hip joint and inferiorly with the tibia at the knee joint. The patella only articulates with the distal end of the femur.

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the **hip joint**. The **fovea capitis** is a minor indentation on the medial side of the femoral head that serves as the site of attachment for the **ligament of the head of the femur**. This ligament spans the femur and acetabulum but is weak and provides little support for the hip joint. It does, however, carry an important artery that supplies the head of the femur.

The narrowed region below the head is the **neck of the femur**. This is a common area for fractures of the femur. The **greater trochanter** is the large, upward bony projection located above the base of the neck. Multiple muscles that act across the hip joint attach to the greater trochanter, which, because of its projection from the femur, gives additional leverage to these muscles. The greater trochanter can be felt just under the skin on the lateral side of your upper thigh. The **lesser trochanter** is a small, bony prominence that lies on the medial aspect of the femur, just below the neck. A single, powerful muscle attaches to the lesser trochanter. Running between the greater and lesser trochanters on the anterior side of the femur is the roughened **intertrochanteric line**. The trochanters are also connected on the posterior side of the femur by the larger **intertrochanteric crest**.

The elongated **shaft of the femur** has a slight anterior bowing or curvature. At its proximal end, the posterior shaft has the **gluteal tuberosity**, a roughened area extending inferiorly from the greater trochanter. More inferiorly, the gluteal tuberosity becomes continuous with the **linea aspera**. This is the roughened ridge that passes distally along the posterior side of the mid-femur. Multiple muscles of the hip and thigh regions make long, thin attachments to the femur along the linea aspera.

The distal end of the femur has medial and lateral bony expansions. On the lateral side, the smooth portion that covers the distal and posterior aspects of the lateral expansion is the **lateral condyle of the femur**. The roughened area on the outer, lateral side of the condyle is the **lateral epicondyle of the femur**. Similarly, the smooth region of the distal and posterior medial femur is the **medial condyle of the femur**, and the irregular outer, medial side of this is the **medial epicondyle of the femur**. The lateral and medial condyles articulate with the tibia to form the knee joint. The epicondyles provide attachment for muscles and supporting ligaments of the knee. Posteriorly, the medial and lateral condyles are separated by a deep depression called the **intercondylar fossa**. Anteriorly, the smooth surfaces of the condyles join together to form a wide groove called the **patellar surface**, which provides for articulation with the patella bone. The combination of the medial and lateral condyles with the patellar surface gives the distal end of the femur a horseshoe (U) shape.

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Interactive Link 8.4

Watch this video (http://oer.aupress.ca/oer-202505/8.4) to view how a fracture of the mid-femur is surgically repaired. How are the two portions of the broken femur stabilized during surgical repair of a fractured femur?

Patella

The patella (kneecap) is the largest sesamoid bone of the body (see Figure 8.12). A sesamoid bone is a bone that is incorporated into the tendon of a muscle where that tendon crosses a joint. The sesamoid bone articulates with the underlying bones to prevent damage to the muscle tendon due to rubbing against the bones during movements of the joint. The patella is found in the tendon of the quadriceps femoris muscle, the large muscle of the anterior thigh that passes across the anterior knee to attach to the tibia. The patella articulates with the patellar surface of the femur and thus prevents rubbing of the muscle tendon against the distal femur. The patella also lifts the tendon away from the knee joint, which increases the leverage power of the quadriceps femoris muscle as it acts across the knee. The patella does not articulate with the tibia.

Interactive Link 8.5

Visit this site (http://oer.aupress.ca/oer-202505/8.5) to watch a virtual knee replacement surgery. The prosthetic knee components must be properly aligned to function properly. How is this alignment ensured?

Tibia

The tibia (shin bone) is the medial bone of the leg and is larger than the fibula, with which it is paired (Figure 8.13). The tibia is the main weight-bearing bone of the lower leg and the second-longest bone of the body, after the femur. The medial side of the tibia is located immediately under the skin, allowing it to be easily palpated down the entire length of the medial leg.

The proximal end of the tibia is greatly expanded. The two sides of this expansion form the **medial condyle of the tibia** and the **lateral condyle of the tibia**. The tibia does not have epicondyles. The top surface of each condyle is smooth and flattened. These areas articulate with the medial and lateral condyles of the femur to form the **knee joint**. Between the articulating surfaces of the tibial condyles is the **intercondylar eminence**, an irregular, elevated

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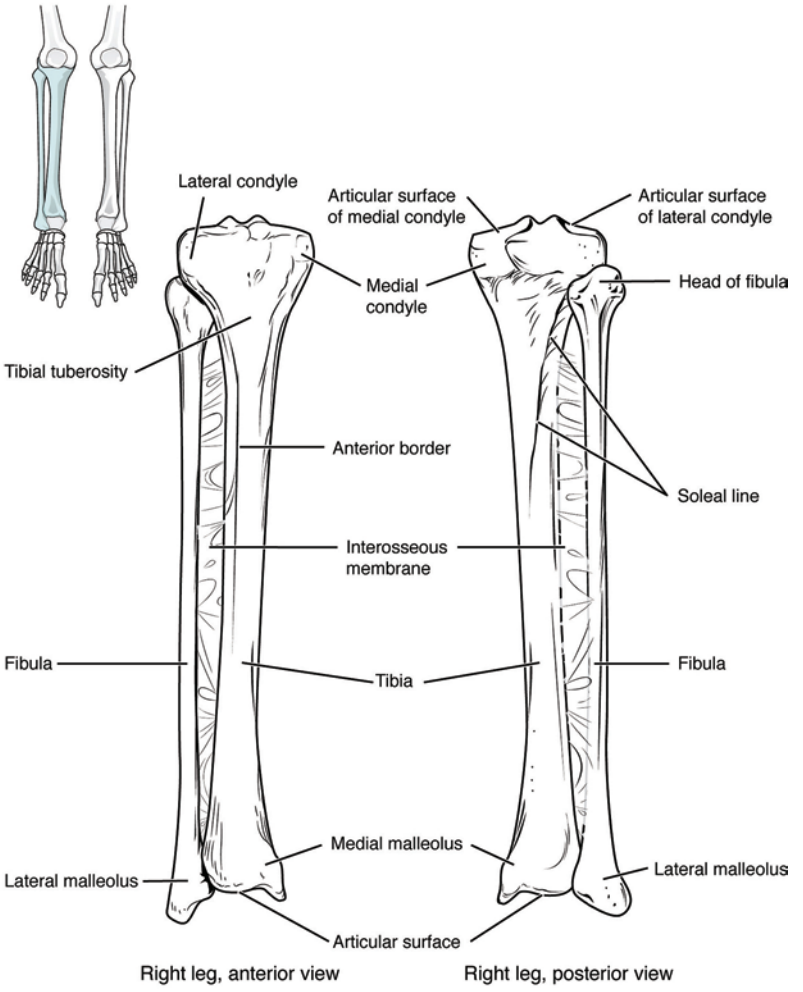


Figure 8.13 Tibia and Fibula. The tibia is the larger, weight-bearing bone located on the medial side of the leg. The fibula is the slender bone of the lateral side of the leg and does not bear weight.

area that serves as the inferior attachment point for two supporting ligaments of the knee.

The **tibial tuberosity** is an elevated area on the anterior side of the tibia, near its proximal end. It is the final site of attachment for the muscle tendon associated with the patella. More inferiorly, the **shaft of the tibia** becomes triangular in shape.

The anterior apex of this triangle forms the **anterior border of the tibia**, which begins at the tibial tuberosity and runs inferiorly along the length of the tibia. Both the anterior border and the medial side of the triangular shaft are located immediately under the skin and can be easily palpated along the entire length of the tibia.

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The large expansion found on the medial side of the distal tibia is the **medial malleolus**. This forms the large bony bump found on the medial side of the ankle region. Both the smooth surface on the inside of the medial malleolus and the smooth area at the distal end of the tibia articulate with the talus bone of the foot as part of the ankle joint. On the lateral side of the distal tibia is a wide groove called the **fibular notch**.

Fibula

The fibula is the slender bone located on the lateral side of the leg (see Figure 8.13). The fibula does not bear weight. It serves primarily for muscle attachments and thus is largely surrounded by muscles. Only the proximal and distal ends of the fibula can be palpated.

The **head of the fibula** is the small, knoblike, proximal end of the fibula. The thin **shaft of the fibula** has the **interosseous border of the fibula**, a narrow ridge running down its medial side for the attachment of the interosseous membrane that spans the fibula and tibia. The distal end of the fibula forms the **lateral malleolus**, which forms the easily palpated bony bump on the lateral side of the ankle. The deep (medial) side of the lateral malleolus articulates with the talus bone of the foot as part of the ankle joint. The distal fibula also articulates with the fibular notch of the tibia.

Tarsal Bones

The posterior half of the foot is formed by seven tarsal bones (Figure 8.14). The most superior bone is the **talus**. This has a relatively square-shaped upper surface that articulates with the tibia and fibula to form the **ankle joint**. Three areas of articulation form the ankle joint: The superomedial surface of the talus bone articulates with the medial malleolus of the tibia, the top of the talus articulates with the distal end of the tibia, and the lateral side of the talus articulates with the lateral malleolus of the fibula. Inferiorly, the talus articulates with the **calcaneus** (heel bone), the largest bone of the foot, which forms the heel. Body weight is transferred from the tibia to the talus to the calcaneus, which rests on the ground.

The **cuboid** bone articulates with the anterior end of the calcaneus bone. The cuboid has a deep groove running across its inferior surface, which provides passage for a muscle tendon. The talus bone articulates anteriorly with the **navicular** bone, which in turn articulates anteriorly with the three cuneiform bones. These bones are the **medial cuneiform**, the **intermediate cuneiform**, and the **lateral cuneiform**. Each of these bones has a broad superior surface and a narrow inferior surface, which together produce the transverse (medial-lateral) curvature of the foot. The navicular and lateral cuneiform bones also articulate with the medial side of the cuboid bone.

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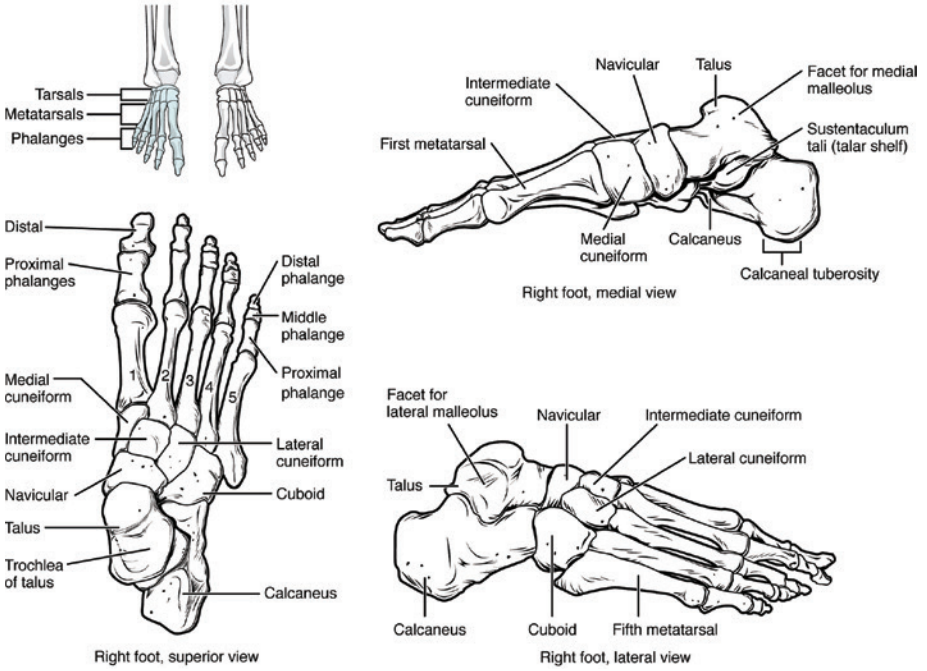


Figure 8.14 Bones of the Foot. The bones of the foot are divided into three groups. The posterior foot is formed by the seven tarsal bones. The midfoot has the five metatarsal bones. The toes contain the phalanges.

Interactive Link 8.6

Use this tutorial (http://oer.aupress.ca/oer-202505/8.6) to review the bones of the foot. Which tarsal bones are in the proximal, intermediate, and distal groups?

Metatarsal Bones

The anterior half of the foot is formed by the five metatarsal bones, which are located between the tarsal bones of the posterior foot and the phalanges of the toes (see Figure 8.14). These elongated bones are numbered 1–5, starting with the medial side of the foot. The first metatarsal bone is shorter and thicker than the others. The second metatarsal is the longest. The **base of the metatarsal bone** is the proximal end of each metatarsal bone. These articulate with the cuboid or cuneiform bones. The base of the fifth metatarsal has a large, lateral expansion that provides for muscle attachments. This expanded base of the fifth metatarsal can be felt as a bony bump at the midpoint along the lateral border of the foot. The expanded distal end of each metatarsal is the **head of the metatarsal bone**.

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Phalanges

The toes contain a total of 14 phalanx bones (phalanges), arranged in a similar manner to that of the phalanges of the fingers (see Figure 8.14). The toes are numbered 1–5, starting with the big toe (**hallux**). The big toe has two phalanx bones, the proximal and distal phalanges. The remaining toes all have proximal, middle, and distal phalanges. A joint between adjacent phalanx bones is called an interphalangeal joint.

Arches of the Foot

When the foot comes into contact with the ground during walking, running, or jumping activities, the impact of the body weight puts a tremendous amount of pressure and force on the foot. During running, the force applied to each foot as it contacts the ground can be up to 2.5 times your body weight. The bones, joints, ligaments, and muscles of the foot absorb this force, thus greatly reducing the amount of shock that is passed superiorly into the lower limb and body. The arches of the foot play an important role in this shock-absorbing ability. When weight is applied to the foot, these arches will flatten somewhat, thus absorbing energy. When the weight is removed, the arch rebounds, giving "spring" to the step. The arches also serve to distribute body weight side to side and to either end of the foot.

The foot has a transverse arch, a medial longitudinal arch, and a lateral longitudinal arch (see Figure 8.14). The transverse arch forms the medial-lateral curvature of the midfoot. It is formed by the wedge shapes of the cuneiform bones and bases (proximal ends) of the first to fourth metatarsal bones. This arch helps distribute body weight from side to side within the foot, thus allowing the foot to accommodate uneven terrain.

The longitudinal arches run down the length of the foot. The lateral longitudinal arch is relatively flat, whereas the medial longitudinal arch is larger (taller). The longitudinal arches are formed by the tarsal bones posteriorly and the metatarsal bones anteriorly. These arches are supported at either end, where they contact the ground. This support is provided posteriorly by the calcaneus bone and anteriorly by the heads (distal ends) of the metatarsal bones.

The talus bone, which receives the weight of the body, is located at the top of the longitudinal arches. Body weight is then conveyed from the talus to the ground by the anterior and posterior ends of these arches. Strong ligaments unite the adjacent foot bones to prevent disruption of the arches during weight-bearing. On the bottom of the foot, additional ligaments tie together the anterior and posterior ends of the arches. These ligaments have elasticity, which allows

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them to stretch somewhat during weight-bearing, thus allowing the longitudinal arches to spread. The stretching of these ligaments stores energy within the foot rather than passing these forces on to the leg. Contraction of the foot muscles also plays an important role in this energy absorption. When the weight is removed, the elastic ligaments recoil and pull the ends of the arches closer together. This recovery of the arches releases the stored energy and improves the energy efficiency of walking.

Key Terms

acetabulum: Large, cup-shaped cavity located on the lateral side of the hip bone; formed by the junction of the ilium, pubis, and ischium portions of the hip bone.

acromial (lateral) end of the clavicle: Lateral end of the clavicle that articulates with the acromion of the scapula.

acromion (acromial process): Flattened bony process that extends laterally from the scapular spine to form the bony tip of the shoulder.

anatomical neck: Line on the humerus located around the outside margin of the humeral head.

ankle joint: Joint that separates the leg and foot portions of the lower limb; formed by the articulations between the talus bone of the foot inferiorly, and the distal end of the tibia, medial malleolus of the tibia, and lateral malleolus of the fibula superiorly.

anterior border of the tibia: Narrow, anterior margin of the tibia that extends inferiorly from the tibial tuberosity.

arm: Region of the upper limb located between the shoulder and elbow joints; contains the humerus bone.

base of the metatarsal bone: Expanded, proximal end of each metatarsal bone.

bony pelvis: The entire structure formed by the two hip bones, the sacrum, and, attached inferiorly to the sacrum, the coccyx.

calcaneus: Heel bone; posterior, inferior tarsal bone that forms the heel of the foot.

capitulum: Knoblike bony structure located anteriorly on the lateral, distal end of the humerus.

carpal bones: Eight small bones that form the wrist and base of the hand; these are grouped as a proximal row consisting of (from lateral to medial) the scaphoid, lunate, triquetrum, and pisiform bones, and a distal row containing (from lateral to medial) the trapezium, trapezoid, capitate, and hamate bones.

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carpal tunnel: Passageway between the anterior forearm and hand formed by the carpal bones and flexor retinaculum.

clavicle: Collarbone; elongated bone that articulates with the manubrium of the sternum medially and the acromion of the scapula laterally.

coracoid process: Short, hooklike process that projects anteriorly and laterally from the superior margin of the scapula.

coronoid process of the ulna: Projecting bony lip located on the anterior, proximal ulna; forms the inferior margin of the trochlear notch.

coxal bone: Hip bone.

cuboid: Tarsal bone that articulates posteriorly with the calcaneus bone, medially with the lateral cuneiform bone, and anteriorly with the fourth and fifth metatarsal bones.

deltoid tuberosity: Roughened, V-shaped region located laterally on the midshaft of the humerus.

elbow joint: Joint located between the upper arm and forearm regions of the upper limb; formed by the articulations between the trochlea of the humerus and the trochlear notch of the ulna, and the capitulum of the humerus and the head of the radius.

femur: Thigh bone; the single bone of the thigh.

fibula: Thin, non-weight-bearing bone found on the lateral side of the leg.

fibular notch: Wide groove on the lateral side of the distal tibia for articulation with the fibula at the distal tibiofibular joint.

flexor retinaculum: Strong band of connective tissue at the anterior wrist that spans the top of the U-shaped grouping of the carpal bones to form the roof of the carpal tunnel.

foot: Portion of the lower limb located distal to the ankle joint.

forearm: Region of the upper limb located between the elbow and wrist joints; contains the radius and ulna bones.

fossa (plural = fossae): Shallow depression on the surface of a bone.

fovea capitis: Minor indentation on the head of the femur that serves as the site of attachment for the ligament to the head of the femur.

glenoid cavity (also glenoid fossa): Shallow depression located on the lateral scapula, between the superior and lateral borders.

gluteal tuberosity: Roughened area on the posterior side of the proximal femur, extending inferiorly from the base of the greater trochanter.

greater pelvis (also greater pelvic cavity or false pelvis): Broad space above the pelvic brim defined laterally by the fanlike portion of the upper ilium.

greater sciatic notch: Large, U-shaped indentation located on the posterior margin of the ilium, superior to the ischial spine.

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greater trochanter: Large, bony expansion of the femur that projects superiorly from the base of the femoral neck.

greater tubercle: Enlarged prominence located on the lateral side of the proximal humerus.

hallux: Big toe; digit 1 of the foot.

hand: Region of the upper limb distal to the wrist joint.

head of the femur: Rounded, proximal end of the femur that articulates with the acetabulum of the hip bone to form the hip joint.

head of the fibula: Small, knoblike, proximal end of the fibula; articulates with the inferior aspect of the lateral condyle of the tibia.

head of the humerus: Smooth, rounded region on the medial side of the proximal humerus; articulates with the glenoid fossa of the scapula to form the glenohumeral (shoulder) joint.

head of the metatarsal bone: Expanded, distal end of each metatarsal bone.

head of the radius: Disc-shaped structure that forms the proximal end of the radius; articulates with the capitulum of the humerus as part of the elbow joint, and with the radial notch of the ulna as part of the proximal radioulnar joint.

head of the ulna: Small, rounded distal end of the ulna; articulates with the ulnar notch of the distal radius, forming the distal radioulnar joint.

hip bone: Coxal bone; one of two paired bones that form the pelvic girdle; each consists of three areas: the ilium, ischium, and pubis.

hip joint: Joint located at the proximal end of the lower limb; formed by the articulation between the acetabulum of the hip bone and the head of the femur.

humerus: Single bone of the upper arm.

iliac crest: Curved, superior margin of the ilium.

iliac fossa: Shallow depression found on the anterior and medial surfaces of the upper ilium.

ilium: Superior portion of the hip bone.

inferior angle of scapula: The most inferior portion of the scapula, particularly important because it serves as the attachment point for several powerful muscles involved in shoulder and upper limb movements.

inferior pubic ramus: Narrow segment of bone that passes inferiorly and laterally from the pubic body; joins with the ischial ramus to form the ischiopubic ramus.

infraspinous fossa: Broad depression located on the posterior scapula, inferior to the spine.

intercondylar eminence: Irregular elevation on the superior end of the tibia, between the articulating surfaces of the medial and lateral condyles.

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intercondylar fossa: Deep depression on the posterior side of the distal femur that separates the medial and lateral condyles.

intermediate cuneiform: Middle of the three cuneiform tarsal bones; articulates posteriorly with the navicular bone, medially with the medial cuneiform bone, laterally with the lateral cuneiform bone, and anteriorly with the second metatarsal bone.

interosseous border of the fibula: Small ridge running down the medial side of the fibular shaft for attachment of the interosseous membrane between the fibula and tibia.

intertrochanteric crest: Short, prominent ridge running between the greater and lesser trochanters on the posterior side of the proximal femur.

intertrochanteric line: Small ridge running between the greater and lesser trochanters on the anterior side of the proximal femur.

ischial ramus: Bony extension projecting anteriorly and superiorly from the ischial tuberosity; joins with the inferior pubic ramus to form the ischiopubic ramus.

ischial spine: Pointed, bony projection from the posterior margin of the ischium that separates the greater sciatic notch and lesser sciatic notch.

ischial tuberosity: Large, roughened protuberance that forms the posteroinferior portion of the hip bone; weight-bearing region of the pelvis when sitting.

ischiopubic ramus: Narrow extension of bone that connects the ischial tuberosity to the pubic body; formed by the junction of the ischial ramus and inferior pubic ramus.

ischium: Posteroinferior portion of the hip bone.

knee joint: Joint that separates the thigh and leg portions of the lower limb; formed by the articulations between the medial and lateral condyles of the femur, and the medial and lateral condyles of the tibia.

lateral condyle of the femur: Smooth, articulating surface that forms the distal and posterior sides of the lateral expansion of the distal femur.

lateral condyle of the tibia: Lateral, expanded region of the proximal tibia that includes the smooth surface that articulates with the lateral condyle of the femur as part of the knee joint.

lateral cuneiform: Most lateral of the three cuneiform tarsal bones; articulates posteriorly with the navicular bone, medially with the intermediate cuneiform bone, laterally with the cuboid bone, and anteriorly with the third metatarsal bone.

lateral epicondyle of the femur: Roughened area of the femur located on the lateral side of the lateral condyle.

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lateral malleolus: Expanded distal end of the fibula.
leg: Portion of the lower limb located between the knee and ankle joints.
lesser pelvis (also lesser pelvic cavity or true pelvis): Narrow space located within the pelvis, defined superiorly by the pelvic brim (pelvic inlet) and inferiorly by the pelvic outlet.
lesser sciatic notch: Shallow indentation along the posterior margin of the ischium, inferior to the ischial spine.
lesser trochanter: Small, bony projection on the medial side of the proximal femur, at the base of the femoral neck.
lesser tubercle: Small, bony prominence located on the anterior side of the proximal humerus.
ligament of the head of the femur: Ligament that spans the acetabulum of the hip bone and the fovea capitis of the femoral head.
linea aspera: Longitudinally running bony ridge located in the middle third of the posterior femur.
medial condyle of the femur: Smooth, articulating surface that forms the distal and posterior sides of the medial expansion of the distal femur.
medial condyle of the tibia: Medial, expanded region of the proximal tibia that includes the smooth surface that articulates with the medial condyle of the femur as part of the knee joint.
medial cuneiform: Most medial of the three cuneiform tarsal bones; articulates posteriorly with the navicular bone, laterally with the intermediate cuneiform bone, and anteriorly with the first and second metatarsal bones.
medial epicondyle of the femur: Roughened area of the distal femur located on the medial side of the medial condyle.
medial malleolus: Bony expansion located on the medial side of the distal tibia.
metacarpal bone: One of the five long bones that form the palm of the hand; numbered 1–5, starting on the lateral (thumb) side of the hand.
metatarsal bone: One of the five elongated bones that form the anterior half of the foot; numbered 1–5, starting on the medial side of the foot.
navicular: Tarsal bone that articulates posteriorly with the talus bone, laterally with the cuboid bone, and anteriorly with the medial, intermediate, and lateral cuneiform bones.
neck of the femur: Narrowed region located inferior to the head of the femur.
neck of the radius: Narrowed region immediately distal to the head of the radius.
obturator foramen: Large opening located in the anterior hip bone, between the pubis and ischium regions.

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olecranon process: Expanded posterior and superior portions of the proximal ulna; forms the bony tip of the elbow.

patella: Kneecap; the largest sesamoid bone of the body; articulates with the distal femur.

patellar surface: Smooth groove located on the anterior side of the distal femur, between the medial and lateral condyles; site of articulation for the patella.

pectoral girdle: Shoulder girdle; the set of bones, consisting of the scapula and clavicle, which attaches each upper limb to the axial skeleton.

pelvic brim: Pelvic inlet; the dividing line between the greater and lesser pelvic regions; formed by the superior margin of the pubic symphysis, the pectineal lines of each pubis, the arcuate lines of each ilium, and the sacral promontory.

pelvic girdle: Hip girdle; consists of a single hip bone, which attaches a lower limb to the sacrum of the axial skeleton.

pelvic inlet: Pelvic brim.

pelvic outlet: Inferior opening of the lesser pelvis; formed by the inferior margin of the pubic symphysis, the right and left ischiopubic rami and sacrotuberous ligaments, and the tip of the coccyx.

pelvis: Ring of bone consisting of the right and left hip bones, the sacrum, and the coccyx.

phalanx bone (plural = phalanges): One of the 28 bones that form the fingers, thumbs, and toes.

pollex: Thumb; digit 1 of the hand.

pubic arch: Bony structure formed by the pubic symphysis and the bodies and inferior pubic rami of the adjacent pubic bones.

pubic body: Enlarged, medial portion of the pubis region of the hip bone.

pubic symphysis: Joint formed by the articulation between the pubic bodies of the right and left hip bones.

pubis: Anterior portion of the hip bone.

radial tuberosity: Oval-shaped, roughened protuberance located on the medial side of the proximal radius.

radiocarpal joint: Wrist joint; located between the forearm and hand regions of the upper limb; articulation formed proximally by the distal end of the radius and the fibrocartilaginous pad that unites the distal radius and ulna bone, and distally by the scaphoid, lunate, and triquetrum carpal bones.

radius: Bone located on the lateral side of the forearm.

sacroiliac joint: Joint formed by the articulation between the auricular surfaces of the sacrum and ilium.

scapula: Shoulder blade bone located on the posterior side of the shoulder.

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shaft of the clavicle: Body of the clavicle bone.
shaft of the femur: Cylindrically shaped region that forms the central portion of the femur.
shaft of the fibula: Elongated, slender portion located between the expanded ends of the fibula.
shaft of the humerus: Narrow, elongated, central region of the humerus.
shaft of the radius: Narrow, elongated, central region of the radius.
shaft of the tibia: Triangular, central portion of the tibia.
shaft of the ulna: Narrow, elongated, central region of the ulna.
spine of the scapula: Prominent ridge passing mediolaterally across the upper portion of the posterior scapular surface.
sternal (medial) end of the clavicle: Medial end of the clavicle that articulates with the manubrium of the sternum.
sternoclavicular joint: Articulation between the manubrium of the sternum and the sternal end of the clavicle; forms the only bony attachment between the pectoral girdle of the upper limb and the axial skeleton.
styloid process of the radius: Pointed projection located on the lateral end of the distal radius.
styloid process of the ulna: Short, bony projection located on the medial end of the distal ulna.
subpubic angle: Inverted V-shape formed by the convergence of the right and left ischiopubic rami; this angle is greater than 80 degrees in females and less than 70 degrees in males.
subscapular fossa: Broad depression located on the anterior (deep) surface of the scapula.
superior pubic ramus: Narrow segment of bone that passes laterally from the pubic body to join the ilium.
suprascapular notch: Small notch located along the superior border of the scapula, medial to the coracoid process.
supraspinous fossa: Narrow depression located on the posterior scapula, superior to the spine.
surgical neck: Region of the humerus where the expanded, proximal end joins with the narrower shaft.
talus: Tarsal bone that articulates superiorly with the tibia and fibula at the ankle joint; also articulates inferiorly with the calcaneus bone and anteriorly with the navicular bone.
tarsal bone: One of the seven bones that make up the posterior foot; includes the calcaneus, talus, navicular, cuboid, medial cuneiform, intermediate cuneiform, and lateral cuneiform bones.
thigh: Portion of the lower limb located between the hip and knee joints.

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tibia: Shin bone; the large, weight-bearing bone located on the medial side of the leg.

tibial tuberosity: Elevated area on the anterior surface of the proximal tibia.

trochlea: Pulley-shaped region located medially at the distal end of the humerus; articulates at the elbow with the trochlear notch of the ulna.

trochlear notch: Large, C-shaped depression located on the anterior side of the proximal ulna; articulates at the elbow with the trochlea of the humerus.

ulna: Bone located on the medial side of the forearm.

ulnar tuberosity: Roughened area located on the anterior, proximal ulna inferior to the coronoid process.

Chapter Review

8.1 The Pectoral Girdles

The pectoral girdle, consisting of the clavicle and the scapula, attaches each upper limb to the axial skeleton. The clavicle is an anterior bone whose sternal end articulates with the manubrium of the sternum at the sternoclavicular joint. The acromial end of the clavicle articulates with the acromion of the scapula at the acromioclavicular joint. This end is also anchored to the coracoid process of the scapula by the coracoclavicular ligament, which provides indirect support for the acromioclavicular joint. The clavicle supports the scapula, transmits the weight and forces from the upper limb to the trunk of the body, and protects the underlying nerves and blood vessels.

The scapula lies on the posterior aspect of the pectoral girdle. It mediates the attachment of the upper limb to the clavicle and contributes to the formation of the glenohumeral (shoulder) joint. This triangular bone has three sides called the medial, lateral, and superior borders. The suprascapular notch is located on the superior border. The scapula also has three corners, two of which are the superior and inferior angles. The third corner is occupied by the glenoid cavity. Posteriorly, the spine separates the supraspinous and infraspinous fossae and then extends laterally as the acromion. The subscapular fossa is located on the anterior surface of the scapula. The coracoid process projects anteriorly and passes beneath the lateral end of the clavicle. The distal carpal bone articulates with the scaphoid proximally, the second metacarpal distally, the trapezium laterally, and the capitate medially.

8.2 Bones of the Upper Limb

Each upper limb is divided into three regions and contains a total of 30 bones. The upper arm is the region located between the shoulder and elbow joints. This area contains the humerus. The proximal humerus consists of the head,

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which articulates with the scapula, the greater and lesser tubercles separated by the intertubercular (bicipital) groove, and the anatomical and surgical necks. The humeral shaft has the roughened area of the deltoid tuberosity on its lateral side. The distal humerus is flattened, forming a lateral ridge that terminates at the small lateral epicondyle. The medial side of the distal humerus has the large, medial epicondyle. The articulating surfaces of the distal humerus consist of the trochlea medially and the capitulum laterally. Depressions on the humerus that accommodate the forearm bones during bending (flexing) and straightening (extending) of the elbow include the radial fossa and the olecranon fossa.

The forearm is the region of the upper limb located between the elbow and wrist joints. This region contains two bones, the ulna medially and the radius on the lateral (thumb) side. The elbow joint is formed by the articulation between the trochlea of the humerus and the trochlear notch of the ulna, plus the articulation between the capitulum of the humerus and the head of the radius. The proximal ulna also has the olecranon process, forming an expanded posterior region, and the coronoid process and ulnar tuberosity on its anterior aspect. On the proximal radius, the narrowed region below the head is the neck; distal to this is the radial tuberosity. The shaft portions of both the ulna and radius have an interosseous border, whereas the distal ends of each bone have a pointed styloid process. The distal end of the radius articulates with the proximal carpal bones, but the ulna does not.

The base of the hand is formed by eight carpal bones. The carpal bones are united into two rows of bones. The proximal and distal carpal rows articulate with each other at the midcarpal joint. The carpal bones, together with the flexor retinaculum, also form the carpal tunnel of the wrist.

The five metacarpal bones form the palm of the hand. The metacarpal bones are numbered 1–5, starting with the thumb side. The first metacarpal bone is freely mobile, but the other bones are united as a group. The digits are also numbered 1–5, with the thumb being number 1. The fingers and thumb contain a total of 14 phalanges (phalanx bones). The thumb contains a proximal and a distal phalanx, whereas the remaining digits each contain proximal, middle, and distal phalanges.

8.3 The Pelvic Girdle and Pelvis

The pelvic girdle, consisting of a hip bone, serves to attach a lower limb to the axial skeleton. The hip bone articulates posteriorly at the sacroiliac joint with the sacrum, which is part of the axial skeleton. The right and left hip bones converge anteriorly and articulate with each other at the pubic symphysis. The combination of the hip bone, the sacrum, and the coccyx forms the pelvis.

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The pelvis has a pronounced anterior tilt. The primary function of the pelvis is to support the upper body and transfer body weight to the lower limbs. It also serves as the site of attachment for multiple muscles.

The hip bone consists of three regions: the ilium, ischium, and pubis. The ilium forms the large, fanlike region of the hip bone. The medial surface of the upper ilium forms the iliac fossa, with the arcuate line marking the inferior limit of this area. The posterior margin of the ilium has the large greater sciatic notch.

The posterolateral portion of the hip bone is the ischium. It has the expanded ischial tuberosity, which supports body weight when sitting. The ischial ramus projects anteriorly and superiorly. The posterior margin of the ischium has the shallow lesser sciatic notch and the ischial spine, which separates the greater and lesser sciatic notches.

The pubis forms the anterior portion of the hip bone. The body of the pubis articulates with the pubis of the opposite hip bone at the pubic symphysis. The inferior pubic ramus projects inferiorly and laterally. The inferior pubic ramus joins the ischial ramus to form the ischiopubic ramus. The subpubic angle is formed by the medial convergence of the right and left ischiopubic rami.

The lateral side of the hip bone has the cuplike acetabulum, which is part of the hip joint. The large anterior opening is the obturator foramen. The sacroiliac joint is supported by the anterior and posterior sacroiliac ligaments. The sacrum is also joined to the hip bone by the sacrospinous ligament, which attaches to the ischial spine, and the sacrotuberous ligament, which attaches to the ischial tuberosity. The sacrospinous and sacrotuberous ligaments contribute to the formation of the greater and lesser sciatic foramina.

The broad space of the upper pelvis is the greater pelvis, and the narrow, inferior space is the lesser pelvis. These areas are separated by the pelvic brim (pelvic inlet). The inferior opening of the pelvis is the pelvic outlet. Compared to the male, the female pelvis is wider to accommodate childbirth, has a larger subpubic angle, and has a broader greater sciatic notch.

8.4 Bones of the Lower Limb

The lower limb is divided into three regions. These are the thigh, located between the hip and knee joints; the leg, located between the knee and ankle joints; and, distal to the ankle, the foot. There are 30 bones in each lower limb. These are the femur, patella, tibia, fibula, seven tarsal bones, five metatarsal bones, and 14 phalanges.

The femur is the single bone of the thigh. Its rounded head articulates with the acetabulum of the hip bone to form the hip joint. The head has the fovea capitis for attachment of the ligament of the head of the femur.

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The narrow neck joins inferiorly with the greater and lesser trochanters. Passing between these bony expansions are the intertrochanteric line on the anterior femur and the larger intertrochanteric crest on the posterior femur. On the posterior shaft of the femur is the gluteal tuberosity proximally and the linea aspera in the midshaft region. The expanded distal end consists of three articulating surfaces: the medial and lateral condyles and the patellar surface. The outside margins of the condyles are the medial and lateral epicondyles.

The patella is a sesamoid bone located within a muscle tendon. It articulates with the patellar surface on the anterior side of the distal femur, thereby protecting the muscle tendon from rubbing against the femur.

The leg contains the large tibia on the medial side and the slender fibula on the lateral side. The tibia bears the weight of the body, whereas the fibula does not bear weight.

The proximal tibia consists of the expanded medial and lateral condyles, which articulate with the medial and lateral condyles of the femur to form the knee joint. Between the tibial condyles is the intercondylar eminence. On the anterior side of the proximal tibia is the tibial tuberosity, which is continuous inferiorly with the anterior border of the tibia. The bony expansion on the medial side of the distal tibia is the medial malleolus. The groove on the lateral side of the distal tibia is the fibular notch.

The head of the fibula forms the proximal end and articulates with the underside of the lateral condyle of the tibia. The distal fibula articulates with the fibular notch of the tibia. The expanded distal end of the fibula is the lateral malleolus.

The posterior foot is formed by the seven tarsal bones. The talus articulates superiorly with the distal tibia, the medial malleolus of the tibia, and the lateral malleolus of the fibula to form the ankle joint. The talus articulates inferiorly with the calcaneus bone. Anterior to the talus is the navicular bone, and anterior to this are the medial, intermediate, and lateral cuneiform bones. The cuboid bone is anterior to the calcaneus.

The five metatarsal bones form the anterior foot. The bases of these bones articulate with the cuboid or cuneiform bones. The metatarsal heads, at their distal ends, articulate with the proximal phalanges of the toes. The big toe (toe number 1) has proximal and distal phalanx bones. The remaining toes have proximal, middle, and distal phalanges.

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9

Joints

Chapter Objectives

After studying this chapter, you will be able to:

- Discuss both functional and structural classifications for body joints
- Describe the characteristic features for fibrous, cartilaginous, and synovial joints and give examples of each
- Define and identify the different body movements
- Discuss the structure of specific body joints and the movements allowed by each

The adult human body has 206 bones, and with the exception of the hyoid bone in the neck, each bone is connected to at least one other bone. Joints are the location where bones come together. Many joints allow for movement between the bones. At these joints, the articulating surfaces of the adjacent bones can move smoothly against each other. However, the bones of other joints may be joined to each other by connective tissue or cartilage. These joints are designed for stability and provide for little or no movement. Importantly, joint stability and movement are related to each other. This means that stable joints allow for little or no mobility between the adjacent bones. Conversely, joints that provide the most movement between bones are the least stable.

Understanding the relationship between joint structure and function will help explain why particular types of joints are found in certain areas of the body.

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9.1 Classification of Joints

Learning Objectives

By the end of this section, you will be able to:

- Distinguish between the functional and structural classifications for joints
- Describe the three functional types of joints and give an example of each
- List the three types of diarthrodial joints

A **joint**, also called an **articulation**, is any place where adjacent bones or bone and cartilage come together (articulate with each other) to form a connection. Joints are classified both structurally and functionally. Structural classifications of joints take into account whether the adjacent bones are strongly anchored to each other by fibrous connective tissue or cartilage, or whether the adjacent bones articulate with each other within a fluid-filled space called a **joint cavity**. Functional classifications describe the degree of movement available between the bones, ranging from immobile to slightly mobile to freely movable joints. The amount of movement available at a particular joint of the body is related to the functional requirements for that joint. Thus immobile or slightly movable joints serve to protect internal organs, give stability to the body, and allow for limited body movement. In contrast, freely movable joints allow for much more extensive movements of the body and limbs.

Structural Classification of Joints

The structural classification of joints is based on whether the articulating surfaces of the adjacent bones are directly connected by fibrous connective tissue or cartilage or contact each other within a fluid-filled joint cavity. These differences serve to divide the joints of the body into three structural classifications. A **fibrous joint** is where the adjacent bones are united by fibrous connective tissue. At a **cartilaginous joint**, the bones are joined by hyaline cartilage or fibrocartilage. At a **synovial joint**, the articulating surfaces of the bones are not directly connected but instead come into contact with each other within a joint cavity that is filled with a lubricating fluid. Synovial joints allow for free movement between the bones and are the most common joints of the body.

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Functional Classification of Joints

The functional classification of joints is determined by the amount of mobility found between the adjacent bones. Joints are thus functionally classified as a synarthrosis or immobile joint, an amphiarthrosis or slightly movable joint, or a diarthrosis, which is a freely movable joint. Depending on their location, fibrous joints may be functionally classified as a synarthrosis (immobile joint) or an amphiarthrosis (slightly mobile joint). Cartilaginous joints are also functionally classified as either a synarthrosis or an amphiarthrosis joint. All synovial joints are functionally classified as diarthrosis joints.

Synarthrosis

An immobile or nearly immobile joint is called a **synarthrosis**. The immobile nature of these joints provide for a strong union between the articulating bones. This is important at locations where the bones provide protection for internal organs.

Examples: Sutures, the fibrous joints between the bones of the skull that surround and protect the brain (Figure 9.1), are synarthrotic joints, as is the manubriosternal joint, the cartilaginous joint that unites the manubrium and body of the sternum for protection of the heart.

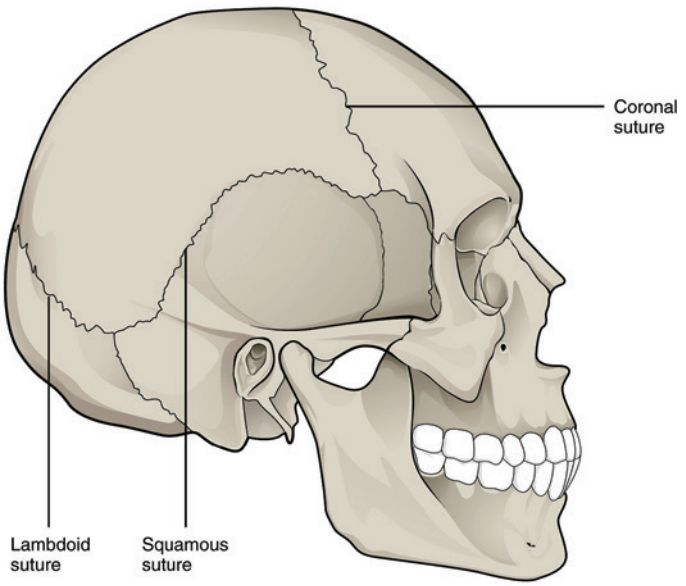


Figure 9.1 Suture Joints of Skull. The suture joints of the skull are an example of a synarthrosis, an immobile or essentially immobile joint.

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Amphiarthrosis

An **amphiarthrosis** is a joint that has limited mobility.

Example: The cartilaginous joint that unites the bodies of adjacent vertebrae is an amphiarthrosis. Filling the gap between the vertebrae is a thick pad of fibrocartilage called an intervertebral disc (Figure 9.2). Each intervertebral disc strongly unites the vertebrae but still allows for a limited amount of movement between them. However, the small movements available between adjacent vertebrae can sum together along the length of the vertebral column to provide for large ranges of body movements.

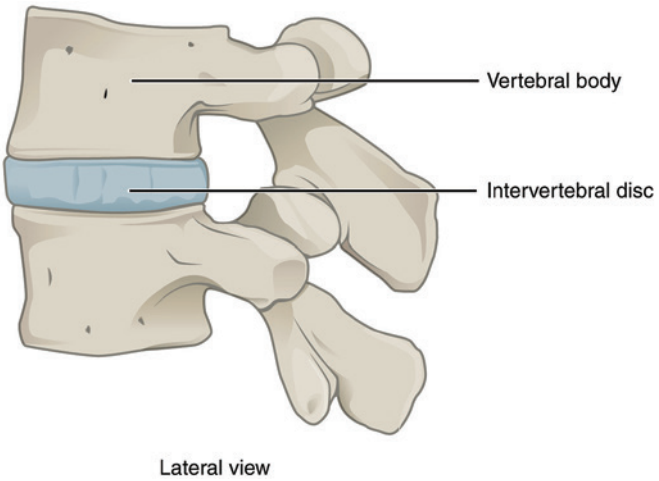


Figure 9.2 Intervertebral Disc. An intervertebral disc unites the bodies of adjacent vertebrae within the vertebral column. Each disc allows for limited movement between the vertebrae and thus functionally forms an amphiarthrosis type of joint. Intervertebral discs are made of fibrocartilage and thereby structurally form a symphysis type of cartilaginous joint.

Example: The pubic symphysis of the pelvis is a cartilaginous joint in which the pubic regions of the right and left hip bones are strongly anchored to each other by fibrocartilage. This joint normally has very little mobility. The strength of the pubic symphysis is important in conferring weight-bearing stability to the pelvis.

Diarthrosis

A freely mobile joint is classified as a **diarthrosis**. These types of joints include all synovial joints of the body, which provide the majority of body movements. Most diarthrotic joints are found in the appendicular skeleton and thus give the limbs a wide range of motion. These joints are divided into three categories based on the number of axes of motion provided by each. An **axis** in anatomy is described as the movements in reference to the three anatomical planes:

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transverse, frontal, and sagittal. Thus, diarthroses are classified as uniaxial (for movement in one plane), biaxial (for movement in two planes), or multiaxial joints (for movement in all three anatomical planes).

A **uniaxial joint** only allows for motion in a single plane (around a single axis). The elbow joint, which only allows for bending or straightening, is an example of a uniaxial joint. A **biaxial joint** allows for motions within two planes. An example of a biaxial joint is a metacarpophalangeal joint (knuckle joint) of the hand. The joint allows for movement along one axis to produce bending or straightening of the finger, and movement along a second axis allows for spreading of the fingers away from each other and bringing them together. A joint that allows for the several directions of movement is called a **multiaxial joint** (or polyaxial or triaxial joint). This type of diarthrotic joint allows for movement along three axes (Figure 9.3).

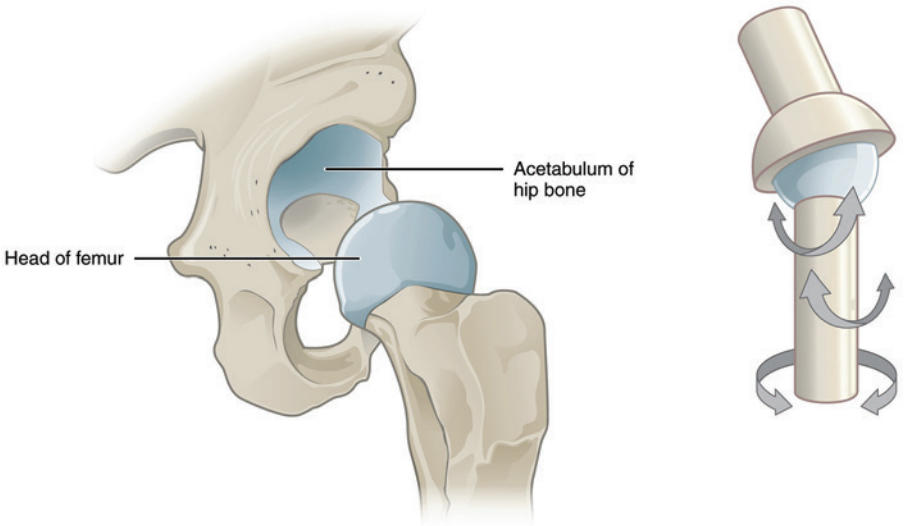


Figure 9.3 Multiaxial Joint. A multiaxial joint, such as the hip joint, allows for three types of movement: anterior-posterior, medial-lateral, and rotational.

Example: The shoulder and hip joints are multiaxial joints. They allow the upper or lower limb to move in an anterior-posterior direction and a medial-lateral direction. In addition, the limb can also be rotated around its long axis. This third movement results in rotation of the limb so that its anterior surface is moved either toward or away from the midline of the body.

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9.2 Fibrous Joints

Learning Objectives

By the end of this section, you will be able to:

- Describe the structural features of fibrous joints
- Distinguish between a suture, syndesmosis, and gomphosis
- Give an example of each type of fibrous joint

At a **fibrous joint**, the adjacent bones are directly connected to each other by fibrous connective tissue, and thus the bones do not have a joint cavity between them (Figure 9.4). The gap between the bones may be narrow or wide.

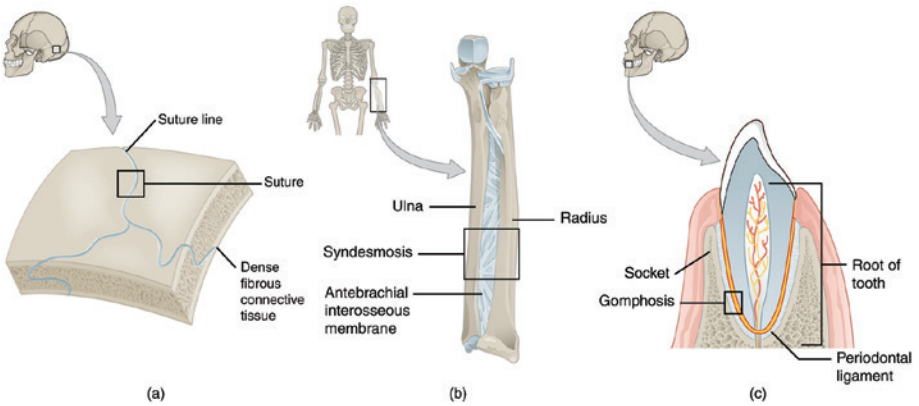


Figure 9.4 Fibrous Joints. Fibrous joints form strong connections between bones. (a) Sutures join most bones of the skull. (b) An interosseous membrane forms a syndesmosis between the radius and ulna bones of the forearm. (c) A gomphosis is a specialized fibrous joint that anchors a tooth to its socket in the jaw.

There are three types of fibrous joints. A suture is the narrow fibrous joint found between most bones of the skull. At a syndesmosis joint, the bones are more widely separated but are held together by a narrow band of fibrous connective tissue called a **ligament** or a wide sheet of connective tissue called an interosseous membrane. This type of fibrous joint is found between the shaft regions of the long bones in the forearm and in the leg. Lastly, a gomphosis is the narrow fibrous joint between the roots of a tooth and the bony socket in the jaw into which the tooth fits.

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Suture

All the bones of the skull, except for the mandible, are joined to one another by a fibrous joint called a **suture**. The fibrous connective tissue found at a suture strongly unites the adjacent skull bones and thus helps protect the brain and form the face. In adults, the skull bones are closely opposed, and fibrous connective tissue fills the narrow gap between the bones. The suture is frequently convoluted, forming a tight union that prevents most movement between the bones. (See Figure 9.4a.) Thus, skull sutures are functionally classified as synarthroses, although some sutures may allow for slight movements between the cranial bones.

In newborns and infants, the areas of connective tissue between the bones are much wider, especially in those areas on the top and sides of the skull that will become the sagittal, coronal, squamous, and lambdoid sutures. These broad areas of connective tissue are called **fontanelles** (Figure 9.5). During birth, the fontanelles provide flexibility to the skull, allowing the bones to push closer together or to overlap slightly, thus aiding movement of the infant's head through the birth canal. After birth, these expanded regions of connective tissue allow for rapid growth of the skull and enlargement of the brain. The fontanelles greatly decrease in width during the first year after birth as the skull bones enlarge. When the connective tissue between the adjacent bones is reduced to a narrow layer, these fibrous joints are then called sutures. At some sutures, the connective tissue will ossify and be converted into bone, causing the adjacent bones to fuse to each other. This fusion between bones is called a **synostosis**.

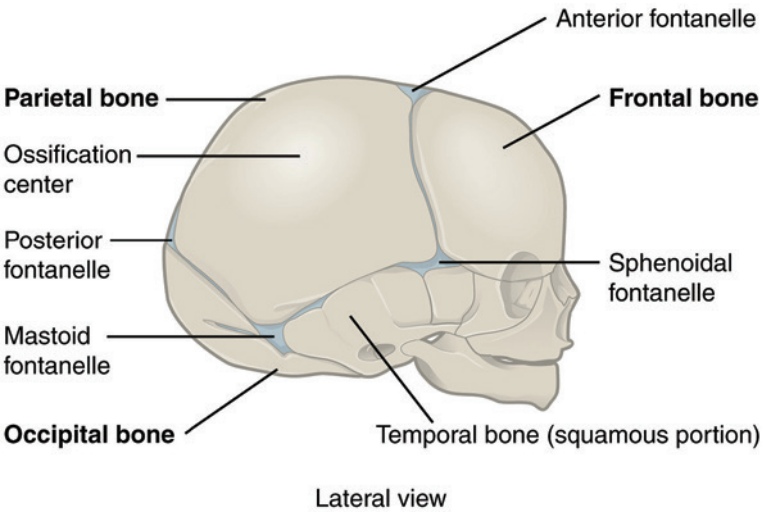


Figure 9.5 The Newborn Skull. The fontanelles of a newborn's skull are broad areas of fibrous connective tissue that form fibrous joints between the bones of the skull.

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Examples of synostosis fusions between cranial bones are found both early and late in life. At the time of birth, the frontal and maxillary bones consist of right and left halves joined together by sutures, which disappear by the eighth year as the halves fuse together to form a single bone. Late in life, the sagittal, coronal, and lambdoid sutures of the skull will begin to ossify and fuse, causing the suture line to gradually disappear.

Syndesmosis

A **syndesmosis** is a type of fibrous joint in which two parallel bones are united to each other by fibrous connective tissue. The gap between the bones may be narrow, with the bones joined by ligaments, or the gap may be wide and filled in by a broad sheet of connective tissue called an **interosseous membrane**.

Example: In the forearm, the shaft of the radius and ulna are separated by a wide gap that is filled by an interosseous membrane. Similarly, in the leg, the shafts of the tibia and fibula are connected along their lengths by an interosseous membrane, which firmly unites the two bones.

Gomphosis

A **gomphosis** is the specialized fibrous joint that anchors the root of a tooth into its bony socket within the maxillary bone (upper jaw) or mandible bone (lower jaw) of the skull. A gomphosis is also known as a peg-and-socket joint. Spanning between the bony walls of the socket and the root of the tooth are numerous short bands of dense connective tissue, each of which is called a **periodontal ligament** (see Figure 9.4c). Due to the immobility of a gomphosis, this type of joint is functionally classified as a synarthrosis.

9.3 Cartilaginous Joints

Learning Objectives

By the end of this section, you will be able to:

- Describe the structural features of cartilaginous joints
- Distinguish between a synchondrosis and symphysis
- Give an example of each type of cartilaginous joint

As the name indicates, at a **cartilaginous joint**, the adjacent bones are united by cartilage, a tough but flexible type of connective tissue. These types of joints lack a joint cavity and involve bones that are joined together by either hyaline cartilage or fibrocartilage (Figure 9.6). There are two types of cartilaginous

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joints. A synchondrosis is a cartilaginous joint where the bones are joined by hyaline cartilage. Also classified as synchondroses are places where bone is united to a cartilage structure, such as between the anterior end of a rib and the costal cartilage of the thoracic cage. The second type of cartilaginous joint is a symphysis, where the bones are joined by fibrocartilage.

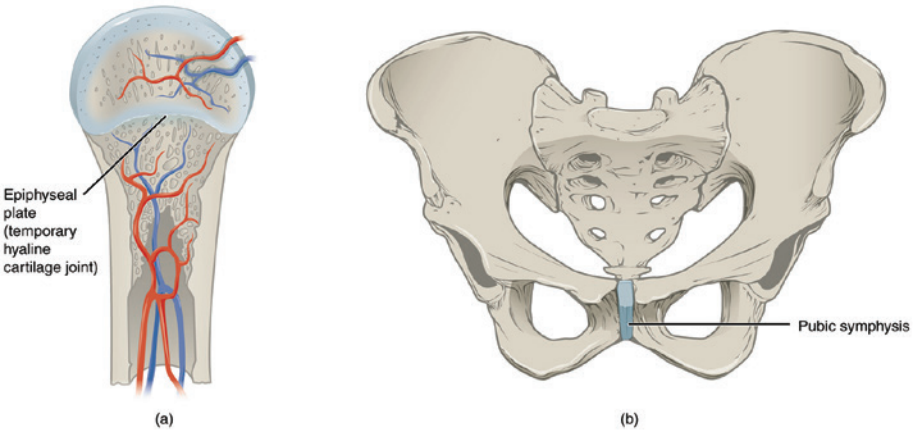


Figure 9.6 Cartilaginous Joints. At cartilaginous joints, bones are united by hyaline cartilage to form a synchondrosis or by fibrocartilage to form a symphysis. (a) The hyaline cartilage of the epiphyseal plate (growth plate) forms a synchondrosis that unites the shaft (diaphysis) and end (epiphysis) of a long bone and allows the bone to grow in length. (b) The pubic portions of the right and left hip bones of the pelvis are joined together by fibrocartilage, forming the pubic symphysis.

Synchondrosis

A **synchondrosis** is a cartilaginous joint where bones are joined together by hyaline cartilage or where bone is united to hyaline cartilage. A synchondrosis may be temporary or permanent. A temporary synchondrosis is the epiphyseal plate (growth plate) of a growing long bone. The epiphyseal plate is the region of growing hyaline cartilage that unites the diaphysis (shaft) of the bone to the epiphysis (end of the bone). Bone lengthening involves growth of the epiphyseal plate cartilage and its replacement by bone, which adds to the diaphysis. For many years during childhood growth, the rates of cartilage growth and bone formation are equal, thus the epiphyseal plate does not change in overall thickness as the bone lengthens. During the late teens and early 20s, growth of the cartilage slows and eventually stops. The epiphyseal plate is then completely replaced by bone, and the diaphysis and epiphysis portions of the bone fuse together to form a single adult bone. This fusion of the diaphysis and epiphysis is a synostosis. Once this occurs, bone lengthening ceases. For this reason,

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the epiphyseal plate is considered to be a temporary synchondrosis. Because cartilage is softer than bone tissue, injury to a growing long bone can damage the epiphyseal plate cartilage, thus stopping bone growth and preventing additional bone lengthening.

Growing layers of cartilage also form synchondroses that join together the ilium, ischium, and pubic portions of the hip bone during childhood and adolescence. When body growth stops, the cartilage disappears and is replaced by bone, forming synostoses and fusing the bony components together into the single hip bone of the adult. Similarly, synostoses unite the sacral vertebrae that fuse together to form the adult sacrum.

Interactive Link 9.1

Watch this video (http://oer.aupress.ca/oer-202505/9.1) to view a radiograph (X-ray image) of a child's hand and wrist. The growing bones of child have an epiphyseal plate that forms a synchondrosis between the shaft and end of a long bone. Being less dense than bone, the area of epiphyseal cartilage is seen on this radiograph as the dark epiphyseal gaps located near the ends of the long bones, including the radius, ulna, metacarpal, and phalanx bones. Which of the bones in this image do not show an epiphyseal plate (epiphyseal gap)?

Examples of permanent synchondroses are found in the thoracic cage. One example is the first sternocostal joint, where the first rib is anchored to the manubrium by its costal cartilage. (The articulations of the remaining costal cartilages to the sternum are all synovial joints.) Additional synchondroses are formed where the anterior end of each of the other 11 ribs is joined to its costal cartilage. Unlike the temporary synchondroses of the epiphyseal plate, these permanent synchondroses retain their hyaline cartilage and thus do not ossify with age. Due to the lack of movement between the bone and cartilage, both temporary and permanent synchondroses are functionally classified as synarthrosis.

Symphysis

A cartilaginous joint where the bones are joined by fibrocartilage is called a **symphysis**. Fibrocartilage is very strong because it contains numerous bundles of thick collagen fibres, giving it a much greater ability to resist pulling and bending forces when compared with hyaline cartilage. This gives symphyses the ability to strongly unite the adjacent bones but can still allow for limited movement to occur. Thus, a symphysis is functionally classified as an

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amphiarthrosis. The gap separating the bones at a symphysis may be narrow or wide.

The gap between the bones is narrow at the pubic symphysis and the manubriosternal joint. At the pubic symphysis, the pubic portions of the right and left hip bones of the pelvis are joined together by fibrocartilage across a narrow gap. Similarly, at the manubriosternal joint, fibrocartilage unites the manubrium and body portions of the sternum. The intervertebral symphysis is a wide symphysis located between the bodies of adjacent vertebrae of the vertebral column. Here, a thick pad of fibrocartilage called an intervertebral disc strongly unites the adjacent vertebrae by filling the gap between them. The width of the intervertebral symphysis is important because it allows for small movements between the adjacent vertebrae. In addition, the thick intervertebral disc provides cushioning between the vertebrae, which is important when carrying heavy objects or during high-impact activities such as running and jumping.

9.4 Synovial Joints

Learning Objectives

By the end of this section, you will be able to:

- Describe the structural features of a synovial joint
- Discuss the function of additional structures associated with synovial joints
- List the six types of synovial joints and give an example of each

Synovial joints are the most common type of joint in the body (Figure 9.7). A key structural characteristic for a synovial joint that is not seen at fibrous or cartilaginous joints is the presence of a joint cavity. This fluid-filled space is the site at which the articulating surfaces of the bones contact each other. Also unlike fibrous or cartilaginous joints, the articulating bone surfaces at a synovial joint are not directly connected to each other with fibrous connective tissue or cartilage. This gives the bones of a synovial joint the ability to move smoothly against each other, allowing for increased joint mobility.

Structural Features of Synovial Joints

Synovial joints are characterized by the presence of a joint cavity. The walls of this space are formed by the **articular capsule**, a fibrous connective tissue structure that is attached to each bone just outside the area of the bone's articulating surface. The bones of the joint articulate with each other within the joint cavity.

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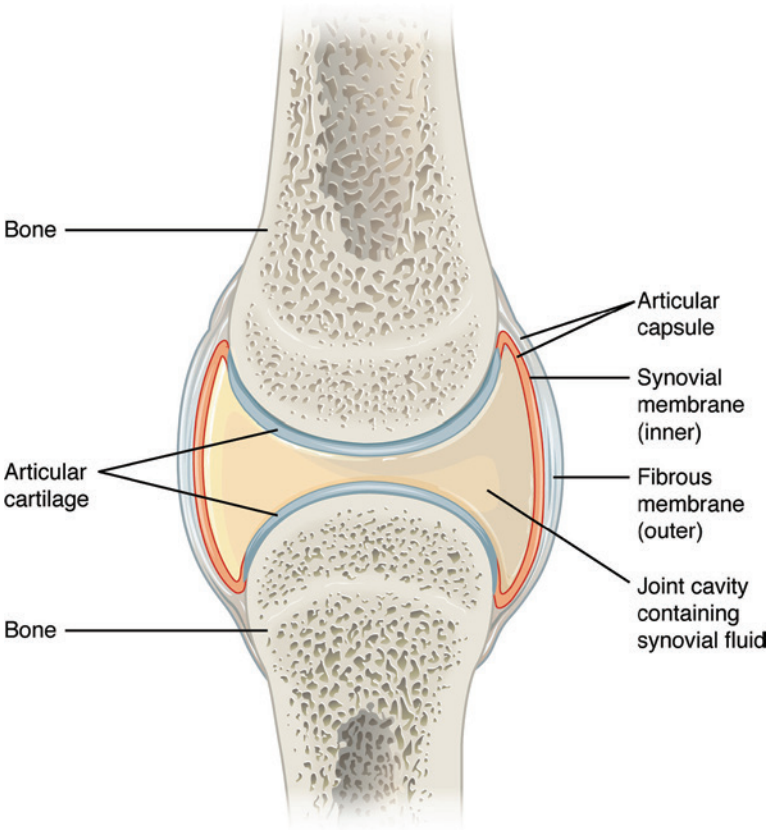


Figure 9.7 Synovial Joints. Synovial joints allow for smooth movements between the adjacent bones. The joint is surrounded by an articular capsule that defines a joint cavity filled with synovial fluid. The articulating surfaces of the bones are covered by a thin layer of articular cartilage. Ligaments support the joint by holding the bones together and resisting excess or abnormal joint motions.

Friction between the bones at a synovial joint is prevented by the presence of the **articular cartilage**, a thin layer of hyaline cartilage that covers the entire articulating surface of each bone. However, unlike at a cartilaginous joint, the articular cartilages of each bone are not continuous with each other. Instead, the articular cartilage acts like a Teflon coating over the bone surface, allowing the articulating bones to move smoothly against each other without damaging the underlying bone tissue. Lining the inner surface of the articular capsule is a thin **synovial membrane**. The cells of this membrane secrete **synovial fluid**: a thick, slimy fluid that provides lubrication to further reduce friction between the bones of the joint. This fluid also provides nourishment to the articular cartilage, which does not contain blood vessels. The ability of the bones to move smoothly against each other within the joint cavity, and

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the freedom of joint movement this provides, means that each synovial joint is functionally classified as a diarthrosis.

Outside of their articulating surfaces, the bones are connected together by ligaments, which are strong bands of fibrous connective tissue. These strengthen and support the joint by anchoring the bones together and preventing their separation. Ligaments allow for normal movements at a joint but limit the range of these motions, thus preventing excessive or abnormal joint movements. Ligaments are classified based on their relationship to the fibrous articular capsule. An **extrinsic ligament** is located outside the articular capsule, an **intrinsic ligament** is fused to or incorporated into the wall of the articular capsule, and an **intracapsular ligament** is located inside the articular capsule.

At many synovial joints, additional support is provided by the muscles and their tendons that act across the joint. A **tendon** is the dense connective tissue structure that attaches a muscle to bone. As forces acting on a joint increase, the body will automatically increase the overall strength of contraction of the muscles crossing that joint, thus allowing the muscle and its tendon to serve as a "dynamic ligament" to resist forces and support the joint. This type of indirect support by muscles is very important at the shoulder joint, for example, where the ligaments are relatively weak.

Additional Structures Associated with Synovial Joints

A few synovial joints of the body have a fibrocartilage structure located between the articulating bones. This is called an **articular disc**, which is generally small and oval-shaped, or a **meniscus**, which is larger and C-shaped. These structures can serve several functions, depending on the specific joint. In some places, an articular disc may act to strongly unite the bones of the joint to each other. Examples of this include the articular discs found at the sternoclavicular joint or between the distal ends of the radius and ulna bones. At other synovial joints, the disc can provide shock absorption and cushioning between the bones, which is the function of each meniscus within the knee joint. Finally, an articular disc can serve to smooth the movements between the articulating bones, as seen at the temporomandibular joint. Some synovial joints also have a fat pad, which can serve as a cushion between the bones.

Additional structures located outside of a synovial joint serve to prevent friction between the bones of the joint and the overlying muscle tendons or skin. A **bursa** (plural = bursae) is a thin connective tissue sac filled with lubricating liquid. They are located in regions where skin, ligaments, muscles, or muscle tendons can rub against one another, usually near a body joint (Figure 9.8). Bursae reduce friction by separating the adjacent structures, preventing them from rubbing directly against each other.

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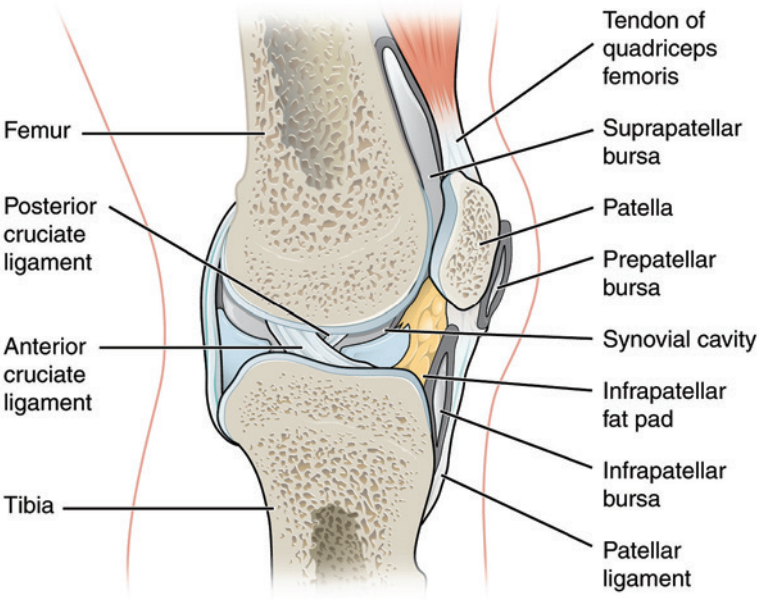


Figure 9.8 Bursae. Bursae are fluid-filled sacs that serve to prevent friction between skin, muscle, or tendon and an underlying bone. Three major bursae and a fat pad are part of the complex joint that unites the femur and tibia of the leg.

A **tendon sheath** is similar in structure to a bursa but smaller. It is a connective tissue sac that surrounds a muscle tendon at places where the tendon crosses a joint. It contains a lubricating fluid that allows for smooth motions of the tendon during muscle contraction and joint movements.

Types of Synovial Joints

Synovial joints are subdivided based on the shapes of the articulating surfaces of the bones that form each joint. The six types of synovial joints are pivot, hinge, condyloid, saddle, plane, and ball-and-socket joints (Figure 9.9).

Pivot Joint

At a **pivot joint**, a rounded portion of a bone is enclosed within a ring formed partially by the articulation with another bone and partially by a ligament (see Figure 9.9a). The bone rotates within this ring. Since the rotation is around a single axis, pivot joints are functionally classified as a uniaxial diarthrosis type of joint.

An example of a pivot joint is the atlantoaxial joint, found between the C1 (atlas) and C2 (axis) vertebrae. Here, the upward projecting dens of the axis articulates with the inner aspect of the atlas, where it is held in place by a ligament. Rotation at this joint allows you to turn your head from side to side.

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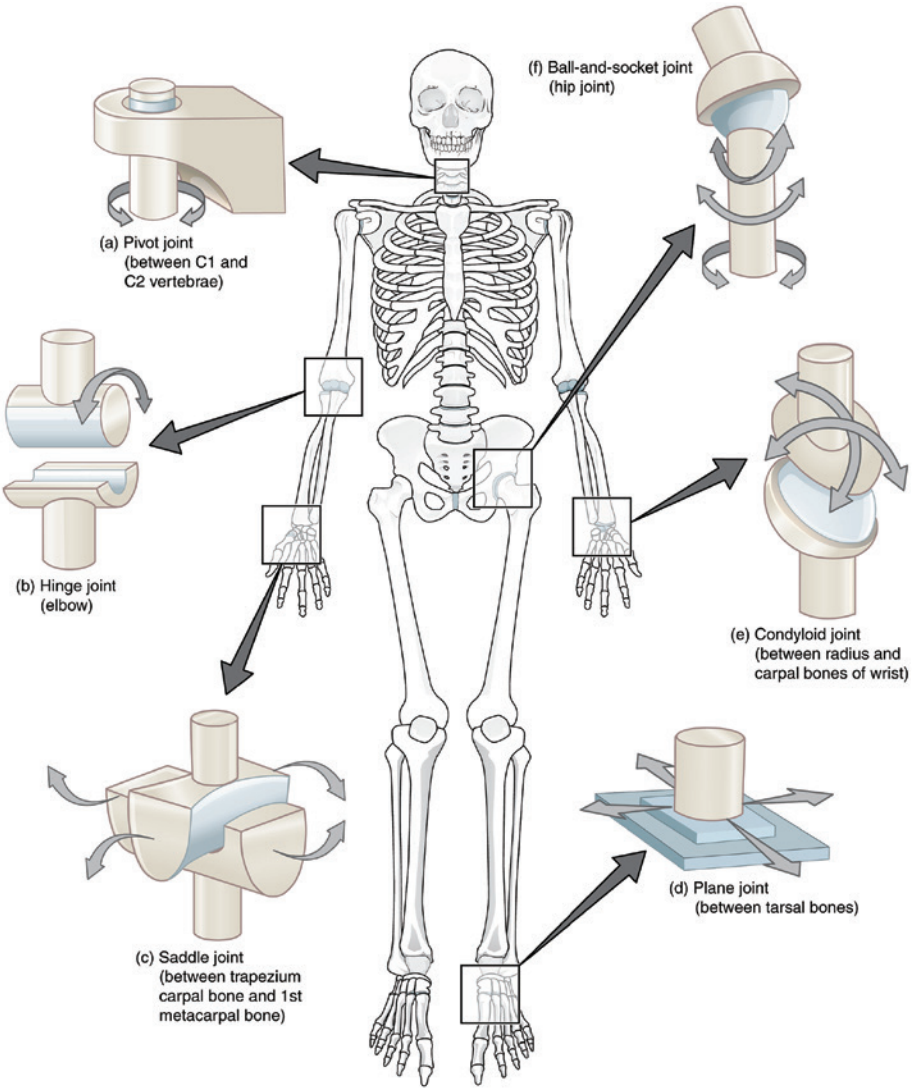


Figure 9.9 Types of Synovial Joints. The six types of synovial joints allow the body to move in a variety of ways. (a) Pivot joints allow for rotation around an axis, such as between the first and second cervical vertebrae, which allows for side-to-side rotation of the head. (b) The hinge joint of the elbow works like a door hinge. (c) The articulation between the trapezium carpal bone and the first metacarpal bone at the base of the thumb is a saddle joint. (d) Plane joints, such as those between the tarsal bones of the foot, allow for limited gliding movements between bones. (e) The radiocarpal joint of the wrist is a condyloid joint. (f) The hip and shoulder joints are the only ball-and-socket joints of the body.

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Hinge Joint

In a **hinge joint**, the convex end of one bone articulates with the concave end of the adjoining bone (see Figure 9.9b). This type of joint allows only for bending and straightening motions along a single axis, thus hinge joints are functionally classified as uniaxial joints.

A good example is the elbow joint, with the articulation between the trochlea of the humerus and the trochlear notch of the ulna.

Condyloid Joint

At a **condyloid joint** (ellipsoid joint), the shallow depression at the end of one bone articulates with a rounded structure from an adjacent bone or bones (see Figure 9.9e). Functionally, condyloid joints are biaxial joints that allow for two planes of movement.

Example: The knuckle (metacarpophalangeal) joints of the hand between the distal end of a metacarpal bone and the proximal phalanx bone are condyloid joints. One movement involves the bending and straightening of the fingers or the anterior-posterior movements of the hand. The second movement is a side-to-side movement, which allows you to spread your fingers apart and bring them together or to move your hand in a medial-going or lateral-going direction.

Saddle Joint

At a **saddle joint**, both of the articulating surfaces for the bones have a saddle shape, which is concave in one direction and convex in the other (see Figure 9.9c). This allows the two bones to fit together like a rider sitting on a saddle. Saddle joints are functionally classified as biaxial joints.

The primary example is the first carpometacarpal joint, between the trapezium (a carpal bone) and the first metacarpal bone at the base of the thumb. This joint provides the thumb the ability to move away from the palm of the hand along two planes. Thus, the thumb can move within the same plane as the palm of the hand, or it can jut out anteriorly, perpendicular to the palm. This movement of the first carpometacarpal joint is what gives humans their distinctive “opposable” thumbs.

Plane Joint

At a **plane joint** (gliding joint), the articulating surfaces of the bones are flat or slightly curved and of approximately the same size, which allows the bones to slide against each other (see Figure 9.9d). The motion at this type of joint is usually small and tightly constrained by surrounding ligaments. Based only on

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their shape, plane joints can allow multiple movements, including rotation. Thus plane joints can be functionally classified as a multiaxial joint.

However, not all these movements are available to every plane joint due to limitations placed on it by ligaments or neighbouring bones. Thus, depending on the specific joint of the body, a plane joint may exhibit only a single type of movement or several movements.

Examples: Plane joints are found between the carpal bones (intercarpal joints) of the wrist or tarsal bones (intertarsal joints) of the foot and between the clavicle and acromion of the scapula (acromioclavicular joint).

Ball-and-Socket Joint

The joint with the greatest range of motion is the **ball-and-socket joint**. At these joints, the rounded head of one bone (the ball) fits into the concave articulation (the socket) of the adjacent bone (see Figure 9.9f).

Examples: The hip joint and the glenohumeral (shoulder) joint are the only ball-and-socket joints of the body. At the hip joint, the head of the femur articulates with the acetabulum of the hip bone, and at the shoulder joint, the head of the humerus articulates with the glenoid cavity of the scapula.

Ball-and-socket joints are classified functionally as multiaxial joints. The femur and the humerus are able to move in both anterior-posterior and medial-lateral directions, and they can also rotate around their long axis. The shallow socket formed by the glenoid cavity allows the shoulder joint an extensive range of motion. In contrast, the deep socket of the acetabulum and the strong supporting ligaments of the hip joint serve to constrain movements of the femur, reflecting the need for stability at and weight-bearing ability of the hip.

Interactive Link 9.2

Watch this video (http://oer.aupress.ca/oer-202505/9.2) to see an animation of synovial joints in action. Synovial joints are places where bones articulate with each other inside of a joint cavity. The different types of synovial joints are the ball-and-socket joint (shoulder joint), hinge joint (knee), pivot joint (atlantoaxial joint, between C1 and C2 vertebrae of the neck), condyloid joint (radiocarpal joint of the wrist), saddle joint (first carpometacarpal joint, between the trapezium carpal bone and the first metacarpal bone, at the base of the thumb), and plane joint (facet joints of vertebral column, between superior and inferior articular processes). Which type of synovial joint allows for the widest range of motion?

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9.5 Types of Body Movements

Learning Objectives

By the end of this section, you will be able to:

- Define the different types of body movements
- Identify the joints that allow for these motions

Synovial joints allow the body a tremendous range of movements. Each movement at a synovial joint results from the contraction or relaxation of the muscles that are attached to the bones on either side of the articulation. The type of movement that can be produced at a synovial joint is determined by its structural type.

While the ball-and-socket joint gives the greatest range of movement at an individual joint, in other regions of the body, several joints may work together to produce a particular movement. Overall, each type of synovial joint is necessary to provide the body with its great flexibility and mobility. There are many types of movement that can occur at synovial joints (Table 9.1). Movement types are generally paired, with one being the opposite of the other. Body movements are always described in relation to the anatomical position of the body: upright stance, with upper limbs to the side of body and palms facing forward. Refer to Figure 9.10 as you go through this section.

Table 9.1 Movements of the Joints

Pivot	Uniaxial joint; allows rotational movement	Atlantoaxial joint (C1–C2 vertebrae articulation); proximal radioulnar joint
Hinge	Uniaxial joint; allows flexion/extension movements	Knee; elbow; ankle; interphalangeal joints of fingers and toes
Condyloid	Biaxial joint; allows flexion/extension, abduction/adduction, and circumduction movements	Metacarpophalangeal (knuckle) joints of fingers; radiocarpal joint of wrist; metatarsophalangeal joints for toes
Saddle	Biaxial joint; allows flexion/extension, abduction/adduction, and circumduction movements	First carpometacarpal joint of the thumb; sternoclavicular joint
Plane	Multiaxial joint; allows inversion and eversion of the foot or flexion, extension, and lateral flexion of the vertebral column	Intertarsal joints of foot; superior-inferior articular process articulations between vertebrae
Ball-and-socket	Multiaxial joint; allows flexion/extension, abduction/adduction, circumduction, and medial/lateral rotation movements	Shoulder and hip joints

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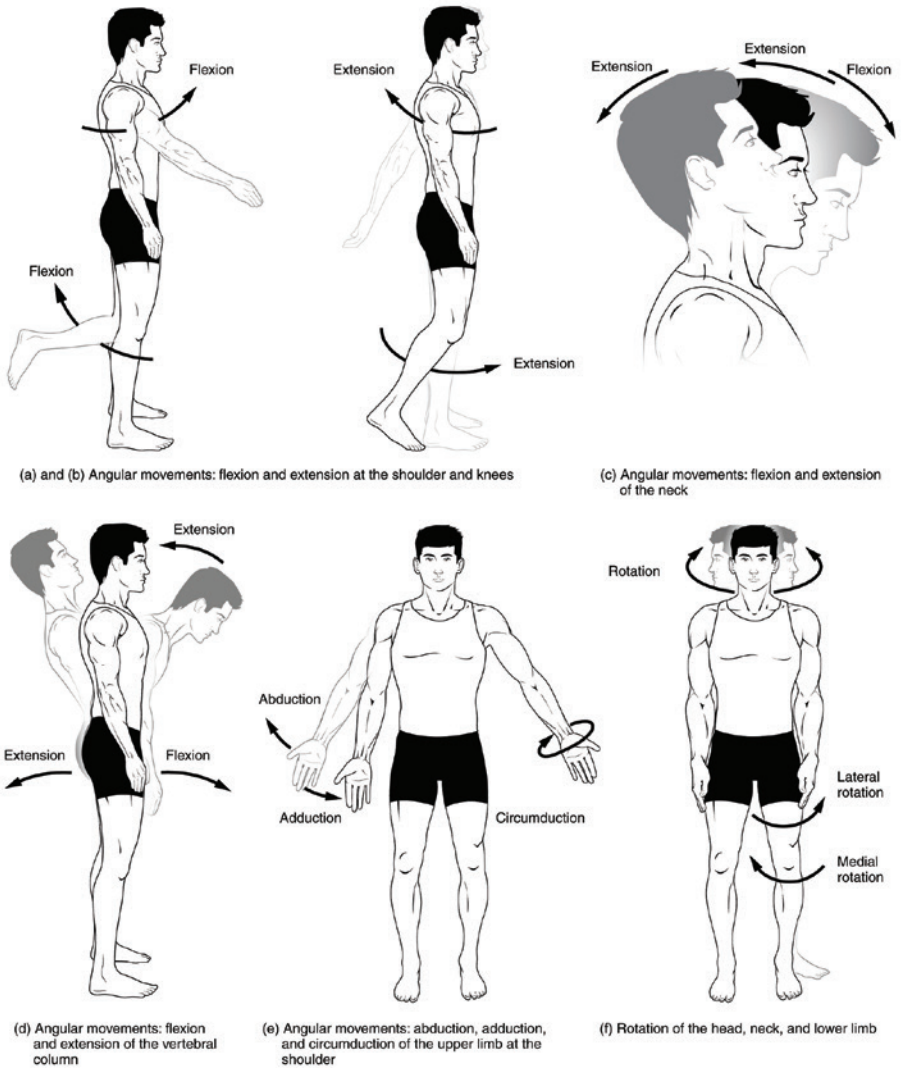


Figure 9.10 Movements of the Body, Part 1**.** Synovial joints give the body many ways in which to move. (a–b) Flexion and extension motions are in the sagittal (anterior-posterior) plane of motion. These movements take place at the shoulder, hip, elbow, knee, wrist, metacarpophalangeal, metatarsophalangeal, and interphalangeal joints. (c–d) Anterior bending of the head or vertebral column is flexion, while any posterior-going movement is extension. (e) Abduction and adduction are motions of the limbs, hand, fingers, or toes in the coronal (medial-lateral) plane of movement. Moving the limb or hand laterally away from the body, or spreading the fingers or toes, is abduction. Adduction brings the limb or hand toward or across the midline of the body or brings the fingers or toes together. Circumduction is the movement of the limb, hand, or fingers in a circular pattern, using the sequential combination of flexion, adduction, extension, and abduction motions. Adduction/abduction and circumduction take place at the shoulder, hip, wrist, metacarpophalangeal, and metatarsophalangeal joints. (f) Turning the head side to side or twisting the body is rotation. Medial and lateral rotation of the upper limb at the shoulder or lower limb at the hip involves turning the anterior surface of the limb toward the midline of the body (medial or internal rotation) or away from the midline (lateral or external rotation).

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Interactive Link 9.3

Watch this video (http://oer.aupress.ca/oer-202505/9.3) to learn about anatomical motions. What motions involve increasing or decreasing the angle of the foot at the ankle?

Flexion and Extension

Flexion and **extension** are typically movements that take place within the sagittal plane and involve anterior or posterior movements of the neck, trunk, or limbs. For the vertebral column, flexion (anterior flexion) is an anterior (forward) bending of the neck or trunk, while extension involves a posterior-directed motion, such as straightening from a flexed position or bending backward. **Lateral flexion** of the vertebral column occurs in the coronal plane and is defined as the bending of the neck or trunk toward the right or left side. These movements of the vertebral column involve both the symphysis joint formed by each intervertebral disc as well as the plane type of synovial joint formed between the inferior articular processes of one vertebra and the superior articular processes of the next lower vertebra.

In the limbs, flexion decreases the angle between the bones (bending of the joint), while extension increases the angle and straightens the joint. For the upper limb, all anterior-going motions are flexion and all posterior-going motions are extension. These include anterior-posterior movements of the arm at the shoulder, the forearm at the elbow, the hand at the wrist, and the fingers at the metacarpophalangeal and interphalangeal joints. For the thumb, extension moves the thumb away from the palm of the hand within the same plane as the palm, while flexion brings the thumb back against the index finger or into the palm. These motions take place at the first carpometacarpal joint. In the lower limb, bringing the thigh forward and upward is flexion at the hip joint, while any posterior-going motion of the thigh is extension. Note that extension of the thigh beyond the anatomical (standing) position is greatly limited by the ligaments that support the hip joint. Knee flexion is the bending of the knee to bring the foot toward the posterior thigh, and extension is the straightening of the knee. Flexion and extension movements are seen at the hinge, condyloid, saddle, and ball-and-socket joints of the limbs (see Figure 9.10a–d).

Hyperextension is the abnormal or excessive extension of a joint beyond its normal range of motion, thus resulting in injury. Similarly, **hyperflexion** is excessive flexion at a joint. Hyperextension injuries are common at hinge joints such as the knee and elbow. In cases of "whiplash" in which the head is suddenly moved backward and then forward, a patient may experience both hyperextension and hyperflexion of the cervical region.

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Abduction and Adduction

Abduction and **adduction** motions occur within the coronal plane and involve medial-lateral motions of the limbs, fingers, toes, or thumbs. Abduction moves the limb laterally away from the midline of the body, while adduction is the opposing movement that brings the limb toward the body or across the midline. For example, abduction is raising the arm at the shoulder joint, moving it laterally away from the body, while adduction brings the arm down to the side of the body. Similarly, abduction and adduction at the wrist move the hand away from or toward the midline of the body. Spreading the fingers or toes apart is also abduction, while bringing the fingers or toes together is adduction. For the thumb, abduction is the anterior movement that brings the thumb to a 90° perpendicular position, pointing straight out from the palm. Adduction moves the thumb back to the anatomical position, next to the index finger. Abduction and adduction movements are seen at condyloid, saddle, and ball-and-socket joints (see Figure 9.10e).

Circumduction

Circumduction is the movement of a body region in a circular manner, in which one end of the body region being moved stays relatively stationary while the other end describes a circle. It involves the sequential combination of flexion, adduction, extension, and abduction at a joint. This type of motion is found at biaxial condyloid and saddle joints and at multiaxial ball-and-sockets joints (see Figure 9.10e).

Rotation

Rotation can occur within the vertebral column, at a pivot joint, or at a ball-and-socket joint. Rotation of the neck or body is the twisting movement produced by the summation of the small rotational movements available between adjacent vertebrae. At a pivot joint, one bone rotates in relation to another bone. This is a uniaxial joint, and thus rotation is the only motion allowed at a pivot joint.

For example, at the atlantoaxial joint, the first cervical (C1) vertebra (atlas) rotates around the dens, the upward projection from the second cervical (C2) vertebra (axis). This allows the head to rotate from side to side as when shaking the head "no." The **proximal radioulnar joint** is a pivot joint formed by the head of the radius and its articulation with the ulna. This joint allows for the radius to rotate along its length during pronation and supination movements of the forearm. Rotation can also occur at the ball-and-socket joints of the shoulder and hip. Here, the humerus and femur rotate around their long axis, which moves the anterior surface of the arm or thigh either toward or away from the midline of the body. Movement that brings the anterior surface of the limb

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toward the midline of the body is called **medial** (**internal**) **rotation**. Conversely, rotation of the limb so that the anterior surface moves away from the midline is **lateral** (**external**) **rotation** (see Figure 9.10f). Be sure to distinguish medial and lateral rotation, which can only occur at the multiaxial shoulder and hip joints, from circumduction, which can occur at either biaxial or multiaxial joints.

Supination and Pronation

Supination and pronation are movements of the forearm. In the anatomical position, the upper limb is held next to the body with the palm facing forward. This is the **supinated position** of the forearm. In this position, the radius and ulna are parallel to each other. When the palm of the hand faces backward, the forearm is in the **pronated position**, and the radius and ulna form an X shape.

Supination and pronation are the movements of the forearm that go between these two positions. **Pronation** is the motion that moves the forearm from the supinated (anatomical) position to the pronated (palm-backward) position. This motion is produced by rotation of the radius at the proximal radioulnar joint accompanied by movement of the radius at the distal radioulnar joint. The proximal radioulnar joint is a pivot joint that allows for rotation of the head of the radius. Because of the slight curvature of the shaft of the radius, this rotation causes the distal end of the radius to cross over the distal ulna at the distal radioulnar joint. This crossing over brings the radius and ulna into an X-shaped position. **Supination** is the opposite motion, in which rotation of the radius returns the bones to their parallel positions and moves the palm to the anterior-facing (supinated) position. It helps to remember that supination is the motion you use when scooping up soup with a spoon (see Figure 9.11g).

Dorsiflexion and Plantar Flexion

Dorsiflexion and **plantar flexion** are movements at the ankle joint, which is a hinge joint. Lifting the front of the foot, so that the top of the foot moves toward the anterior leg, is dorsiflexion, while lifting the heel of the foot from the ground or pointing the toes downward is plantar flexion. These are the only movements available at the ankle joint (see Figure 9.11h).

Inversion and Eversion

Inversion and eversion are complex movements that involve the multiple plane joints among the tarsal bones of the posterior foot (intertarsal joints) and thus are not motions that take place at the ankle joint. **Inversion** is the turning of the foot to angle the bottom of the foot toward the midline, while **eversion** turns the bottom of the foot away from the midline. The foot has a greater range of

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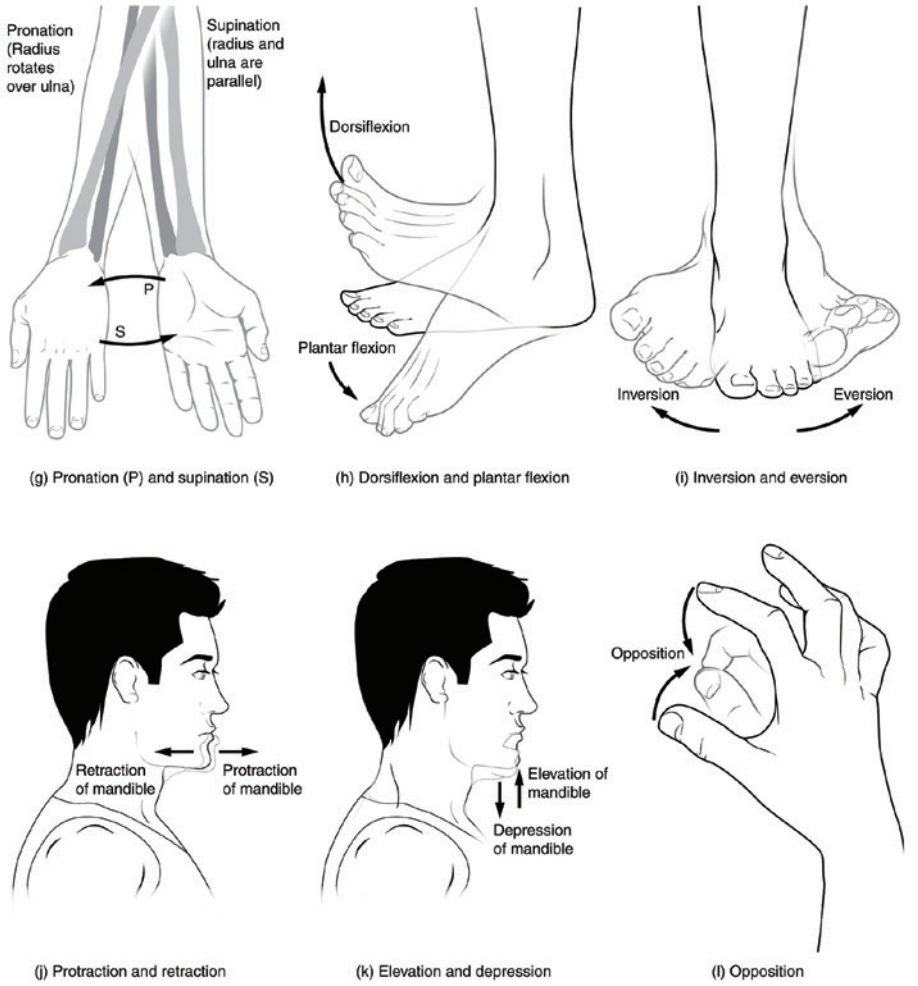


Figure 9.11 Movements of the Body, Part 2**.** (g) Supination of the forearm turns the hand to the palm forward position in which the radius and ulna are parallel, while forearm pronation turns the hand to the palm backward position in which the radius crosses over the ulna to form an X. (h) Dorsiflexion of the foot at the ankle joint moves the top of the foot toward the leg, while plantar flexion lifts the heel and points the toes. (i) Eversion of the foot moves the bottom (sole) of the foot away from the midline of the body, while foot inversion faces the sole toward the midline. (j) Protraction of the mandible pushes the chin forward, and retraction pulls the chin back. (k) Depression of the mandible opens the mouth, while elevation closes it. (l) Opposition of the thumb brings the tip of the thumb into contact with the tip of the fingers of the same hand, and reposition brings the thumb back next to the index finger.

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inversion than eversion motion. These are important motions that help stabilize the foot when walking or running on an uneven surface and aid in the quick side-to-side changes in direction used during active sports such as basketball, racquetball, and soccer (see Figure 9.11i).

Protraction and Retraction

Protraction and **retraction** are anterior-posterior movements of the scapula or mandible. Protraction of the scapula occurs when the shoulder is moved forward, as when pushing against something or throwing a ball. Retraction is the opposite motion, with the scapula being pulled posteriorly and medially, toward the vertebral column. For the mandible, protraction occurs when the lower jaw is pushed forward to stick out the chin, while retraction pulls the lower jaw backward (see Figure 9.11j).

Depression and Elevation

Depression and **elevation** are downward and upward movements of the scapula or mandible. The upward movement of the scapula and shoulder is elevation, while a downward movement is depression. These movements are used to shrug your shoulders. Similarly, elevation of the mandible is the upward movement of the lower jaw used to close the mouth or bite on something, and depression is the downward movement that produces opening of the mouth (see Figure 9.11k).

Excursion

Excursion is the side-to-side movement of the mandible. **Lateral excursion** moves the mandible away from the midline, toward either the right or left side. **Medial excursion** returns the mandible to its resting position at the midline.

Superior Rotation and Inferior Rotation

Superior and inferior rotation are movements of the scapula and are defined by the direction of movement of the glenoid cavity. These motions involve rotation of the scapula around a point inferior to the scapular spine and are produced by combinations of muscles acting on the scapula. During **superior rotation**, the glenoid cavity moves upward as the medial end of the scapular spine moves downward. This is a very important motion that contributes to upper limb abduction. Without superior rotation of the scapula, the greater tubercle of the humerus would hit the acromion of the scapula, thus preventing any abduction of the arm above shoulder height. Superior rotation of the scapula is thus required for full abduction of the upper limb. Superior rotation is also used without arm abduction when carrying a heavy load with your hand

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or on your shoulder. You can feel this rotation when you pick up a load such as a heavy backpack and carry it on only one shoulder. To increase its weight-bearing support for the bag, the shoulder lifts as the scapula superiorly rotates. **Inferior rotation** occurs during limb adduction and involves the downward motion of the glenoid cavity with upward movement of the medial end of the scapular spine.

Opposition and Reposition

Opposition is the thumb movement that brings the tip of the thumb in contact with the tip of a finger. This movement is produced at the first carpometacarpal joint, which is a saddle joint formed between the trapezium carpal bone and the first metacarpal bone. Thumb opposition is produced by a combination of flexion and abduction of the thumb at this joint. Returning the thumb to its anatomical position next to the index finger is called **reposition** (see Figure 9.11l).

9.6 Anatomy of Selected Synovial Joints

Learning Objectives

By the end of this section, you will be able to:

- Describe the bones that articulate together to form selected synovial joints
- Discuss the movements available at each joint
- Describe the structures that support and prevent excess movement at each joint

Each synovial joint of the body is specialized to perform certain movements. The movements that are allowed are determined by the structural classification for each joint. For example, a multiaxial ball-and-socket joint has much more mobility than a uniaxial hinge joint. However, the ligaments and muscles that support a joint may place restrictions on the total range of motion available. Thus, the ball-and-socket joint of the shoulder has little in the way of ligament support, which gives the shoulder a very large range of motion. In contrast, movements at the hip joint are restricted by strong ligaments, which reduce its range of motion but confer stability during standing and weight-bearing.

This section will examine the anatomy of selected synovial joints of the body. Anatomical names for most joints are derived from the names of the bones that articulate at that joint, although joints such as the elbow, hip, and knee are exceptions to this general naming scheme.

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Articulations of the Vertebral Column

In addition to being held together by the intervertebral discs, adjacent vertebrae also articulate with each other at synovial joints formed between the superior and inferior articular processes called zygapophysial joints (facet joints; see Figure 9.2). These are plane joints that provide for only limited motions between the vertebrae. The orientation of the articular processes at these joints varies in different regions of the vertebral column and serves to determine the types of motions available in each vertebral region. The cervical and lumbar regions have the greatest ranges of motion.

In the neck, the articular processes of cervical vertebrae are flattened and generally face upward or downward. This orientation provides the cervical vertebral column with extensive ranges of motion for flexion, extension, lateral flexion, and rotation. In the thoracic region, the downward projecting and overlapping spinous processes, along with the attached thoracic cage, greatly limit flexion, extension, and lateral flexion. However, the flattened and vertically positioned thoracic articular processes allow for the greatest range of rotation within the vertebral column. The lumbar region allows for considerable extension, flexion, and lateral flexion, but the orientation of the articular processes largely prohibits rotation.

The articulations formed between the skull, the atlas (C1 vertebra), and the axis (C2 vertebra) differ from the articulations in other vertebral areas and play important roles in movements of the head. The **atlanto-occipital joint** is formed by the articulations between the superior articular processes of the atlas and the occipital condyles on the base of the skull. This articulation has a pronounced U-shaped curvature, oriented along the anterior-posterior axis. This allows the skull to rock forward and backward, producing flexion and extension of the head. This moves the head up and down, as when nodding your head "yes."

The **atlantoaxial joint**, between the atlas and axis, consists of three articulations. The paired superior articular processes of the axis articulate with the inferior articular processes of the atlas. These articulating surfaces are relatively flat and oriented horizontally. The third articulation is the pivot joint formed between the dens, which projects upward from the body of the axis, and the inner aspect of the anterior arch of the atlas (Figure 9.12). A strong ligament passes posterior to the dens to hold it in position against the anterior arch. These articulations allow the atlas to rotate on top of the axis, moving the head toward the right or left, as when shaking your head "no."

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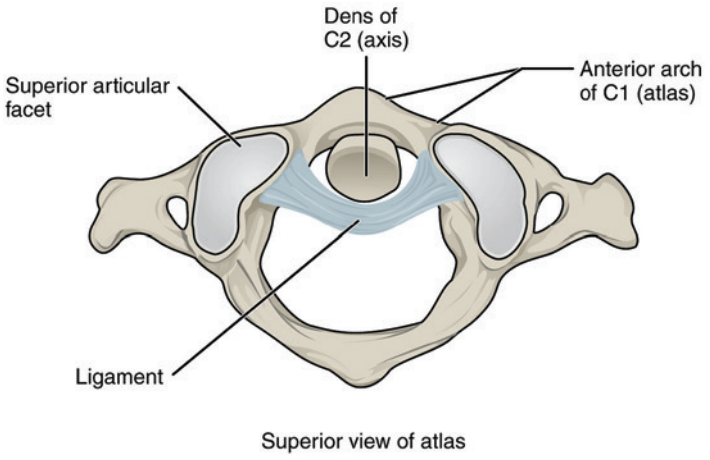


Figure 9.12 Atlantoaxial Joint. The atlantoaxial joint is a pivot type of joint between the dens portion of the axis (C2 vertebra) and the anterior arch of the atlas (C1 vertebra), with the dens held in place by a ligament.

Shoulder Joint

The shoulder joint is called the **glenohumeral joint**. This is a ball-and-socket joint formed by the articulation between the head of the humerus and the glenoid cavity of the scapula (Figure 9.13). This joint has the largest range of motion of any joint in the body. However, this freedom of movement is due to the lack of structural support, thus the enhanced mobility is offset by a loss of stability.

The large range of motion at the shoulder joint is provided by the articulation of the large, rounded humeral head with the small and shallow glenoid cavity, which is only about one-third of the size of the humeral head. The socket formed by the glenoid cavity is deepened slightly by a small lip of fibrocartilage called the **glenoid labrum**, which extends around the outer margin of the cavity. The articular capsule that surrounds the glenohumeral joint is relatively thin and loose to allow for large motions of the upper limb. Some structural support for the joint is provided by thickening of the articular capsule walls that form weak intrinsic ligaments.

However, the primary support for the shoulder joint is provided by muscles crossing the joint, particularly the four **rotator cuff** muscles. These muscles (supraspinatus, infraspinatus, teres minor, and subscapularis) arise from the scapula and attach to the greater or lesser tubercles of the humerus. As these muscles cross the shoulder joint, their tendons encircle the head of the humerus and become fused to the anterior, superior, and posterior walls of the articular capsule.

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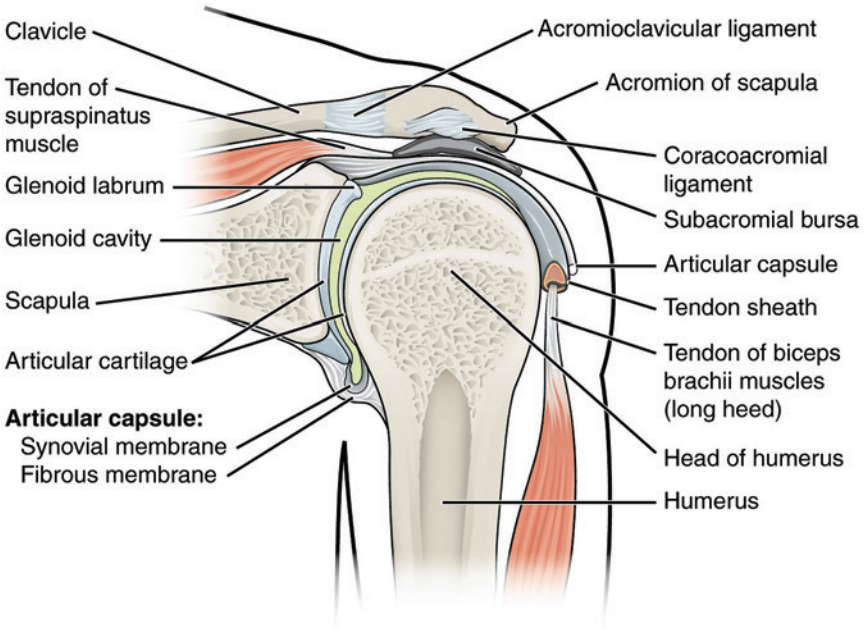


Figure 9.13 Glenohumeral Joint. The glenohumeral (shoulder) joint is a ball-and-socket joint that provides the widest range of motions. It has a loose articular capsule and is supported by ligaments and the rotator cuff muscles.

Interactive Link 9.4

Watch this video (http://oer.aupress.ca/oer-202505/9.4) for a tutorial on the anatomy of the shoulder joint. What movements are available at the shoulder joint?

Interactive Link 9.5

Watch this video (http://oer.aupress.ca/oer-202505/9.5) to learn more about the anatomy of the shoulder joint, including bones, joints, muscles, nerves, and blood vessels. What is the shape of the glenoid labrum in cross-section, and what is the importance of this shape?

Elbow Joint

The **elbow joint** is a uniaxial hinge joint formed by the **humeroulnar joint**, the articulation between the trochlea of the humerus and the trochlear notch of the ulna. Also associated with the elbow are the **humeroradial joint** and the proximal radioulnar joint. All three of these joints are enclosed within a single articular capsule (Figure 9.14).

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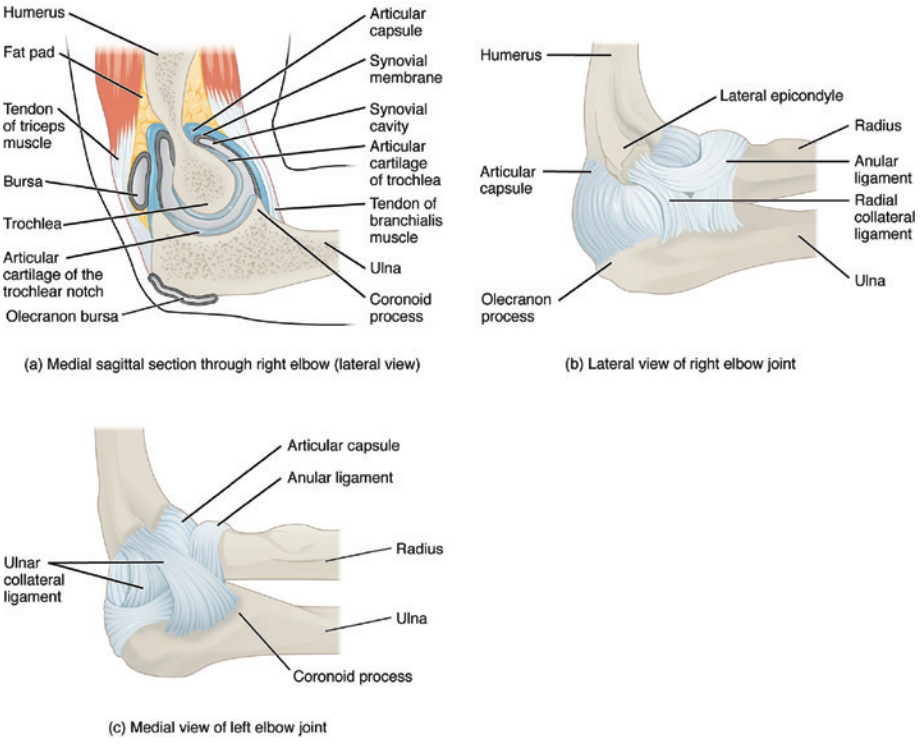


Figure 9.14 Elbow Joint. (a) The elbow is a hinge joint that allows only for flexion and extension of the forearm. (b) It is supported by the ulnar and radial collateral ligaments. (c) The annular ligament supports the head of the radius at the proximal radioulnar joint, the pivot joint that allows for rotation of the radius.

The articular capsule of the elbow is thin on its anterior and posterior aspects but is thickened along its outside margins by strong intrinsic ligaments. These ligaments prevent side-to-side movements and hyperextension. The lateral side of the elbow is supported by the **radial collateral ligament**, and the medial side of the elbow is supported by the **ulnar collateral ligament**. This arises from the lateral epicondyle of the humerus and then blends into the lateral side of the annular ligament. The **annular ligament** encircles the head of the radius. This ligament supports the head of the radius as it articulates with the radial notch of the ulna at the proximal radioulnar joint. This is a pivot joint that allows for rotation of the radius during supination and pronation of the forearm.

Interactive Link 9.6

Watch this animation (http://oer.aupress.ca/oer-202505/9.6) to learn more about the anatomy of the elbow joint. Which structures provide the main stability for the elbow?

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Interactive Link 9.7

Watch this video (http://oer.aupress.ca/oer-202505/9.7) to learn more about the anatomy of the elbow joint, including bones, joints, muscles, nerves, and blood vessels. What are the functions of the articular cartilage?

Knee Joint

The **knee joint** is the largest joint of the body (Figure 9.15). It actually consists of three articulations. The **femoropatellar joint** is found between the patella and the distal femur. The **medial tibiofemoral joint** and **lateral tibiofemoral joint** are located between the medial and lateral condyles of the femur and the medial and lateral condyles of the tibia. All these articulations are enclosed within a single articular capsule. The knee functions as a hinge joint, allowing flexion and extension of the leg. This action is generated by both rolling and gliding motions of the femur on the tibia. In addition, some rotation of the leg is available when the knee is flexed but not when extended. The knee is well constructed for weight-bearing in its extended position, but it is vulnerable to injuries associated with hyperextension, twisting, or blows to the medial or lateral side of the joint, particularly while bearing weight.

At the femoropatellar joint, the patella slides vertically within a groove on the distal femur. The patella is a sesamoid bone incorporated into the tendon of the quadriceps femoris muscle, the large muscle of the anterior thigh. The patella serves to protect the quadriceps tendon from friction against the distal femur. Continuing from the patella to the anterior tibia just below the knee is the **patellar ligament**. Acting via the patella and patellar ligament, the quadriceps femoris is a powerful muscle that acts to extend the leg at the knee. It also serves as a "dynamic ligament" to provide very important support and stabilization for the knee joint.

The medial and lateral tibiofemoral joints are the articulations between the rounded condyles of the femur and the relatively flat condyles of the tibia. During flexion and extension motions, the condyles of the femur both roll and glide over the surfaces of the tibia. The rolling action produces flexion or extension, while the gliding action serves to maintain the femoral condyles centred over the tibial condyles, thus ensuring maximal bony, weight-bearing support for the femur in all knee positions. As the knee comes into full extension, the femur undergoes a slight medial rotation in relation to the tibia. The rotation results because the lateral condyle of the femur is slightly smaller than

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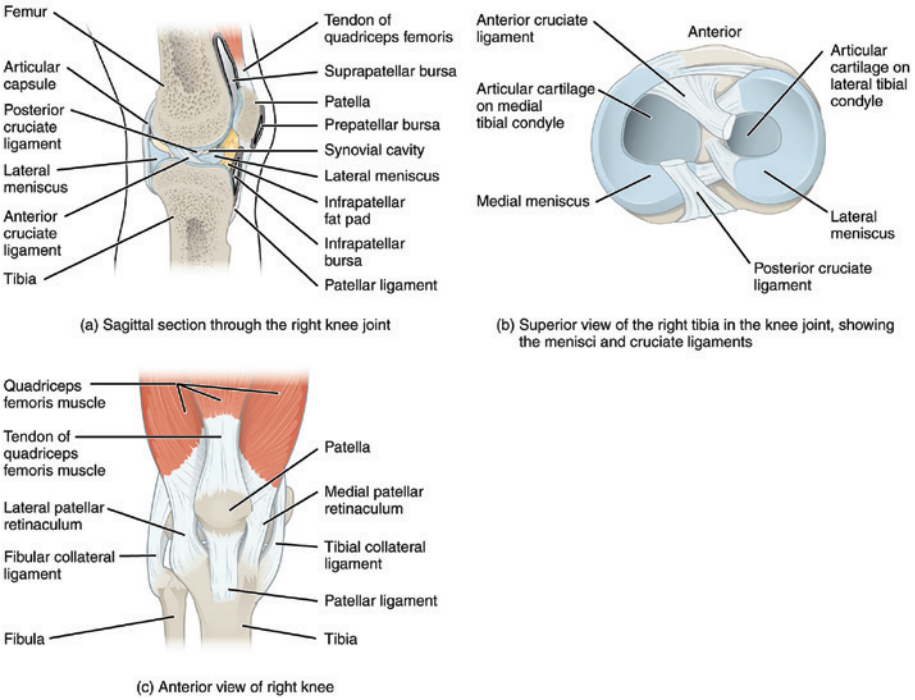


Figure 9.15 Knee Joint. (a) The knee joint is the largest joint of the body. (b–c) It is supported by the tibial and fibular collateral ligaments, located on the sides of the knee outside of the articular capsule, and the anterior and posterior cruciate ligaments found inside the capsule. The medial and lateral menisci provide padding and support between the femoral condyles and tibial condyles.

the medial condyle. Thus, the lateral condyle finishes its rolling motion first, followed by the medial condyle.

The resulting small medial rotation of the femur serves to "lock" the knee into its fully extended and most stable position. Flexion of the knee is initiated by a slight lateral rotation of the femur on the tibia, which "unlocks" the knee. This lateral rotation motion is produced by the popliteus muscle of the posterior leg.

The knee joint has multiple ligaments that provide support, particularly in the extended position (see Figure 9.15c). Outside the articular capsule, located at the sides of the knee, are two extrinsic ligaments called the **tibial collateral ligament** and the **fibular collateral ligament**. The articular capsule of the posterior knee is thickened by intrinsic ligaments that help resist knee hyperextension. Inside the knee are two intracapsular ligaments: the **anterior cruciate ligament** and **posterior cruciate ligament**. These ligaments are anchored inferiorly to the tibia at the intercondylar eminence, the roughened area between the tibial condyles. The cruciate ligaments are named for whether they are attached anteriorly or posteriorly to this tibial region. Each ligament

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runs diagonally upward to attach to the inner aspect of a femoral condyle. The cruciate ligaments are named for the X shape formed as they pass each other (cruciate means "cross"). The posterior cruciate ligament is the stronger ligament. It serves to support the knee when it is flexed and weight-bearing, as when walking downhill. In this position, the posterior cruciate ligament prevents the femur from sliding anteriorly off the top of the tibia. The anterior cruciate ligament becomes tight when the knee is extended and thus resists hyperextension.

Located between the articulating surfaces of the femur and tibia are two articular discs, the **medial meniscus** and **lateral meniscus** (see Figure 9.15b). Each is a C-shaped fibrocartilage structure that is thin along its inside margin and thick along the outer margin. They are attached to their tibial condyles but do not attach to the femur. While both menisci are free to move during knee motions, the medial meniscus shows less movement because it is anchored at its outer margin to the articular capsule and tibial collateral ligament. The menisci provide padding between the bones and help fill the gap between the round femoral condyles and flattened tibial condyles. Some areas of each meniscus lack an arterial blood supply; thus they heal poorly if damaged.

Interactive Link 9.8

Watch this video (http://oer.aupress.ca/oer-202505/9.8) to learn more about the flexion and extension of the knee, as the femur both rolls and glides on the tibia to maintain stable contact between the bones in all knee positions. The patella glides along a groove on the anterior side of the distal femur. The collateral ligaments on the sides of the knee become tight in the fully extended position to help stabilize the knee. The posterior cruciate ligament supports the knee when flexed, and the anterior cruciate ligament becomes tight when the knee comes into full extension to resist hyperextension. What are the ligaments that support the knee joint?

Interactive Link 9.9

Watch this video (http://oer.aupress.ca/oer-202505/9.9) to learn more about the anatomy of the knee joint, including bones, joints, muscles, nerves, and blood vessels. Which ligament of the knee keeps the tibia from sliding too far forward in relation to the femur, and which ligament keeps the tibia from sliding too far backward?

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Key Terms

abduction: Movement in the coronal plane that moves a limb laterally away from the body; spreading of the fingers.

adduction: Movement in the coronal plane that moves a limb medially toward or across the midline of the body; bringing fingers together.

amphiarthrosis: Slightly mobile joint.

annular ligament: Intrinsic ligament of the elbow articular capsule that surrounds and supports the head of the radius at the proximal radioulnar joint.

anterior cruciate ligament: Intracapsular ligament of the knee; extends from anterior, superior surface of the tibia to the inner aspect of the lateral condyle of the femur; resists hyperextension of knee.

articular capsule: Connective tissue structure that encloses the joint cavity of a synovial joint.

articular cartilage: Thin layer of hyaline cartilage that covers the articulating surfaces of bones at a synovial joint.

articular disc: Meniscus; a fibrocartilage structure found between the bones of some synovial joints; provides padding or smooths movements between the bones; strongly unites the bones together.

articulation: Joint of the body.

atlantoaxial joint: Series of three articulations between the atlas (C1) vertebra and the axis (C2) vertebra, consisting of the joints between the inferior articular processes of C1 and the superior articular processes of C2, and the articulation between the dens of C2 and the anterior arch of C1.

atlanto-occipital joint: Articulation between the occipital condyles of the skull and the superior articular processes of the atlas (C1 vertebra).

ball-and-socket joint: Synovial joint formed between the spherical end of one bone (the ball) that fits into the depression of a second bone (the socket); found at the hip and shoulder joints; functionally classified as a multiaxial joint.

biaxial joint: Type of diarthrosis; a joint that allows for movements within two planes (two axes).

bursa: Connective tissue sac containing lubricating fluid that prevents friction between adjacent structures, such as skin and bone, tendons and bone, or two muscles.

cartilaginous joint: Joint at which the bones are united by hyaline cartilage (synchondrosis) or fibrocartilage (symphysis).

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circumduction: Circular motion of the arm, thigh, hand, thumb, or finger that is produced by the sequential combination of flexion, abduction, extension, and adduction.

condyloid joint: Synovial joint in which the shallow depression at the end of one bone receives a rounded end from a second bone or a rounded structure formed by two bones; found at the metacarpophalangeal joints of the fingers or the radiocarpal joint of the wrist; functionally classified as a biaxial joint.

depression: Downward (inferior) motion of the scapula or mandible.

diarthrosis: Freely mobile joint.

dorsiflexion: Movement at the ankle that brings the top of the foot toward the anterior leg.

elbow joint: Humeroulnar joint.

elevation: Upward (superior) motion of the scapula or mandible.

eversion: Foot movement involving the intertarsal joints of the foot in which the bottom of the foot is turned laterally, away from the midline.

extension: Movement in the sagittal plane that increases the angle of a joint (straightens the joint); motion involving posterior bending of the vertebral column or returning to the upright position from a flexed position.

extrinsic ligament: Ligament located outside of the articular capsule of a synovial joint.

femoropatellar joint: Portion of the knee joint consisting of the articulation between the distal femur and the patella.

fibrous joint: Joint where the articulating areas of the adjacent bones are connected by fibrous connective tissue.

fibular collateral ligament: The second extrinsic ligaments of the knee.

flexion: Movement in the sagittal plane that decreases the angle of a joint (bends the joint); motion involving anterior bending of the vertebral column.

fontanelles: Expanded areas of fibrous connective tissue that separate the braincase bones of the skull prior to birth and during the first year after birth.

glenohumeral joint: Shoulder joint; articulation between the glenoid cavity of the scapula and head of the humerus; multiaxial ball-and-socket joint that allows for flexion/extension, abduction/adduction, circumduction, and medial/lateral rotation of the humerus.

glenoid labrum: Lip of fibrocartilage located around the outside margin of the glenoid cavity of the scapula.

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gomphosis: Type of fibrous joint in which the root of a tooth is anchored into its bony jaw socket by strong periodontal ligaments.

hinge joint: Synovial joint at which the convex surface of one bone articulates with the concave surface of a second bone; includes the elbow, knee, ankle, and interphalangeal joints; functionally classified as a uniaxial joint.

humeroradial joint: Articulation between the capitulum of the humerus and head of the radius.

humeroulnar joint: Articulation between the trochlea of humerus and the trochlear notch of the ulna; uniaxial hinge joint that allows for flexion/extension of the forearm.

hyperextension: Excessive extension of a joint, beyond the normal range of movement.

hyperflexion: Excessive flexion of a joint, beyond the normal range of movement.

inferior rotation: Movement of the scapula during upper limb adduction in which the glenoid cavity of the scapula moves in a downward direction as the medial end of the scapular spine moves in an upward direction.

interosseous membrane: Wide sheet of fibrous connective tissue that fills the gap between two parallel bones, forming a syndesmosis; found between the radius and ulna of the forearm and between the tibia and fibula of the leg.

intracapsular ligament: Ligament that is located within the articular capsule of a synovial joint.

intrinsic ligament: Ligament that is fused to or incorporated into the wall of the articular capsule of a synovial joint.

inversion: Foot movement involving the intertarsal joints of the foot in which the bottom of the foot is turned toward the midline.

joint: Site at which two or more bones or bone and cartilage come together (articulate).

joint cavity: Space enclosed by the articular capsule of a synovial joint that is filled with synovial fluid and contains the articulating surfaces of the adjacent bones.

knee joint: Joint between the femur, tibia, and patella; the largest joint of the body.

lateral (external) rotation: Movement of the arm at the shoulder joint or the thigh at the hip joint that moves the anterior surface of the limb away from the midline of the body.

lateral excursion: Side-to-side movement of the mandible away from the midline toward either the right or left side.

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lateral flexion: Bending of the neck or body toward the right or left side.

lateral meniscus: C-shaped fibrocartilage articular disc located at the knee, between the lateral condyle of the femur and the lateral condyle of the tibia.

lateral tibiofemoral joint: Portion of the knee consisting of the articulation between the lateral condyle of the tibia and the lateral condyle of the femur; allows for flexion/extension at the knee.

ligament: Strong band of dense connective tissue spanning between bones.

medial (internal) rotation: Movement of the arm at the shoulder joint or the thigh at the hip joint that brings the anterior surface of the limb toward the midline of the body.

medial excursion: Side-to-side movement that returns the mandible to the midline.

medial meniscus: C-shaped fibrocartilage articular disc located at the knee, between the medial condyle of the femur and medial condyle of the tibia.

medial tibiofemoral joint: Portion of the knee consisting of the articulation between the medial condyle of the tibia and the medial condyle of the femur; allows for flexion/extension at the knee.

meniscus: Articular disc.

multiaxial joint: Type of diarthrosis; a joint that allows for movements within three planes (three axes).

opposition: Thumb movement that brings the tip of the thumb in contact with the tip of a finger.

patellar ligament: Ligament spanning from the patella to the anterior tibia; serves as the final attachment for the quadriceps femoris muscle.

periodontal ligament: Band of dense connective tissue that anchors the root of a tooth into the bony jaw socket.

pivot joint: Synovial joint at which the rounded portion of a bone rotates within a ring formed by a ligament and an articulating bone; functionally classified as uniaxial joint.

plane joint: Synovial joint formed between the flattened articulating surfaces of adjacent bones; functionally classified as a multiaxial joint.

plantar flexion: Foot movement at the ankle in which the heel is lifted off the ground.

posterior cruciate ligament: Intracapsular ligament of the knee; extends from the posterior, superior surface of the tibia to the inner aspect of the medial condyle of the femur; prevents anterior displacement of the femur when the knee is flexed and weight-bearing.

pronated position: Forearm position in which the palm faces backward.

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pronation: Forearm motion that moves the palm of the hand from the palm forward to the palm backward position.

protraction: Anterior motion of the scapula or mandible.

proximal radioulnar joint: Articulation between head of radius and radial notch of ulna; uniaxial pivot joint that allows for rotation of radius during pronation/supination of the forearm.

radial collateral ligament: Intrinsic ligament on the lateral side of the elbow joint; runs from the lateral epicondyle of humerus to merge with the annular ligament.

reposition: Movement of the thumb from opposition back to the anatomical position (next to index finger).

retraction: Posterior motion of the scapula or mandible.

rotation: Movement of a bone around a central axis (atlantoaxial joint) or around its long axis (proximal radioulnar joint; shoulder or hip joint); twisting of the vertebral column resulting from the summation of small motions between adjacent vertebrae.

rotator cuff: Strong connective tissue structure formed by the fusion of four rotator cuff muscle tendons to the articular capsule of the shoulder joint; surrounds and supports superior, anterior, lateral, and posterior sides of the humeral head.

saddle joint: Synovial joint in which the articulating ends of both bones are convex and concave in shape, such as the first carpometacarpal joint at the base of the thumb; functionally classified as a biaxial joint.

superior rotation: Movement of the scapula during upper limb abduction in which the glenoid cavity of the scapula moves in an upward direction as the medial end of the scapular spine moves in a downward direction.

supinated position: Forearm position in which the palm faces anteriorly (anatomical position).

supination: Forearm motion that moves the palm of the hand from the palm backward to the palm forward position.

suture: Fibrous joint that connects the bones of the skull (except the mandible); an immobile joint (synarthrosis).

symphysis: Type of cartilaginous joint where the bones are joined by fibrocartilage.

synarthrosis: Immobile or nearly immobile joint.

synchondrosis: Type of cartilaginous joint where the bones are joined by hyaline cartilage.

syndesmosis: Type of fibrous joint in which two separated, parallel bones are connected by an interosseous membrane.

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synostosis: Site at which adjacent bones or bony components have fused together.

synovial fluid: Thick, lubricating fluid that fills the interior of a synovial joint.

synovial joint: Joint at which the articulating surfaces of the bones are located within a joint cavity formed by an articular capsule.

synovial membrane: Thin layer that lines the inner surface of the joint cavity at a synovial joint; produces the synovial fluid.

tendon: Dense connective tissue structure that anchors a muscle to bone.

tendon sheath: Connective tissue that surrounds a tendon at places where the tendon crosses a joint; contains a lubricating fluid to prevent friction and allow smooth movements of the tendon.

tibial collateral ligament: Extrinsic ligament of knee joint that spans from the medial epicondyle of the femur to the medial tibia; resists hyperextension and rotation of extended knee.

ulnar collateral ligament: Intrinsic ligament on the medial side of the elbow joint; spans from the medial epicondyle of the humerus to the medial ulna.

uniaxial joint: Type of diarthrosis; joint that allows for motion within only one plane (one axis).

Chapter Review

9.1 Classification of Joints

Structural classifications of the body joints are based on how the bones are held together and articulate with each other. At fibrous joints, the adjacent bones are directly united to each other by fibrous connective tissue. Similarly, at a cartilaginous joint, the adjacent bones are united by cartilage. In contrast, at a synovial joint, the articulating bone surfaces are not directly united to each other but come together within a fluid-filled joint cavity.

The functional classification of body joints is based on the degree of movement found at each joint. A synarthrosis is a joint that is essentially immobile. This type of joint provides for a strong connection between the adjacent bones, which serves to protect internal structures such as the brain or heart. Examples include the fibrous joints of the skull sutures and the cartilaginous manubriosternal joint. A joint that allows for limited movement is an amphiarthrosis. An example is the pubic symphysis of the pelvis, the cartilaginous joint that strongly unites the right and left hip bones of the pelvis. The cartilaginous joints in which vertebrae are united by intervertebral discs provide for small movements between the adjacent vertebrae and are also an amphiarthrotic

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type of joint. Thus, based on their movement ability, both fibrous and cartilaginous joints are functionally classified as synarthroses or amphiarthroses.

The most common type of joint is the diarthrosis, which is a freely movable joint. All synovial joints are functionally classified as diarthroses. A uniaxial diarthrosis, such as the elbow, is a joint that only allows for movement within a single anatomical plane. Joints that allow for movements in two planes are biaxial joints, such as the metacarpophalangeal joints of the fingers. A multiaxial joint, such as the shoulder or hip joint, allows for three planes of motion.

9.2 Fibrous Joints

Fibrous joints are where adjacent bones are strongly united by fibrous connective tissue. The gap filled by connective tissue may be narrow or wide. The three types of fibrous joints are sutures, gomphoses, and syndesmoses. A suture is the narrow fibrous joint that unites most bones of the skull. At a gomphosis, the root of a tooth is anchored across a narrow gap by periodontal ligaments to the walls of its socket in the bony jaw. A syndesmosis is the type of fibrous joint found between parallel bones. The gap between the bones may be wide and filled with a fibrous interosseous membrane, or it may be narrow with ligaments spanning between the bones. Syndesmoses are found between the bones of the forearm (radius and ulna) and the leg (tibia and fibula). Fibrous joints strongly unite adjacent bones and thus provide protection for internal organs, strength to body regions, or weight-bearing stability.

9.3 Cartilaginous Joints

There are two types of cartilaginous joints. A synchondrosis is formed when adjacent bones are united by hyaline cartilage. A temporary synchondrosis is formed by the epiphyseal plate of a growing long bone, which is lost when the epiphyseal plate ossifies as the bone reaches maturity. The synchondrosis is thus replaced by a synostosis. Permanent synchondroses that do not ossify are found at the first sternocostal joint and between the anterior ends of the bony ribs and the junction with their costal cartilage. A symphysis is where the bones are joined by fibrocartilage, and the gap between the bones may be narrow or wide. A narrow symphysis is found at the manubriosternal joint and at the pubic symphysis. A wide symphysis is the intervertebral symphysis in which the bodies of adjacent vertebrae are united by an intervertebral disc.

9.4 Synovial Joints

Synovial joints are the most common type of joints in the body. They are characterized by the presence of a joint cavity, inside of which the bones of the joint articulate with each other. The articulating surfaces of the bones at a

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synovial joint are not directly connected to each other by connective tissue or cartilage, which allows the bones to move freely against each other. The walls of the joint cavity are formed by the articular capsule. Friction between the bones is reduced by a thin layer of articular cartilage covering the surfaces of the bones and by a lubricating synovial fluid, which is secreted by the synovial membrane.

Synovial joints are strengthened by the presence of ligaments, which hold the bones together and resist excessive or abnormal movements of the joint. Ligaments are classified as extrinsic ligaments if they are located outside the articular capsule, intrinsic ligaments if they are fused to the wall of the articular capsule, or intracapsular ligaments if they are located inside the articular capsule. Some synovial joints also have an articular disc (meniscus), which can provide padding between the bones, smooth their movements, or strongly join them together to strengthen the joint. Muscles and their tendons acting across a joint can also increase their contractile strength when needed, thus providing indirect support for the joint.

Bursae contain a lubricating fluid that serves to reduce friction between structures. Subcutaneous bursae prevent friction between the skin and an underlying bone, submuscular bursae protect muscles from rubbing against a bone or another muscle, and a subtendinous bursa prevents friction between bone and a muscle tendon. Tendon sheaths contain a lubricating fluid and surround tendons to allow for smooth movement of the tendon as it crosses a joint.

Based on the shape of the articulating bone surfaces and the types of movement allowed, synovial joints are classified into six types. At a pivot joint, one bone is held within a ring by a ligament and its articulation with a second bone. Pivot joints only allow for rotation around a single axis. These are found at the articulation between the C1 (atlas) and the dens of the C2 (axis) vertebrae, which provides the side-to-side rotation of the head, or at the proximal radioulnar joint between the head of the radius and the radial notch of the ulna, which allows for rotation of the radius during forearm movements. Hinge joints, such as at the elbow, knee, ankle, and interphalangeal joints between phalanx bones of the fingers and toes, only allow for bending and straightening of the joint. Pivot and hinge joints are functionally classified as uniaxial joints.

Condyloid joints are found where the shallow depression of one bone receives a rounded bony area formed by one or two bones. Condyloid joints are found at the base of the fingers (metacarpophalangeal joints) and at the wrist (radiocarpal joint). At a saddle joint, the articulating bones fit together like a rider and a saddle. An example is the first carpometacarpal joint located at the base of the thumb. Both condyloid and saddle joints are functionally classified as biaxial joints.

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Plane joints are formed between the small, flattened surfaces of adjacent bones. These joints allow the bones to slide or rotate against each other, but the range of motion is usually slight and tightly limited by ligaments or surrounding bones. This type of joint is found between the articular processes of adjacent vertebrae, at the acromioclavicular joint, and at the intercarpal joints of the hand and intertarsal joints of the foot. Ball-and-socket joints, in which the rounded head of a bone fits into a large depression or socket, are found at the shoulder and hip joints. Both plane and ball-and-sockets joints are classified functionally as multiaxial joints. However, ball-and-socket joints allow for large movements, while the motions between bones at a plane joint are small.

9.5 Types of Body Movements

The variety of movements provided by the different types of synovial joints allows for a large range of body motions and gives you tremendous mobility. These movements allow you to flex or extend your body or limbs, medially rotate and adduct your arms and flex your elbows to hold a heavy object against your chest, raise your arms above your head, rotate or shake your head, and bend to touch your toes (with or without bending your knees).

Each of the different structural types of synovial joints also allows for specific motions. The atlantoaxial pivot joint provides side-to-side rotation of the head, while the proximal radioulnar articulation allows for rotation of the radius during pronation and supination of the forearm. Hinge joints, such as at the knee and elbow, only allow for flexion and extension. Similarly, the hinge joint of the ankle only allows for dorsiflexion and plantar flexion of the foot.

Condyloid and saddle joints are biaxial. These allow for flexion/extension and abduction/adduction.

The sequential combination of flexion, adduction, extension, and abduction produces circumduction. Multiaxial plane joints provide for only small motions, but these can add together over several adjacent joints to produce body movement, such as inversion and eversion of the foot. Similarly, plane joints allow for flexion, extension, and lateral flexion movements of the vertebral column. The multiaxial ball-and-socket joints allow for flexion/extension, abduction/adduction, and circumduction. In addition, these allow for medial (internal) and lateral (external) rotation. Ball-and-socket joints have the greatest range of motion of all synovial joints.

9.6 Anatomy of Selected Synovial Joints

Although synovial joints share many common features, each joint of the body is specialized for certain movements and activities. The joints of the upper

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limb provide for large ranges of motion, which give the upper limb great mobility, thus enabling actions such as the throwing of a ball or typing on a keyboard. The joints of the lower limb are more robust, giving them greater strength and the stability needed to support the body weight during running, jumping, or kicking activities.

The joints of the vertebral column include the symphysis joints formed by each intervertebral disc and the plane synovial joints between the superior and inferior articular processes of adjacent vertebrae. Each of these joints provides for limited motions, but these sum together to produce flexion, extension, lateral flexion, and rotation of the neck and body. The range of motion available in each region of the vertebral column varies, with all these motions available in the cervical region. Only rotation is allowed in the thoracic region; the lumbar region has considerable extension, flexion, and lateral flexion, but rotation is prevented. The atlanto-occipital joint allows for flexion and extension of the head, while the atlantoaxial joint is a pivot joint that provides for rotation of the head.

The temporomandibular joint is the articulation between the condyle of the mandible and the mandibular fossa and articular tubercle of the skull temporal bone. An articular disc is located between the bony components of this joint. A combination of gliding and hinge motions of the mandibular condyle allows for elevation/depression, protraction/retraction, and side-to-side motions of the lower jaw.

The glenohumeral (shoulder) joint is a multiaxial ball-and-socket joint that provides flexion/extension, abduction/adduction, circumduction, and medial/lateral rotation of the humerus. The head of the humerus articulates with the glenoid cavity of the scapula. The glenoid labrum extends around the margin of the glenoid cavity. However, the primary support comes from muscles crossing the joint whose tendons form the rotator cuff. The elbow is a uniaxial hinge joint that allows for flexion/extension of the forearm. It includes the humeroulnar joint and the humeroradial joint. The medial elbow is supported by the ulnar collateral ligament, and the radial collateral ligament supports the lateral side. These ligaments prevent side-to-side movements and resist hyperextension of the elbow. The proximal radioulnar joint is a pivot joint that allows for rotation of the radius during pronation/supination of the forearm. The annular ligament surrounds the head of the radius to hold it in place at this joint.

The hip joint is a ball-and-socket joint whose motions are more restricted than at the shoulder to provide greater stability during weight-bearing. The hip joint is the articulation between the head of the femur and the acetabulum of the hip bone.

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The knee includes three articulations. The femoropatellar joint is between the patella and distal femur. The patella, a sesamoid bone incorporated into the tendon of the quadriceps femoris muscle of the anterior thigh, serves to protect this tendon from rubbing against the distal femur during knee movements. The medial and lateral tibiofemoral joints, between the condyles of the femur and condyles of the tibia, are modified hinge joints that allow for knee extension and flexion. During these movements, the condyles of the femur both roll and glide over the surface of the tibia. As the knee comes into full extension, a slight medial rotation of the femur serves to "lock" the knee into its most stable weight-bearing position. The reverse motion, a small lateral rotation of the femur, is required to initiate knee flexion. When the knee is flexed, some rotation of the leg is available.

Two extrinsic ligaments, the tibial collateral ligament on the medial side and the fibular collateral ligament on the lateral side, serve to resist hyperextension or rotation of the extended knee joint. Two intracapsular ligaments, the anterior cruciate ligament and posterior cruciate ligament, span between the tibia and the inner aspects of the femoral condyles. The anterior cruciate ligament resists hyperextension of the knee, while the posterior cruciate ligament prevents anterior sliding of the femur, thus supporting the knee when it is flexed and weight-bearing. The medial and lateral menisci, located between the femoral and tibial condyles, are articular discs that provide padding and improve the fit between the bones.

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10

Muscle Tissue

Chapter Objectives

After studying this chapter, you will be able to:

- Explain the organization of muscle tissue
- Describe the function and structure of skeletal, cardiac, and smooth muscle
- Explain how muscles work with tendons to move the body
- Describe how muscles contract and relax
- Define the process of muscle metabolism
- Explain how the nervous system controls muscle tension

When most people think of muscles, they think of the muscles that are visible just under the skin, particularly of the limbs. These are skeletal muscles, so named because most of them move the skeleton. But there are two other types of muscle in the body, with distinctly different jobs. Cardiac muscle, found in the heart, is concerned with pumping blood through the circulatory system. Smooth muscle is concerned with various involuntary movements, such as having one's hair stand on end when cold or frightened or moving food through the digestive system. This chapter will examine the structure and function of these three types of muscle.

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10.1 Overview of Muscle Tissues

Learning Objectives

By the end of this section, you will be able to:

- Describe the different types of muscle
- Explain contractibility and extensibility

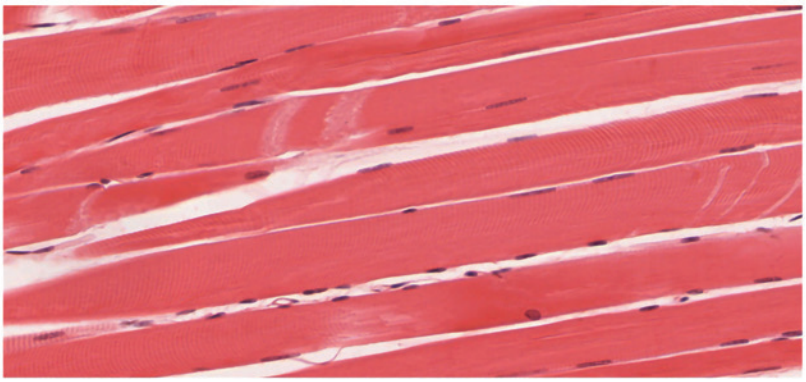
Muscle is one of the four primary tissue types of the body, and the body contains three types of muscle tissue: skeletal muscle, cardiac muscle, and smooth muscle (Figure 10.1). All three muscle tissues have some properties in common: They all exhibit a quality called **excitability**, as their plasma membranes can change their electrical states (from polarized to depolarized) and send an electrical wave called an action potential along the entire length of the membrane. While the nervous system can influence the excitability of cardiac and smooth muscle to some degree, skeletal muscle completely depends on signalling from the nervous system to work properly. On the other hand, both cardiac muscle and smooth muscle can respond to other stimuli, such as hormones and local stimuli.

The muscles all begin the actual process of contracting (shortening) when a protein called actin is pulled by a protein called myosin. This occurs in striated muscle (skeletal and cardiac) after specific binding sites on the actin have been exposed in response to the interaction between calcium ions (Ca^{++}) and proteins (troponin and tropomyosin) that "shield" the actin-binding sites. Ca^{++} is also required for the contraction of smooth muscle, although its role is different: Here, Ca^{++} activates enzymes, which in turn activate myosin heads. All muscles require adenosine triphosphate (ATP) to continue the process of contracting, and they all relax when the Ca^{++} is removed and the actin-binding sites are reshielded.

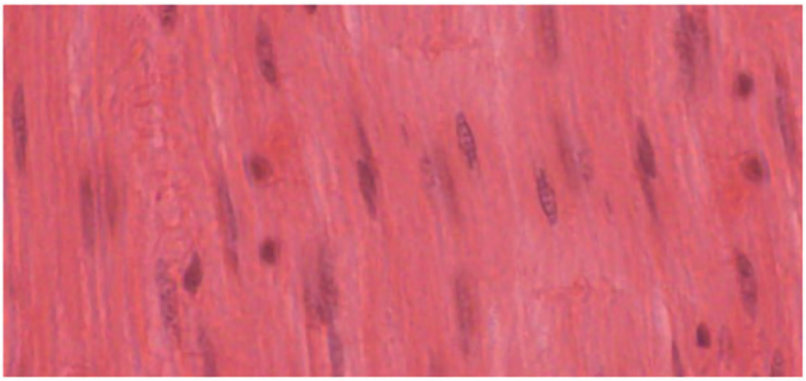
A muscle can return to its original length when relaxed due to a quality of muscle tissue called **elasticity**. It can recoil back to its original length due to elastic fibres. Muscle tissue also has the quality of **extensibility**; it can stretch or extend. **Contractility** allows muscle tissue to pull on its attachment points and shorten with force.

Differences among the three muscle types include the microscopic organization of their contractile proteins—actin and myosin. The actin and myosin proteins are arranged very regularly in the cytoplasm of individual muscle cells (referred to as fibres) in both skeletal muscle and cardiac muscle, which creates a pattern, or stripes, called striations. The striations are visible with a

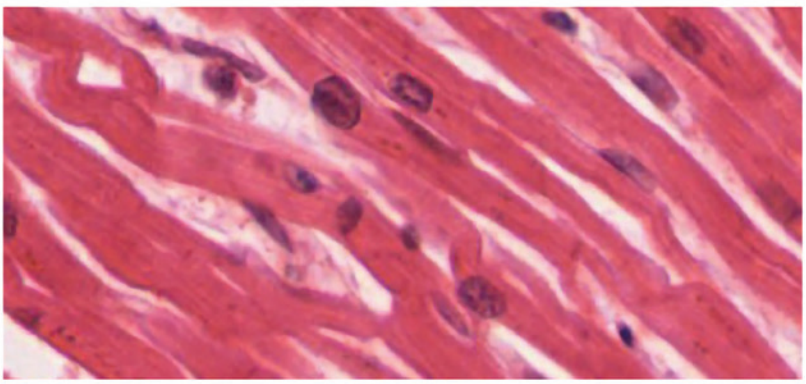
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(a)



(b)



(c)

Figure 10.1 The Three Types of Muscle Tissue. The body contains three types of muscle tissue: (a) skeletal muscle, (b) smooth muscle, and (c) cardiac muscle. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)

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light microscope under high magnification (see Figure 10.1). **Skeletal muscle** fibres are multinucleated structures that compose the skeletal muscle. **Cardiac muscle** fibres each have one to two nuclei and are physically and electrically connected to one another so that the entire heart contracts as one unit (called a syncytium).

Because the actin and myosin are not arranged in such a regular fashion in **smooth muscle**, the cytoplasm of a smooth muscle fibre (which has only a single nucleus) has a uniform, nonstriated appearance (resulting in the name smooth muscle). However, the less organized appearance of smooth muscle should not be interpreted as less efficient. Smooth muscle in the walls of arteries is a critical component that regulates the blood pressure necessary to push blood through the circulatory system; likewise, smooth muscle in the skin, visceral organs, and internal passageways is essential for moving all materials through the body.

10.2 Skeletal Muscle

Learning Objectives

By the end of this section, you will be able to:

- Describe the layers of connective tissues packaging skeletal muscle
- Explain how muscles work with tendons to move the body
- Identify areas of the skeletal muscle fibres
- Describe excitation-contraction coupling

The best-known feature of skeletal muscle is its ability to contract and cause movement. Skeletal muscles act not only to produce movement but also to stop movement, such as resisting gravity to maintain posture. Small, constant adjustments of the skeletal muscles are needed to hold a body upright or balanced in any position. Muscles also prevent excess movement of the bones and joints, maintaining skeletal stability and preventing skeletal structure damage or deformation. Joints can become misaligned or dislocated entirely by pulling on the associated bones; muscles work to keep joints stable. Skeletal muscles are located throughout the body at the openings of internal tracts to control the movement of various substances. These muscles allow functions such as swallowing, urination, and defecation to be under voluntary control. Skeletal muscles also protect internal organs (particularly abdominal and pelvic organs) by acting as an external barrier or shield to external trauma and by supporting the weight of the organs.

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Skeletal muscles contribute to the maintenance of homeostasis in the body by generating heat. Muscle contraction requires energy, and when ATP is broken down, heat is produced. This heat is very noticeable during exercise, when sustained muscle movement causes body temperature to rise, and in cases of extreme cold, when shivering produces random skeletal muscle contractions to generate heat.

Each skeletal muscle is an organ that consists of various integrated tissues. These tissues include the skeletal muscle fibres, blood vessels, nerve fibres, and connective tissue. Each skeletal muscle has three layers of connective tissue (called "mysia") that enclose it, providing structure to the muscle as a whole and also compartmentalizing the muscle fibres within the muscle (Figure 10.2).

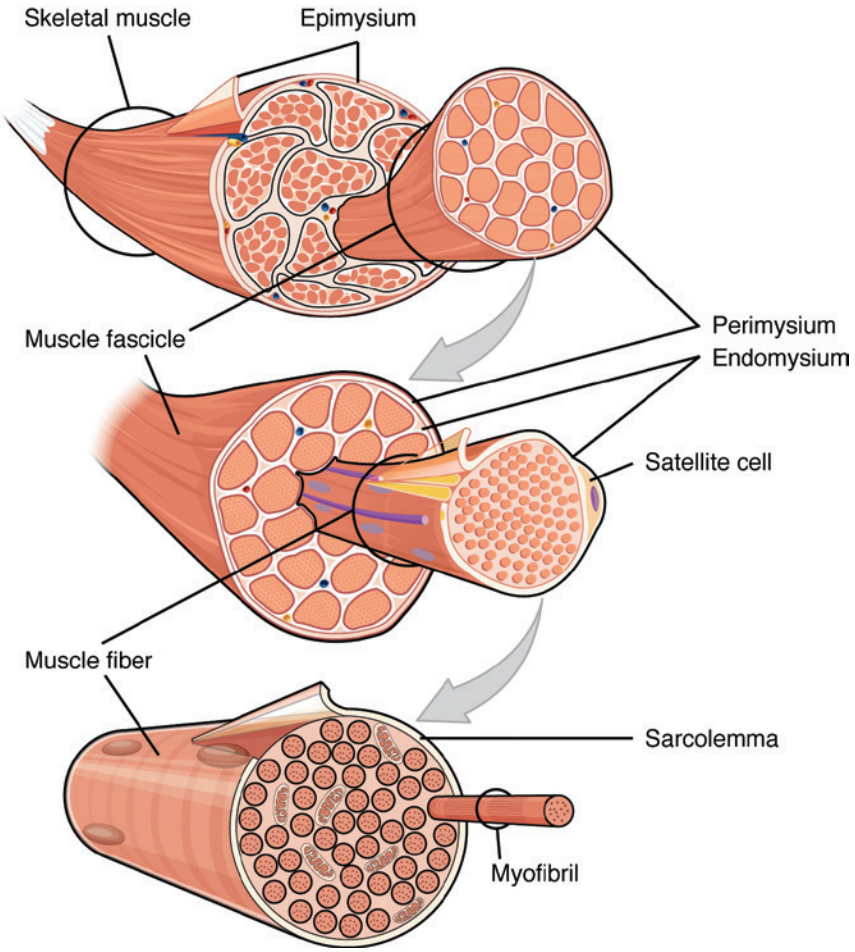


Figure 10.2 The Three Connective Tissue Layers. Bundles of muscle fibres, called fascicles, are covered by the perimysium. Muscle fibres are covered by the endomysium.

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Each muscle is wrapped in a sheath of dense irregular connective tissue called the **epimysium**, which allows a muscle to contract and move powerfully while maintaining its structural integrity. The epimysium also separates muscle from other tissues and organs in the area, allowing the muscle to move independently.

Inside each skeletal muscle, muscle fibres are organized into individual bundles, each called a **fascicle**, by a middle layer of connective tissue called the **perimysium**. This fascicular organization is common in muscles of the limbs; it allows the nervous system to trigger a specific movement of a muscle by activating a subset of muscle fibres within a fascicle of the muscle. Inside each fascicle, each muscle fibre is encased in a thin connective tissue layer of collagen and reticular fibres called the **endomysium**. The endomysium contains the extracellular fluid and nutrients to support the muscle fibre. These nutrients are supplied via blood to the muscle tissue.

In skeletal muscles that work with tendons to pull on bones, the collagen in the three tissue layers (the mysia) intertwines with the collagen of a tendon. At the other end of the tendon, it fuses with the periosteum coating the bone. The tension created by contraction of the muscle fibres is then transferred through the mysia, to the tendon, and then to the periosteum to pull on the bone for movement of the skeleton. In other places, the mysia may fuse with a broad, tendonlike sheet called an **aponeurosis** or with fascia, the connective tissues between skin and bones. The broad sheet of connective tissue in the lower back that the latissimus dorsi muscles (the "lats") fuse into is an example of an aponeurosis.

Every skeletal muscle is also richly supplied by blood vessels for nourishment, oxygen delivery, and waste removal. In addition, every muscle fibre in a skeletal muscle is supplied by the axon branch of a somatic motor neuron, which signals the fibre to contract. Unlike cardiac and smooth muscle, the only way to functionally contract a skeletal muscle is through signalling from the nervous system.

Skeletal Muscle Fibres

Because skeletal muscle cells are long and cylindrical, they are commonly referred to as **muscle fibres**. Skeletal muscle fibres can be quite large for human cells, with diameters up to 100 μm and lengths up to 30 cm (11.8 in) in the sartorius of the upper leg. During early development each myoblast, with its own nucleus, fuses with up to hundreds of other myoblasts to form the multinucleated skeletal muscle fibres. Multiple nuclei mean multiple copies of genes, permitting the production of the large amounts of proteins and enzymes needed for muscle contraction.

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The plasma membrane of muscle fibres is called the **sarcolemma**, the cytoplasm is referred to as **sarcoplasm**, and the specialized smooth endoplasmic reticulum—which stores, releases, and retrieves calcium ions (Ca^{++})—is called the **sarcoplasmic reticulum** (**SR**; Figure 10.3). As will soon be described, the functional unit of a skeletal muscle fibre is the sarcomere, a highly organized arrangement of the contractile **myofilaments actin** (thin filament) and **myosin** (thick filament), along with other support proteins.

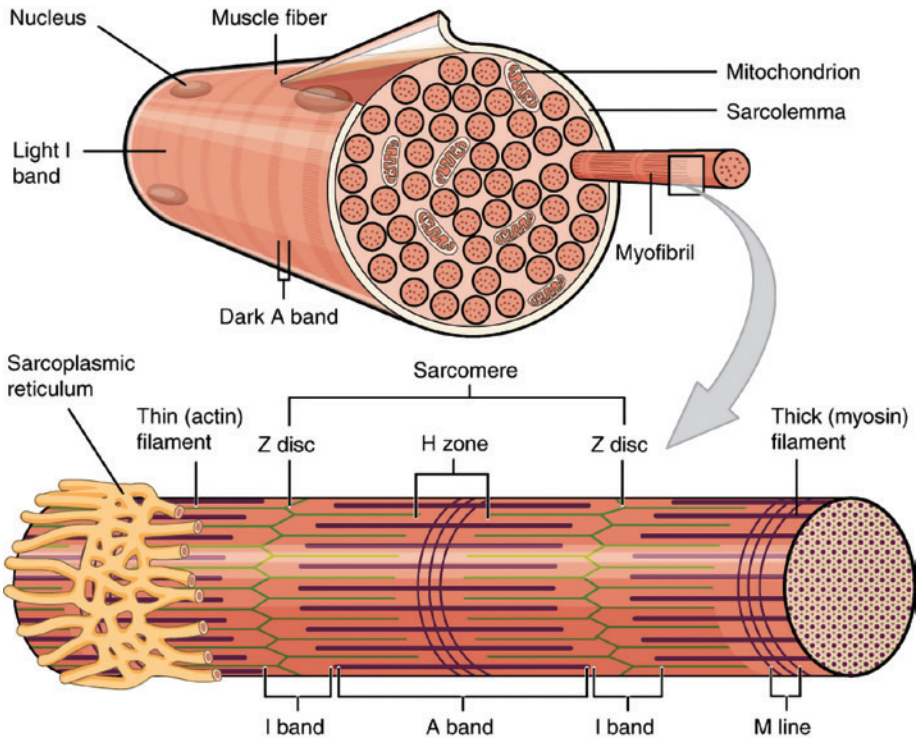


Figure 10.3 Muscle Fibre. A skeletal muscle fibre is surrounded by a plasma membrane called the sarcolemma, which contains sarcoplasm, the cytoplasm of muscle cells. A muscle fibre is composed of many fibrils, which give the cell its striated appearance.

The Sarcomere

The striated appearance of skeletal muscle fibres is due to the arrangement of the myofilaments of actin and myosin in sequential order from one end of the muscle fibre to the other. Each packet of these microfilaments and their regulatory proteins, **troponin** and **tropomyosin** (along with other proteins), is called a **sarcomere**.

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Interactive Link 10.1

Watch this video (http://oer.aupress.ca/oer-202505/10.1) to learn more about macro- and microstructures of skeletal muscles. (a) What are the names of the "junction points" between sarcomeres? (b) What are the names of the "subunits" within the myofibrils that run the length of skeletal muscle fibres? (c) What is the "double strand of pearls" described in the video? (d) What gives a skeletal muscle fibre its striated appearance?

The sarcomere is the functional unit of the muscle fibre. The sarcomere itself is bundled within the myofibril that runs the entire length of the muscle fibre and attaches to the sarcolemma at its end. As myofibrils contract, the entire muscle cell contracts. Because myofibrils are only approximately 1.2 µm in diameter, hundreds to thousands (each with thousands of sarcomeres) can be found inside one muscle fibre. Each sarcomere is approximately 2 µm in length with a three-dimensional cylinder-like arrangement and is bordered by structures called **Z discs** (also called Z lines, because pictures are two-dimensional), to which the actin myofilaments are anchored (Figure 10.4).

The components of a sarcomere are organized into a variety of bands and zones. The darker middle part of the sarcomere is the A band, which extends the entire length of the thick filaments. Toward each end of the A band is a zone of overlap, where the thick and thin filaments lie side by side. The I band is a lighter, less dense area that contains the rest of the thin filaments but no thick filaments, and a Z disc passes through the centre of each I band. The alternating dark A bands and light I bands create the striations that can be seen in both myofibrils and whole skeletal and cardiac muscle fibres. A narrow H band in the centre of each A band contains thick but not thin filaments. A mnemonic that will help you remember the composition of the I and H bands is as follows: The letter I is thin (contains thin filaments), while the letter H is thick (contains thick filaments). Supporting proteins that hold the thick filaments together at the centre of the H band form the M line, so named because it is at the middle of the sarcomere.

Because the actin and its troponin-tropomyosin complex (projecting from the Z discs toward the centre of the sarcomere) form strands that are thinner than the myosin, it is called the **thin filament** of the sarcomere. Likewise, because the myosin strands and their multiple heads (projecting from the centre of the sarcomere, toward but not all the way to the Z discs) have more mass and are thicker, they are called the **thick filaments** of the sarcomere.

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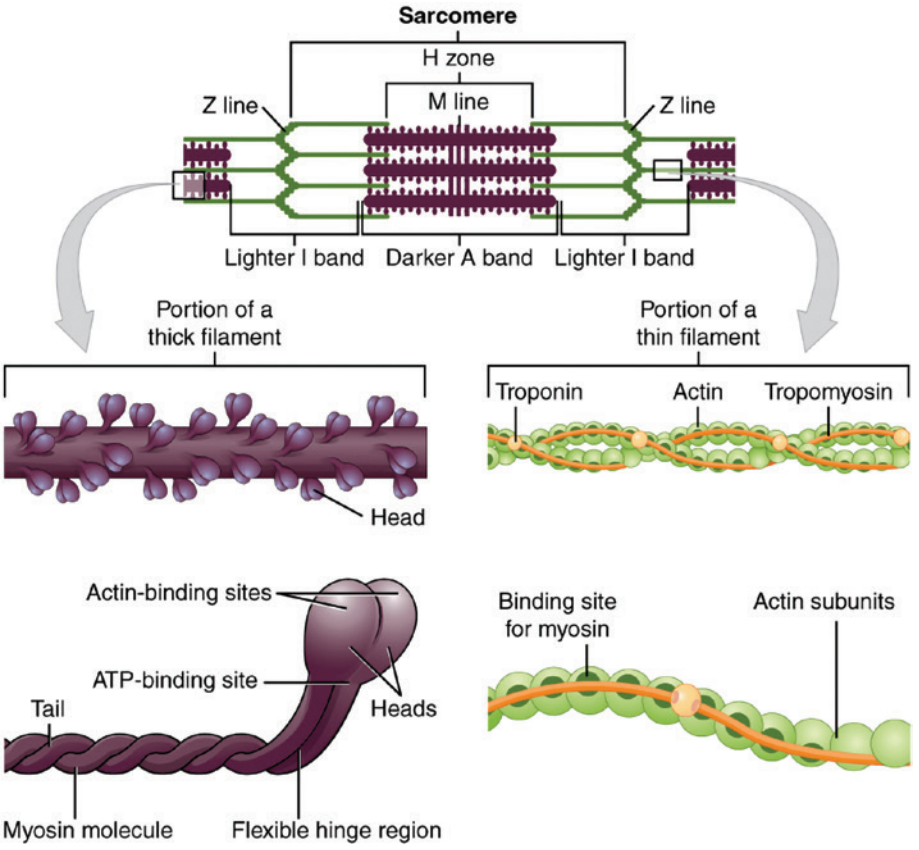


Figure 10.4 The Sarcomere. The sarcomere, the region from one Z line to the next Z line, is the functional unit of a skeletal muscle fibre.

The Neuromuscular Junction

Another specialization of skeletal muscle is the site where a motor neuron's terminal meets the muscle fibre—called the **neuromuscular junction** (**NMJ**). This is where the muscle fibre first responds to signalling by the motor neuron. Every skeletal muscle fibre in every skeletal muscle is innervated by a motor neuron at the NMJ. Excitation signals from the neuron are the only way to functionally activate the fibre to contract.

Interactive Link 10.2

Every skeletal muscle fibre is supplied by a motor neuron at the NMJ. Watch this video (http://oer.aupress.ca/oer-202505/10.2) to learn more about what happens at the NMJ. (a) What is the definition of a motor unit? (b) What is the structural and functional difference between a

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large motor unit and a small motor unit? (c) Can you give an example of each? (d) Why is the neurotransmitter acetylcholine degraded after binding to its receptor?

Excitation-Contraction Coupling

All living cells have membrane potentials, or electrical gradients across their membranes. The inside of the membrane is usually around −60 to −90 mV relative to the outside. This is the cell's membrane potential. Neurons and muscle cells can use their membrane potentials to generate electrical signals. They do this by controlling the movement of charged particles, called ions, across their membranes to create electrical currents. This is achieved by opening and closing specialized proteins in the membrane called ion channels. Although the currents generated by ions moving through these channel proteins are very small, they form the basis of both neural signalling and muscle contraction.

Both neurons and skeletal muscle cells are electrically excitable, meaning that they are able to generate action potentials. An action potential is a special type of electrical signal that can travel along a cell membrane as a wave. This allows a signal to be transmitted quickly and faithfully over long distances. **Excitation-contraction coupling** comes down to this: For a skeletal muscle fibre to contract, its membrane must first be "excited"—in other words, it must be stimulated to fire an action potential. The muscle fibre action potential, which sweeps along the sarcolemma as a wave, is "coupled" to the actual contraction through the release of calcium ions (Ca^{++}) from the SR. Once released, the Ca^{++} interacts with the shielding proteins, forcing them to move aside so that the actin-binding sites are available for attachment by myosin heads. The myosin then pulls the actin filaments toward the centre, shortening the muscle fibre. In skeletal muscle, this sequence begins with signals from the somatic motor division of the nervous system. In other words, the "excitation" step in skeletal muscles is always triggered by signalling from the nervous system (Figure 10.5).

The motor neurons that tell the skeletal muscle fibres to contract originate in the spinal cord, with a smaller number located in the brain stem for activation of skeletal muscles of the face, head, and neck. These neurons have long processes, called axons, which are specialized to transmit action potentials long distances—in this case, all the way from the spinal cord to the muscle itself (which may be up to 1 m away). The axons of multiple neurons bundle together to form nerves, like wires bundled together in a cable. Signalling begins when a neuronal **action potential** travels along the axon of a motor neuron, and then

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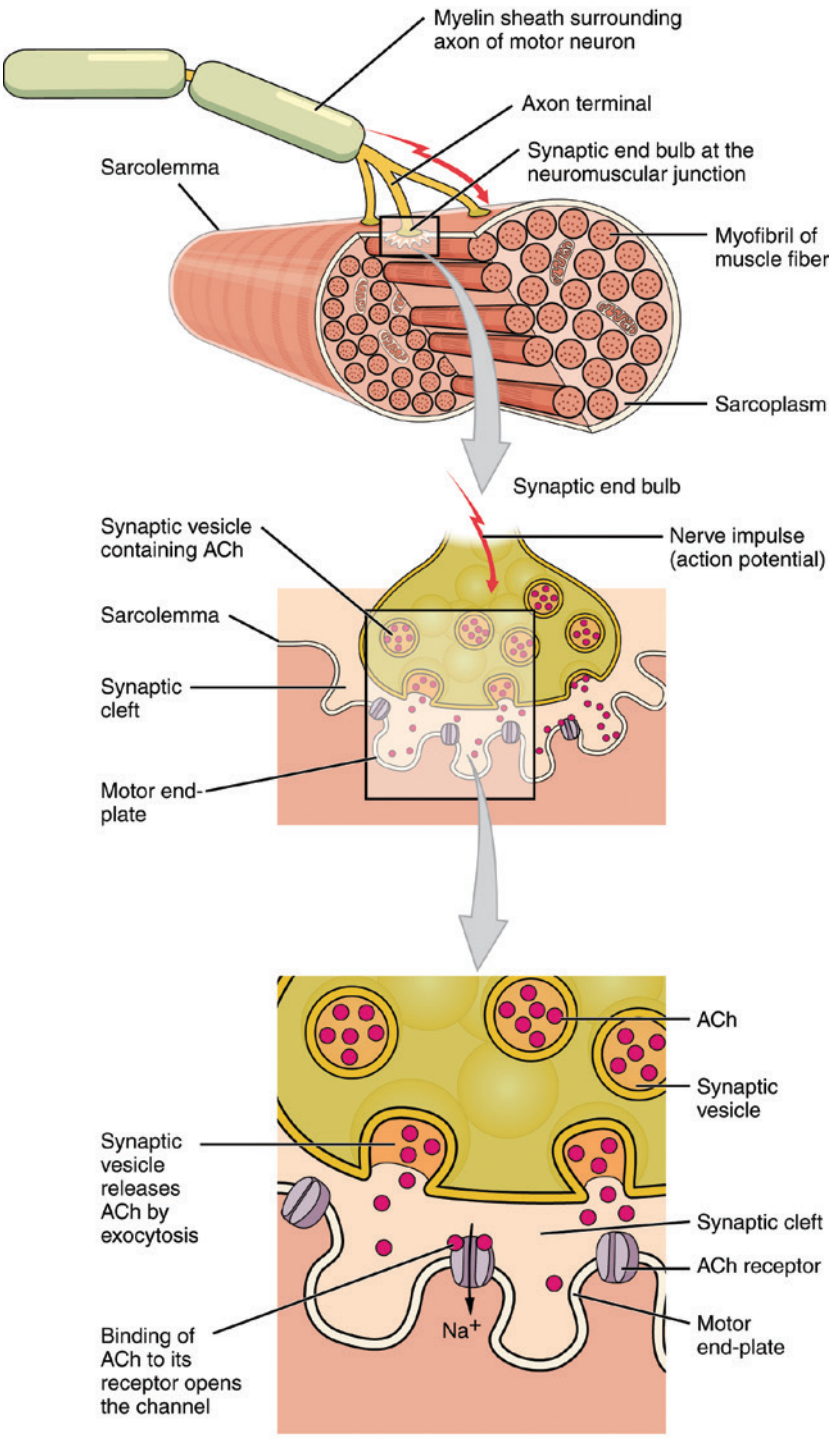


Figure 10.5 Motor End-Plate and Innervation. At the NMJ, the axon terminal releases ACh. The motor end-plate is the location of the ACh-receptors in the muscle fibre sarcolemma. When ACh molecules are released, they diffuse across a minute space called the synaptic cleft and bind to the receptors.

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along the individual branches to terminate at the NMJ. At the NMJ, the axon terminal releases a chemical messenger, or **neurotransmitter**, called **acetylcholine** (**ACh**). The ACh molecules diffuse across a minute space called the **synaptic cleft** and bind to ACh receptors located within the **motor end-plate** of the sarcolemma on the other side of the synapse. Once ACh binds, a channel in the ACh receptor opens, and positively charged ions can pass through into the muscle fibre, causing it to **depolarize**, meaning that the membrane potential of the muscle fibre becomes less negative (closer to zero).

As the membrane depolarizes, another set of ion channels called **voltage-gated sodium channels** is triggered to open. Sodium ions enter the muscle fibre, and an action potential rapidly spreads (or "fires") along the entire membrane to initiate excitation-contraction coupling.

Things happen very quickly in the world of excitable membranes (just think about how quickly you can snap your fingers as soon as you decide to do it). Immediately following depolarization of the membrane, it repolarizes, reestablishing the negative membrane potential. Meanwhile, the ACh in the synaptic cleft is degraded by the enzyme acetylcholinesterase (AChE) so that the ACh cannot rebind to a receptor and reopen its channel, which would cause unwanted extended muscle excitation and contraction.

Propagation of an action potential along the sarcolemma is the excitation portion of excitation-contraction coupling. Recall that this excitation actually triggers the release of calcium ions (Ca^{++}) from their storage in the cell's SR. For the action potential to reach the membrane of the SR, there are periodic invaginations in the sarcolemma, called **T-tubules** ("T" stands for "transverse"). You will recall that the diameter of a muscle fibre can be up to 100 μm, so these T-tubules ensure that the membrane can get close to the SR in the sarcoplasm. The arrangement of a T-tubule with the membranes of SR on either side is called a **triad** (Figure 10.6). The triad surrounds the cylindrical structure called a **myofibril**, which contains actin and myosin.

The T-tubules carry the action potential into the interior of the cell, which triggers the opening of calcium channels in the membrane of the adjacent SR, causing Ca^{++} to diffuse out of the SR and into the sarcoplasm. It is the arrival of Ca^{++} in the sarcoplasm that initiates contraction of the muscle fibre by its contractile units, or sarcomeres.

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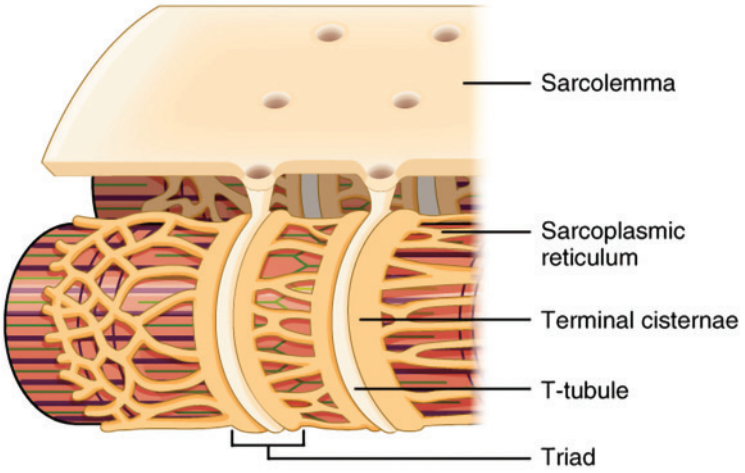


Figure 10.6 The T-Tubule. Narrow T-tubules permit the conduction of electrical impulses. The SR functions to regulate intracellular levels of calcium. Two terminal cisternae (where enlarged SR connects to the T-tubule) and one T-tubule comprise a triad—a "threesome" of membranes, with those of SR on two sides and the T-tubule sandwiched between them.

10.3 Muscle Fibre Contraction and Relaxation

Learning Objectives

By the end of this section, you will be able to:

- Describe the components involved in a muscle contraction
- Explain how muscles contract and relax
- Describe the sliding filament model of muscle contraction

The sequence of events that result in the contraction of an individual muscle fibre begins with a signal—the neurotransmitter, ACh—from the motor neuron innervating that fibre. The local membrane of the fibre will depolarize as positively charged sodium ions (Na^+) enter, triggering an action potential that spreads to the rest of the membrane that will depolarize, including the T-tubules. This triggers the release of calcium ions (Ca^{++}) from storage in the sarcoplasmic reticulum (SR). The Ca^{++} then initiates contraction, which is sustained by ATP (Figure 10.7). As long as Ca^{++} ions remain in the sarcoplasm to bind to troponin (which keeps the actin-binding sites "unshielded") and as long as ATP is available to drive the cross-bridge cycling and the pulling of actin strands by myosin, the muscle fibre will continue to shorten to an anatomical limit.

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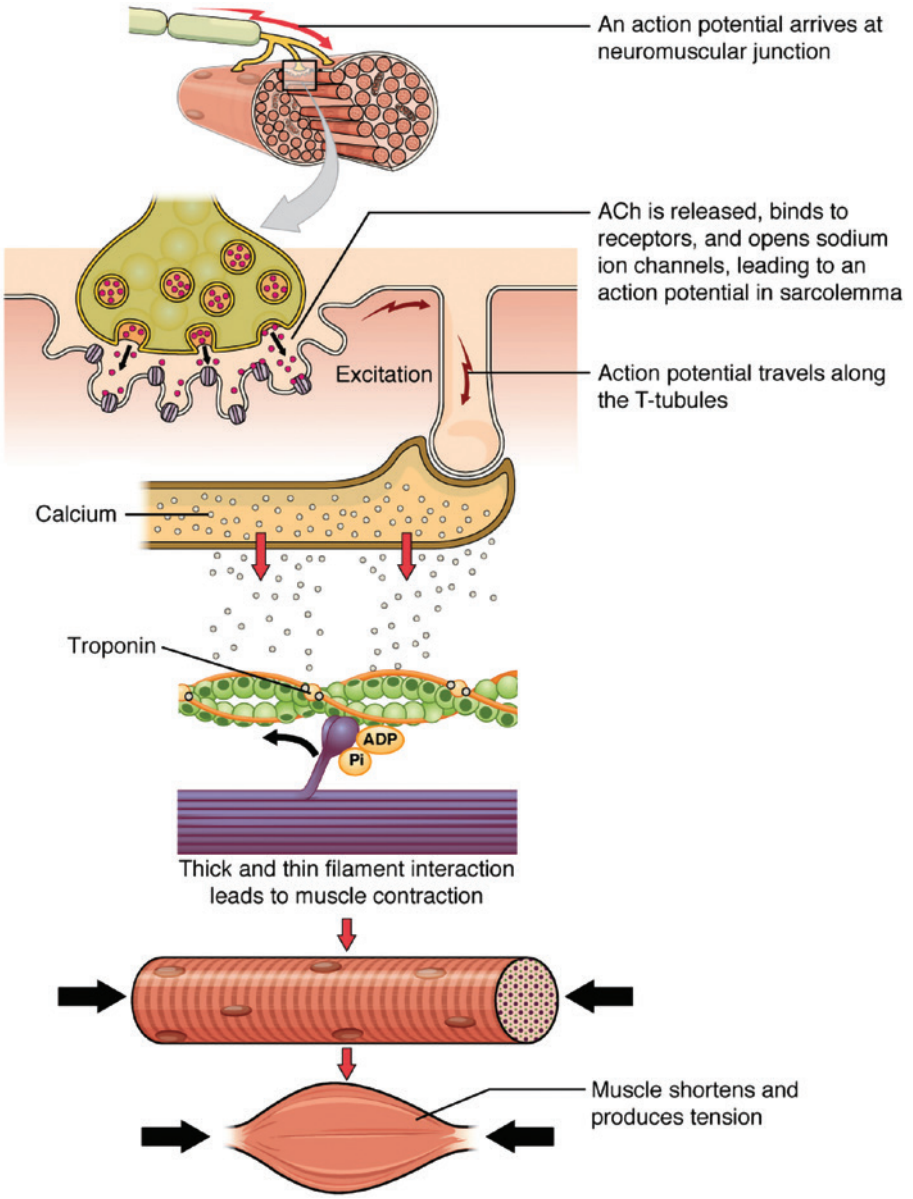


Figure 10.7 Contraction of a Muscle Fibre. A cross-bridge forms between actin and the myosin heads, triggering contraction. As long as Ca^{++} ions remain in the sarcoplasm to bind to troponin, and as long as ATP is available, the muscle fibre will continue to shorten.

Muscle contraction usually stops when signalling from the motor neuron ends, which repolarizes the sarcolemma and T-tubules, and closes the voltage-gated calcium channels in the SR. Ca^{++} ions are then pumped back into the SR, which causes the tropomyosin to reshield (or recover) the binding sites on the actin strands. A muscle can also stop contracting when it runs out of ATP and becomes fatigued (Figure 10.8).

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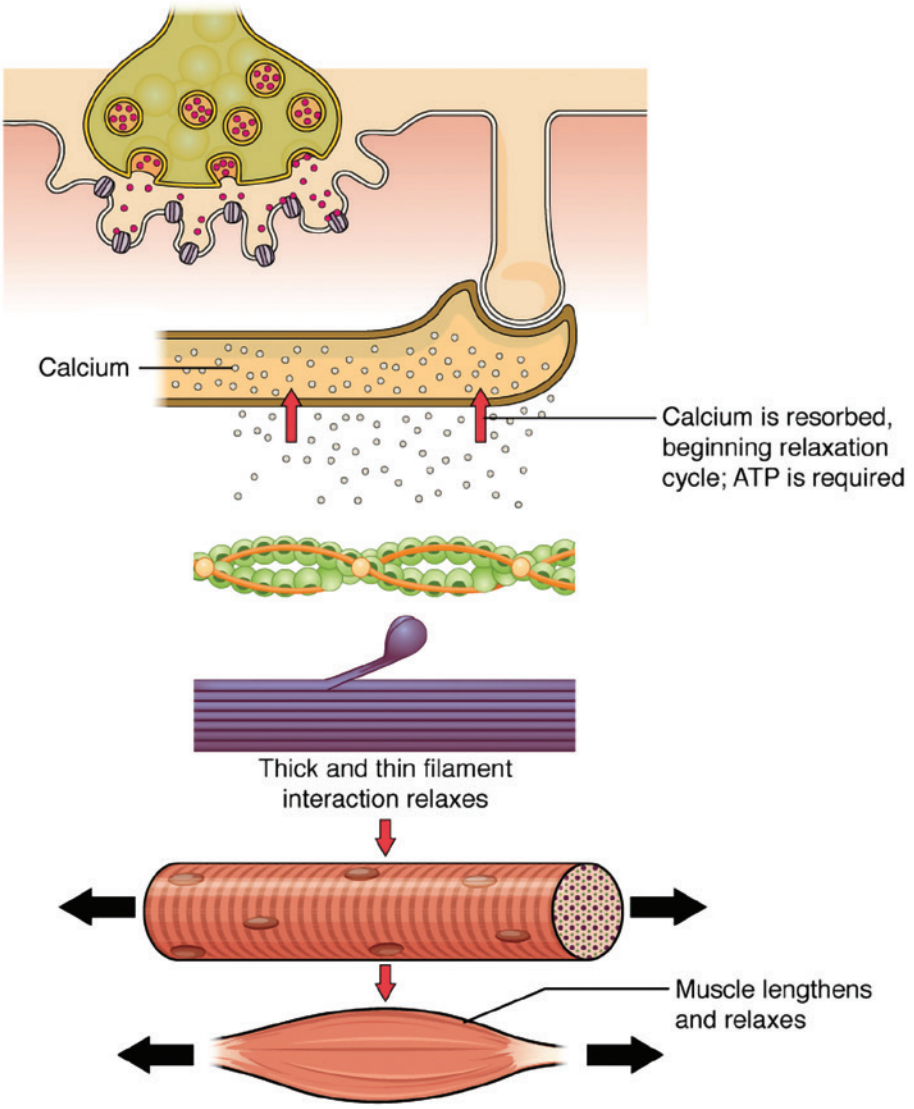


Figure 10.8 Relaxation of a Muscle Fibre. Ca^{++} ions are pumped back into the SR, which causes the tropomyosin to reshield the binding sites on the actin strands. A muscle may also stop contracting when it runs out of ATP and becomes fatigued.

Interactive Link 10.3

The release of calcium ions initiates muscle contractions. Watch this video (http://oer.aupress.ca/oer-202505/10.3) to learn more about the role of calcium. (a) What are "T-tubules" and what is their role? (b) Please describe how actin-binding sites are made available for cross-bridging with myosin heads during contraction.

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The molecular events of muscle fibre shortening occur within the fibre's sarcomeres (see Figure 10.9). The contraction of a striated muscle fibre occurs as the sarcomeres, linearly arranged within myofibrils, shorten as myosin heads pull on the actin filaments.

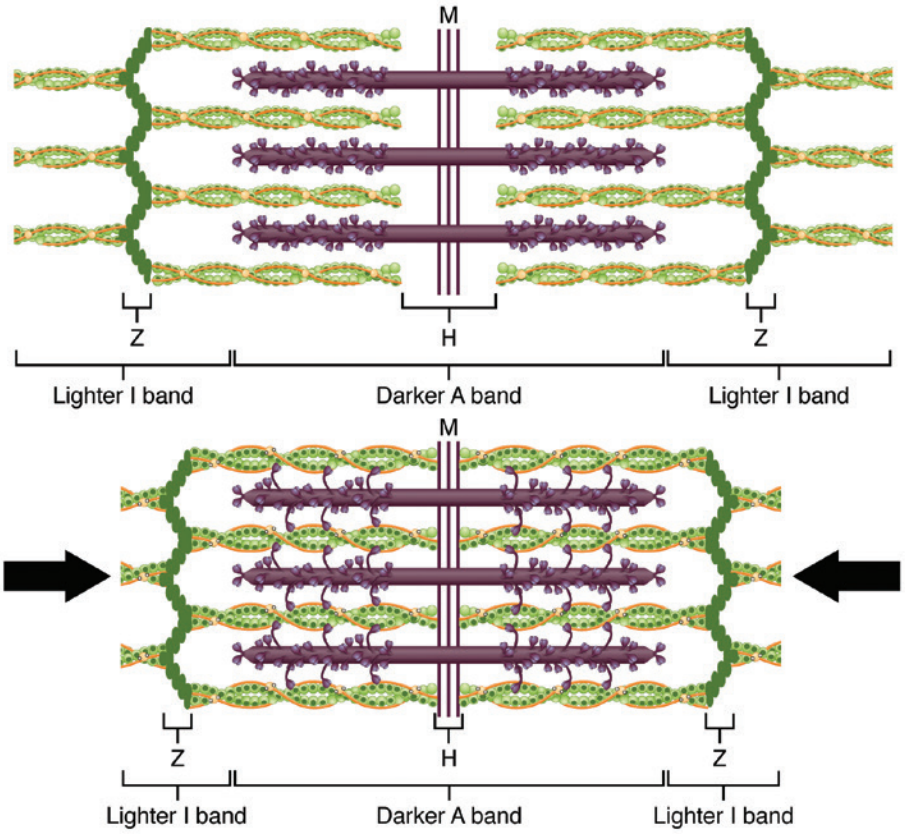


Figure 10.9 The Sliding Filament Model of Muscle Contraction. When a sarcomere contracts, the Z lines move closer together, and the I band becomes smaller. The A band stays the same width. At full contraction, the thin and thick filaments overlap completely.

The region where thick and thin filaments overlap has a dense appearance, as there is little space between the filaments. This zone, where thin and thick filaments overlap, is very important to muscle contraction, as it is the site where filament movement starts. Thin filaments, anchored at their ends by the Z discs, do not extend completely into the central region, which only contains thick filaments, anchored at their bases at a spot called the M line. A myofibril is composed of many sarcomeres running along its length; thus, myofibrils and muscle cells contract as the sarcomeres contract.

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The Sliding Filament Model of Contraction

When signalled by a motor neuron, a skeletal muscle fibre contracts as the thin filaments are pulled and then slide past the thick filaments within the fibre's sarcomeres. This process is known as the **sliding filament model of muscle contraction** (Figure 10.9). The sliding can only occur when myosin-binding sites on the actin filaments are exposed by a series of steps that begins with Ca^{++} entry into the sarcoplasm.

Tropomyosin is a protein that winds around the chains of the actin filament and covers the myosin-binding sites to prevent actin from binding to myosin. Tropomyosin binds to troponin to form a troponin-tropomyosin complex. The troponin-tropomyosin complex prevents the myosin "heads" from binding to the active sites on the actin microfilaments. Troponin also has a binding site for Ca^{++} ions.

To initiate muscle contraction, tropomyosin has to expose the myosin-binding site on an actin filament to allow cross-bridge formation between the actin and myosin microfilaments. The first step in the process of contraction is for Ca^{++} to bind to troponin so that tropomyosin can slide away from the binding sites on the actin strands. This allows the myosin heads to bind to these exposed binding sites and form cross-bridges. The thin filaments are then pulled by the myosin heads to slide past the thick filaments toward the centre of the sarcomere. But each head can only pull a very short distance before it has reached its limit and must be "recocked" before it can pull again, a step that requires ATP.

ATP and Muscle Contraction

For thin filaments to continue to slide past thick filaments during muscle contraction, myosin heads must pull the actin at the binding sites, detach, recock, attach to more binding sites, pull, detach, recock, and so on. This repeated movement is known as the cross-bridge cycle. This motion of the myosin heads is similar to the motion of oars when an individual rows a boat: The paddles of the oars (the myosin heads) pull, then they are lifted from the water (detach), repositioned (recocked), and immersed again to pull (Figure 10.10). Each cycle requires energy, and the action of the myosin heads in the sarcomeres repetitively pulling on the thin filaments also requires energy, which is provided by ATP.

Cross-bridge formation occurs when the myosin head attaches to the actin while adenosine diphosphate (ADP) and inorganic phosphate (P_i) are still bound to myosin (Figure 10.10a and b). P_i is then released, causing myosin to form a stronger attachment to the actin, after which the myosin head moves toward the M line, pulling the actin along with it. As actin is pulled, the filaments move

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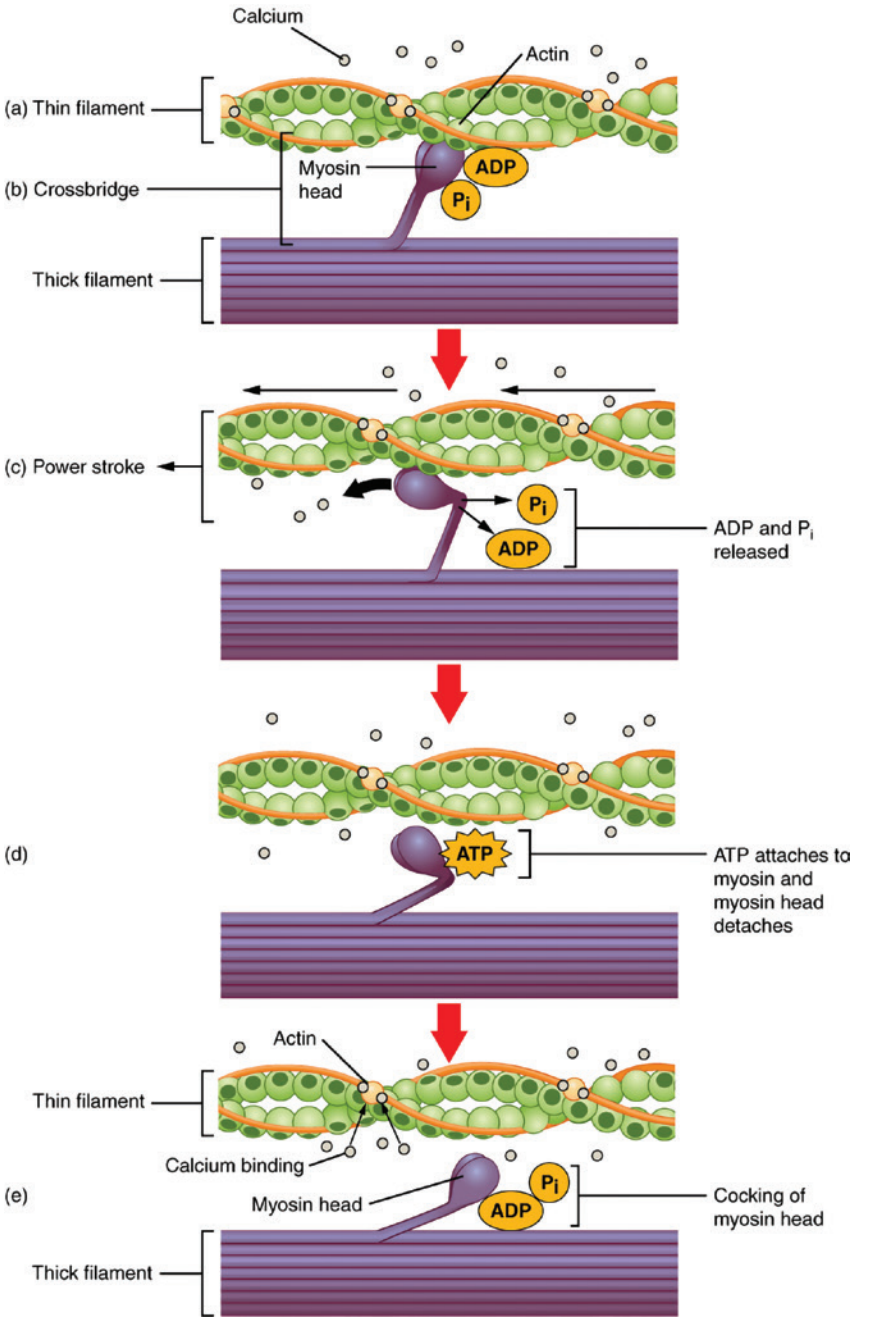


Figure 10.10 Skeletal Muscle Contraction. (a) The active site on actin is exposed as calcium binds to troponin. (b) The myosin head is attracted to actin, and myosin binds actin at its actin-binding site, forming the cross-bridge. (c) During the power stroke, the phosphate generated in the previous contraction cycle is released. This results in the myosin head pivoting toward the centre of the sarcomere, after which the attached ADP and phosphate group are released. (d) A new molecule of ATP attaches to the myosin head, causing the cross-bridge to detach. (e) The myosin head hydrolyzes ATP to ADP and phosphate, which returns the myosin to the cocked position.

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approximately 10 nm toward the M line. This movement is called the **power stroke**, as movement of the thin filament occurs at this step (Figure 10.10c). In the absence of ATP, the myosin head will not detach from actin.

One part of the myosin head attaches to the binding site on the actin, but the head has another binding site for ATP.

ATP binding causes the myosin head to detach from the actin (Figure 10.10d). After this occurs, ATP is converted to ADP and P_i by the intrinsic **ATPase** activity of myosin. The energy released during ATP hydrolysis changes the angle of the myosin head into a cocked position (Figure 10.10e). The myosin head is now in position for further movement.

When the myosin head is cocked, myosin is in a high-energy configuration. This energy is expended as the myosin head moves through the power stroke, and at the end of the power stroke, the myosin head is in a low-energy position. After the power stroke, ADP is released; however, the formed cross-bridge is still in place, and actin and myosin are bound together. As long as ATP is available, it readily attaches to myosin, the cross-bridge cycle can recur, and muscle contraction can continue.

Note that each thick filament of roughly 300 myosin molecules has multiple myosin heads, and many cross-bridges form and break continuously during muscle contraction. Multiply this by all the sarcomeres in one myofibril, all the myofibrils in one muscle fibre, and all the muscle fibres in one skeletal muscle, and you can understand why so much energy (ATP) is needed to keep skeletal muscles working. In fact, it is the loss of ATP that results in the rigor mortis observed soon after someone dies. With no further ATP production possible, there is no ATP available for myosin heads to detach from the actin-binding sites, so the cross-bridges stay in place, causing rigidity in the skeletal muscles.

Sources of ATP

ATP supplies the energy for muscle contraction to take place. In addition to its direct role in the cross-bridge cycle, ATP also provides the energy for the active transport Ca^{++} pumps in the SR. Muscle contraction does not occur without sufficient amounts of ATP. The amount of ATP stored in muscle is very low, only sufficient to power a few seconds' worth of contractions. As it is broken down, ATP must therefore be regenerated and replaced quickly to allow for sustained contraction. There are three mechanisms by which ATP can be regenerated in muscle cells: creatine phosphate metabolism, anaerobic glycolysis, and aerobic respiration.

Creatine phosphate is a molecule that can store energy in its phosphate bonds. In a resting muscle, excess ATP transfers its energy to creatine, producing

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ADP and creatine phosphate. This acts as an energy reserve that can be used to quickly create more ATP. When the muscle starts to contract and needs energy, creatine phosphate transfers its phosphate back to ADP to form ATP and creatine. This reaction is catalyzed by the enzyme creatine kinase and occurs very quickly; thus, creatine phosphate-derived ATP powers the first few seconds of muscle contraction. However, creatine phosphate can only provide approximately 15 seconds' worth of energy, at which point another energy source has to be used.

As the ATP produced by creatine phosphate is depleted, muscles turn to glycolysis as an ATP source. **Glycolysis** is an anaerobic (oxygen-independent) process that breaks down glucose (sugar) to produce ATP; however, glycolysis cannot generate ATP as quickly as creatine phosphate. Thus, the switch to glycolysis results in a slower rate of ATP availability to the muscle. The sugar used in glycolysis can be provided by blood glucose or by metabolizing glycogen that is stored in the muscle. The breakdown of one glucose molecule produces two ATPs and two molecules of **pyruvic acid**, which can be used in aerobic respiration or, when oxygen levels are low, converted to lactic acid.

If oxygen is available, pyruvic acid is used in aerobic respiration. However, if oxygen is not available (**anaerobic metabolism**), pyruvic acid is converted to **lactic acid**, which may contribute to muscle fatigue. This conversion allows the recycling of the enzyme NAD^+ from NADH, which is needed for glycolysis to continue. This occurs during strenuous exercise when high amounts of energy are needed but oxygen cannot be sufficiently delivered to the muscle. Glycolysis itself cannot be sustained for very long (approximately one minute of muscle activity), but it is useful in facilitating short bursts of high-intensity output. This is because glycolysis does not utilize glucose very efficiently, producing a net gain of two ATPs per molecule of glucose and the end product of lactic acid, which may contribute to muscle fatigue as it accumulates.

Aerobic respiration is the breakdown of glucose or other nutrients in the presence of oxygen (O_2) to produce carbon dioxide, water, and ATP. Approximately 95 percent of the ATP required for resting or moderately active muscles is provided by aerobic respiration, which takes place in mitochondria. The inputs for aerobic respiration include glucose circulating in the bloodstream, pyruvic acid, and fatty acids. Aerobic respiration is much more efficient than anaerobic glycolysis, producing approximately 36 ATPs per molecule of glucose versus four from glycolysis.

However, aerobic respiration cannot be sustained without a steady supply of O_2 to the skeletal muscle and is much slower. To compensate, muscles store a small amount of excess oxygen in proteins called myoglobin, allowing for more efficient muscle contractions and less fatigue. Aerobic training also

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increases the efficiency of the circulatory system so that O_2 can be supplied to the muscles for longer periods of time.

Muscle fatigue occurs when a muscle can no longer contract in response to signals from the nervous system. The exact causes of muscle fatigue are not fully known, although certain factors have been correlated with the decreased muscle contraction that occurs during fatigue. ATP is needed for normal muscle contraction, and as ATP reserves are reduced, muscle function may decline. This may be more of a factor in brief, intense muscle output rather than sustained, lower intensity efforts. Lactic acid buildup may lower intracellular pH, affecting enzyme and protein activity. Imbalances in Na^+ and K^+ levels as a result of membrane depolarization may disrupt Ca^{++} flow out of the SR. Long periods of sustained exercise may damage the SR and the sarcolemma, resulting in impaired Ca^{++} regulation.

Intense muscle activity results in an **oxygen debt**, which is the amount of oxygen needed to compensate for ATP produced without oxygen during muscle contraction. Oxygen is required to restore ATP and creatine phosphate levels, convert lactic acid to pyruvic acid, and convert lactic acid into glucose or glycogen in the liver. Other systems used during exercise also require oxygen, and all these combined processes result in the increased breathing rate that occurs with exercise. Until the oxygen debt has been met, oxygen intake is elevated, even after exercise has stopped.

Relaxation of a Skeletal Muscle

Relaxing skeletal muscle fibres, and ultimately, the skeletal muscle, begins with the motor neuron, which stops releasing its chemical signal, ACh, into the synapse at the NMJ. The muscle fibre will repolarize, which closes the gates in the SR where Ca^{++} was being released. ATP-driven pumps will move Ca^{++} out of the sarcoplasm back into the SR. This results in the "reshielding" of the actin-binding sites on the thin filaments. Without the ability to form cross-bridges between the thin and thick filaments, the muscle fibre loses its tension and relaxes.

Muscle Strength

The number of skeletal muscle fibres in a given muscle is genetically determined and does not change. Muscle strength is directly related to the amount of myofibrils and sarcomeres within each fibre. Factors, such as hormones and stress (and artificial anabolic steroids), acting on the muscle can increase the production of sarcomeres and myofibrils within the muscle fibres, a change called hypertrophy, which results in the increased mass and bulk in a skeletal muscle. Likewise, decreased use of a skeletal muscle results in atrophy, where

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the number of sarcomeres and myofibrils is significantly reduced (but not the number of muscle fibres). It is common for a limb in a cast to show atrophied muscles when the cast is removed, and certain diseases, such as polio, also cause atrophied muscles.

10.4 Nervous System Control of Muscle Tension

Learning Objectives

By the end of this section, you will be able to:

- Explain concentric, isotonic, and eccentric contractions
- Describe the length-tension relationship
- Describe the three phases of a muscle twitch
- Define wave summation, tetanus, and treppe

To move an object, referred to as a load, the sarcomeres in the muscle fibres of the skeletal muscle must shorten. The force generated by the contraction of the muscle (or shortening of the sarcomeres) is called **muscle tension**.

However, muscle tension is also generated when the muscle is contracting against a load that does not move, resulting in two main types of skeletal muscle contractions: isotonic contractions and isometric contractions.

In **isotonic contractions**, where the tension in the muscle stays constant, a load is moved as the length of the muscle changes (shortens). There are two types of isotonic contractions: concentric and eccentric. A **concentric contraction** involves the muscle shortening to move a load. An example of this is the biceps brachii muscle contracting when a hand weight is brought upward with increasing muscle tension. As the biceps brachii contract, the angle of the elbow joint decreases as the forearm is brought toward the body. Here, the biceps brachii contracts as sarcomeres in its muscle fibres are shortening and cross-bridges form; the myosin heads pull the actin. An **eccentric contraction** occurs as the muscle tension diminishes and the muscle lengthens. In this case, the hand weight is lowered in a slow and controlled manner as the amount of cross-bridges being activated by nervous system stimulation decreases. In this case, as tension is released from the biceps brachii, the angle of the elbow joint increases. Eccentric contractions are also used for movement and balance of the body (Figure 10.11).

An **isometric contraction** occurs as the muscle produces tension without changing the angle of a skeletal joint. Isometric contractions involve sarcomere shortening and increasing muscle tension, but do not move a load, as the force

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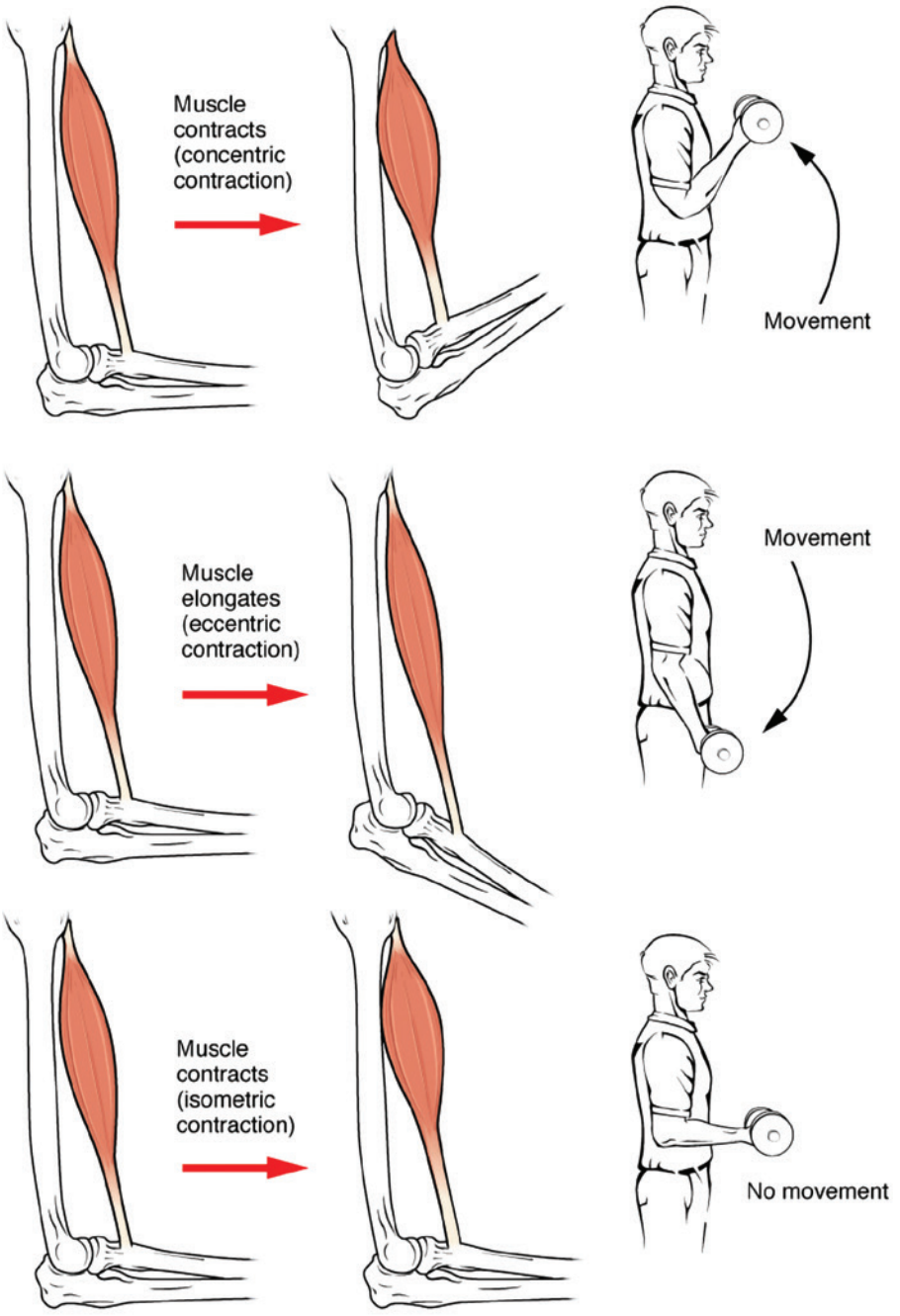


Figure 10.11 Types of Muscle Contractions. During isotonic contractions, muscle length changes to move a load. During isometric contractions, muscle length does not change because the load exceeds the tension the muscle can generate.

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produced cannot overcome the resistance provided by the load. For example, if one attempts to lift a hand weight that is too heavy, there will be sarcomere activation and shortening to a point, and ever-increasing muscle tension, but no change in the angle of the elbow joint. In everyday living, isometric contractions are active in maintaining posture and maintaining bone and joint stability. However, holding your head in an upright position occurs not because the muscles cannot move the head but because the goal is to remain stationary and not produce movement. Most actions of the body are the result of a combination of isotonic and isometric contractions working together to produce a wide range of outcomes.

All these muscle activities are under the exquisite control of the nervous system. Neural control regulates concentric, eccentric and isometric contractions, muscle fibre recruitment, and muscle tone. A crucial aspect of the nervous system's control of skeletal muscles is the role of motor units.

Motor Units

As you have learned, every skeletal muscle fibre must be innervated by the axon terminal of a motor neuron in order to contract. Each muscle fibre is innervated by only one motor neuron. The actual group of muscle fibres in a muscle innervated by a single motor neuron is called a **motor unit**. The size of a motor unit is variable depending on the nature of the muscle.

A **small motor unit** is an arrangement where a single motor neuron supplies a small number of muscle fibres in a muscle. Small motor units permit very fine motor control of the muscle. The best example in humans is the small motor units of the extraocular eye muscles that move the eyeballs. There are thousands of muscle fibres in each muscle, but every six or so fibres are supplied by a single motor neuron, as the axons branch to form synaptic connections at their individual NMJs. This allows for exquisite control of eye movements so that both eyes can quickly focus on the same object. Small motor units are also involved in the many fine movements of the fingers and thumb of the hand for grasping, texting, and so on.

A **large motor unit** is an arrangement where a single motor neuron supplies a large number of muscle fibres in a muscle. Large motor units are concerned with simple, or "gross," movements, such as powerfully extending the knee joint. The best example is the large motor units of the thigh muscles or back muscles, where a single motor neuron will supply thousands of muscle fibres in a muscle, as its axon splits into thousands of branches.

There is a wide range of motor units within many skeletal muscles, which gives the nervous system a wide range of control over the muscle. The small motor units in the muscle will have smaller, lower-threshold motor neurons

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that are more excitable, firing first to their skeletal muscle fibres, which also tend to be the smallest. Activation of these smaller motor units results in a relatively small degree of contractile strength (tension) generated in the muscle. As more strength is needed, larger motor units with bigger, higher-threshold motor neurons are enlisted to activate larger muscle fibres. This increasing activation of motor units produces an increase in muscle contraction known as **recruitment**. As more motor units are recruited, the muscle contraction grows progressively stronger. In some muscles, the largest motor units may generate a contractile force 50 times greater than the smallest motor units in the muscle. This allows a feather to be picked up using the biceps brachii arm muscle with minimal force, and a heavy weight to be lifted by the same muscle by recruiting the largest motor units.

When necessary, the maximal number of motor units in a muscle can be recruited simultaneously, producing the maximum force of contraction for that muscle, but this cannot last for very long because of the energy requirements to sustain the contraction. To prevent complete muscle fatigue, motor units are generally not all simultaneously active, but instead some motor units rest while others are active, which allows for longer muscle contractions. The nervous system uses recruitment as a mechanism to efficiently utilize a skeletal muscle.

The Length-Tension Range of a Sarcomere

When a skeletal muscle fibre contracts, myosin heads attach to actin to form cross-bridges, followed by the thin filaments sliding over the thick filaments as the heads pull the actin, and this results in sarcomere shortening, creating the tension of the muscle contraction. The cross-bridges can only form where thin and thick filaments already overlap, so that the length of the sarcomere has a direct influence on the force generated when the sarcomere shortens. This is called the length-tension relationship.

The ideal length of a sarcomere to produce maximal tension occurs at 80 percent to 120 percent of its resting length, with 100 percent being the state where the medial edges of the thin filaments are just at the most-medial myosin heads of the thick filaments (Figure 10.12). This length maximizes the overlap of actin-binding sites and myosin heads. If a sarcomere is stretched past this ideal length (beyond 120 percent), thick and thin filaments do not overlap sufficiently, which results in less tension produced. If a sarcomere is shortened beyond 80 percent, the zone of overlap is reduced, with the thin filaments jutting beyond the last of the myosin heads, and shrinks the H zone, which is normally composed of myosin tails. Eventually, there is nowhere else for the thin filaments to go, and the amount of tension is diminished. If the muscle is

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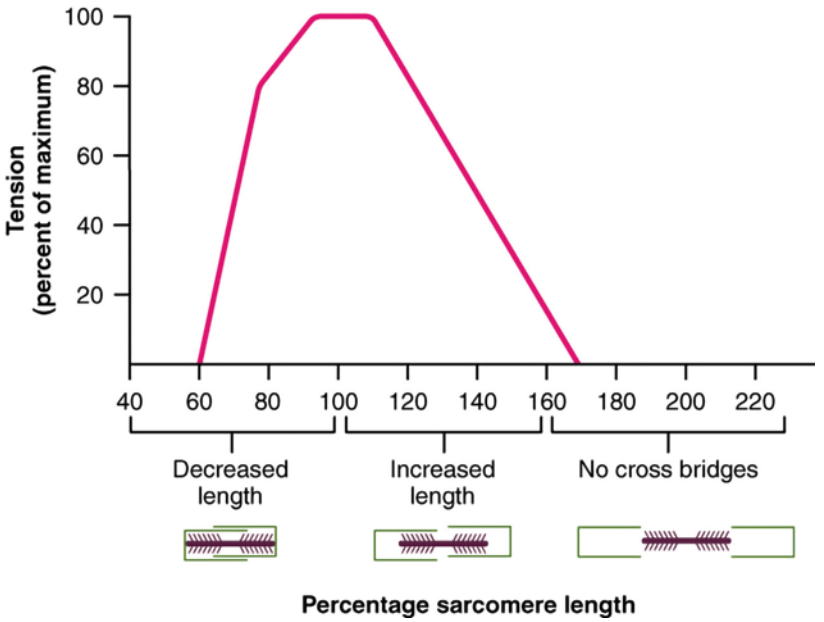


Figure 10.12 The Ideal Length of a Sarcomere. Sarcomeres produce maximal tension when thick and thin filaments overlap between about 80 percent to 120 percent.

stretched to the point where thick and thin filaments do not overlap at all, no cross-bridges can be formed, and no tension is produced in that sarcomere. This amount of stretching does not usually occur, as accessory proteins and connective tissue oppose extreme stretching.

The Frequency of Motor Neuron Stimulation

A single action potential from a motor neuron will produce a single contraction in the muscle fibres of its motor unit. This isolated contraction is called a **twitch**. A twitch can last for a few milliseconds (ms) or 100 ms, depending on the muscle type. The tension produced by a single twitch can be measured by a **myogram**, an instrument that measures the amount of tension produced over time (Figure 10.13). Each twitch undergoes three phases. The first phase is the **latent period**, during which the action potential is being propagated along the sarcolemma and Ca^{++} ions are released from the SR. This is the phase during which excitation and contraction are being coupled but contraction has yet to occur. The **contraction phase** occurs next. The Ca^{++} ions in the sarcoplasm have bound to troponin, tropomyosin has shifted away from actin-binding sites, cross-bridges have formed, and sarcomeres are actively shortening to the point of peak tension. The last phase is the **relaxation phase**, when tension decreases as contraction stops. Ca^{++} ions are pumped out of the sarcoplasm into the SR, and cross-bridge cycling stops, returning the muscle fibres to their resting state.

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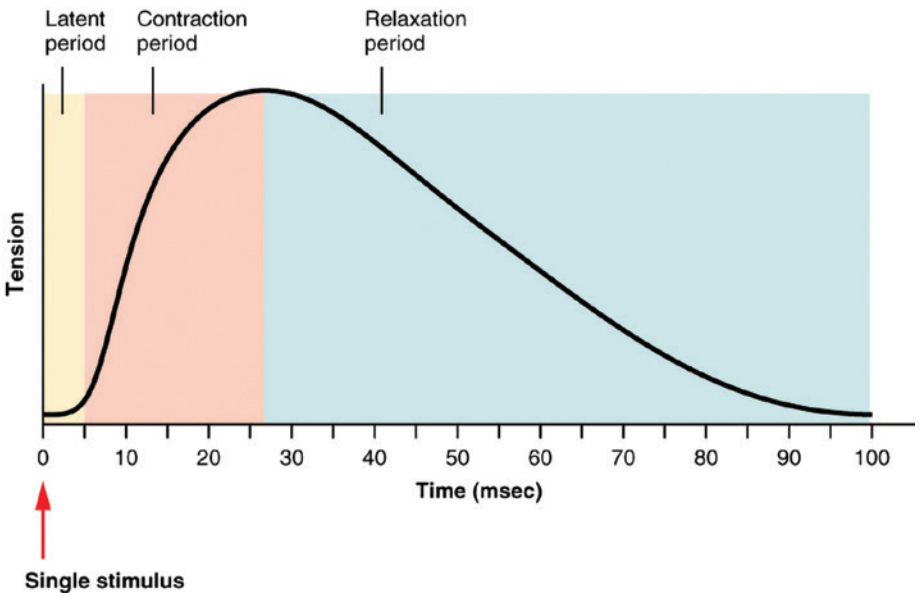


Figure 10.13 A Myogram of a Muscle Twitch. A single muscle twitch has a latent period, a contraction phase when tension increases, and a relaxation phase when tension decreases. During the latent period, the action potential is being propagated along the sarcolemma. During the contraction phase, Ca^{++} ions in the sarcoplasm bind to troponin, tropomyosin moves from actin-binding sites, cross-bridges form, and sarcomeres shorten. During the relaxation phase, tension decreases as Ca^{++} ions are pumped out of the sarcoplasm and cross-bridge cycling stops.

Although a person can experience a muscle "twitch," a single twitch does not produce any significant muscle activity in a living body. A series of action potentials to the muscle fibres is necessary to produce a muscle contraction that can produce work. Normal muscle contraction is more sustained, and it can be modified by input from the nervous system to produce varying amounts of force; this is called a **graded muscle response**. The frequency of action potentials (nerve impulses) from a motor neuron and the number of motor neurons transmitting action potentials both affect the tension produced in skeletal muscle.

The rate at which a motor neuron fires action potentials affects the tension produced in the skeletal muscle. If the fibres are stimulated while a previous twitch is still occurring, the second twitch will be stronger. This response is called **wave summation** because the excitation-contraction coupling effects of successive motor neuron signalling are summed, or added together (Figure 10.14a). At the molecular level, summation occurs because the second stimulus triggers the release of more Ca^{++} ions, which become available to activate additional sarcomeres while the muscle is still contracting from the first stimulus. Summation results in greater contraction of the motor unit.

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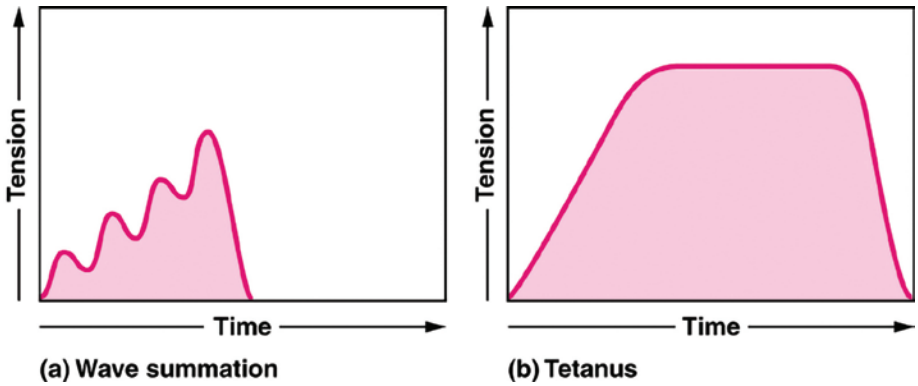


Figure 10.14 Wave Summation and Tetanus. (a) The excitation-contraction coupling effects of successive motor neuron signalling are added together, which is referred to as wave summation. The bottom of each wave, the end of the relaxation phase, represents the point of stimulus. (b) When the stimulus frequency is so high that the relaxation phase disappears completely, the contractions become continuous; this is called tetanus.

If the frequency of motor neuron signalling increases, summation and subsequent muscle tension in the motor unit continue to rise until they reach a peak point. The tension at this point is about three to four times greater than the tension of a single twitch, a state referred to as incomplete tetanus. During incomplete tetanus, the muscle goes through quick cycles of contraction with a short relaxation phase for each. If the stimulus frequency is so high that the relaxation phase disappears completely, contractions become continuous in a process called complete **tetanus** (Figure 10.14b).

During tetanus, the concentration of Ca^{++} ions in the sarcoplasm allows virtually all the sarcomeres to form cross-bridges and shorten, so that a contraction can continue uninterrupted (until the muscle fatigues and can no longer produce tension).

Treppe

When a skeletal muscle has been dormant for an extended period and then activated to contract, with all other things being equal, the initial contractions generate about half the force of later contractions. The muscle tension increases in a graded manner that, to some, looks like a set of stairs. This tension increase is called **treppe**, a condition where muscle contractions become more efficient. It's also known as the "staircase effect" (Figure 10.15).

It is believed that treppe results from a higher concentration of Ca^{++} in the sarcoplasm from the steady stream of signals from the motor neuron. It can only be maintained with adequate ATP.

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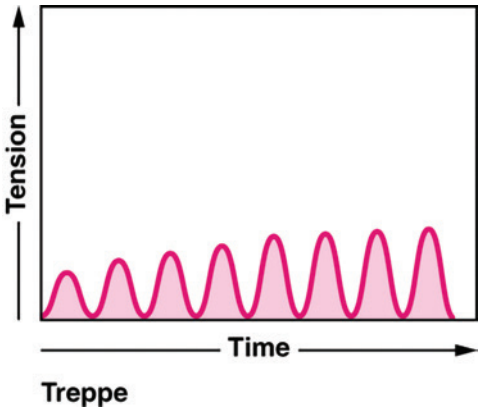


Figure 10.15 Treppe. When muscle tension increases in a graded manner that looks like a set of stairs, it is called treppe. The bottom of each wave represents the point of stimulus.

Muscle Tone

Skeletal muscles are rarely completely relaxed, or flaccid. Even if a muscle is not producing movement, it is contracted a small amount to maintain its contractile proteins and produce **muscle tone**. The tension produced by muscle tone allows muscles to continually stabilize joints and maintain posture.

Muscle tone is accomplished by a complex interaction between the nervous system and skeletal muscles that results in the activation of a few motor units at a time, most likely in a cyclical manner. In this manner, muscles never fatigue completely, as some motor units can recover while others are active.

The absence of the low-level contractions that lead to muscle tone is referred to as **hypotonia**, and it can result from damage to parts of the central nervous system (CNS), such as the cerebellum, or from loss of innervations to a skeletal muscle, as in poliomyelitis. Hypotonic muscles have a flaccid appearance and display functional impairments, such as weak reflexes. Conversely, excessive muscle tone is referred to as **hypertonia**, accompanied by hyperreflexia (excessive reflex responses), often the result of damage to upper motor neurons in the CNS. Hypertonia can present with muscle rigidity (as seen in Parkinson's disease) or spasticity, a phasic change in muscle tone, where a limb will "snap" back from passive stretching (as seen in some strokes).

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10.5 Types of Muscle Fibres

Learning Objectives

By the end of this section, you will be able to:

- Describe the types of skeletal muscle fibres
- Explain fast and slow muscle fibres

Two criteria to consider when classifying the types of muscle fibres are how fast some fibres contract relative to others, and how fibres produce ATP. Using these criteria, there are three main types of skeletal muscle fibres. **Slow oxidative** (**SO**) fibres contract relatively slowly and use aerobic respiration (oxygen and glucose) to produce ATP. **Fast oxidative** (**FO**) fibres have fast contractions and primarily use aerobic respiration, but because they may switch to anaerobic respiration (glycolysis), they can fatigue more quickly than SO fibres. Lastly, **fast glycolytic** (**FG**) fibres have fast contractions and primarily use anaerobic glycolysis. The FG fibres fatigue more quickly than the others. Most skeletal muscles in a human contain(s) all three types, although in varying proportions.

The speed of contraction is dependent on how quickly myosin's ATPase hydrolyzes ATP to produce cross-bridge action. Fast fibres hydrolyze ATP approximately twice as quickly as slow fibres, resulting in much quicker cross-bridge cycling (which pulls the thin filaments toward the centre of the sarcomeres at a faster rate). The primary metabolic pathway used by a muscle fibre determines whether the fibre is classified as oxidative or glycolytic. If a fibre primarily produces ATP through aerobic pathways, it is oxidative. More ATP can be produced during each metabolic cycle, making the fibre more resistant to fatigue. Glycolytic fibres primarily create ATP through anaerobic glycolysis, which produces less ATP per cycle. As a result, glycolytic fibres fatigue at a quicker rate.

The oxidative fibres contain many more mitochondria than the glycolytic fibres, because aerobic metabolism, which uses oxygen (O_2) in the metabolic pathway, occurs in the mitochondria. The SO fibres possess a large number of mitochondria and are capable of contracting for longer periods because of the large amount of ATP they can produce, but they have a relatively small diameter and do not produce a large amount of tension. SO fibres are extensively supplied with blood capillaries to supply O_2 from the red blood cells in the bloodstream. The SO fibres also possess myoglobin, an O_2-carrying molecule similar to O_2-carrying hemoglobin in the red blood cells. The myoglobin stores some of the

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needed O_2 within the fibres themselves (and gives SO fibres their red colour). All these features allow SO fibres to produce large quantities of ATP, which can sustain muscle activity without fatiguing for long periods of time.

The fact that SO fibres can function for long periods without fatiguing makes them useful in maintaining posture, producing isometric contractions, stabilizing bones and joints, and making small movements that happen often but do not require large amounts of energy. They do not produce high tension, and thus they are not used for powerful, fast movements that require high amounts of energy and rapid cross-bridge cycling.

FO fibres are sometimes called intermediate fibres because they possess characteristics that are intermediate between fast fibres and slow fibres. They produce ATP relatively quickly, more quickly than SO fibres, and thus can produce relatively high amounts of tension. They are oxidative because they produce ATP aerobically, possess high amounts of mitochondria, and do not fatigue quickly. However, FO fibres do not possess significant myoglobin, giving them a lighter colour than the red SO fibres. FO fibres are used primarily for movements, such as walking, that require more energy than postural control but less energy than an explosive movement, such as sprinting. FO fibres are useful for this type of movement because they produce more tension than SO fibres but are more fatigue-resistant than FG fibres.

FG fibres primarily use anaerobic glycolysis as their ATP source. They have a large diameter and possess high amounts of glycogen, which is used in glycolysis to generate ATP quickly to produce high levels of tension. Because they do not primarily use aerobic metabolism, they do not possess substantial numbers of mitochondria or significant amounts of myoglobin and therefore have a white colour. FG fibres are used to produce rapid, forceful contractions to make quick, powerful movements. These fibres fatigue quickly, permitting them to only be used for short periods. Most muscles possess a mixture of each fibre type. The predominant fibre type in a muscle is determined by the primary function of the muscle.

10.6 Cardiac Muscle Tissue

Learning Objectives

By the end of this section, you will be able to:

- Describe intercalated discs and gap junctions
- Describe a desmosome

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Cardiac muscle tissue is only found in the heart. Highly coordinated contractions of cardiac muscle pump blood into the vessels of the circulatory system. Similar to skeletal muscle, cardiac muscle is striated and organized into sarcomeres, possessing the same banding organization as skeletal muscle (Figure 10.16). However, cardiac muscle fibres are shorter than skeletal muscle fibres and usually contain only one nucleus, which is located in the central region of the cell. Cardiac muscle fibres also possess many mitochondria and myoglobin, as ATP is produced primarily through aerobic metabolism. Cardiac muscle fibre cells are also extensively branched and are connected to one another at their ends by intercalated discs. An **intercalated disc** allows the cardiac muscle cells to contract in a wavelike pattern so that the heart can work as a pump.

Interactive Link 10.4

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/10.4) to explore the tissue sample in greater detail.

Intercalated discs are part of the sarcolemma and contain two structures important in cardiac muscle contraction: gap junctions and desmosomes. A **gap**

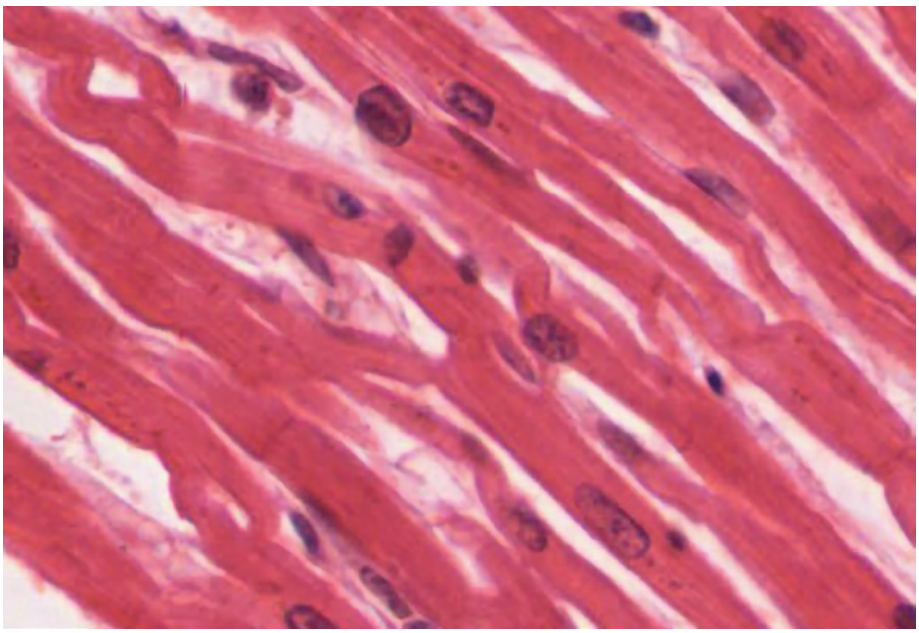


Figure 10.16 Cardiac Muscle Tissue. Cardiac muscle tissue is only found in the heart. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

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junction forms channels between adjacent cardiac muscle fibres that allow the depolarizing current produced by cations to flow from one cardiac muscle cell to the next. (Figure 10.17).

This joining is called electric coupling, and in cardiac muscle, it allows the quick transmission of action potentials and the coordinated contraction of the entire heart. This network of electrically connected cardiac muscle cells creates a functional unit of contraction called a syncytium. The remainder of the intercalated disc is composed of desmosomes. A **desmosome** is a cell structure that anchors the ends of cardiac muscle fibres together so the cells do not pull apart during the stress of individual fibres contracting.

Contractions of the heart (heartbeats) are controlled by specialized cardiac muscle cells called pacemaker cells that directly control heart rate. Although cardiac muscle cannot be consciously controlled, the pacemaker cells respond to signals from the autonomic nervous system (ANS) to speed up or slow down the heart rate. The pacemaker cells can also respond to various hormones that modulate heart rate to control blood pressure.

The wave of contraction that allows the heart to work as a unit, called a functional syncytium, begins with the pacemaker cells. This group of cells is self-excitable; they are able to depolarize until they reach the threshold potential and fire action potentials on their own, a feature called **autorhythmicity**; they do this at set intervals, which determine heart rate. Because they are connected with gap junctions to surrounding muscle fibres and the specialized fibres of the heart's conduction system, the pacemaker cells are able to transfer the depolarization to the other cardiac muscle fibres in a manner that allows the heart to contract in a coordinated manner.

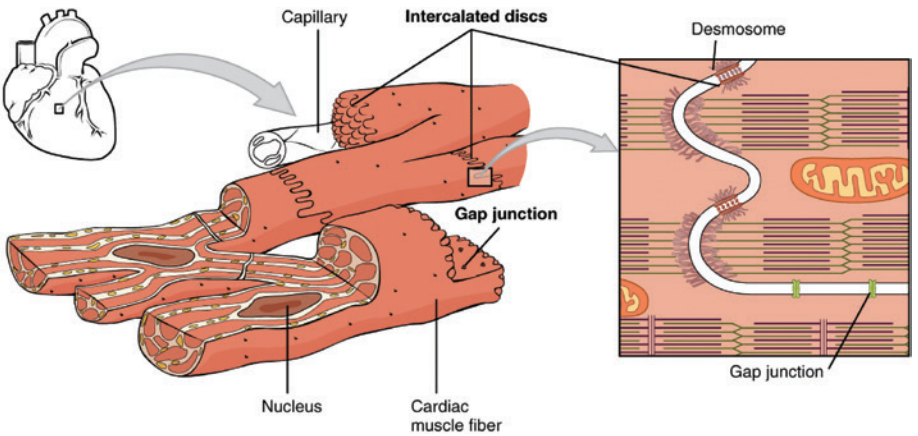


Figure 10.17 Cardiac Muscle. Intercalated discs are part of the cardiac muscle sarcolemma, and they contain gap junctions and desmosomes.

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Another feature of cardiac muscle is its relatively long action potentials in its fibres, having a sustained depolarization "plateau." The plateau is produced by Ca^{++} entry through voltage-gated calcium channels in the sarcolemma of cardiac muscle fibres. This sustained depolarization (and Ca^{++} entry) provides for a longer contraction than is produced by an action potential in skeletal muscle. Unlike skeletal muscle, a large percentage of the Ca^{++} that initiates contraction in cardiac muscles comes from outside the cell rather than from the SR.

10.7 Smooth Muscle

Learning Objectives

By the end of this section, you will be able to:

- Describe a dense body
- Explain how smooth muscle works with internal organs and passageways through the body
- Explain how smooth muscles differ from skeletal and cardiac muscles
- Explain the difference between single-unit and multiunit smooth muscle

Smooth muscle (so named because the cells do not have striations) is present in the walls of hollow organs like the urinary bladder, uterus, stomach, intestines, and in the walls of passageways, such as the arteries and veins of the circulatory system, and the tracts of the respiratory, urinary, and reproductive systems (Figure 10.18). Smooth muscle is also present in the eyes, where it functions to change the size of the iris and alter the shape of the lens, and in the skin, where it causes hair to stand erect in response to cold temperature or fear.

Interactive Link 10.5

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/10.5) to explore the tissue sample in greater detail.

Smooth muscle fibres are spindle-shaped (wide in the middle and tapered at both ends, somewhat like a football) and have a single nucleus; they range from

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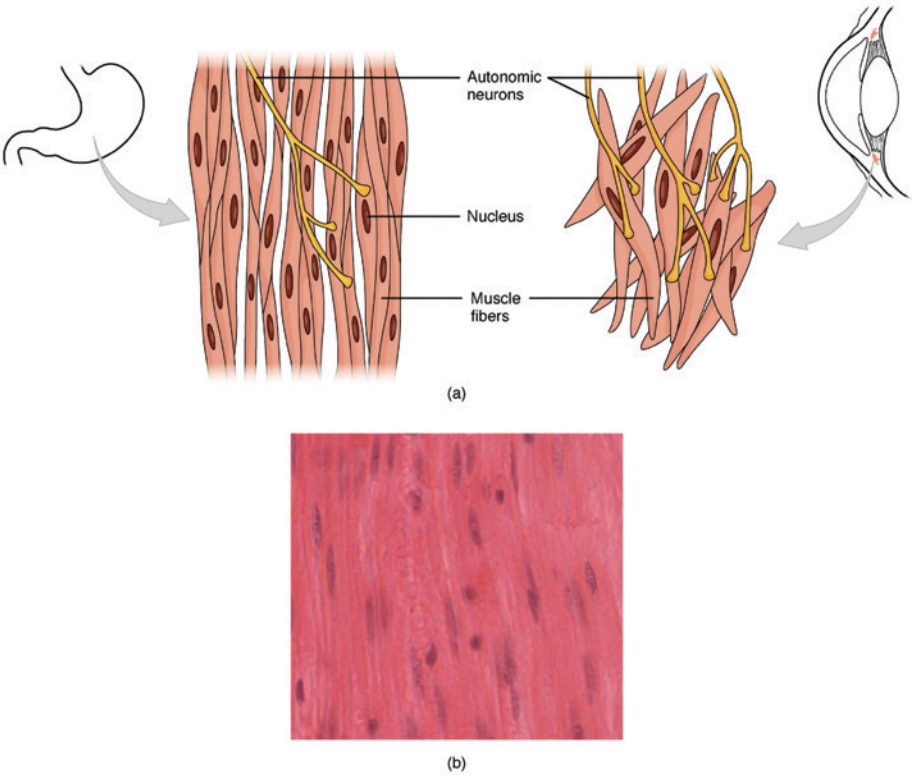


Figure 10.18 Smooth Muscle Tissue. Smooth muscle tissue is found around organs in the digestive, respiratory, reproductive tracts, and the iris of the eye. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

about 30 to 200 μm (thousands of times shorter than skeletal muscle fibres), and they produce their own connective tissue, endomysium. Although they do not have striations and sarcomeres, smooth muscle fibres do have actin and myosin contractile proteins, and thick and thin filaments.

These thin filaments are anchored by dense bodies. A **dense body** is analogous to the Z discs of skeletal and cardiac muscle fibres and is fastened to the sarcolemma. Calcium ions are supplied by the SR in the fibres and by sequestration from the extracellular fluid through membrane indentations called calveoli.

Because smooth muscle cells do not contain troponin, cross-bridge formation is not regulated by the troponin-tropomyosin complex but instead by the regulatory protein **calmodulin**. In a smooth muscle fibre, external Ca^{++} ions passing through opened calcium channels in the sarcolemma, and additional Ca^{++} released from SR, bind to calmodulin. The Ca^{++}-calmodulin complex then activates an enzyme called myosin (light chain) kinase, which, in turn, activates the myosin heads by phosphorylating them (converting ATP to ADP and P_i, with the P_i attaching to the head). The heads can then attach to actin-binding

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sites and pull on the thin filaments. The thin filaments are also anchored to the dense bodies, or the structures invested in the inner membrane of the sarcolemma (at adherens junctions) that also have cordlike intermediate filaments attached to them. When the thin filaments slide past the thick filaments, they pull on the dense bodies, which then pull on the intermediate filament networks throughout the sarcoplasm. This arrangement causes the entire muscle fibre to contract in a manner whereby the ends are pulled toward the centre, causing the midsection to bulge in a corkscrew motion (Figure 10.19).

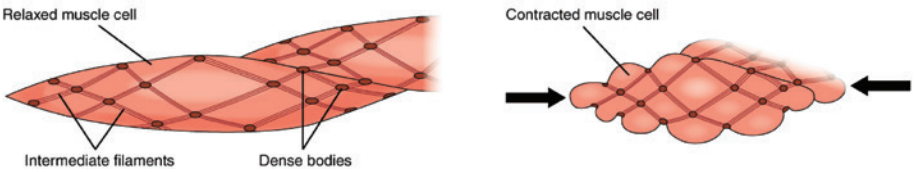


Figure 10.19 Muscle Contraction. The dense bodies and intermediate filaments are networked through the sarcoplasm, which causes the muscle fibre to contract.

Although smooth muscle contraction relies on the presence of Ca^{++} ions, smooth muscle fibres have a much smaller diameter than skeletal muscle cells. T-tubules are not required to reach the interior of the cell and therefore are not necessary to transmit an action potential deep into the fibre. Smooth muscle fibres have a limited calcium-storing SR but have calcium channels in the sarcolemma (similar to cardiac muscle fibres) that open during the action potential along the sarcolemma. The influx of extracellular Ca^{++} ions, which diffuse into the sarcoplasm to reach the calmodulin, accounts for most of the Ca^{++} that triggers contraction of a smooth muscle cell.

Muscle contraction continues until ATP-dependent calcium pumps actively transport Ca^{++} ions back into the SR and out of the cell. However, a low concentration of calcium remains in the sarcoplasm to maintain **muscle tone**. This remaining calcium keeps the muscle slightly contracted, which is important in certain tracts and around blood vessels.

Because most smooth muscles must function for long periods without rest, their power output is relatively low, but contractions can continue without using large amounts of energy. Some smooth muscle can also maintain contractions even as Ca^{++} is removed and myosin kinase is inactivated/dephosphorylated. This can happen as a subset of cross-bridges between myosin heads and actin, called **latch-bridges**, keep the thick and thin filaments linked together for a prolonged period, without the need for ATP. This allows for the maintenance of muscle "tone" in smooth muscle that lines arterioles and other visceral organs with very little energy expenditure.

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Smooth muscle is not under voluntary control; thus, it is called involuntary muscle. The triggers for smooth muscle contraction include hormones, neural stimulation by the ANS, and local factors. In certain locations, such as the walls of visceral organs, stretching the muscle can trigger its contraction (the stress-relaxation response). Axons of neurons in the ANS do not form the highly organized NMJs with smooth muscle, as seen between motor neurons and skeletal muscle fibres. Instead, there is a series of neurotransmitter-filled bulges called varicosities as an axon courses through smooth muscle, loosely forming motor units (Figure 10.20).

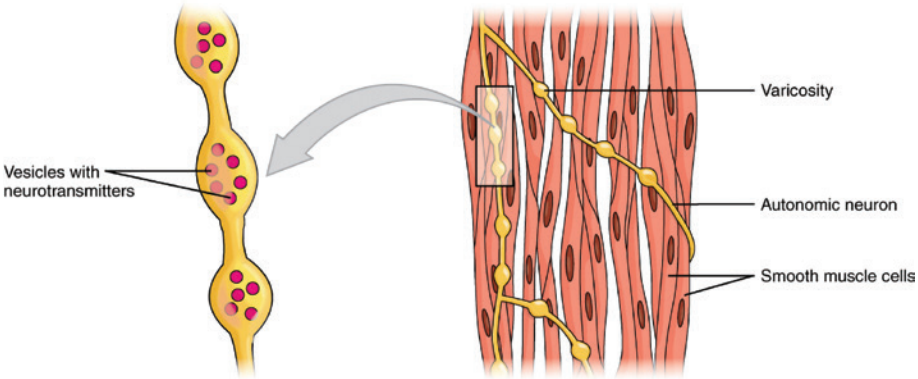


Figure 10.20 Motor Units. A series of axon-like swellings, called varicosities or "boutons," from autonomic neurons form motor units through the smooth muscle.

Smooth muscle is organized in two ways: as single-unit smooth muscle, which is much more common, and as multiunit smooth muscle. The two types have different locations in the body and have different characteristics. Single-unit smooth muscle has its muscle fibres joined by gap junctions so that the muscle contracts as a single unit. This type of smooth muscle is found in the walls of all visceral organs except the heart (which has cardiac muscle in its walls), and so it is commonly called **visceral muscle**. Because the muscle fibres are not constrained by the organization and stretchability limits of sarcomeres, visceral smooth muscle has a **stress-relaxation response**. This means that as the muscle of a hollow organ is stretched when it fills, the mechanical stress of the stretching will trigger contraction, but this is immediately followed by relaxation so that the organ does not empty its contents prematurely. This is important for hollow organs, such as the stomach or urinary bladder, which continuously expand as they fill. The smooth muscle around these organs can also maintain a muscle tone when the organ empties and shrinks, a feature that prevents "flabbiness" in the empty organ. In general, visceral smooth muscle

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produces slow, steady contractions that allow substances, such as food in the digestive tract, to move through the body.

Multiunit smooth muscle cells rarely possess gap junctions and thus are not electrically coupled. As a result, contraction does not spread from one cell to the next but is instead confined to the cell that was originally stimulated. Stimuli for multiunit smooth muscles come from autonomic nerves or hormones but not from stretching. This type of tissue is found around large blood vessels, in the respiratory airways, and in the eyes.

Hyperplasia in Smooth Muscle

Similar to skeletal and cardiac muscle cells, smooth muscle can undergo **hypertrophy** to increase in size. Unlike other muscle, smooth muscle can also divide to produce more cells, a process called **hyperplasia**. This can most evidently be observed in the uterus at puberty, which responds to increased estrogen levels by producing more uterine smooth muscle fibres and greatly increasing the size of the myometrium.

Key Terms

acetylcholine (ACh): Neurotransmitter that binds at a motor end-plate to trigger depolarization.

actin: Protein that makes up most of the thin myofilaments in a sarcomere muscle fibre.

action potential: Change in voltage of a cell membrane in response to a stimulus that results in transmission of an electrical signal; unique to neurons and muscle fibres.

aerobic respiration: Production of ATP in the presence of oxygen.

anaerobic metabolism: Process during periods of reduced oxygen when pyruvic acid is converted to lactic acid, which may contribute to muscle fatigue.

aponeurosis: Broad, tendonlike sheet of connective tissue that attaches a skeletal muscle to another skeletal muscle or to a bone.

ATPase: Enzyme that hydrolyzes ATP to ADP.

autorhythmicity: Heart's ability to control its own contractions.

calmodulin: Regulatory protein that facilitates contraction in smooth muscles.

cardiac muscle: Striated muscle found in the heart; joined to one another at intercalated discs and under the regulation of pacemaker cells, which contract as one unit to pump blood through the circulatory system. Cardiac muscle is under involuntary control.

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concentric contraction: Muscle contraction that shortens the muscle to move a load.
contractility: Ability to shorten (contract) forcibly.
contraction phase: Twitch contraction phase when tension increases.
creatine phosphate: Phosphagen used to store energy from ATP and transfer it to muscle.
dense body: Sarcoplasmic structure that attaches to the sarcolemma and shortens the muscle as thin filaments slide past thick filaments.
depolarize: Process where the membrane potential of muscle fibre becomes less negative (closer to zero).
desmosome: Cell structure that anchors the ends of cardiac muscle fibres to allow contraction to occur.
eccentric contraction: Muscle contraction that lengthens the muscle as the tension is diminished.
elasticity: Ability to stretch and rebound.
endomysium: Loose, well-hydrated connective tissue covering each muscle fibre in a skeletal muscle.
epimysium: Outer layer of connective tissue around a skeletal muscle.
excitability: Ability to undergo neural stimulation.
excitation-contraction coupling: Sequence of events from motor neuron signalling to a skeletal muscle fibre to contraction of the fibre's sarcomeres.
extensibility: Ability to lengthen (extend).
fascicle: Bundle of muscle fibres within a skeletal muscle.
fast glycolytic (FG): Muscle fibre that primarily uses anaerobic glycolysis.
fast oxidative (FO): Intermediate muscle fibre that is between slow oxidative and fast glycolytic fibres.
gap junction: Channels between adjacent cardiac muscle fibres that allow the depolarizing current produced by cations to flow from one cardiac muscle cell to the next.
glycolysis: Anaerobic breakdown of glucose to ATP.
graded muscle response: Modification of contraction strength.
hyperplasia: Process in which one cell splits to produce new cells.
hypertonia: Abnormally high muscle tone.
hypertrophy: Addition of structural proteins to muscle fibres.
hypotonia: Abnormally low muscle tone caused by the absence of low-level contractions.
intercalated disc: Part of the sarcolemma that connects cardiac tissue and contains gap junctions and desmosomes.

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isometric contraction: Muscle contraction that occurs with no change in muscle length.

isotonic contraction: Muscle contraction that involves changes in muscle length.

lactic acid: Product of anaerobic glycolysis.

large motor unit: Arrangement where a single motor neuron supplies a large number of muscle fibres in a muscle; concerned with simple, or "gross," movements.

latch-bridges: Subset of a cross-bridge in which actin and myosin remain locked together.

latent period: The time when a twitch does not produce contraction.

motor end-plate: Sarcolemma of muscle fibre at the neuromuscular junction, with receptors for the neurotransmitter acetylcholine.

motor unit: A motor neuron and the group of muscle fibres it innervates.

muscle fatigue: Occurs when a muscle can no longer contract in response to signals from the nervous system.

muscle fibre: Skeletal muscle cells; they are long and cylindrical.

muscle tension: Force generated by the contraction of the muscle; tension generated during isotonic contractions and isometric contractions.

muscle tone: Low levels of muscle contraction that occur when a muscle is not producing movement.

myofibril: Long, cylindrical organelle that runs parallel within the muscle fibre and contains the sarcomeres.

myofilaments: Highly organized arrangement of the contractile fibres in the sarcomere.

myogram: Instrument used to measure twitch tension.

myosin: Protein that makes up most of the thick cylindrical myofilament within a sarcomere muscle fibre.

neuromuscular junction (NMJ): Synapse between the axon terminal of a motor neuron and the section of the membrane of a muscle fibre with receptors for the acetylcholine released by the terminal.

neurotransmitter: Signalling chemical released by nerve terminals that binds to and activates receptors on target cells.

oxygen debt: Amount of oxygen needed to compensate for ATP produced without oxygen during muscle contraction.

perimysium: Connective tissue that bundles skeletal muscle fibres into fascicles within a skeletal muscle.

power stroke: Action of myosin pulling actin inward (toward the M line).

pyruvic acid: Product of glycolysis that can be used in aerobic respiration or converted to lactic acid.

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recruitment: Increase in the number of motor units involved in contraction.
relaxation phase: Period after twitch contraction when tension decreases.
sarcolemma: Plasma membrane of a skeletal muscle fibre.
sarcomere: Longitudinally repeating functional unit of skeletal muscle, with all the contractile and associated proteins involved in contraction.
sarcoplasm: Cytoplasm of a muscle cell.
sarcoplasmic reticulum (SR): Specialized smooth endoplasmic reticulum, which stores, releases, and retrieves Ca^{++}.
skeletal muscle: Striated, multinucleated muscle that requires signalling from the nervous system to trigger contraction; most skeletal muscles are referred to as voluntary muscles that move bones and produce movement.
sliding filament model of muscle contraction: Skeletal muscle fibre contracts as the thin filaments are pulled and then slide past the thick filaments within the fibre's sarcomeres.
slow oxidative (SO): Muscle fibre that primarily uses aerobic respiration.
small motor unit: Arrangement where a single motor neuron supplies a small number of muscle fibres; permits very fine motor control of the muscle.
smooth muscle: Nonstriated, mononucleated muscle in the skin that is associated with hair follicles; assists in moving materials in the walls of internal organs, blood vessels, and internal passageways.
stress-relaxation response: Relaxation of smooth muscle tissue after being stretched.
synaptic cleft: Space between a nerve (axon) terminal and a motor end-plate.
tetanus: A continuous fused contraction.
thick filament: The thick myosin strands and their multiple heads projecting from the centre of the sarcomere toward, but not all the way to, the Z discs.
thin filament: Thin strands of actin and its troponin-tropomyosin complex projecting from the Z discs toward the centre of the sarcomere.
treppe: Stepwise increase in contraction tension.
triad: A grouping of one T-tubule and two terminal cisternae.
tropomyosin: Regulatory protein that covers myosin-binding sites to prevent actin from binding to myosin.
troponin: Regulatory protein that binds to actin, tropomyosin, and calcium.
T-tubule: Projection of the sarcolemma into the interior of the cell.
twitch: Single contraction produced by one action potential.
varicosity: Enlargement of neurons that release neurotransmitters into synaptic clefts.
visceral muscle: Smooth muscle found in the walls of visceral organs.

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voltage-gated sodium channels: Membrane proteins that open sodium channels in response to a sufficient voltage change and initiate and transmit the action potential as Na^+ enters through the channel.

wave summation: Addition of successive neural stimuli to produce greater contraction.

Z discs: Three-dimensional cylinder-like arrangement of sarcomere.

Chapter Review

10.1 Overview of Muscle Tissues

Muscle is the tissue in animals that allows for active movement of the body or materials within the body. There are three types of muscle tissue: skeletal muscle, cardiac muscle, and smooth muscle. Most of the body's skeletal muscle produces movement by acting on the skeleton. Cardiac muscle is found in the wall of the heart and pumps blood through the circulatory system.

Smooth muscle is found in the skin, where it is associated with hair follicles; it is also found in the walls of internal organs, blood vessels, and internal passageways, where it assists in moving materials.

10.2 Skeletal Muscle

Skeletal muscles contain connective tissue, blood vessels, and nerves. There are three layers of connective tissue: epimysium, perimysium, and endomysium. Skeletal muscle fibres are organized into groups called fascicles. Blood vessels and nerves enter the connective tissue and branch in the cell. Muscles attach to bones directly or through tendons or aponeuroses. Skeletal muscles maintain posture, stabilize bones and joints, control internal movement, and generate heat.

Skeletal muscle fibres are long, multinucleated cells. The membrane of the cell is the sarcolemma; the cytoplasm of the cell is the sarcoplasm. The sarcoplasmic reticulum (SR) is a form of endoplasmic reticulum. Muscle fibres are composed of myofibrils. The striations are created by the organization of actin and myosin, resulting in the banding pattern of myofibrils.

10.3 Muscle Fibre Contraction and Relaxation

A sarcomere is the smallest contractile portion of a muscle. Myofibrils are composed of thick and thin filaments. Thick filaments are composed of the protein myosin; thin filaments are composed of the protein actin. Troponin and tropomyosin are regulatory proteins.

Muscle contraction is described by the sliding filament model of contraction. ACh is the neurotransmitter that binds at the neuromuscular junction

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(NMJ) to trigger depolarization, and an action potential travels along the sarcolemma to trigger calcium release from the SR. The actin sites are exposed after Ca^{++} enters the sarcoplasm from its SR storage to activate the troponin-tropomyosin complex so that the tropomyosin shifts away from the sites. The cross-bridging of myosin heads docking into actin-binding sites is followed by the "power stroke"—the sliding of the thin filaments by thick filaments. The power strokes are powered by ATP. Ultimately, the sarcomeres, myofibrils, and muscle fibres shorten to produce movement.

10.4 Nervous System Control of Muscle Tension

The number of cross-bridges formed between actin and myosin determines the amount of tension produced by a muscle. The length of a sarcomere is optimal when the zone of overlap between thin and thick filaments is greatest. Muscles that are stretched or compressed too greatly do not produce maximal amounts of power. A motor unit is formed by a motor neuron and all the muscle fibres that are innervated by that same motor neuron. A single contraction is called a twitch. A muscle twitch has a latent period, a contraction phase, and a relaxation phase. A graded muscle response allows variation in muscle tension. Summation occurs as successive stimuli are added together to produce a stronger muscle contraction. Tetanus is the fusion of contractions to produce a continuous contraction. Increasing the number of motor neurons involved increases the number of motor units activated in a muscle, which is called recruitment. Muscle tone is the constant, low-level contractions that allow for posture and stability.

10.5 Types of Muscle Fibres

ATP provides the energy for muscle contraction. The three mechanisms for ATP regeneration are creatine phosphate, anaerobic glycolysis, and aerobic metabolism. Creatine phosphate provides about the first 15 seconds of ATP at the beginning of muscle contraction. Anaerobic glycolysis produces small amounts of ATP in the absence of oxygen for a short period. Aerobic metabolism utilizes oxygen to produce much more ATP, allowing a muscle to work for longer periods. Muscle fatigue, which has many contributing factors, occurs when a muscle can no longer contract. An oxygen debt is created as a result of muscle use. The three types of muscle fibre are slow oxidative (SO), fast oxidative (FO), and fast glycolytic (FG). SO fibres use aerobic metabolism to produce low-power contractions over long periods and are slow to fatigue. FO fibres use aerobic metabolism to produce ATP but produce higher tension contractions than SO fibres. FG fibres use anaerobic metabolism to produce powerful, high-tension contractions but fatigue quickly.

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10.6 Cardiac Muscle Tissue

Cardiac muscle is striated muscle that is present only in the heart. Cardiac muscle fibres have a single nucleus, are branched, and joined to one another by intercalated discs that contain gap junctions for depolarization between cells and desmosomes to hold the fibres together when the heart contracts.

Contraction in each cardiac muscle fibre is triggered by Ca^{++} ions in a similar manner as skeletal muscle, but here the Ca^{++} ions come from SR and through voltage-gated calcium channels in the sarcolemma. Pacemaker cells stimulate the spontaneous contraction of cardiac muscle as a functional unit, called a syncytium.

10.7 Smooth Muscle

Smooth muscle is found throughout the body around various organs and tracts. Smooth muscle cells have a single nucleus and are spindle-shaped. Smooth muscle cells can undergo hyperplasia, mitotically dividing to produce new cells. The smooth cells are nonstriated, but their sarcoplasm is filled with actin and myosin, along with dense bodies in the sarcolemma to anchor the thin filaments and a network of intermediate filaments involved in pulling the sarcolemma toward the fibre's middle, shortening it in the process. Ca^{++} ions trigger contraction when they are released from SR and enter through opened voltage-gated calcium channels. Smooth muscle contraction is initiated when the Ca^{++} binds to intracellular calmodulin, which then activates an enzyme called myosin kinase that phosphorylates myosin heads so they can form the cross-bridges with actin and then pull on the thin filaments. The fibres in some smooth muscle have latch-bridges, cross-bridges that cycle slowly without the need for ATP; these muscles can maintain low-level contractions for long periods. Single-unit smooth muscle tissue contains gap junctions to synchronize membrane depolarization and contractions so that the muscle contracts as a single unit. Single-unit smooth muscle in the walls of the viscera, called visceral muscle, has a stress-relaxation response that permits the muscle to stretch, contract, and relax as the organ expands. Multi-unit smooth muscle cells do not possess gap junctions, and contraction does not spread from one cell to the next.

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11

The Muscular System

Chapter Objectives

After studying this chapter, you will be able to:

- Describe the actions and roles of agonists and antagonists
- Explain the structure and organization of muscle fascicles and their role in generating force
- Explain the criteria used to name skeletal muscles
- Identify the skeletal muscles and their actions on the skeleton and soft tissues of the body
- Identify the origins and insertions of skeletal muscles and the prime movements

Think about the things that you do each day—talking, walking, sitting, standing, and running—all these activities require movement of particular skeletal muscles. Skeletal muscles are even used during sleep. The diaphragm is a sheet of skeletal muscle that has to contract and relax for you to breathe day and night. If you recall from your study of the skeletal system and joints, body movement occurs around the joints in the body. The focus of this chapter is on skeletal muscle organization. The system for naming skeletal muscles will be explained; in some cases, the muscle is named by its shape, and in other cases, it is named by its location or attachments to the skeleton. If you understand the meaning of the name of the muscle, it will often help you remember its location and/or what it does. This chapter will also describe how skeletal muscles are arranged to accomplish movement, and how other muscles may assist, or be arranged on the skeleton to resist or carry out the opposite movement. The actions of the skeletal muscles will be covered in a regional manner, working from the head down to the toes.

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11.1 Interactions of Skeletal Muscles, Their Fascicle Arrangement, and Their Lever Systems

Learning Objectives

By the end of this section, you will be able to:

- Compare and contrast agonist and antagonist muscles
- Describe how fascicles are arranged within a skeletal muscle
- Explain the major events of a skeletal muscle contraction within a muscle in generating force

To move the skeleton, the tension created by the contraction of the fibres in most skeletal muscles is transferred to the tendons. The tendons are strong bands of dense regular connective tissue that connect muscles to bones. The bone connection is why this muscle tissue is called skeletal muscle.

Interactions of Skeletal Muscles in the Body

To pull on a bone—that is, to change the angle at its synovial joint, which essentially moves the skeleton—a skeletal muscle must also be attached to a fixed part of the skeleton. The movable end of the muscle that attaches to the bone being pulled is called the muscle's **insertion**, and the end of the muscle attached to a fixed (stabilized) bone is called the **origin**. During forearm **flexion**—bending the elbow—the brachioradialis assists the brachialis.

Although a number of muscles may be involved in an action, the principal muscle involved is called the **prime mover**, or **agonist**. To lift a cup, a muscle called the biceps brachii is actually the prime mover; however, because it can be assisted by the brachialis, the brachialis is called a **synergist** in this action (Figure 11.1). A synergist can also be a **fixator** that stabilizes the bone that is the attachment for the prime mover's origin.

A muscle with the opposite action of the prime mover is called an **antagonist**. Antagonists play two important roles in muscle function: (1) They maintain body or limb position, such as holding the arm out or standing erect, and (2) they control rapid movement, as in shadow boxing without landing a punch or the ability to check the motion of a limb.

For example, to extend the knee, a group of four muscles called the quadriceps femoris in the anterior compartment of the thigh are activated (and would be called the agonists of knee extension). However, to flex the knee joint, an opposite or antagonistic set of muscles called the hamstrings is activated.

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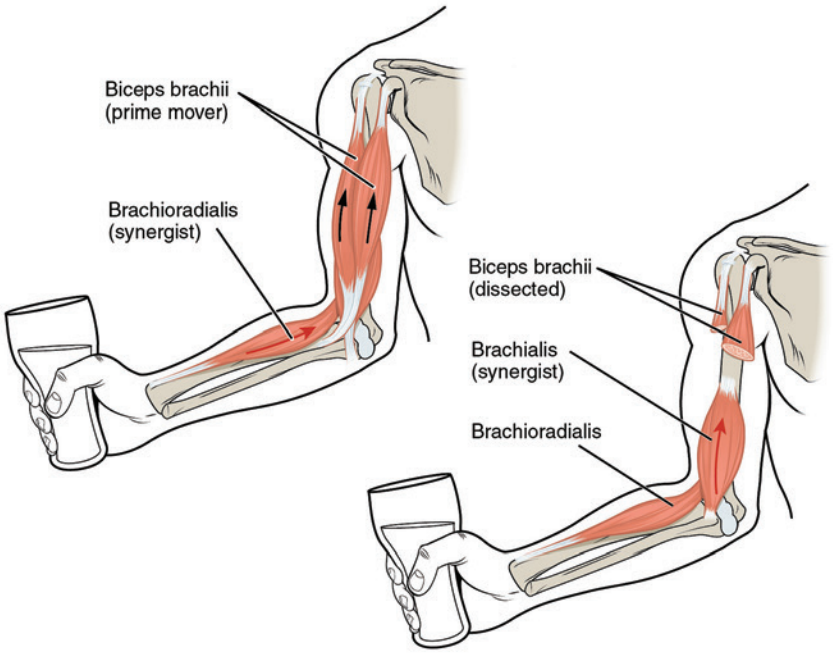


Figure 11.1 Prime Movers and Synergists. The biceps brachii flex the lower arm. The brachoradialis, in the forearm, and the brachialis, located deep to the biceps in the upper arm, are both synergists that aid in this motion.

As you can see, these terms would also be reversed for the opposing action. If you consider the first action as the knee bending, the hamstrings would be called the agonists, and the quadriceps femoris would then be called the antagonists.

There are also skeletal muscles that do not pull against the skeleton for movements. For example, there are the muscles that produce facial expressions. The insertions and origins of facial muscles are in the skin, so that certain individual muscles contract to form a smile or frown, form sounds or words, and raise the eyebrows. There are also skeletal muscles in the tongue, and the external urinary and anal sphincters that allow for voluntary regulation of urination and defecation, respectively. In addition, the diaphragm contracts and relaxes to change the volume of the pleural cavities, but it does not move the skeleton to do this.

Patterns of Fascicle Organization

Skeletal muscle is enclosed in connective tissue scaffolding at three levels. Each muscle fibre (cell) is covered by endomysium, and the entire muscle is covered by epimysium. When a group of muscle fibres is "bundled" as a unit within the whole muscle by an additional covering of a connective tissue called perimysium,

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that bundled group of muscle fibres is called a **fascicle**. Fascicle arrangement by perimysia is correlated to the force generated by a muscle; it also affects the range of motion of the muscle. Based on the patterns of fascicle arrangement, skeletal muscles can be classified in several ways. What follows are the most common fascicle arrangements.

Parallel muscles have fascicles that are arranged in the same direction as the long axis of the muscle (Figure 11.2). The majority of skeletal muscles in the body have this type of organization. Some parallel muscles are flat sheets that expand at the ends to make broad attachments. Other parallel muscles are rotund, with tendons at one or both ends. Muscles that seem to be plump have a large mass of tissue located in the middle of the muscle, between the insertion and the origin, which is known as the central body. A more common name for this muscle is the **belly**. When a muscle contracts, the contractile fibres shorten it to an even larger bulge. When a parallel muscle has a central, large belly that is spindle-shaped, meaning it tapers as it extends to its origin and insertion, it is sometimes called **fusiform**.

Circular muscles are also called sphincters (see Figure 11.2). When they relax, the sphincters' concentrically arranged bundles of muscle fibres increase the size of the opening, and when they contract, the size of the opening shrinks to the point of closure. The orbicularis oris muscle is a circular muscle that surrounds the mouth. When it contracts, the oral opening becomes smaller, as when puckering the lips for whistling. Another example is the orbicularis oculi, one of which surrounds each eye. Consider, for example, the names of the two orbicularis muscles (orbicularis oris and orbicularis oculi), where part of the first name of both muscles is the same. The first part of the word *orbicularis*, *orb* (*orb* = "circular"), is a reference to a round or circular structure; it may also make one think of orbit, such as the moon's path around the earth. The word *oris* (*oris* = "oral") refers to the oral cavity, or the mouth. The word *oculi* (*ocular* = "eye") refers to the eye.

There are other muscles throughout the body named by their shape or location. The deltoid is a large, triangular muscle that covers the shoulder. It is so named because the Greek letter delta looks like a triangle. The rectus abdominis (*rector* = "straight") is the straight muscle in the anterior wall of the abdomen, while the rectus femoris is the straight muscle in the anterior compartment of the thigh.

When a muscle has a widespread expansion over a sizable area, but then the fascicles come to a single, common attachment point, the muscle is called **convergent**. The attachment point for a convergent muscle could be a tendon, an aponeurosis (a flat, broad tendon), or a raphe (a very slender tendon). The large muscle on the chest, the pectoralis major, is an example of a convergent

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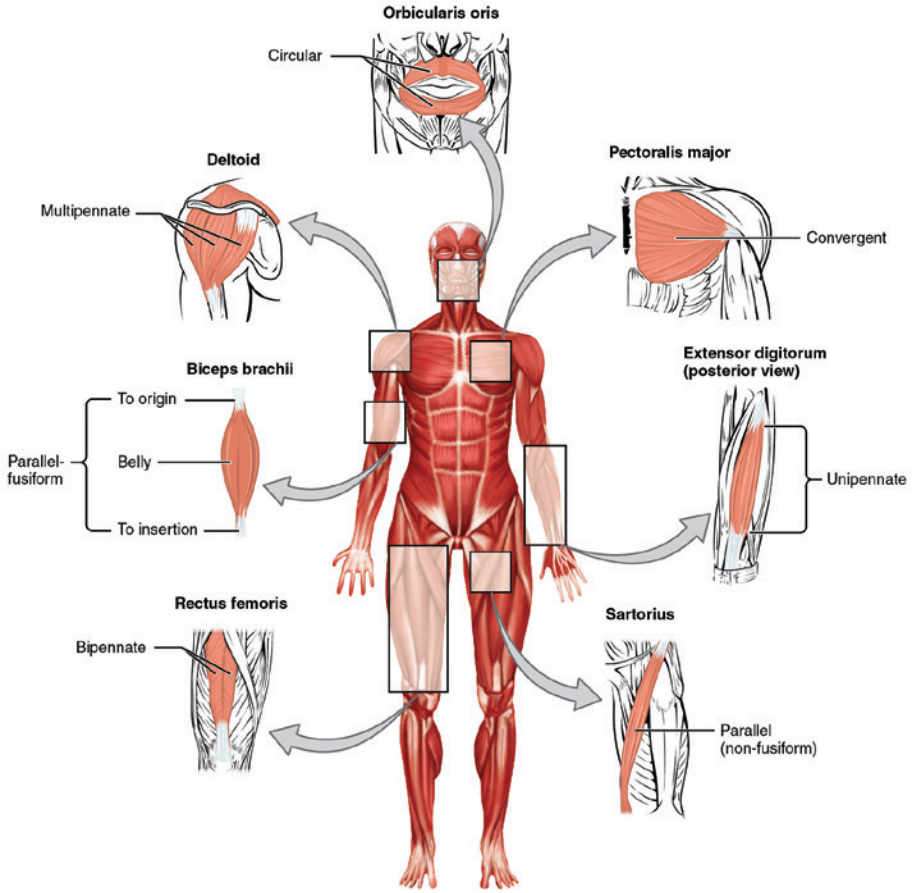


Figure 11.2 Muscle Shapes and Fibre Alignment. The skeletal muscles of the body typically come in seven different general shapes.

muscle because it converges on the greater tubercle of the humerus via a tendon. The temporalis muscle of the cranium is another.

Pennate muscles (*penna* = "feathers") blend into a tendon that runs through the central region of the muscle for its whole length, somewhat like the quill of a feather, with the muscle arranged similarly to the vane of the feather. Due to this design, the muscle fibres in a pennate muscle can only pull at an angle, and as a result, contracting pennate muscles do not move their tendons very far. However, because a pennate muscle generally can hold more muscle fibres within it, it can produce relatively more tension for its size. There are three subtypes of pennate muscles.

In a **unipennate** muscle, the fascicles are located on one side of the tendon. The extensor digitorum of the forearm is an example of a unipennate muscle. A **bipennate** muscle has fascicles on both sides of the tendon. In some pennate muscles, the muscle fibres wrap around the tendon, sometimes

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forming individual fascicles in the process. This arrangement is referred to as **multipennate**. A common example is the deltoid muscle of the shoulder, which covers the shoulder but has a single tendon that inserts on the deltoid tuberosity of the humerus.

Because of fascicles, a portion of a multipennate muscle like the deltoid can be stimulated by the nervous system to change the direction of the pull. For example, when the deltoid muscle contracts, the arm abducts (moves away from midline in the sagittal plane), but when only the anterior fascicle is stimulated, the arm will abduct and flex (move anteriorly at the shoulder joint).

The Lever System of Muscle and Bone Interactions

Skeletal muscles do not work by themselves. Muscles are arranged in pairs based on their functions. For muscles attached to the bones of the skeleton, the connection determines the force, speed, and range of movement. These characteristics depend on each other and can explain the general organization of the muscular and skeletal systems.

The skeleton and muscles act together to move the body. Have you ever used the back of a hammer to remove a nail from wood? The handle acts as a lever, and the head of the hammer acts as a **fulcrum**, the fixed point that the force is applied to when you pull back or push down on the handle. The **effort** applied to this system is the pulling or pushing on the handle to remove the nail, which is the **load**, or "resistance" to the movement of the handle in the system. Our musculoskeletal system works in a similar manner, with bones being stiff levers and the articular endings of the bones—encased in synovial joints—acting as fulcrums. The load would be an object being lifted or any resistance to a movement (your head is a load when you are lifting it), and the effort, or applied force, comes from contracting skeletal muscle.

11.2 Naming Skeletal Muscles

Learning Objectives

By the end of this section, you will be able to:

- Describe the criteria used to name skeletal muscles
- Explain how understanding the muscle names helps describe shapes, locations, and actions of various muscles

The large number of muscles in the body and unfamiliar words can make learning the names of the muscles in the body seem daunting, but understanding the

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etymology can help. Etymology is the study of how the root of a particular word entered a language and how the use of the word evolved over time. Taking the time to learn the roots of words is crucial to understanding the vocabulary of anatomy and physiology. When you understand the names of muscles, it will help you remember where the muscles are located and what they do (Table 11.1, Figure 11.3, and Table 11.2).

Pronunciation of words and terms will take a bit of time to master, but after you have some basic information, the correct names and pronunciations will become easier.

Table 11.1 Understanding a Muscle Name from the Latin

Example	Word	Latin root 1	Latin root 2	Meaning	Translation
abductor digiti minimi	abductor	*ab* = away from	*duct* = to move	a muscle that moves away from	A muscle that moves the little finger or toe away
	digiti	*digitus* = digit		refers to a finger or toe	
	minimi			little	
adductor digiti minimi	adductor	*ad* = toward	*duct* = to move	a muscle that moves toward	A muscle that moves the little finger or toe toward
	digiti	*digitus* = digit		refers to a finger or toe	
	minimi	*minimus* = mini, tiny		little	

Anatomists name the skeletal muscles according to a number of criteria, each of which describes the muscle in some way. These include naming the muscle after its shape, its size compared to other muscles in the area, its location in the body or the location of its attachments to the skeleton, how many origins it has, or its action.

The skeletal muscle's anatomical location or its relationship to a particular bone often determines its name. For example, the frontalis muscle is located on top of the frontal bone of the skull. Similarly, the shapes of some muscles are very distinctive, and the names, such as orbicularis, reflect the shape. For the buttocks, the size of the muscles influences the names: gluteus **maximus** (largest), gluteus **medius** (medium), and gluteus **minimus** (smallest). Names were given to indicate length—**brevis** (short), **longus** (long)—and to

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Table 11.2 Mnemonic Devices for Latin Roots

Example	Latin or Greek translation	Mnemonic device
ad	to; toward	ADvance toward your goal.
ab	away from	n/a
sub	under	SUBmarines move underwater.
ductor	something that moves	A conDUCTOR makes a train move.
anti	against	If you are ANTIsocial, you are against engaging in social activities.
epi	on top of	n/a
apo	to the side of	n/a
longissimus	longest	*Longissimus* is longer than the word *long*.
longus	long	long
brevis	short	brief
maximus	large	max
medius	medium	"Medius" and "medium" both begin with "med."
minimus	tiny; little	mini
rectus	straight	To RECTify a situation is to straighten it out.
multi	many	If something is MULTIcoloured, it has many colours.
uni	one	A UNIcorn has one horn.
bi/di	two	If a ring is DIcast, it is made of two metals.
tri	three	TRIple the amount of money is three times as much.
quad	four	QUADruplets are four children born at one birth.
externus	outside	EXternal
internus	inside	INternal

identify position relative to the midline: **lateralis** (to the outside away from the midline) and **medialis** (toward the midline). The direction of the muscle fibres and fascicles is used to describe muscles relative to the midline, such as the **rectus** (straight) abdominis or the **oblique** (at an angle) muscles of the abdomen.

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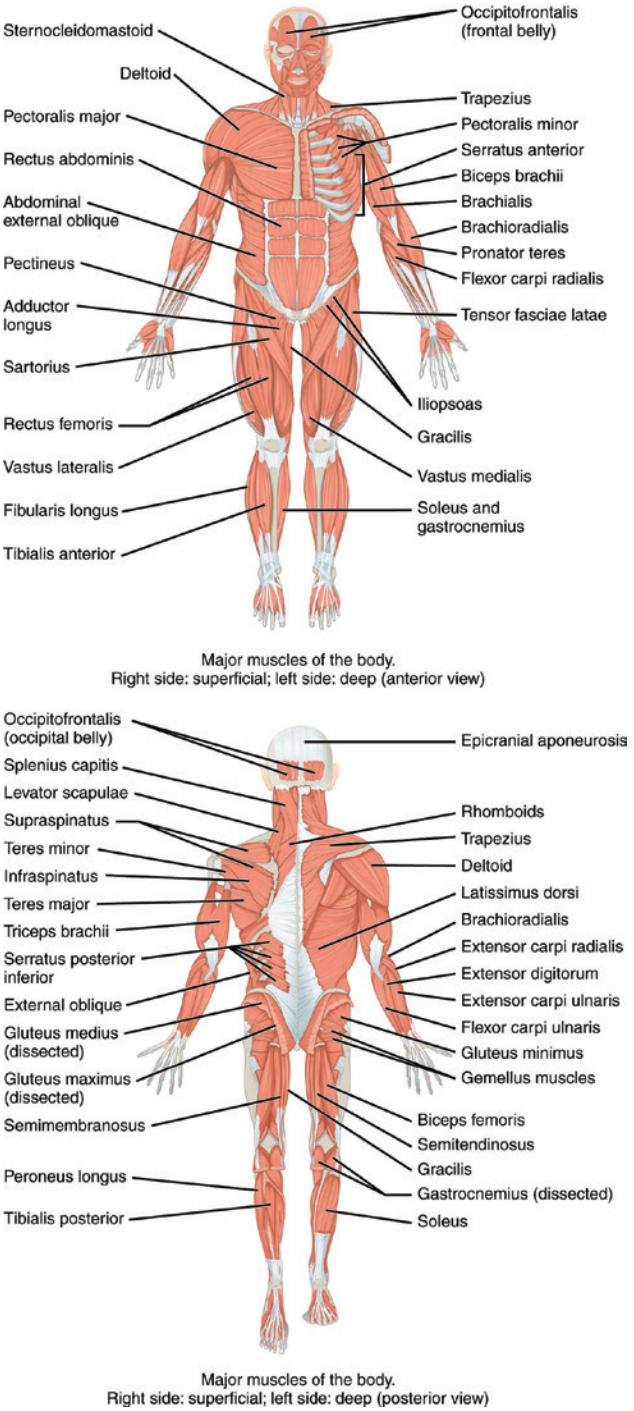


Figure 11.3 Overview of the Muscular System. On the anterior and posterior views of the muscular system, superficial muscles (those at the surface) are shown on the right side of the body, while deep muscles (those underneath the superficial muscles) are shown on the left half of the body. For the legs, superficial muscles are shown in the anterior view, while the posterior view shows both superficial and deep muscles.

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Some muscle names indicate the number of muscles in a group. One example of this is the quadriceps, a group of four muscles located on the anterior (front) thigh. Other muscle names can provide information as to how many origins a particular muscle has, such as the biceps brachii. The prefix **bi** indicates that the muscle has two origins, and **tri** indicates three origins.

The location of a muscle's attachment can also appear in its name. When the name of a muscle is based on the attachments, the **origin** is always named first. For instance, the sternocleidomastoid muscle of the neck has a dual origin on the sternum (sterno) and clavicle (cleido), and it inserts on the mastoid process of the temporal bone. The last feature by which to name a muscle is its action. When muscles are named for the movement they produce, one can find action words in their name. Some examples are **flexor** (decreases the angle at the joint), **extensor** (increases the angle at the joint), **abductor** (moves the bone away from the midline), and **adductor** (moves the bone toward the midline).

11.3 Axial Muscles of the Head, Neck, and Back

Learning Objectives

By the end of this section, you will be able to:

- Identify the axial muscles of the face, head, and neck
- Identify the movement and function of the face, head, and neck muscles

The skeletal muscles are divided into **axial** (muscles of the trunk and head) and **appendicular** (muscles of the arms and legs) categories. This system reflects the bones of the skeletal system, which are also arranged in this manner. The axial muscles are grouped based on location, function, or both. Some of the axial muscles may seem to blur the boundaries because they cross over to the appendicular skeleton. The first grouping of the axial muscles you will review includes the muscles of the head and neck, then you will review the muscles of the vertebral column, and finally, you will review the oblique and rectus muscles.

Muscles That Create Facial Expression

The origins of the muscles of facial expression are on the surface of the skull (remember, the origin of a muscle does not move). The insertions of these muscles have fibres intertwined with connective tissue and the dermis of the skin. Because the muscles insert in the skin rather than on bone, when they contract, the skin moves to create facial expression (Figure 11.4).

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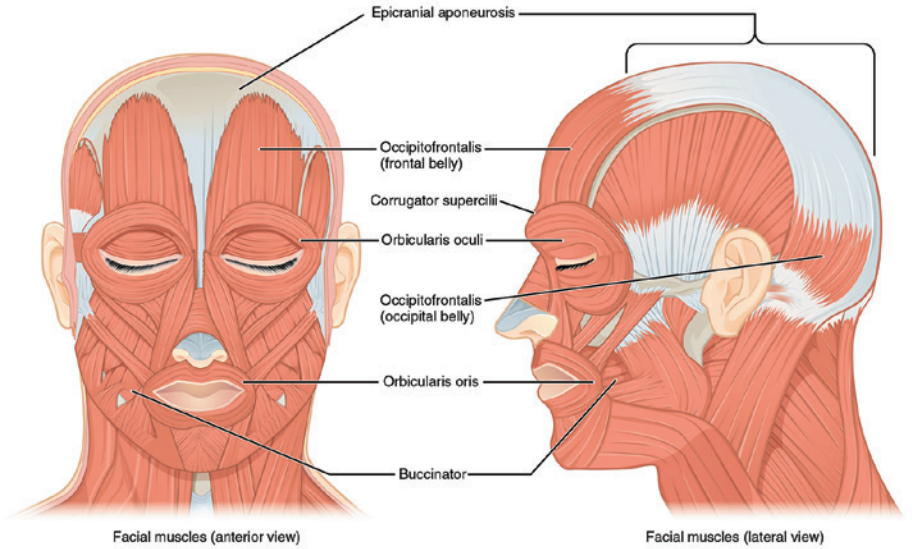


Figure 11.4 Muscles of Facial Expression. Many of the muscles of facial expression insert into the skin surrounding the eyelids, nose, and mouth, producing facial expressions by moving the skin rather than bones.

The **orbicularis oris** is a circular muscle that moves the lips, and the **orbicularis oculi** is a circular muscle that closes the eye. The **occipitofrontalis** muscle moves up the scalp and eyebrows. The muscle has a frontal belly and an occipital (near the occipital bone on the posterior part of the skull) belly. In other words, there is a muscle on the forehead (**frontalis**) and one on the back of the head (**occipitalis**), but there is no muscle across the top of the head.

A large portion of the face is composed of the **buccinator** muscle, which compresses the cheek. This muscle allows you to whistle, blow, and suck, and it contributes to the action of chewing.

Muscles That Move the Lower Jaw

In anatomical terminology, chewing is called **mastication**. Muscles involved in chewing must be able to exert enough pressure to bite through and then chew food before it is swallowed (Figure 11.5). The **masseter** muscle is the main muscle used for chewing because it elevates the mandible (lower jaw) to close the mouth. The origins of the masseter are the maxilla and zygomatic arch. Its insertion is at the angle and ramus of the mandible. It is assisted by the **temporalis** muscle, which retracts the mandible. The origin of the temporalis is the temporal bone, and its insertion is at the coronoid process and ramus of the mandible. Although the masseter and temporalis are responsible for elevating and closing the jaw to break food into digestible pieces, the medial and lateral pterygoid muscles provide the side-to-side and forward movements necessary for grinding and thoroughly chewing the food.

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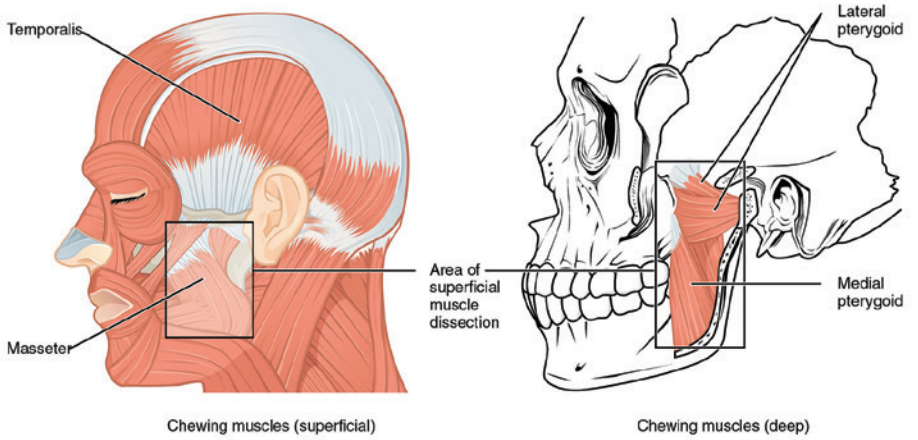


Figure 11.5 Muscles That Move the Lower Jaw. The muscles that move the lower jaw are typically located within the cheek and originate from processes in the skull. This provides the jaw muscles with the large amount of leverage needed for chewing.

Muscles of the Anterior Neck

The muscles of the anterior neck assist in **deglutition** (swallowing) and speech by controlling the positions of the larynx (voice box), and the hyoid bone, a horseshoe-shaped bone that functions as a solid foundation on which the tongue can move. The muscles of the neck are categorized according to their position relative to the hyoid bone (Figure 11.6). **Suprahyoid muscles** are superior to it, and the **infrahyoid muscles** are located inferiorly.

The suprahyoid muscles raise the hyoid bone, the floor of the mouth, and the larynx during deglutition. These include the **digastric** muscle, which has anterior and posterior bellies that work to elevate the hyoid bone and larynx when one swallows; it also depresses the mandible.

Muscles That Move the Head

The head, attached to the top of the vertebral column, is balanced, moved, and rotated by the neck muscles. When these muscles act unilaterally, the head rotates. When they contract bilaterally, the head flexes or extends. The major muscle that laterally flexes and rotates the head is the **sternocleidomastoid**. In addition, both muscles working together are the flexors of the head. This muscle divides the neck into anterior and posterior triangles when viewed from the side. The origin of the sternal head is the manubrium of the sternum. The origin of the clavicular head is the medial third of the clavicle. Their insertion is at the mastoid process of the temporal bone and the lateral half of the superior nuchal line of the occipital bone (Figure 11.7).

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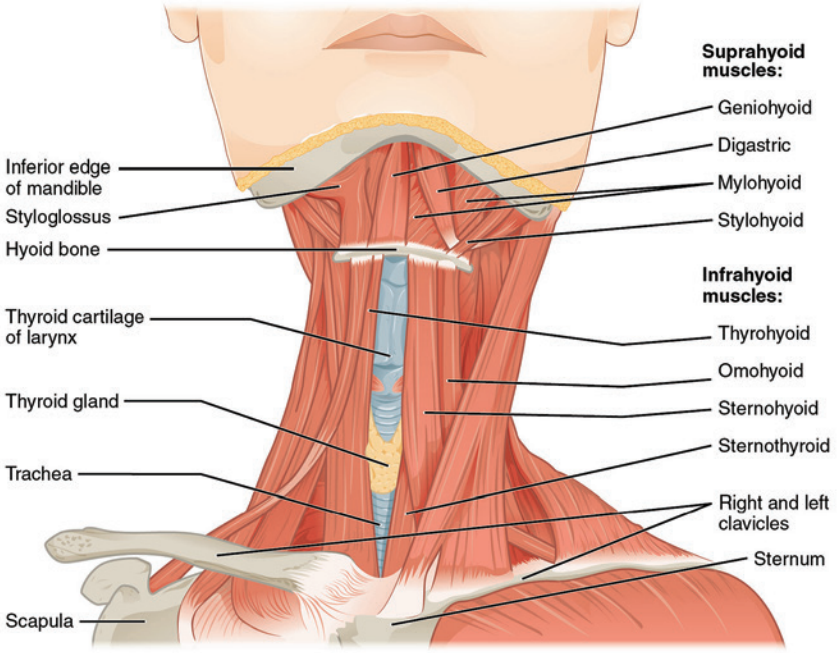


Figure 11.6 Muscles of the Anterior Neck. The anterior muscles of the neck facilitate swallowing and speech. The suprahyoid muscles originate from above the hyoid bone in the chin region. The infrahyoid muscles originate below the hyoid bone in the lower neck.

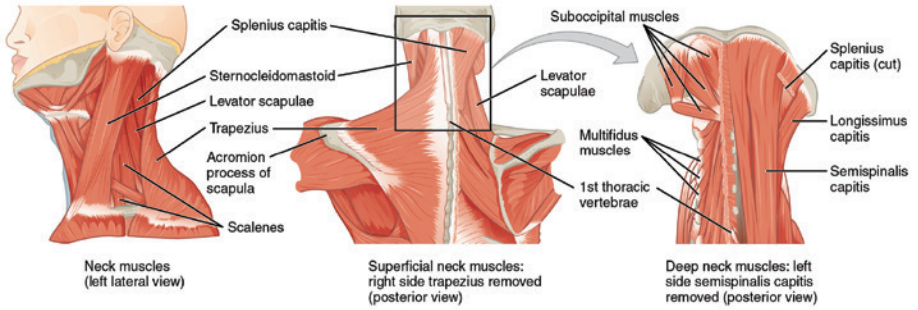


Figure 11.7 Posterior and Lateral Views of the Neck. The superficial and deep muscles of the neck are responsible for moving the head, cervical vertebrae, and scapulae.

Muscles of the Posterior Neck and the Back

The posterior muscles of the neck are primarily concerned with head movements, like extension. The back muscles stabilize and move the vertebral column and are grouped according to the lengths and direction of the fascicles.

The **splenius** muscles originate at the midline and run laterally and superiorly to their insertions. These muscles can extend the head, laterally flex it, and rotate it (Figure 11.8).

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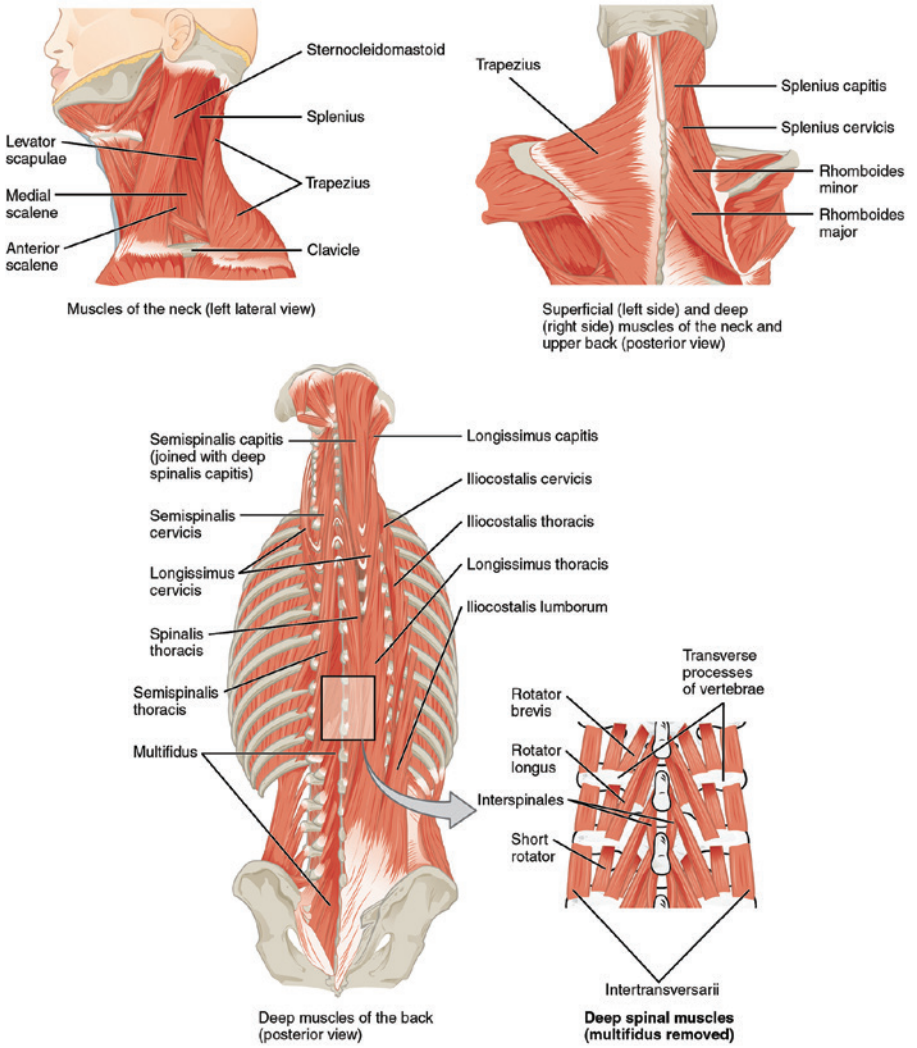


Figure 11.8 Muscles of the Neck and Back. The large, complex muscles of the neck and back move the head, shoulders, and vertebral column.

The **erector spinae group** forms the majority of the muscle mass of the back, and it is the primary extensor of the vertebral column. It controls flexion, lateral flexion, and rotation of the vertebral column and maintains the lumbar curve. The erector spinae comprises the iliocostalis (laterally placed) group, the longissimus (intermediately placed) group, and the spinalis (medially placed) group.

The **iliocostalis group** includes the **iliocostalis cervicis**, associated with the cervical region; the **iliocostalis thoracis**, associated with the thoracic region; and the **iliocostalis lumborum**, associated with the lumbar region. The **scalene muscles** work together to flex, laterally flex, and rotate the head. They also contribute to deep inhalation.

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11.4 Axial Muscles of the Abdominal Wall and Thorax

Learning Objectives

By the end of this section, you will be able to:

- Identify the intrinsic skeletal muscles of the back and neck, and the skeletal muscles of the abdominal wall and thorax
- Identify the movement and function of the intrinsic skeletal muscles of the back and neck, and the skeletal muscles of the abdominal wall and thorax

It is a complex job to balance the body on two feet and walk upright. The muscles of the vertebral column, thorax, and abdominal wall extend, flex, and stabilize different parts of the body's trunk. The deep muscles of the core of the body help maintain posture as well as carry out other functions. The brain sends out electrical impulses to these various muscle groups to control posture by alternate contraction and relaxation. This is necessary so that no single muscle group becomes fatigued too quickly. If any one group fails to function, body posture will be compromised.

Muscles of the Abdomen

There are four pairs of abdominal muscles that cover the anterior and lateral abdominal region and meet at the anterior midline. These muscles of the anterolateral abdominal wall can be divided into four groups: the external obliques, the internal obliques, the transversus abdominis, and the rectus abdominis (Figure 11.9).

There are three flat skeletal muscles in the anterolateral wall of the abdomen. The **external oblique**, closest to the surface, extends inferiorly and medially, in the direction of sliding one's four fingers into pants pockets. Perpendicular to it is the intermediate **internal oblique**, extending superiorly and medially, the direction the thumbs usually go when the other fingers are in the pants pocket. The deep muscle, the **transversus abdominis**, is arranged transversely around the abdomen, similar to the front of a belt on a pair of pants. This arrangement of three bands of muscles in different orientations allows various movements and rotations of the trunk. The three layers of muscle also help protect the internal abdominal organs in an area where there is no bone.

The **linea alba** is a white, fibrous band that is made of the bilateral **rectus sheaths** that join at the anterior midline of the body. These enclose the

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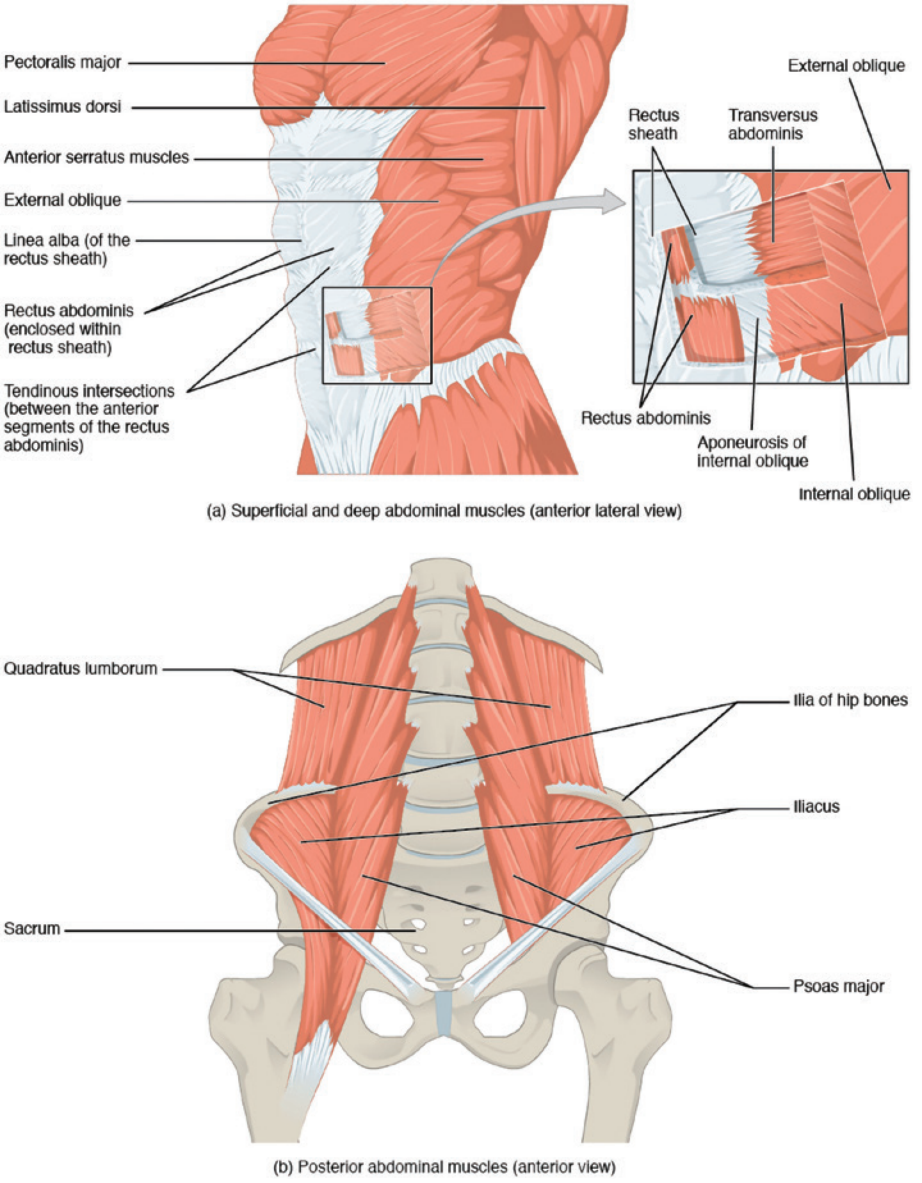


Figure 11.9 Muscles of the Abdomen. (a) The anterior abdominal muscles include the medially located rectus abdominis, which is covered by a sheet of connective tissue called the rectus sheath. On the flanks of the body, medial to the rectus abdominis, the abdominal wall is composed of three layers. The external oblique muscles form the superficial layer, while the internal oblique muscles form the middle layer, and the transversus abdominis forms the deepest layer. (b) The muscles of the lower back move the lumbar spine but also assist in femur movements.

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rectus abdominis muscles (a pair of long, linear muscles, commonly called the "sit-up" muscles). The rectus abdominis originates at the pubic crest and the symphysis and inserts on the cartilage of ribs 5–7 and the xiphoid process. It extends the length of the body's trunk. The rectus abdominis flexes the vertebral column, especially the lumbar portion, and compresses the abdomen to aid in defecation, urination, forced exhalation, and childbirth; it flexes the pelvis on the vertebral column.

Muscles of the Thorax

The muscles of the chest serve to facilitate breathing by changing the size of the thoracic cavity. When you inhale, your chest rises because the cavity expands. Alternatively, when you exhale, your chest falls because the thoracic cavity decreases in size.

The Diaphragm

The change in volume of the thoracic cavity during breathing is due to the alternate contraction and relaxation of the **diaphragm** (Figure 11.10). It separates the thoracic and abdominal cavities and is dome-shaped at rest. The superior surface of the diaphragm is convex, creating the elevated floor of

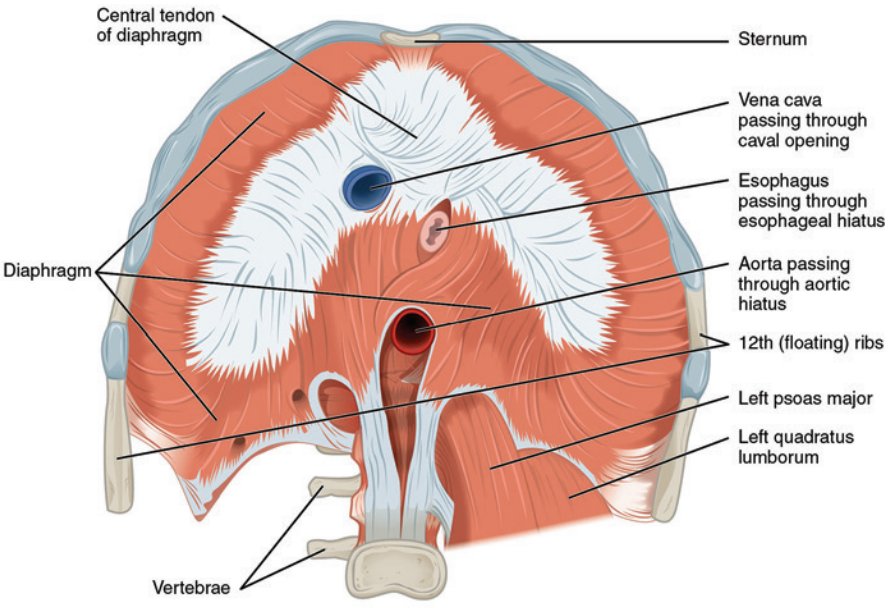


Figure 11.10 Muscles of the Diaphragm. The diaphragm separates the thoracic and abdominal cavities.

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the thoracic cavity. The inferior surface is concave, creating the curved roof of the abdominal cavity.

Defecating, urination, and even childbirth involve cooperation between the diaphragm and abdominal muscles (this cooperation is referred to as the "Valsalva manoeuvre"). You hold your breath by a steady contraction of the diaphragm; this stabilizes the volume and pressure of the peritoneal cavity. When the abdominal muscles contract, the pressure cannot push the diaphragm up, so it increases pressure on the intestinal tract (defecation), urinary tract (urination), or reproductive tract (childbirth).

The inferior surface of the pericardial sac and the inferior surfaces of the pleural membranes (parietal pleura) fuse onto the central tendon of the diaphragm. To the sides of the tendon are the skeletal muscle portions of the diaphragm, which insert into the tendon while having a number of origins, including the xiphoid process of the sternum anteriorly, the inferior six ribs and their cartilages laterally, and the lumbar vertebrae and 12th ribs posteriorly.

The Intercostal Muscles

There are three sets of muscles, called **intercostal muscles**, that span each of the intercostal spaces. The principal role of the intercostal muscles is to assist in breathing by changing the dimensions of the rib cage (Figure 11.11).

The 11 pairs of superficial **external intercostal** muscles aid in inspiration of air during breathing because when they contract, they raise the rib cage,

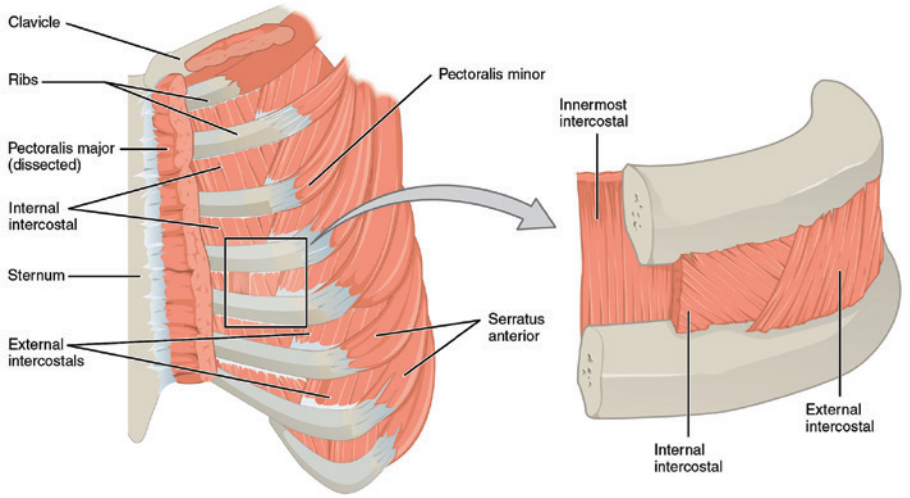


Figure 11.11 Intercostal Muscles. The external intercostals are located laterally on the sides of the body. The internal intercostals are located medially near the sternum. The innermost intercostals are located deep to both the internal and external intercostals.

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which expands it. The 11 pairs of **internal intercostal** muscles, just under the externals, are used for expiration because they draw the ribs together to constrict the rib cage. The **innermost intercostal** muscles are the deepest, and they act as synergists for the action of the internal intercostals.

11.5 Muscles of the Pectoral Girdle and Upper Limbs

Learning Objectives

By the end of this section, you will be able to:

- Identify the muscles of the pectoral girdle and upper limbs
- Identify the movement and function of the pectoral girdle and upper limbs

Muscles of the shoulder and upper limb can be divided into four groups: muscles that stabilize and position the pectoral girdle, muscles that move the arm, muscles that move the forearm, and muscles that move the wrists, hands, and fingers. The **pectoral girdle**, or shoulder girdle, consists of the lateral ends of the clavicle and scapula, along with the proximal end of the humerus, and the muscles covering these three bones to stabilize the shoulder joint. The girdle creates a base from which the head of the humerus, in its ball-and-socket joint with the glenoid fossa of the scapula, can move the arm in multiple directions.

Muscles That Position the Pectoral Girdle

Muscles that position the pectoral girdle are located either on the anterior thorax or on the posterior thorax (Figure 11.12). The anterior muscles include the **subclavius**, **pectoralis minor**, and **serratus anterior**. The posterior muscles include the **trapezius**, **rhomboid major**, and **rhomboid minor**. When the rhomboids are contracted, your scapula moves medially, which can pull the shoulder and upper limb posteriorly. The origin of the trapezius is the superior nuchal line of the occipital bone, the ligamentum nuchae, and the spines of C7–T12; it inserts on the clavicle, the acromion, and the spine of the scapula. The rhomboid major originates at the spines of T2–T5, and its insertion is at the vertebral border of the scapula inferior to the spine.

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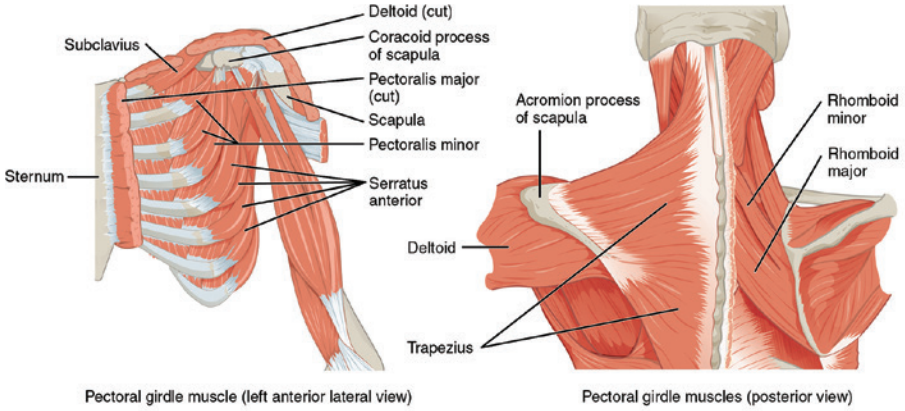


Figure 11.12 Muscles That Position the Pectoral Girdle. The muscles that stabilize the pectoral girdle make it a steady base upon which other muscles can move the arm. Note that the pectoralis major and deltoid, which move the humerus, are cut here to show the deeper positioning muscles.

Muscles That Move the Humerus

Similar to the muscles that position the pectoral girdle, muscles that cross the shoulder joint and move the humerus bone of the arm include both axial and scapular muscles (Figure 11.13). The two axial muscles are the pectoralis major and the latissimus dorsi. The **pectoralis major** is thick and fan-shaped, covering much of the superior portion of the anterior thorax. Its origins are the clavicle (clavicular head), sternum, and costal cartilages of ribs 2–6 and sometimes also of ribs 1–7 (sternocostal head). The insertion of the pectoralis major is the greater tubercle and lateral lip of intertubercular sulcus of humerus. The broad, triangular **latissimus dorsi** is located on the inferior part of the back, where it inserts into a thick connective tissue sheath called an aponeurosis.

The rest of the shoulder muscles originate on the scapula. The anatomical and ligamental structure of the shoulder joint and the arrangements of the muscles covering it allow the arm to carry out different types of movements. The **deltoid**, the thick muscle that creates the rounded lines of the shoulder, is the major abductor of the arm, but it also facilitates flexing and medial rotation, as well as extension and lateral rotation. The origin of the deltoid is the acromial extremity of the clavicle, the acromion of the scapula, and the spine of the scapula. It inserts on the deltoid tuberosity of the humerus. The **subscapularis** originates on the anterior scapula and medially rotates the arm. Named for their locations, the **supraspinatus** (superior to the spine of the scapula) and the **infraspinatus** (inferior to the spine of the scapula) abduct the arm and laterally rotate the arm, respectively. The supraspinatus originates from the supraspinous fossa of the scapula and inserts at the greater tubercle of the humerus. The

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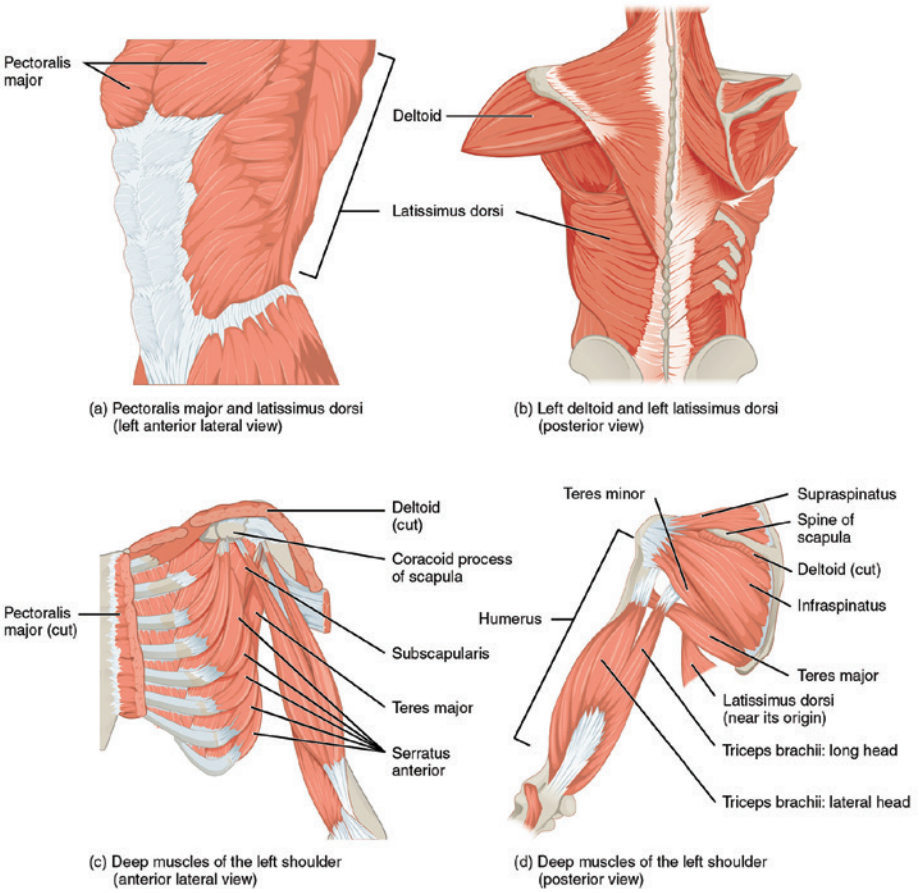


Figure 11.13 Muscles That Move the Humerus. (a, c) The muscles that move the humerus anteriorly are generally located on the anterior side of the body and originate from the sternum (e.g., pectoralis major) or the anterior side of the scapula (e.g., subscapularis). (b) The muscles that move the humerus superiorly generally originate from the superior surfaces of the scapula and/or the clavicle (e.g., deltoids). The muscles that move the humerus inferiorly generally originate from the middle or lower back (e.g., latissimus dorsi). (d) The muscles that move the humerus posteriorly are generally located on the posterior side of the body and insert into the scapula (e.g., infraspinatus).

thick and flat **teres major** is inferior to the teres minor, extends the arm, and assists in adduction and medial rotation. The long **teres minor** laterally rotates and extends the arm.

The tendons of the deep subscapularis, supraspinatus, infraspinatus, and teres minor connect the scapula to the humerus, forming the **rotator cuff** (musculotendinous cuff), the circle of tendons around the shoulder joint. When baseball pitchers undergo shoulder surgery, it is usually on the rotator cuff, which becomes pinched and inflamed, and may tear away from the bone due to the repetitive motion of bringing the arm overhead to throw a fast pitch.

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Muscles That Move the Forearm

The forearm, made of the radius and ulna bones, has four main types of action at the hinge of the elbow joint: flexion, extension, pronation, and supination. The forearm flexors include the biceps brachii, brachialis, and brachioradialis. The extensors are the **triceps brachii** and **anconeus**. The triceps brachii originates at the glenoid cavity of the scapula, the lateral surface of the humerus, and the posterior surface of the humerus. It inserts at the olecranon of the ulna. The forearm pronators are the **pronator teres** and the **pronator quadratus**, and the **supinator** is the only one that turns the forearm anteriorly. When the forearm faces anteriorly, it is supinated. When the forearm faces posteriorly, it is pronated.

The biceps brachii, brachialis, and brachioradialis flex the forearm. The two-headed **biceps brachii** crosses the shoulder and elbow joints to flex the forearm, also taking part in supinating the forearm at the radioulnar joints and flexing the arm at the shoulder joint. Its long head originates from the tubercle above the glenoid cavity of the scapula, and its short head originates from the coracoid process of the scapula. The insertion of the biceps brachii is at the radial tuberosity of the radius and the bicipital aponeurosis. Deep to the biceps brachii, the **brachialis** provides additional power in flexing the forearm. Finally, the **brachioradialis** can flex the forearm quickly or help lift a load slowly (Figure 11.14).

Muscles That Move the Wrist, Hand, and Fingers

Wrist, hand, and finger movements are facilitated by two groups of muscles. The forearm is the origin of the **extrinsic muscles of the hand**. The palm is the origin of the intrinsic muscles of the hand.

Muscles of the Arm That Move the Wrists, Hands, and Fingers

The muscles in the anterior compartment of the forearm originate on the humerus and insert onto different parts of the hand (Figure 11.14). These make up the bulk of the forearm. From lateral to medial, the superficial anterior compartment of the forearm includes the **flexor carpi radialis**, **palmaris longus**, **flexor carpi ulnaris**, and **flexor digitorum superficialis**. The flexor carpi radialis originates at the medial epicondyle of the humerus, and its insertion is at metacarpals 2 and 3. The flexor digitorum superficialis flexes the hand as well as the digits at the knuckles, which allows for rapid finger movements, as in typing or playing a musical instrument.

The muscles in the superficial posterior compartment of the forearm originate on the humerus. One of these is the **extensor radialis longus**.

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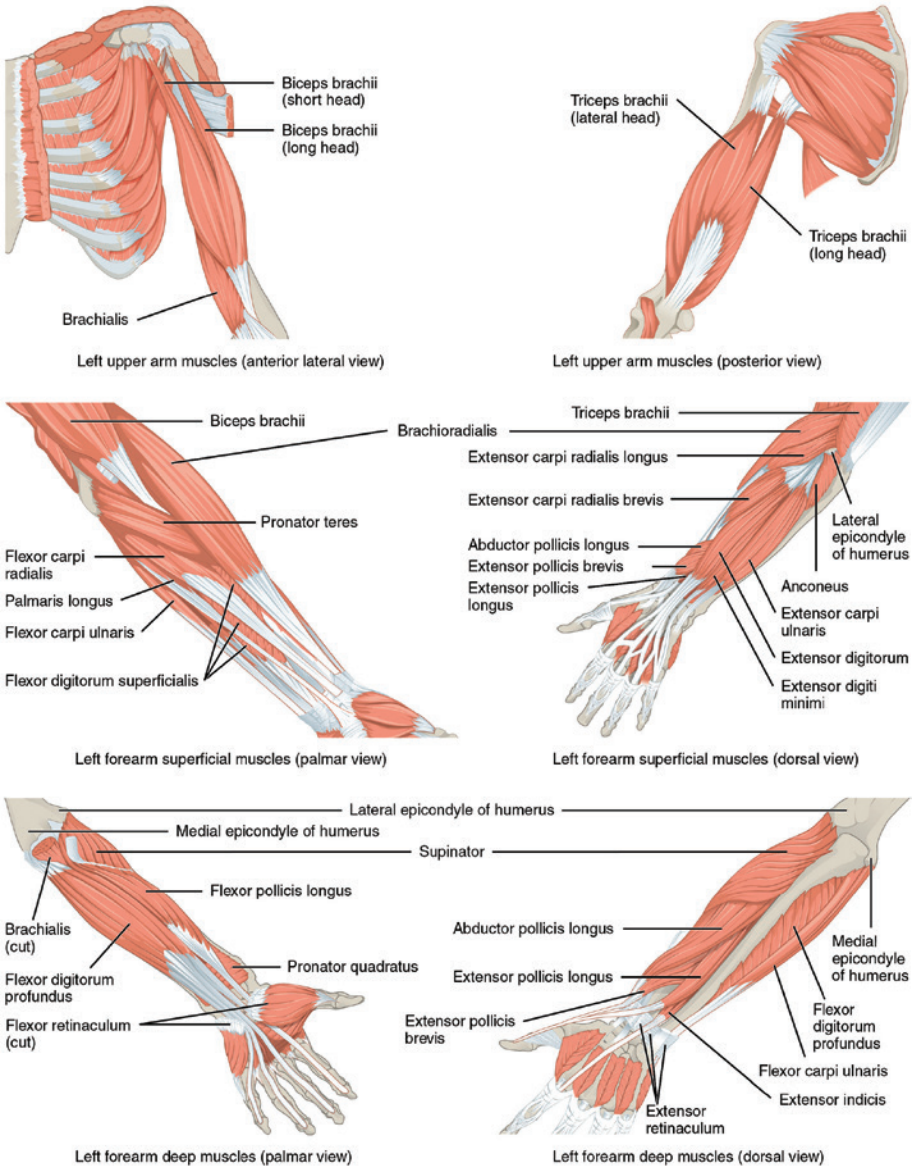


Figure 11.14 Muscles That Move the Forearm. The muscles originating in the upper arm flex, extend, pronate, and supinate the forearm. The muscles originating in the forearm move the wrists, hands, and fingers.

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11.6 Appendicular Muscles of the Pelvic Girdle and Lower Limbs

Learning Objectives

By the end of this section, you will be able to:

- Identify the appendicular muscles of the pelvic girdle and lower limb
- Identify the movement and function of the pelvic girdle and lower limb

The appendicular muscles of the lower body position and stabilize the **pelvic girdle**, which serves as a foundation for the lower limbs. Comparatively, there is much more movement at the pectoral girdle than at the pelvic girdle. There is very little movement of the pelvic girdle because of its connection with the sacrum at the base of the axial skeleton. The pelvic girdle has less range of motion because it was designed to stabilize and support the body.

Muscles of the Thigh

Walking would expend more energy if the heads of the femurs were not secured in the acetabula of the pelvis. The body's centre of gravity is in the area of the pelvis. If the centre of gravity were not to remain fixed, standing up would be difficult as well. Therefore, what the leg muscles lack in range of motion and versatility, they make up for in size and power, facilitating the body's stabilization, posture, and movement.

Gluteal Region Muscles That Move the Femur

Most muscles that insert on the femur (the thigh bone) and move it originate on the pelvic girdle. The **psoas major** and **iliacus** make up the **iliopsoas group**. The origin of the psoas major is the transverse processes and bodies of the lumbar vertebrae. Its insertion is at the lesser trochanter of the femur. Some of the largest and most powerful muscles in the body are the gluteal muscles or **gluteal group**. The **gluteus maximus** is the largest; deep to the gluteus maximus is the **gluteus medius**, and deep to the gluteus medius is the **gluteus minimus**, the smallest of the trio (Figure 11.15). These muscles attach the leg to the hip and help extend the hip joint. The origin of the gluteus medius is the lateral surface of the ilium. Its insertion is at the greater trochanter of the femur.

The **tensor fascia latae** is a thick, squarish muscle in the superior aspect of the lateral thigh. It acts as a synergist of the gluteus medius and the iliopsoas in flexing and abducting the thigh. The **adductor longus**, **adductor brevis**, and

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adductor magnus can rotate the thigh both medially and laterally, depending on the placement of the foot. The adductor longus flexes the thigh, whereas the adductor magnus extends it.

Thigh Muscles That Move the Femur, Tibia, and Fibula

Deep fascia in the thigh separates it into medial, anterior, and posterior compartments (see Figure 11.15). The muscles in the medial compartment of the thigh are responsible for adducting the femur at the hip. Along with the adductor longus, adductor brevis, adductor magnus, and pectineus, the straplike **gracilis** adducts the thigh in addition to flexing the leg at the knee.

The muscles of the anterior compartment of the thigh flex the thigh and extend the leg. This compartment contains the **quadriceps femoris group**, which actually comprises four muscles that extend and stabilize the knee. The **rectus femoris** is on the anterior aspect of the thigh. Its origin is the anterior inferior iliac spine and its insertion at the patella via the quadriceps tendon and then the tibial tuberosity via the patellar ligament. The **vastus lateralis** is on the lateral aspect of the thigh, the **vastus medialis** is on the medial aspect of the thigh, and the **vastus intermedius** is between the vastus lateralis and vastus medialis and deep to the rectus femoris. The tendon common to all four is the **quadriceps tendon** (patellar tendon), which inserts into the patella and continues below it as the **patellar ligament**. The patellar ligament attaches to the tibial tuberosity. In addition to the quadriceps femoris, the **sartorius** is a bandlike muscle that extends from the anterior superior iliac spine to the medial side of the proximal tibia. This versatile muscle flexes the leg at the knee and flexes, abducts, and laterally rotates the leg at the hip. This muscle allows us to sit cross-legged.

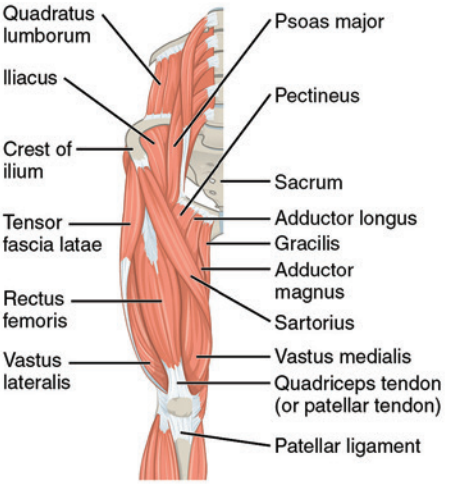
The posterior compartment of the thigh includes muscles that flex the leg and extend the thigh. The three long muscles on the back of the knee are the **hamstring group**, which flexes the knee. These are the **biceps femoris**, **semitendinosus**, and **semimembranosus**. The tendons of these muscles form the **popliteal fossa**, the diamond-shaped space at the back of the knee. The origin of the biceps femoris is the ischial tuberosity and the linea aspera of the femur. Its insertion is at the head of the fibula and the lateral condyle of the tibia.

Muscles That Move the Feet and Toes

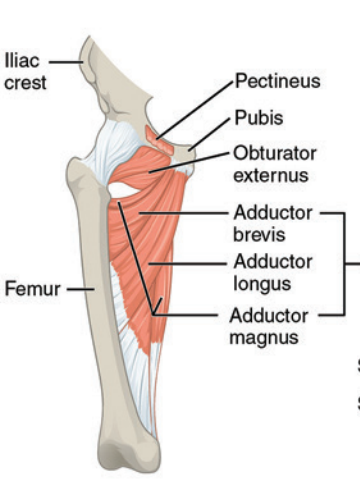
Similar to the thigh muscles, the muscles of the leg are divided by deep fascia into compartments, although the leg has three: anterior, lateral, and posterior (Figure 11.16).

The muscles in the anterior compartment of the leg are the **tibialis anterior**, a long and thick muscle on the lateral surface of the tibia; the **extensor**

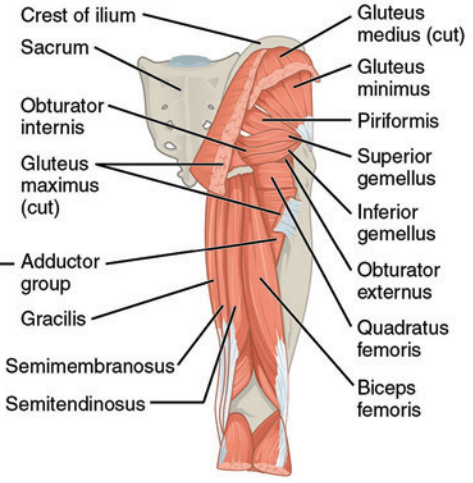
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Superficial pelvic and thigh muscles of right leg (anterior view)



Deep pelvic and thigh muscles of right leg (anterior view)



Pelvic and thigh muscles of right leg (posterior view)

Figure 11.15 Hip and Thigh Muscles. The large and powerful muscles of the hip that move the femur generally originate on the pelvic girdle and insert into the femur. The muscles that move the lower leg typically originate on the femur and insert into the bones of the knee joint. The anterior muscles of the femur extend the lower leg but also aid in flexing the thigh. The posterior muscles of the femur flex the lower leg but also aid in extending the thigh. A combination of gluteal and thigh muscles also adduct, abduct, and rotate the thigh and lower leg.

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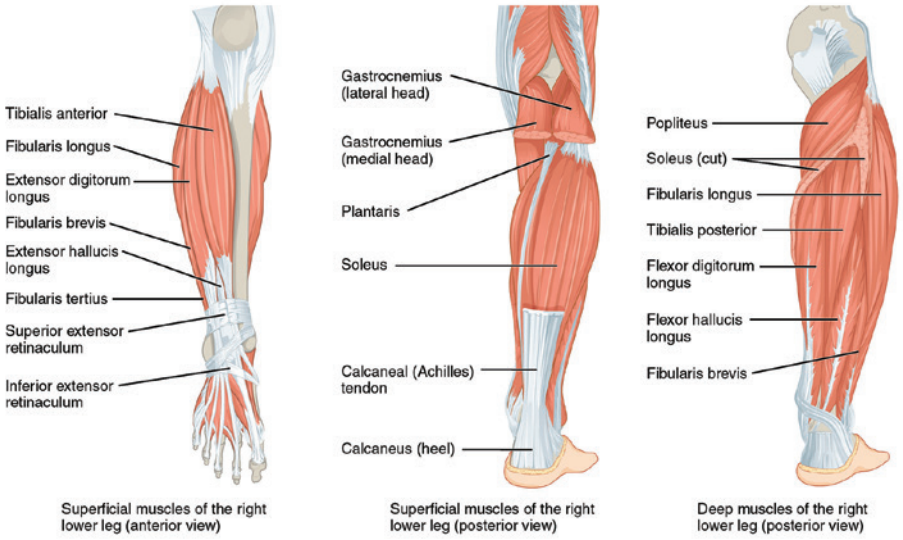


Figure 11.16 Muscles of the Lower Leg. The muscles of the anterior compartment of the lower leg are generally responsible for dorsiflexion, and the muscles of the posterior compartment of the lower leg are generally responsible for plantar flexion. The lateral and medial muscles in both compartments invert, evert, and rotate the foot.

hallucis longus, deep under it; and the **extensor digitorum longus**, lateral to it. These all contribute to raising the front of the foot when they contract. The origin of the tibialis anterior is the lateral condyle and the body of the tibia and interosseous membrane. Its insertion is at the metatarsal I and the tarsal bone. The origin of the extensor digitorum longus is the lateral condyle of the tibia, the anterior surface of the fibula, and the interosseous membrane. Its insertion is at the middle and distal phalanges of toes 2–5.

The lateral compartment of the leg includes two muscles: the **fibularis longus** (peroneus longus) and the **fibularis brevis** (peroneus brevis). The superficial muscles in the posterior compartment of the leg all insert onto the **calcaneal tendon** (Achilles tendon), a strong tendon that inserts into the calcaneal bone of the ankle. The muscles in this compartment are large and strong, and they keep humans upright. The most superficial, largest, and visible muscle of the calf is the **gastrocnemius**. Its origin is the lateral and medial condyles of the femur and the articular capsule of the knee. Its insertion is at the calcaneus by way of the calcaneal tendon. Deep to the gastrocnemius is the wide, flat **soleus**. There are four deep muscles in the posterior compartment of the leg as well: the **popliteus**, flexor digitorum longus, flexor hallucis longus, and tibialis posterior.

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EXERCISE

For each of the following muscles, learn the name, location, and action. Additionally, for each of the muscles marked with an asterisk, also learn the origin and insertion.

- occipitofrontalis: frontal belly and occipital belly
- orbicularis oris
- buccinator
- orbicularis oculi
- *masseter
- *temporalis
- *sternocleidomastoid
- *rectus abdominis
- external oblique
- internal oblique
- transversus abdominis
- *diaphragm
- external intercostal
- internal intercostal
- innermost intercostal
- pectoralis minor
- *trapezius
- *rhomboid major
- *pectoralis major
- latissimus dorsi
- *deltoid
- subscapularis
- *supraspinatus
- infraspinatus
- teres major
- teres minor
- *biceps brachii
- brachialis
- brachioradialis
- *triceps brachii
- pronator teres
- supinator
- *flexor carpi radialis
- palmaris longus
- flexor carpi ulnaris
- flexor digitorum superficialis
- iliocostalis group
- *psoas major
- iliacus
- gluteus maximus
- *gluteus medius
- adductor longus
- adductor magnus
- *rectus femoris
- vastus lateralis
- vastus medialis
- vastus intermedius
- sartorius
- *biceps femoris
- semitendinosus
- semimembranosus
- *tibialis anterior
- *extensor digitorum longus
- fibularis longus
- *gastrocnemius
- soleus

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Key Terms

abductor: Moves the bone away from the midline.
adductor: Moves the bone toward the midline.
adductor brevis: Muscle that adducts and medially rotates the thigh.
adductor longus: Muscle that adducts, medially rotates, and flexes the thigh.
adductor magnus: Muscle with an anterior fascicle that adducts, medially rotates, and flexes the thigh and a posterior fascicle that assists in thigh extension.
agonist (also prime mover): Muscle whose contraction is responsible for producing a particular motion.
anconeus: Small muscle on the lateral posterior elbow that extends the forearm.
antagonist: Muscle that opposes the action of an agonist.
appendicular: Of the arms and legs.
axial: Of the trunk and head.
belly: Bulky central body of a muscle.
bi: Two.
biceps brachii: Two-headed muscle that crosses the shoulder and elbow joints to flex the forearm while assisting in supinating it and flexing the arm at the shoulder.
biceps femoris: Hamstring muscle.
bipennate: Pennate muscle that has fascicles that are located on both sides of the tendon.
brachialis: Muscle deep to the biceps brachii that provides power in flexing the forearm.
brachioradialis: Muscle that can flex the forearm quickly or help lift a load slowly.
brevis: Short.
buccinator: Muscle that compresses the cheek.
calcaneal tendon (also Achilles tendon): Strong tendon that inserts into the calcaneal bone of the ankle.
circular (also sphincter): Fascicles that are concentrically arranged around an opening.
convergent: Fascicles that extend over a broad area and converge on a common attachment site.
deglutition: Swallowing.
deltoid: Shoulder muscle that abducts the arm as well as flexes and medially rotates it and extends and laterally rotates it.

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diaphragm: Skeletal muscle that separates the thoracic and abdominal cavities and is dome-shaped at rest.
digastric: Muscle that has anterior and posterior bellies and elevates the hyoid bone and larynx when one swallows; it also depresses the mandible.
effort: Force applied to the handle of a lever.
erector spinae group: Large muscle mass of the back; primary extensor of the vertebral column.
extensor: Muscle that increases the angle at the joint.
extensor digitorum longus: Muscle that is lateral to the tibialis anterior.
extensor hallucis longus: Muscle that is partly deep to the tibialis anterior and extensor digitorum longus.
extensor radialis longus: Muscle that extends and abducts the hand at the wrist.
external intercostal: Superficial intercostal muscles that raise the rib cage.
external oblique: Superficial abdominal muscle with fascicles that extend inferiorly and medially.
extrinsic muscles of the hand: Muscles that move the wrists, hands, and fingers and originate on the arm.
fascicle: Muscle fibres bundled by perimysium into a unit.
fibularis brevis (also peroneus brevis): Muscle that plantar flexes the foot at the ankle and everts it at the intertarsal joints.
fibularis longus (also peroneus longus): Muscle that plantar flexes the foot at the ankle and everts it at the intertarsal joints.
fixator: Synergist that assists an agonist by preventing or reducing movement at another joint, thereby stabilizing the origin of the agonist.
flexion: Movement that decreases the angle of a joint.
flexor: Muscle that decreases the angle at the joint.
flexor carpi radialis: Muscle that flexes and abducts the hand at the wrist.
flexor carpi ulnaris: Muscle that flexes and adducts the hand at the wrist.
flexor digitorum superficialis: Muscle that flexes the hand and the digits.
frontalis: Front part of the occipitofrontalis muscle.
fulcrum: Fixed point that a force is applied to on the handle of a lever.
fusiform: Muscle that has fascicles that are spindle-shaped to create large bellies.
gastrocnemius: Most superficial muscle of the calf.
gluteal group: Muscle group that extends, flexes, rotates, adducts, and abducts the femur.
gluteus maximus: Largest of the gluteus muscles that extends the femur.

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gluteus medius: Muscle deep to the gluteus maximus that abducts the femur at the hip.
gluteus minimus: Smallest of the gluteal muscles; deep to the gluteus medius.
gracilis: Muscle that adducts the thigh and flexes the leg at the knee.
hamstring group: Three long muscles on the back of the leg.
iliacus: Muscle that, along with the psoas major, makes up the iliopsoas.
iliocostalis cervicis: Muscle of the iliocostalis group associated with the cervical region.
iliocostalis group: Laterally placed muscles of the erector spinae.
iliocostalis lumborum: Muscle of the iliocostalis group associated with the lumbar region.
iliocostalis thoracis: Muscle of the iliocostalis group associated with the thoracic region.
iliopsoas group: Muscle group consisting of iliacus and psoas major muscles; flexes the thigh at the hip, rotates it laterally, and flexes the trunk of the body onto the hip.
infrahyoid muscles: Anterior neck muscles that are attached to, and inferior to, the hyoid bone.
infraspinatus: Muscle that laterally rotates the arm.
innermost intercostal: The deepest intercostal muscles that draw the ribs together.
insertion: End of a skeletal muscle that is attached to the structure (usually a bone) that is moved when the muscle contracts.
intercostal muscles: Muscles that span the spaces between the ribs.
internal intercostal: Intermediate intercostal muscles that draw the ribs together.
internal oblique: Flat, intermediate abdominal muscle with fascicles that run perpendicular to those of the external oblique.
lateralis: To the outside.
latissimus dorsi: Broad, triangular axial muscle located on the inferior part of the back.
linea alba: White, fibrous band that runs along the midline of the trunk.
load: Resistance to the movement of the handle in a lever system.
longus: Long.
masseter: Main muscle for chewing that elevates the mandible to close the mouth.
mastication: Chewing.
maximus: Largest.

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medialis: To the inside.
medius: Medium.
minimus: Smallest.
multipennate: Pennate muscle that has a tendon branching within it.
oblique: At an angle.
occipitalis: Posterior part of the occipitofrontalis muscle.
occipitofrontalis: Muscle that makes up the scalp with a frontal belly and an occipital belly.
orbicularis oculi: Circular muscle that closes the eye.
orbicularis oris: Circular muscle that moves the lips.
origin: End of a skeletal muscle that is attached to another structure (usually a bone) in a fixed position.
palmaris longus: Muscle that provides weak flexion of the hand at the wrist.
parallel: Fascicles that extend in the same direction as the long axis of the muscle.
patellar ligament: Extension of the quadriceps tendon below the patella.
pectoral girdle: Shoulder girdle, made up of the clavicle and scapula.
pectoralis major: Thick, fan-shaped axial muscle that covers much of the superior thorax.
pectoralis minor: Muscle that moves the scapula and assists in inhalation.
pelvic girdle: Hips; a foundation for the lower limb.
pennate: Fascicles that are arranged differently based on their angles to the tendon.
popliteal fossa: Diamond-shaped space at the back of the knee.
popliteus: Muscle that flexes the leg at the knee and creates the floor of the popliteal fossa.
prime mover (also agonist): Principal muscle involved in an action.
pronator quadratus: Pronator that originates on the ulna and inserts on the radius.
pronator teres: Pronator that originates on the humerus and inserts on the radius.
psoas major: Muscle that, along with the iliacus, makes up the iliopsoas.
quadriceps femoris group: Four muscles that extend and stabilize the knee.
quadriceps tendon (also patellar tendon): Tendon common to all four quadriceps muscles, inserts into the patella.
rectus: Straight.
rectus abdominis: Long, linear muscle that extends along the middle of the trunk.
rectus femoris: Quadricep muscle on the anterior aspect of the thigh.

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rectus sheaths: Tissue that makes up the linea alba.
rhomboid major: Muscle that attaches the vertebral border of the scapula to the spinous process of the thoracic vertebrae.
rhomboid minor: Muscle that attaches the vertebral border of the scapula to the spinous process of the thoracic vertebrae.
rotator cuff (also musculotendinous cuff): The circle of tendons around the shoulder joint.
sartorius: Bandlike muscle that flexes, abducts, and laterally rotates the leg at the hip.
scalene muscles: Flex, laterally flex, and rotate the head; contribute to deep inhalation.
semimembranosus: Hamstring muscle.
semitendinosus: Hamstring muscle.
serratus anterior: Large and flat muscle that originates on the ribs and inserts onto the scapula.
soleus: Wide, flat muscle deep to the gastrocnemius.
splenius: Posterior neck muscles.
sternocleidomastoid: Major muscle that laterally flexes and rotates the head.
subclavius: Muscle that stabilizes the clavicle during movement.
subscapularis: Muscle that originates on the anterior scapula and medially rotates the arm.
supinator: Muscle that moves the palm and forearm anteriorly.
suprahyoid muscles: Neck muscles that are superior to the hyoid bone.
supraspinatus: Muscle that abducts the arm.
synergist: Muscle whose contraction helps a prime mover in an action.
temporalis: Muscle that retracts the mandible.
tensor fascia lata: Muscle that flexes and abducts the thigh.
teres major: Muscle that extends the arm and assists in adduction and medial rotation of it.
teres minor: Muscle that laterally rotates and extends the arm.
tibialis anterior: Muscle located on the lateral surface of the tibia.
transversus abdominis: Deep layer of the abdomen that has fascicles arranged transversely around the abdomen.
trapezius: Muscle that stabilizes the upper part of the back.
tri: Three.
triceps brachii: Three-headed muscle that extends the forearm.
unipennate: Pennate muscle that has fascicles located on one side of the tendon.

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vastus intermedius: Quadricep muscle that is between the vastus lateralis and vastus medialis and is deep to the rectus femoris.
vastus lateralis: Quadricep muscle on the lateral aspect of the thigh.
vastus medialis: Quadricep muscle on the medial aspect of the thigh.

Chapter Review

11.1 Interactions of Skeletal Muscles, Their Fascicle Arrangement, and Their Lever Systems

Skeletal muscles each have an origin and an insertion. The end of the muscle that attaches to the bone being pulled is called the muscle's insertion, and the end of the muscle attached to a fixed, or stabilized, bone is called the origin. The muscle primarily responsible for a movement is called the prime mover, and muscles that assist in this action are called synergists. A synergist that makes the insertion site more stable is called a fixator. Meanwhile, a muscle with the opposite action of the prime mover is called an antagonist.

Several factors contribute to the force generated by a skeletal muscle. One is the arrangement of the fascicles in the skeletal muscle. Fascicles can be parallel, circular, convergent, pennate, fusiform, or triangular. Each arrangement has its own range of motion and ability to do work.

11.2 Naming Skeletal Muscles

Muscle names are based on many characteristics. The location of a muscle in the body is important. Some muscles are named based on their size and location, such as the gluteal muscles of the buttocks. Other muscle names can indicate the location in the body or bones with which the muscle is associated, such as the tibialis anterior. The shapes of some muscles are distinctive; for example, the direction of the muscle fibres is used to describe muscles of the body midline. The origin and/or insertion can also be features used to name a muscle; examples include the biceps brachii, triceps brachii, and the pectoralis major.

11.3 Axial Muscles of the Head, Neck, and Back

Muscles are either axial muscles or appendicular. The axial muscles are grouped based on location, function, or both. Some axial muscles cross over to the appendicular skeleton. The muscles of the head and neck are all axial. The muscles in the face create facial expression by inserting into the skin rather than onto bone. Muscles that move the eyeballs are extrinsic, meaning they originate outside of the eye and insert onto it. The muscles of the anterior neck facilitate swallowing and speech, stabilize the hyoid bone, and

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position the larynx. The muscles of the neck stabilize and move the head. The sternocleidomastoid divides the neck into anterior and posterior triangles.

The muscles of the back and neck that move the vertebral column are complex, overlapping, and can be divided into five groups. The erector spinae has three subgroups. The iliocostalis group includes the iliocostalis cervicis, the iliocostalis thoracis, and the iliocostalis lumborum. The longissimus group includes the longissimus capitis, the longissimus cervicis, and the longissimus thoracis. The spinalis group includes the spinalis capitis, the spinalis cervicis, and the spinalis thoracis.

11.4 Axial Muscles of the Abdominal Wall and Thorax

Made of skin, fascia, and four pairs of muscles, the anterior abdominal wall protects the organs located in the abdomen and moves the vertebral column. These muscles include the rectus abdominis, which extends through the entire length of the trunk, the external oblique, the internal oblique, and the transversus abdominis.

The muscles of the thorax play a large role in breathing, especially the dome-shaped diaphragm. When it contracts and flattens, the volume inside the pleural cavities increases, which decreases the pressure within them. As a result, air will flow into the lungs. The external and internal intercostal muscles span the space between the ribs and help change the shape of the rib cage and the volume-pressure ratio inside the pleural cavities during inspiration and expiration.

11.5 Muscles of the Pectoral Girdle and Upper Limbs

The clavicle and scapula make up the pectoral girdle, which provides a stable origin for the muscles that move the humerus. The muscles that position and stabilize the pectoral girdle are located on the thorax. The anterior thoracic muscles are the subclavius, pectoralis minor, and the serratus anterior. The posterior thoracic muscles are the trapezius, rhomboid major, and rhomboid minor. Nine muscles cross the shoulder joint to move the humerus. The ones that originate on the axial skeleton are the pectoralis major and the latissimus dorsi. The deltoid, subscapularis, supraspinatus, infraspinatus, teres major, teres minor, and coracobrachialis originate on the scapula.

The forearm flexors include the biceps brachii, brachialis, and brachioradialis. The extensors are the triceps brachii and anconeus. The pronators are the pronator teres and the pronator quadratus. The supinator is the only muscle that turns the forearm anteriorly.

The extrinsic muscles of the hands originate along the forearm and insert into the hand in order to facilitate crude movements of the wrists, hands, and

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fingers. These muscles are the flexor carpi radialis, palmaris longus, flexor carpi ulnaris, and the flexor digitorum superficialis. The rest of the compartments produce extension. The deep posterior compartment includes the abductor longus and the extensor pollicis longus.

11.6 Appendicular Muscles of the Pelvic Girdle and Lower Limbs

The pelvic girdle attaches the legs to the axial skeleton. The hip joint is where the pelvic girdle and the leg come together. The hip is joined to the pelvic girdle by many muscles. In the gluteal region, the psoas major and iliacus form the iliopsoas. The large and strong gluteus maximus, gluteus medius, and gluteus minimus extend and abduct the femur. On the medial part of the thigh, the adductor longus, adductor brevis, and adductor magnus adduct the thigh and medially rotate it. The pectineus muscle adducts and flexes the femur at the hip.

The thigh muscles that move the femur, tibia, and fibula are divided into medial, anterior, and posterior compartments. The medial compartment includes the adductors, pectineus, and the gracilis. The anterior compartment comprises the quadriceps femoris, quadriceps tendon, patellar ligament, and sartorius. The quadriceps femoris is made of four muscles: the rectus femoris, the vastus lateralis, the vastus medius, and the vastus intermedius, which together extend the knee. The posterior compartment of the thigh includes the hamstrings: the biceps femoris, semitendinosus, and the semimembranosus, which all flex the knee.

The muscles of the leg that move the foot and toes are divided into anterior, lateral, superficial-posterior, and deep-posterior compartments. The anterior compartment includes the tibialis anterior, the extensor hallucis longus, the extensor digitorum longus, and the fibularis (peroneus) tertius. The lateral compartment houses the fibularis (peroneus) longus and the fibularis (peroneus) brevis. The superficial posterior compartment has the gastrocnemius, soleus, and plantaris, and the deep posterior compartment has the popliteus.

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PART 3

Regulation, Integration, and Control

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12

The Nervous System and Nervous Tissue

Chapter Objectives

After studying this chapter, you will be able to:

- Name the major divisions of the nervous system, both anatomical and functional
- Describe the functional and structural differences between grey matter and white matter structures
- Name the parts of the multipolar neuron in order of polarity
- List the types of glial cells, along with their function(s), and assign each to the proper division of the nervous system
- Distinguish the major functions of the nervous system: sensation, integration, and response
- Describe the components of the membrane that establish the resting membrane potential
- Describe the changes that occur to the membrane that result in the action potential
- Explain the differences between types of graded potentials
- Categorize the major neurotransmitters by chemical type and effect

The nervous system is a very complex organ system. In Peter D. Kramer's book *Listening to Prozac*, a pharmaceutical researcher is quoted as saying, "If the human brain were simple enough for us to understand, we would be too simple to understand it" (1994). That quote is from the early 1990s; in the three decades since, progress has continued at an amazing rate within the scientific disciplines of neuroscience. It is an interesting conundrum to consider that

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the complexity of the nervous system may be too complex for it (that is, for us) to completely unravel. But our current level of understanding is probably nowhere close to that limit. The focus of this chapter is on nervous (neural) tissue, both its structure and its function. But before you learn about that, you will see a big picture of the system—actually, a few big pictures.

12.1 Basic Structure and Function of the Nervous System

Learning Objectives

By the end of this section, you will be able to:

- Identify the anatomical and functional divisions of the nervous system
- Relate the functional and structural differences between grey matter and white matter structures of the nervous system to the structure of neurons
- List the basic functions of the nervous system

The picture you have in your mind of the nervous system probably includes the **brain**, the nervous tissue contained within the cranium, and the **spinal cord**, the extension of nervous tissue within the vertebral column. That suggests it is made of two organs—and you may not even think of the spinal cord as an organ—but the nervous system is a very complex structure. Within the brain, many different and separate regions are responsible for many different and separate functions. It is as if the nervous system is composed of many organs that all look similar and can only be differentiated using tools such as the microscope or electrophysiology. In comparison, it is easy to see that the stomach is different than the esophagus or the liver, so you can imagine the digestive system as a collection of specific organs.

The Central and Peripheral Nervous Systems

The nervous system can be divided into two major regions: the central and peripheral nervous systems. The **central nervous system** (**CNS**) is the brain and spinal cord, and the **peripheral nervous system** (**PNS**) is everything else (Figure 12.1). The brain is contained within the cranial cavity of the skull, and the spinal cord is contained within the vertebral cavity of the vertebral column. It is a bit of an oversimplification to say that the CNS is what is inside these two cavities and the peripheral nervous system is outside of them,

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but that is one way to start to think about it. In actuality, there are some elements of the peripheral nervous system that are within the cranial or vertebral cavities. The peripheral nervous system is so named because it is on the periphery—meaning beyond the brain and spinal cord. Depending on different aspects of the nervous system, the dividing line between central and peripheral is not necessarily universal.

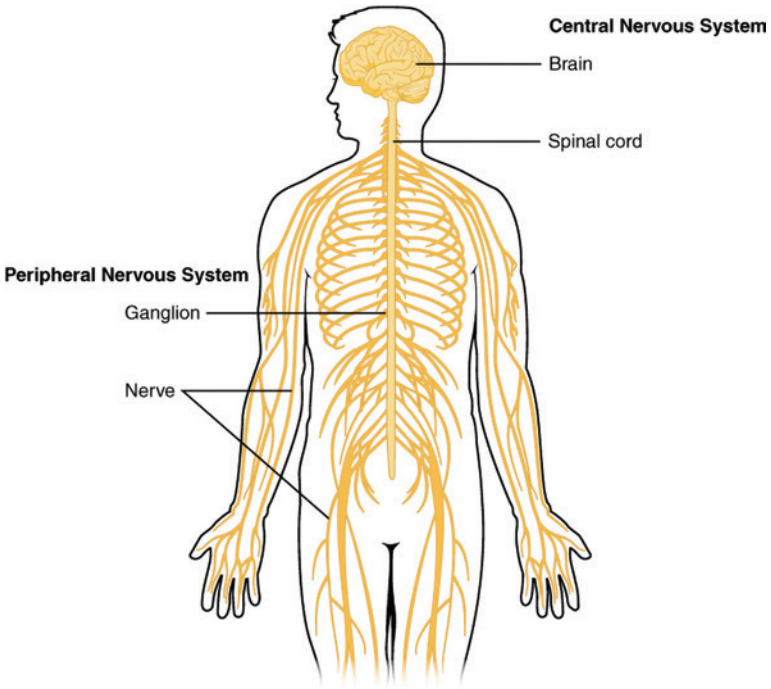


Figure 12.1 Central and Peripheral Nervous System. The structures of the PNS are referred to as ganglia and nerves, which can be seen as distinct structures. The equivalent structures in the CNS are not obvious from this overall perspective and are best examined in prepared tissue under the microscope.

Nervous tissue, present in both the CNS and PNS, contains two basic types of cells: neurons and glial cells. A **glial cell** is one of a variety of cells that provide a framework of tissue that supports the neurons and their activities. The **neuron** is the more functionally important of the two, in terms of the communicative function of the nervous system. To describe the functional divisions of the nervous system, it is important to understand the structure of a neuron. Neurons are cells and therefore have a **soma**, or **cell body**, but they also have extensions of the cell; each extension is generally referred to as a **process**. There is one important process that every neuron has called an **axon**, which is the fibre that connects a neuron with its target. Another type of process that branches off

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from the soma is the **dendrites**. Dendrites are responsible for receiving most of the input from other neurons. Looking at nervous tissue, there are regions that predominantly contain cell bodies and regions that are largely composed of just axons. These two regions within nervous system structures are often referred to as **grey matter** (the regions with many cell bodies and dendrites) or **white matter** (the regions with many axons). Figure 12.2 demonstrates the appearance of these regions in the brain and spinal cord. The colours ascribed to these regions are what would be seen in "fresh," or unstained, nervous tissue. Grey matter is not necessarily grey. It can be pinkish because of blood content, or even slightly tan, depending on how long the tissue has been preserved. But white matter is white because axons are insulated by a lipid-rich substance called **myelin**. Lipids can appear as white ("fatty") material, much like the fat on a raw piece of chicken or beef. Actually, grey matter may have that colour ascribed to it because next to the white matter, it is just darker—hence, grey.

The distinction between grey matter and white matter is most often applied to central nervous tissue, which has large regions that can be seen with the unaided eye. When looking at peripheral structures, often a microscope is used and the tissue is stained with artificial colours. That is not to say that central nervous tissue cannot be stained and viewed under a microscope, but unstained tissue is most likely from the CNS—for example, a frontal section of the brain or cross-section of the spinal cord.

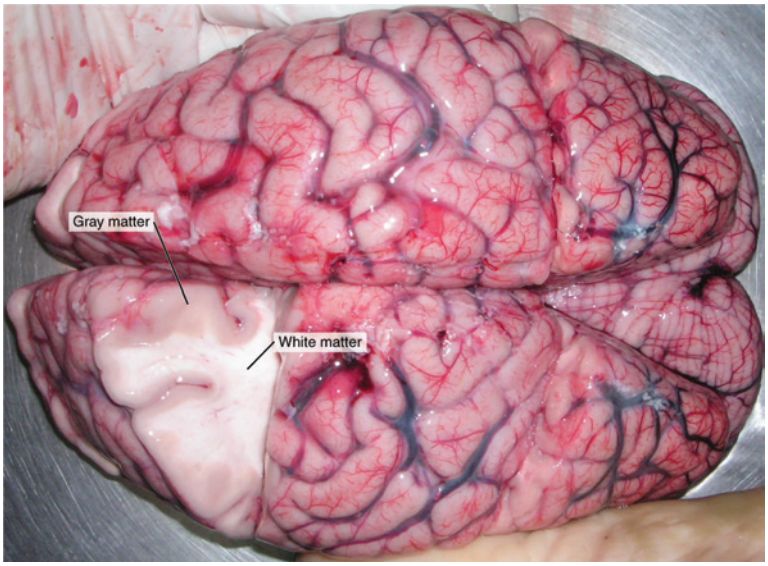


Figure 12.2 Grey Matter and White Matter. A brain removed during an autopsy, with a partial section removed, shows white matter surrounded by grey matter. Grey matter makes up the outer cortex of the brain. (credit: modification of work by "Suseno"/Wikimedia Commons)

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Regardless of the appearance of stained or unstained tissue, the cell bodies of neurons or axons can be located in discrete anatomical structures that need to be named. Those names are specific to whether the structure is central or peripheral. A localized collection of neuron cell bodies in the CNS is referred to as a **nucleus**. In the PNS, a cluster of neuron cell bodies is referred to as a **ganglion**. Figure 12.3 indicates how the term *nucleus* has a few different meanings within anatomy and physiology. It is the centre of an atom, where protons and neutrons are found; it is the centre of a cell, where the DNA is found; and it is the centre of some function in the CNS. There is also a potentially confusing use of the word *ganglion* (plural = ganglia) that has a historical explanation. In the central nervous system, there is a group of nuclei that are connected together and were once called the basal ganglia before "ganglion" became accepted as a description for a peripheral structure. Some sources refer to this group of nuclei as the "basal nuclei" to avoid confusion.

Terminology applied to bundles of axons also differs depending on location. A bundle of axons, or fibres, found in the CNS is called a **tract**, whereas the same thing in the PNS would be called a **nerve**. There is an important point to make about these terms, which is that they can both be used to refer to the same bundle of axons. The most obvious example of this is the axons that project from the retina into the brain. Those axons are called the optic nerve as they leave the eye, but when they are inside the cranium, they are referred to as the optic tract. There is a specific place where the name changes, which is the optic chiasm, but they are still the same axons (Figure 12.4). A similar situation outside of science can be described for some roads. Imagine a road

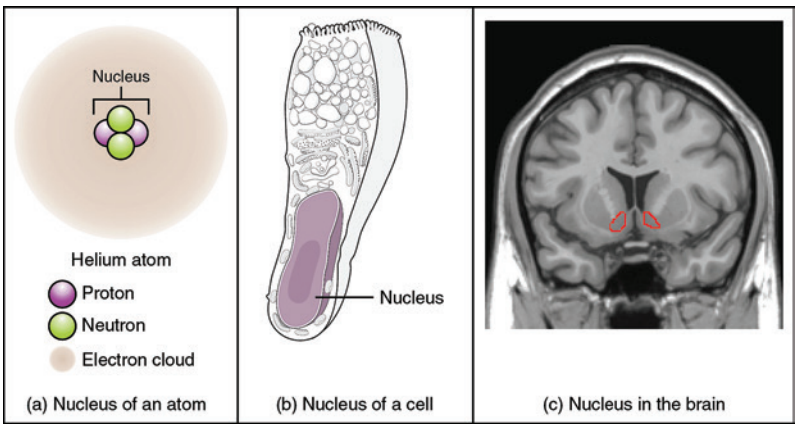


Figure 12.3 What Is a Nucleus? (a) The nucleus of an atom contains its protons and neutrons. (b) The nucleus of a cell is the organelle that contains DNA. (c) A nucleus in the CNS is a localized centre of function with the cell bodies of several neurons, shown here circled in red. (credit c: "Was a bee"/Wikimedia Commons)

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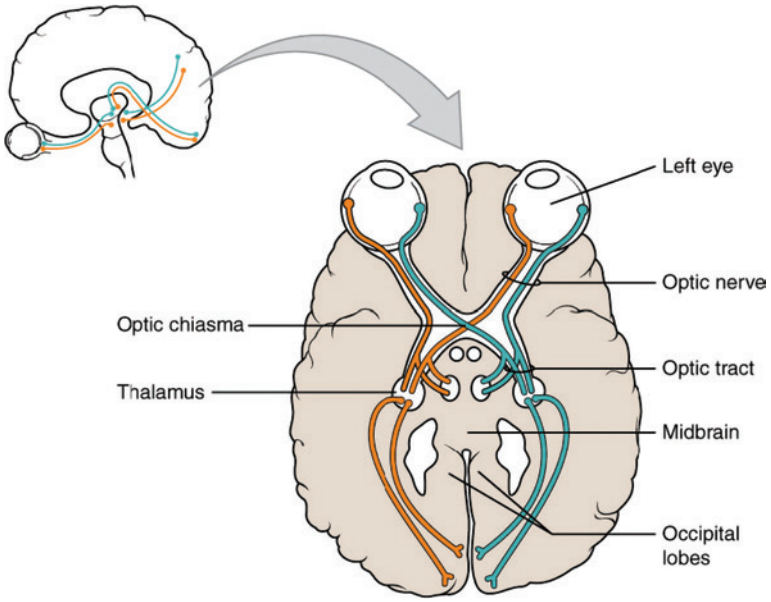


Figure 12.4 Optic Nerve Versus Optic Tract. This drawing of the connections of the eye to the brain shows the optic nerve extending from the eye to the chiasm, where the structure continues as the optic tract. The same axons extend from the eye to the brain through these two bundles of fibres, but the chiasm represents the border between peripheral and central.

called "Broad Street" in a town called "Anyville." The road leaves Anyville and goes to the next town over, called "Hometown." When the road crosses the line between the two towns and is in Hometown, its name changes to "Main Street." That is the idea behind the naming of the retinal axons. In the PNS, they are collectively called the optic nerve, and in the CNS, they are the optic tract. Table 12.1 helps clarify which of these terms apply to the central or peripheral nervous systems.

Table 12.1 Structures of the CNS and PNS

	CNS	PNS
Group of Neuron Cell Bodies (i.e., grey matter)	Nucleus	Ganglion
Bundle of Axons (i.e., white matter)	Tract	Nerve

Functional Divisions of the Nervous System

The nervous system can also be divided on the basis of its functions, but anatomical divisions and functional divisions are different. The CNS and the PNS both contribute to the same functions, but those functions can be attributed to

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different regions of the brain (such as the cerebral cortex or the hypothalamus) or to different ganglia in the periphery. The problem with trying to fit functional differences into anatomical divisions is that sometimes the same structure can be part of several functions. For example, the optic nerve carries signals from the retina that are used either for the conscious perception of visual stimuli, which takes place in the cerebral cortex, or for the reflexive responses of smooth muscle tissue that are processed through the hypothalamus.

There are two ways to consider how the nervous system is divided functionally. First, the basic functions of the nervous system are sensation, integration, and response. Secondly, control of the body can be somatic or autonomic—divisions that are largely defined by the structures that are involved in the response. There is also a region of the peripheral nervous system, called the enteric nervous system, that is responsible for a specific set of functions within the realm of autonomic control related to gastrointestinal functions.

Basic Functions

The nervous system is involved in receiving information about the environment around us (sensation) and generating responses to that information (motor responses). The nervous system can be divided into regions that are responsible for **sensation** (sensory functions) and for the **response** (motor functions). But there is a third function that needs to be included. Sensory input needs to be integrated with other sensations, as well as with memories, emotional state, or learning (cognition). Some regions of the nervous system are termed **integration** or **association areas**. The process of integration combines sensory perceptions and higher cognitive functions such as memories, learning, and emotion to produce a response.

Sensation. The first major function of the nervous system is sensation—receiving information about the environment to gain input about what is happening outside the body (or, sometimes, within the body). The sensory functions of the nervous system register the presence of a change from homeostasis or a particular event in the environment, known as a **stimulus**. The senses we think of most are the "big five": taste, smell, touch, sight, and hearing. The stimuli for taste and smell are both chemical substances (molecules, compounds, ions, etc.), touch is the physical or mechanical stimuli that interact with the skin, sight is light stimuli, and hearing is the perception of sound, which is a physical stimulus similar to some aspects of touch. There are actually more senses than just those, but that list represents the major senses. Those five are all senses that receive stimuli from the outside world and of which there is conscious perception. Additional

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sensory stimuli might be from the internal environment (inside the body), such as the stretch of an organ wall or the concentration of certain ions in the blood.

Response. The nervous system produces a response on the basis of the stimuli perceived by sensory structures. An obvious response would be the movement of muscles, such as withdrawing a hand from a hot stove, but there are broader uses of the term. The nervous system can cause the contraction of all three types of muscle tissue. For example, skeletal muscle contracts to move the skeleton, cardiac muscle is influenced as heart rate increases during exercise, and smooth muscle contracts as the digestive system moves food along the digestive tract.

Responses also include the neural control of glands in the body, such as the production and secretion of sweat by the eccrine and merocrine sweat glands found in the skin to lower body temperature.

Responses can be divided into those that are voluntary or conscious (contraction of skeletal muscle) and those that are involuntary (contraction of smooth muscles, regulation of cardiac muscle, activation of glands). Voluntary responses are governed by the somatic nervous system, and involuntary responses are governed by the autonomic nervous system, which is discussed in the next section.

Integration. Stimuli that are received by sensory structures are communicated to the nervous system, where that information is processed. This is called integration. Stimuli are compared with, or integrated with, other stimuli, memories of previous stimuli, or the state of a person at a particular time. This leads to the specific response that will be generated. Seeing a baseball pitched to a batter will not automatically cause the batter to swing. The trajectory of the ball and its speed will need to be considered. Maybe the count is three balls and one strike, and the batter wants to let this pitch go by in the hope of getting a walk to first base. Or maybe the batter's team is so far ahead, it would be fun to just swing away.

Controlling the Body

The nervous system can be divided into two parts mostly on the basis of a functional difference in responses. The **somatic nervous system** (**SNS**) is responsible for conscious perception and voluntary motor responses. Voluntary motor response means the contraction of skeletal muscle, but those contractions are not always voluntary in the sense that you have to want to perform them. Some somatic motor responses are reflexes and often happen without a conscious decision to perform them. If your friend jumps out from behind a corner and yells "Boo!" you will be startled, and you might scream or

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leap back. You didn't decide to do that, and you may not have wanted to give your friend a reason to laugh at your expense, but it is a reflex involving skeletal muscle contractions. Other motor responses become automatic (in other words, unconscious) as a person learns motor skills (referred to as "habit-learning" or "procedural memory").

The **autonomic nervous system** (**ANS**) is responsible for involuntary control of the body, usually for the sake of homeostasis (regulation of the internal environment). Sensory input for autonomic functions can be from sensory structures tuned to external or internal environmental stimuli. The motor output extends to smooth and cardiac muscle as well as glandular tissue. The role of the autonomic system is to regulate the organ systems of the body, which usually means to control homeostasis. Sweat glands, for example, are controlled by the autonomic system. When you are hot, sweating helps cool your body down. That is a homeostatic mechanism. But when you are nervous, you might also start sweating. That is not homeostatic; it is the physiological response to an emotional state.

There is another division of the nervous system that describes functional responses. The **enteric nervous system** (**ENS**) is responsible for controlling the smooth muscle and glandular tissue in your digestive system. It is a large part of the PNS, and it is not dependent on the CNS. It is sometimes valid, however, to consider the enteric system to be a part of the autonomic system because the neural structures that make up the enteric system are a component of the autonomic output that regulates digestion. There are some differences between the two, but for our purposes here, there will be a good bit of overlap. See Figure 12.5 for examples of where these divisions of the nervous system can be found.

Interactive Link 12.1

Visit this site (http://oer.aupress.ca/oer-202505/12.1) to read about a woman who notices that her daughter is having trouble walking up the stairs. This leads to the discovery of a hereditary condition that affects the brain and spinal cord. The electromyography and MRI tests indicated deficiencies in the spinal cord and cerebellum, both of which are responsible for controlling coordinated movements. To what functional division of the nervous system would these structures belong?

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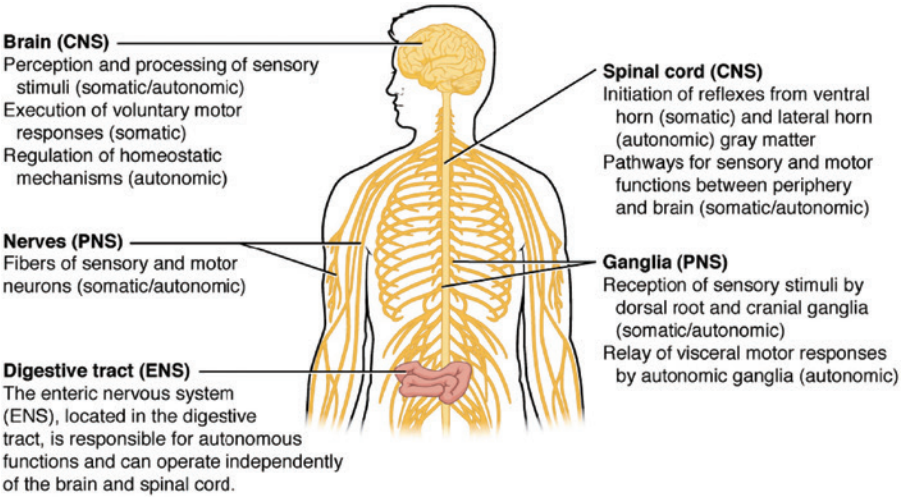


Figure 12.5 Somatic, Autonomic, and Enteric Structures of the Nervous System. Somatic structures include the spinal nerves, both motor and sensory fibres, as well as the sensory ganglia (posterior root ganglia and cranial nerve ganglia). Autonomic structures are also found in the nerves, including the sympathetic and parasympathetic ganglia. The enteric nervous system includes the nervous tissue within the organs of the digestive tract.

12.2 Nervous Tissue

Learning Objectives

By the end of this section, you will be able to:

- Describe the basic structure of a neuron
- Identify the different types of neurons on the basis of polarity
- List the glial cells of the CNS and describe their function
- List the glial cells of the PNS and describe their function

Nervous tissue is composed of two types of cells, neurons and glial cells. Neurons are the primary type of cell that most people associate with the nervous system. They are responsible for the computation and communication that the nervous system provides. They are electrically active and release chemical signals to target cells. Glial cells, or glia, are known to play a supporting role for nervous tissue. Ongoing research pursues an expanded role that glial cells might play in signalling, but neurons are still considered the basis of this function. Neurons are important, but without glial support, they would not be able to perform their function.

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Neurons

Neurons are the cells considered to be the basis of nervous tissue. They are responsible for the electrical signals that communicate information about sensations and that produce movements in response to those stimuli, along with inducing thought processes within the brain. An important part of the function of neurons is in their structure, or shape. The three-dimensional shape of these cells makes the immense number of connections within the nervous system possible.

Parts of a Neuron

As you learned in the first section, the main part of a neuron is the cell body, which is also known as the soma (*soma* = "body"). The cell body contains the nucleus and most of the major organelles. But what makes neurons special is that they have many extensions of their cell membranes, which are generally referred to as processes. Neurons are usually described as having one, and only one, axon—a fibre that emerges from the cell body and projects to target cells. That single axon can branch repeatedly to communicate with many target cells. It is the axon that propagates the nerve impulse, which is communicated to one or more cells. The other processes of the neuron are **dendrites**, which receive information from other neurons at specialized areas of contact called **synapses**. The dendrites are usually highly branched processes, providing locations for other neurons to communicate with the cell body.

Information flows through a neuron from the dendrites, across the cell body, and down the axon. This gives the neuron a polarity—meaning that information flows in this one direction. Figure 12.6 shows the relationship of these parts to one another.

Where the axon emerges from the cell body, there is a small elevated region referred to as the **axon hillock**. This is a tapering of the cell body toward the axon fibre. Within the axon hillock, the cytoplasm changes to a solution of limited components called **axoplasm**. Because the axon hillock represents the first segment of the cell body toward the axon, the next segment is considered the proximal segment of the axon, called the **initial segment**.

Many axons are wrapped by an insulating substance called myelin, which is actually made from glial cells. Myelin acts as insulation, much like the plastic or rubber that is used to insulate electrical wires. A key difference between myelin and the insulation on a wire is that there are gaps in the myelin covering of an axon. Each gap is called a **node of Ranvier** and is important to the way that electrical signals travel down the axon. The length of the axon between each gap, which is wrapped in myelin, is referred to as an **axon segment**. At the end of the axon is the **axon terminal**, where there are usually several branches

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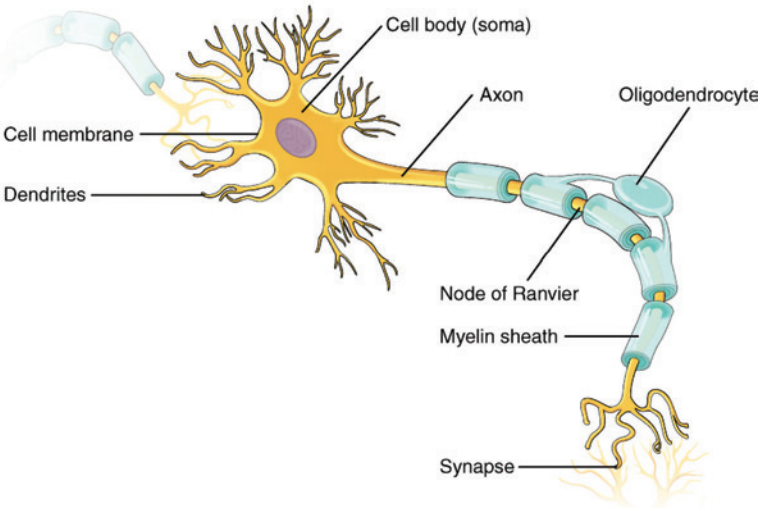


Figure 12.6 Parts of a Neuron. The major parts of the neuron are labelled on a multipolar neuron from the CNS.

extending toward the target cell, each of which ends in an enlargement called a **synaptic end bulb**. These bulbs are what make the connection with the target cell at the synapse.

Types of Neurons

There are many neurons in the nervous system—a number in the trillions. And there are many different types of neurons. They can be classified by many different criteria. The first way to classify them is by the number of processes attached to the cell body. Using the standard model of neurons, one of these processes is the axon, and the rest are dendrites. Because information flows through the neuron from dendrites or cell bodies toward the axon, these names are based on the neuron's polarity (Figure 12.7).

Unipolar cells have only one process emerging from the cell. True unipolar cells are only found in invertebrate animals, so the unipolar cells in humans are more appropriately called "pseudounipolar" cells. Invertebrate unipolar cells do not have dendrites. Human unipolar cells have an axon that emerges from the cell body, but it splits so that the axon can extend along a very long distance. At one end of the axon are dendrites, and at the other end, the axon forms synaptic connections with a target. Unipolar cells are exclusively sensory neurons and have two unique characteristics. First, their dendrites are receiving sensory information, sometimes directly from the stimulus itself. Secondly, the cell bodies of unipolar neurons are always found in ganglia. Sensory reception is a peripheral function (those dendrites are in the periphery,

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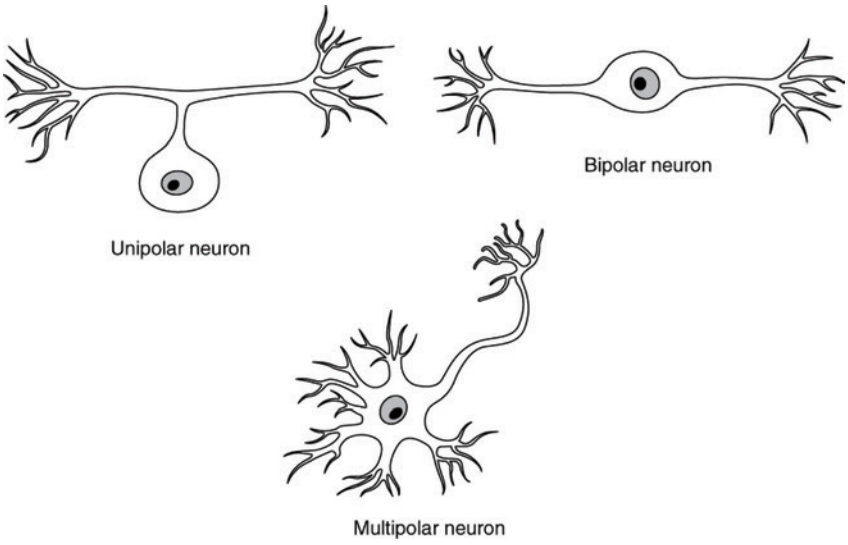


Figure 12.7 Neuron Classification by Shape. Unipolar cells have one process that includes both the axon and dendrite. Bipolar cells have two processes: the axon and a dendrite. Multipolar cells have more than two processes: the axon and two or more dendrites.

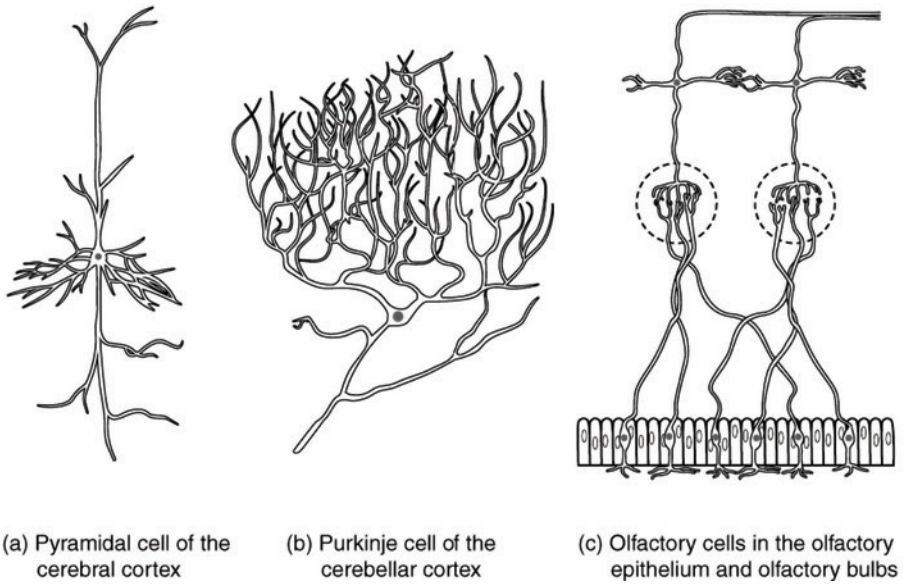
perhaps in the skin), so the cell body is in the periphery, though it is closer to the CNS in a ganglion. The axon projects from the dendrite endings, past the cell body in a ganglion, and into the central nervous system.

Bipolar cells have two processes, which extend from each end of the cell body, opposite of each other. One is the axon, and one is the dendrite. Bipolar cells are not very common. They are found mainly in the olfactory epithelium (where smell stimuli are sensed) and as part of the retina.

Multipolar neurons are all the neurons that are not unipolar or bipolar. They have one axon and two or more dendrites (usually many more). With the exceptions of the unipolar sensory ganglion cells and the two specific bipolar cells mentioned previously, all other neurons are multipolar. Some cutting-edge research suggests that certain neurons in the CNS do not conform to the standard model of "one and only one" axon. Some sources describe a fourth type of neuron, called an anaxonic neuron. The name suggests that it has no axon (*an-* = "without"), but this is not accurate. Anaxonic neurons are very small, and if you look through a microscope at the standard resolution used in histology (approximately 400× to 1000× total magnification), you will not be able to distinguish any process specifically as an axon or a dendrite. Any of those processes can function as an axon depending on the conditions at any given time. Nevertheless, even if they cannot be easily seen, and one specific process is definitively the axon, these neurons have multiple processes and are therefore multipolar.

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Neurons can also be classified on the basis of where they are found, who found them, what they do, or even what chemicals they use to communicate with each other. Some neurons referred to in this section on the nervous system are named on the basis of those sorts of classifications (Figure 12.8). For example, a multipolar neuron that has a very important role to play in a part of the brain called the cerebellum is known as a **Purkinje cell**.



(a) Pyramidal cell of the cerebral cortex

(b) Purkinje cell of the cerebellar cortex

(c) Olfactory cells in the olfactory epithelium and olfactory bulbs

Figure 12.8 Other Neuron Classifications. Three examples of neurons that are classified on the basis of other criteria. (a) The pyramidal cell is a multipolar cell with a cell body that is shaped somewhat like a pyramid. (b) The Purkinje cell in the cerebellum was named after the scientist who originally described it. (c) Olfactory neurons are named for the functional group with which they belong.

Glial Cells

Glial cells, or neuroglia or simply glia, are the other type of cell found in nervous tissue. They are considered to be supporting cells, and many functions are directed at helping neurons complete their function for communication. The name *glia* comes from the Greek word that means "glue" and was coined by the German pathologist Rudolph Virchow, who wrote in 1856, "This connective substance, which is in the brain, the spinal cord, and the special sense nerves, is a kind of glue (neuroglia) in which the nervous elements are planted." Today, research into nervous tissue has shown that there are many deeper roles that these cells play. And research may find much more about them in the future.

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There are six types of glial cells. Four of them are found in the CNS, and two are found in the PNS. Table 12.2 outlines some common characteristics and functions.

Table 12.2 Glial Cell Types by Location and Basic Function

CNS glia	PNS glia	Basic function
Astrocyte	Satellite cell	Support
Oligodendrocyte	Schwann cell	Insulation, myelination
Microglia	—	Immune surveillance and phagocytosis
Ependymal cell	—	Creating CSF

Glial Cells of the CNS

One cell providing support to neurons of the CNS is the **astrocyte**, so named because it appears to be star-shaped under the microscope (*astro-* = "star"). Astrocytes have many processes extending from their main cell body (not axons or dendrites like neurons, just cell extensions). Those processes extend to interact with neurons, blood vessels, or the connective tissue covering the CNS, which is called the pia mater (Figure 12.9). Generally, they are supporting cells for the neurons in the central nervous system. Some ways in which they support neurons in the central nervous system are by maintaining the concentration of chemicals in the extracellular space, removing excess signalling molecules, reacting to tissue damage, and contributing to the **blood-brain barrier** (**BBB**). The blood-brain barrier is a physiological barrier that keeps many substances that circulate in the rest of the body from getting into the central nervous system, restricting what can cross from circulating blood into the CNS. Nutrient molecules, such as glucose or amino acids, can pass through the BBB, but other molecules cannot. This actually causes problems with drug delivery to the CNS. Pharmaceutical companies are challenged to design drugs that can cross the BBB as well as have an effect on the nervous system.

Like a few other parts of the body, the brain has a privileged blood supply. Very little can pass through by diffusion. Most substances that cross the wall of a blood vessel into the CNS must do so through an active transport process. Because of this, only specific types of molecules can enter the CNS. Glucose—the primary energy source—is allowed, as are amino acids. Water and some other small particles, like gases and ions, can enter. But most everything else cannot, including white blood cells, which are one of the body's main lines of defence.

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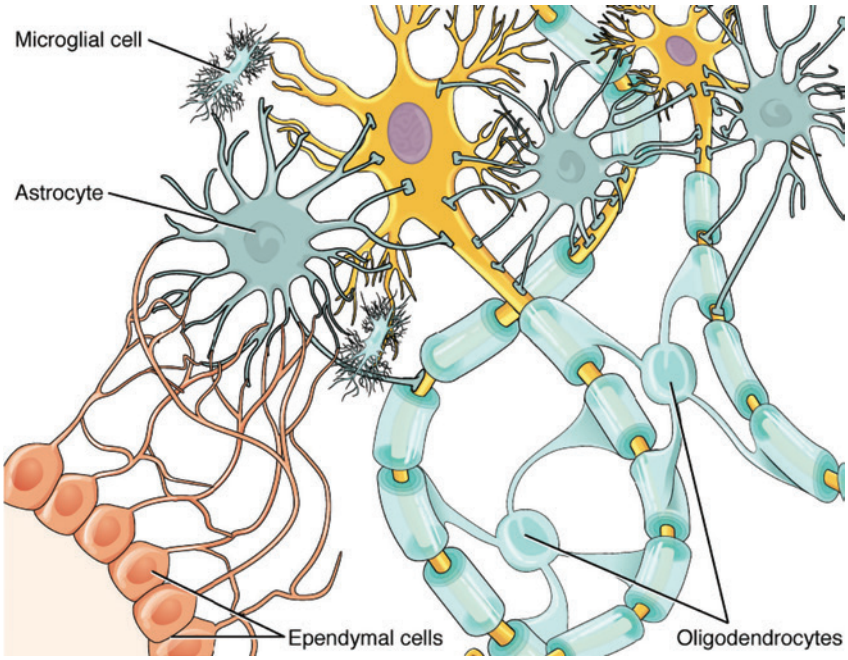


Figure 12.9 Glial Cells of the CNS. The CNS has astrocytes, oligodendrocytes, microglia, and ependymal cells that support the neurons of the CNS in several ways.

While this barrier protects the CNS from exposure to toxic or pathogenic substances, it also keeps out the cells that could protect the brain and spinal cord from disease and damage. The BBB also makes it harder for pharmaceuticals to be developed that can affect the nervous system. Aside from finding efficacious substances, the means of delivery is also crucial.

Also found in CNS tissue is the **oligodendrocyte**, sometimes called just "oligo," which is the glial cell type that insulates axons in the CNS. There are a few processes that extend from the cell body. Each one reaches out and surrounds an axon to insulate it in myelin. One oligodendrocyte will provide the myelin for multiple axon segments, either for the same axon or for separate axons. The function of myelin will be discussed in a later section.

Microglia are, as the name implies, smaller than most of the other glial cells. Ongoing research into these cells, although not entirely conclusive, suggests that they may originate as white blood cells, called macrophages, that become part of the CNS during early development. While their origin is not conclusively determined, their function is related to what macrophages do in the rest of the body. When macrophages encounter diseased or damaged cells in the rest of the body, they ingest and digest those cells or the pathogens that cause disease. Microglia are the cells in the CNS that can do this in

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normal, healthy tissue, and they are therefore also referred to as CNS-resident macrophages.

The **ependymal cell** is a glial cell that filters blood to make **cerebrospinal fluid** (**CSF**), the fluid that circulates through the CNS. Because of the privileged blood supply inherent in the BBB, the extracellular space in nervous tissue does not easily exchange components with the blood. Ependymal cells line each **ventricle**, one of four central cavities that are remnants of the hollow centre of the neural tube formed during the embryonic development of the brain. The **choroid plexus** is a specialized structure in the ventricles where ependymal cells come in contact with blood vessels and filter and absorb components of the blood to produce cerebrospinal fluid. Because of this, ependymal cells can be considered a component of the BBB, or a place where the BBB breaks down. These glial cells appear similar to epithelial cells, making a single layer of cells with little intracellular space and tight connections between adjacent cells. They also have cilia on their apical surface to help move the CSF through the ventricular space. The relationship of these glial cells to the structure of the CNS is seen in Figure 12.9.

Glial Cells of the PNS

One of the two types of glial cells found in the PNS is the **satellite cell**. Satellite cells are found in sensory and autonomic ganglia, where they surround the cell bodies of neurons. This accounts for the name, based on their appearance under the microscope. They provide support, performing similar functions in the periphery as astrocytes do in the CNS—except, of course, for establishing the BBB.

The second type of glial cell is the **Schwann cell**, which insulates axons with myelin in the periphery. Schwann cells are different than oligodendrocytes in that a Schwann cell wraps around a portion of only one axon segment and no others. Oligodendrocytes have processes that reach out to multiple axon segments, whereas the entire Schwann cell surrounds just one axon segment. The nucleus and cytoplasm of the Schwann cell are on the edge of the myelin sheath. The relationship of these two types of glial cells to ganglia and nerves in the PNS is seen in Figure 12.10.

Myelin

The insulation for axons in the nervous system is provided by glial cells, oligodendrocytes in the CNS, and Schwann cells in the PNS. Whereas the manner in which either cell is associated with the axon segment(s) that it insulates is different, the means of myelinating an axon segment is mostly the same in the

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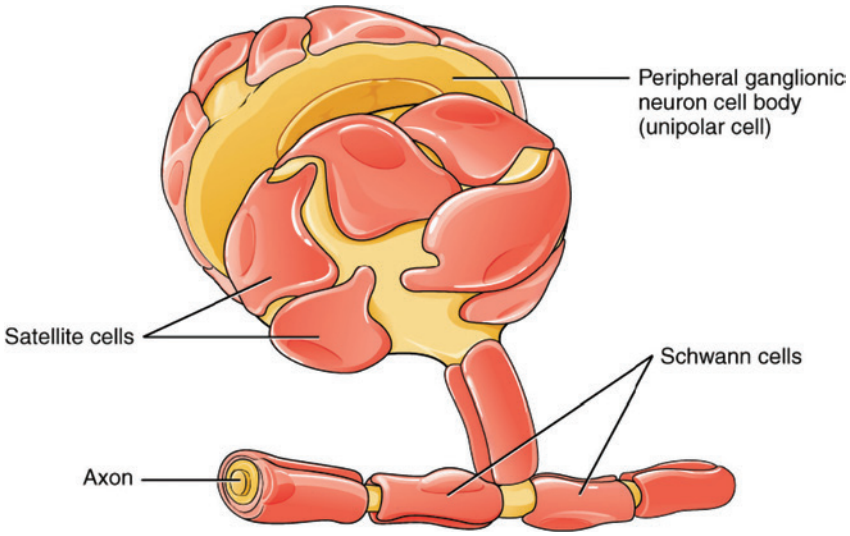


Figure 12.10 Glial Cells of the PNS. The PNS has satellite cells and Schwann cells.

two situations. Myelin is a lipid-rich sheath that surrounds the axon and, by doing so, creates a **myelin sheath** that facilitates the transmission of electrical signals along the axon. The lipids are essentially the phospholipids of the glial cell membrane. Myelin, however, is more than just the membrane of the glial cell. It also includes important proteins that are integral to that membrane. Some of the proteins help hold the layers of the glial cell membrane closely together.

The appearance of the myelin sheath can be thought of as similar to the pastry wrapped around a hot dog for "pigs in a blanket" or a similar food. The glial cell is wrapped around the axon several times with little to no cytoplasm between the glial cell layers. For oligodendrocytes, the rest of the cell is separate from the myelin sheath as a cell process extends back toward the cell body. A few other processes provide the same insulation for other axon segments in the area. For Schwann cells, the outermost layer of the cell membrane contains cytoplasm and the nucleus of the cell as a bulge on one side of the myelin sheath. During development, the glial cell is loosely or incompletely wrapped around the axon (Figure 12.11a). The edges of this loose enclosure extend toward each other, and one end tucks under the other. The inner edge wraps around the axon, creating several layers, and the other edge closes around the outside so that the axon is completely enclosed.

Myelin sheaths can extend for one or two millimetres, depending on the diameter of the axon. Axon diameters can be as small as 1 to 20 micrometres (μm). Because a micrometre is 1/1000 of a millimetre, this means that the length of

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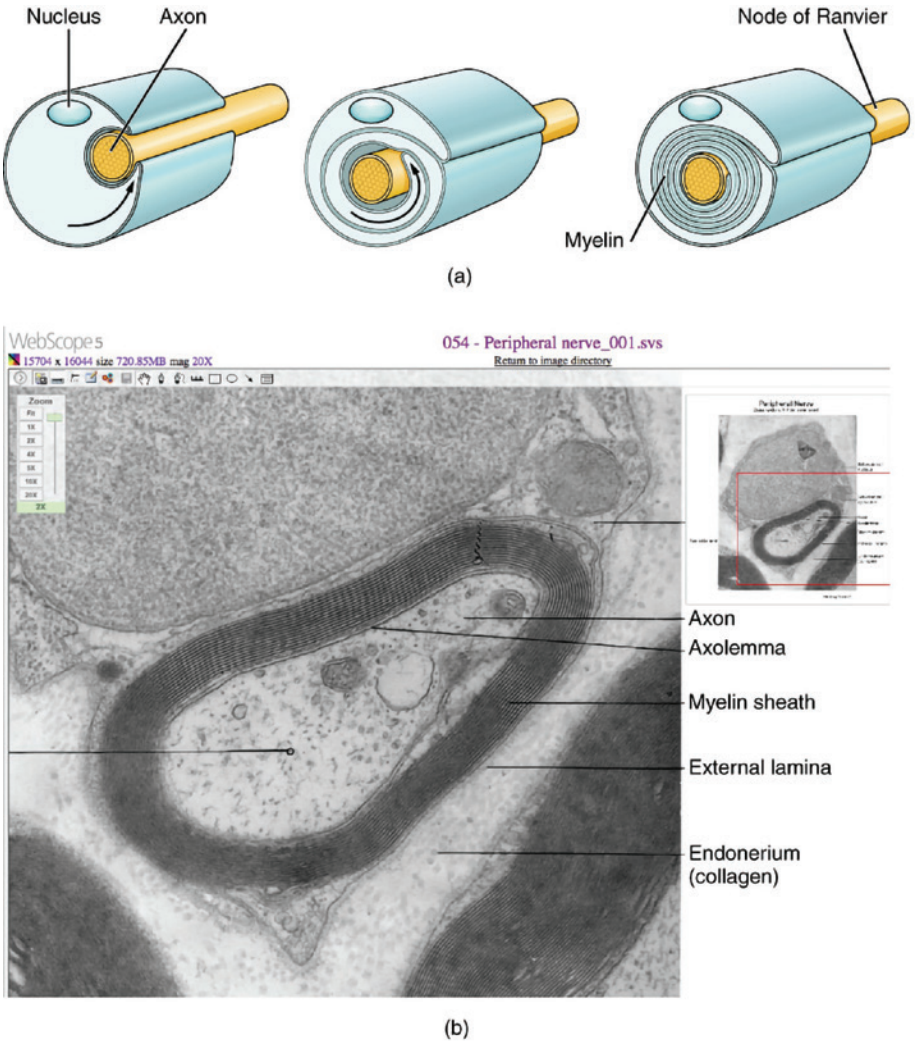


Figure 12.11 The Process of Myelination. Myelinating glia wrap several layers of cell membrane around the cell membrane of an axon segment. A single Schwann cell insulates a segment of a peripheral nerve, whereas in the CNS, an oligodendrocyte may provide insulation for a few separate axon segments. EM × 1,460,000. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

a myelin sheath can be 100–1000 times the diameter of the axon. Figure 12.6, Figure 12.9, and Figure 12.10 show the myelin sheath surrounding an axon segment but are not to scale. If the myelin sheath were drawn to scale, the neuron would have to be immense—possibly covering an entire wall of the room in which you are sitting.

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12.3 The Functions of Nervous Tissue

Learning Objectives

By the end of this section, you will be able to:

- Distinguish the major functions of the nervous system: sensation, integration, and response
- List the sequence of events in a simple sensory receptor–motor response pathway

Having looked at the components of nervous tissue and the basic anatomy of the nervous system, next comes an understanding of how nervous tissue is capable of communicating within the nervous system. Before getting to the nuts and bolts of how this works, an illustration of how the components come together will be helpful. An example is summarized in Figure 12.12.

Imagine you are about to take a shower in the morning before going to school. You have turned on the tap to start the water as you prepare to get in the shower. After a few minutes, you expect the water to be at a temperature that will be comfortable to enter. So you put your hand out into the spray of water. What happens next depends on how your nervous system interacts with the stimulus of the water temperature and what you do in response to that stimulus.

Found in the skin of your fingers or toes is a type of **sensory receptor** that is sensitive to temperature, called a **thermoreceptor**. When you place your hand under the shower (Figure 12.13), the cell membrane of the thermoreceptors changes its electrical state (voltage). The amount of change is dependent on the strength of the stimulus (how hot the water is). This is called a **graded potential**. If the stimulus is strong, the voltage of the cell membrane will change enough to generate an electrical signal that will travel down the axon. You have learned about this type of signalling before, with respect to the interaction of nerves and muscles at the neuromuscular junction. The voltage at which such a signal is generated is called the **threshold**, and the resulting electrical signal is called an **action potential**. In this example, the action potential travels—a process known as **propagation**—along the axon from the axon hillock to the axon terminals and into the synaptic end bulbs. When this signal reaches the end bulbs, it causes the release of a signalling molecule called a **neurotransmitter**.

The neurotransmitter diffuses across the short distance of the synapse and binds to a receptor protein of the target neuron. When the molecular signal binds to the receptor, the cell membrane of the target neuron changes its electrical state, and a new graded potential begins. If that graded potential is

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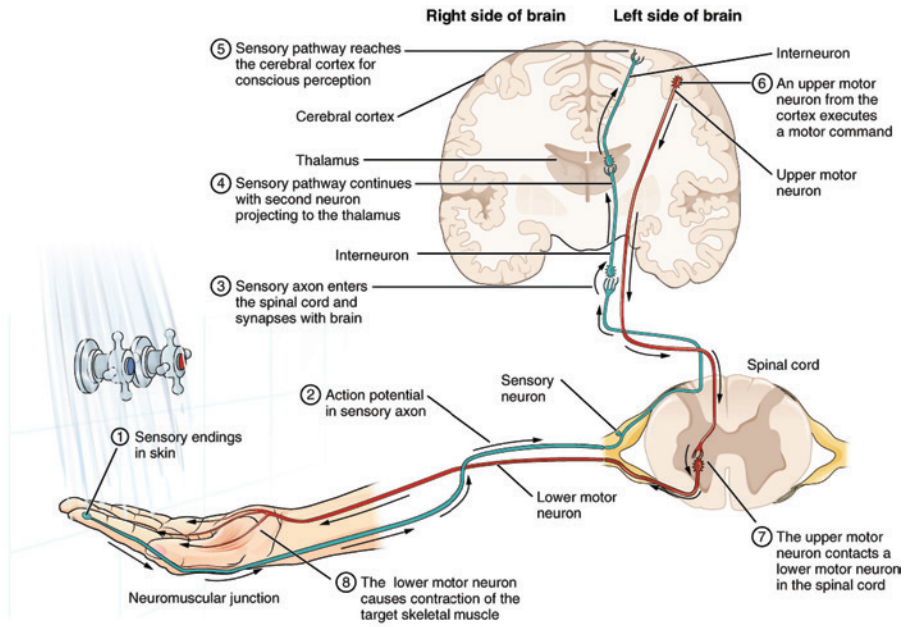


Figure 12.12 Testing the Water. (1) The sensory neuron has endings in the skin that sense a stimulus such as water temperature. The strength of the signal that starts here is dependent on the strength of the stimulus. (2) The graded potential from the sensory endings, if strong enough, will initiate an action potential at the initial segment of the axon (which is immediately adjacent to the sensory endings in the skin). (3) The axon of the peripheral sensory neuron enters the spinal cord and contacts another neuron in the grey matter. The contact is a synapse where another graded potential is caused by the release of a chemical signal from the axon terminals. (4) An action potential is initiated at the initial segment of this neuron and travels up the sensory pathway to a region of the brain called the thalamus. Another synapse passes the information along to the next neuron. (5) The sensory pathway ends when the signal reaches the cerebral cortex. (6) After integration with neurons in other parts of the cerebral cortex, a motor command is sent from the precentral gyrus of the frontal cortex. (7) The upper motor neuron sends an action potential down to the spinal cord. The target of the upper motor neuron is the dendrites of the lower motor neuron in the grey matter of the spinal cord. (8) The axon of the lower motor neuron emerges from the spinal cord in a nerve and connects to a muscle through a neuromuscular junction to cause contraction of the target muscle.

strong enough to reach the threshold, the second neuron generates an action potential at its axon hillock. The target of this neuron is another neuron in the **thalamus** of the brain, the part of the CNS that acts as a relay for sensory information. At another synapse, a neurotransmitter is released and binds to its receptor. The thalamus then sends the sensory information to the **cerebral cortex**, the outermost layer of grey matter in the brain, where conscious perception of that water temperature begins.

Within the cerebral cortex, information is processed among many neurons, integrating the stimulus of the water temperature with other sensory stimuli,

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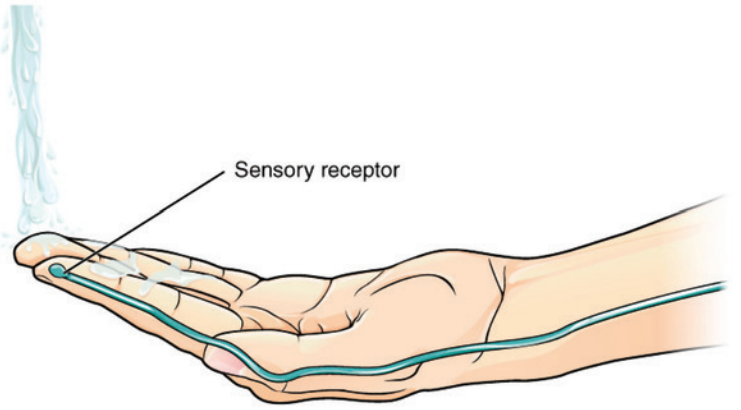


Figure 12.13 The Sensory Input. Receptors in the skin sense the temperature of the water.

such as your emotional state (you just aren't ready to wake up; the bed is calling to you) and memories (perhaps of the lab notes you have to study before a quiz). Finally, a plan is developed about what to do, whether that is to turn the temperature up, turn the whole shower off and go back to bed, or step into the shower. To do any of these things, the cerebral cortex has to send a command out to your body to move your muscles (Figure 12.14).

A region of the cortex is specialized for sending signals down to the spinal cord for movement. The **upper motor neuron** is in this region, which has an axon that extends all the way down the spinal cord. At the level of the spinal cord at which this axon makes a synapse, a graded potential occurs in the cell membrane of a **lower motor neuron**. This second motor neuron is responsible for causing muscle fibres to contract. In the manner described in the chapter on muscle tissue, an action potential travels along the motor neuron axon into the periphery. The axon terminates on muscle fibres at the neuromuscular junction.

Acetylcholine is released at this specialized synapse, which causes the muscle action potential to begin, following a large potential known as an end-plate potential. When the lower motor neuron excites the muscle fibre, it contracts. All this occurs in a fraction of a second, but this story is the basis of how the nervous system functions.

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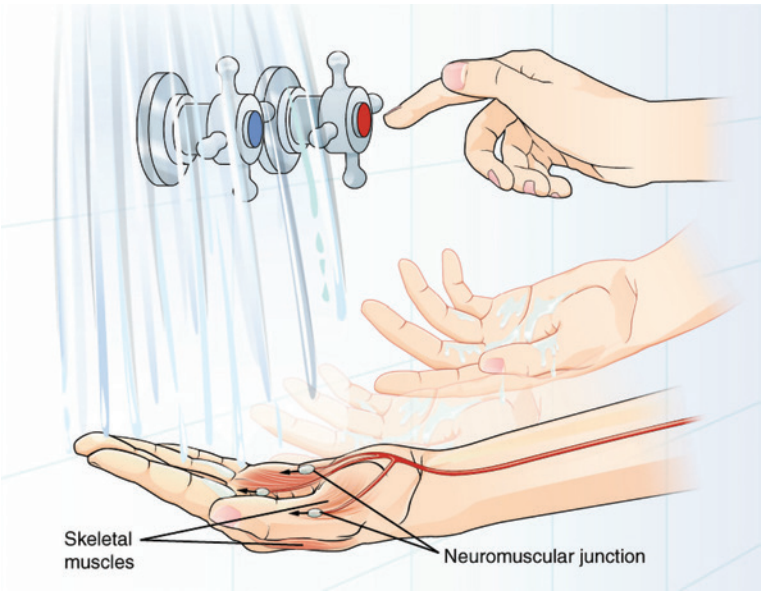


Figure 12.14 The Motor Response. On the basis of the sensory input and the integration in the CNS, a motor response is formulated and executed.

12.4 The Action Potential

Learning Objectives

By the end of this section, you will be able to:

- Describe the components of the membrane that establish the resting membrane potential
- Describe the changes that occur to the membrane that result in the action potential

The functions of the nervous system—sensation, integration, and response—depend on the functions of the neurons underlying these pathways. To understand how neurons are able to communicate, it is necessary to describe the role of an **excitable membrane** in generating these signals. The basis of this communication is the action potential, which demonstrates how changes in the membrane can constitute a signal. Looking at the way these signals work in more variable circumstances involves a look at graded potentials, which will be covered in the next section.

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Electrically Active Cell Membranes

Most cells in the body make use of charged particles, ions, to build up a charge across the cell membrane. Previously, this was shown to be a part of how muscle cells work. For skeletal muscles to contract, based on excitation-contraction coupling, requires input from a neuron. Both of the cells make use of the cell membrane to regulate ion movement between the extracellular fluid and cytosol.

As you learned in the chapter on cells, the cell membrane is primarily responsible for regulating what can cross the membrane and what stays on only one side. The cell membrane is a phospholipid bilayer, so only substances that can pass directly through the hydrophobic core can diffuse through unaided. Charged particles, which are hydrophilic by definition, cannot pass through the cell membrane without assistance (Figure 12.15).

Transmembrane proteins, specifically channel proteins, make this possible. Several passive transport channels, as well as active transport pumps, are necessary to generate a transmembrane potential and an action potential. Of special interest is the carrier protein referred to as the **sodium-potassium pump** that moves sodium ions (Na^+) out of a cell and potassium ions (K^+) into a cell, thus regulating ion concentration on both sides of the cell membrane. Therefore, it is considered to be an electrogenic pump.

The sodium-potassium pump requires energy in the form of adenosine triphosphate (ATP), so it is also referred to as an **ATPase**. As was explained in the cell chapter, the concentration of Na^+ is higher outside the cell than inside, and the concentration of K^+ is higher inside the cell than outside. That means that

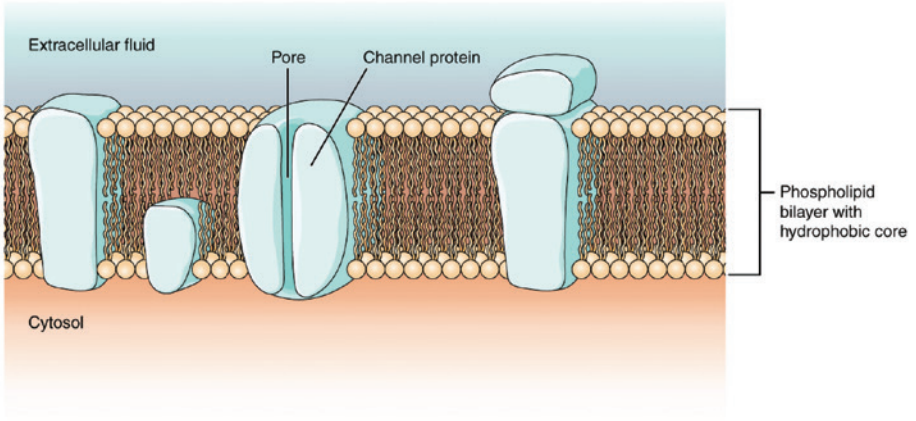


Figure 12.15 Cell Membrane and Transmembrane Proteins. The cell membrane is composed of a phospholipid bilayer and has many transmembrane proteins, including different types of channel proteins that serve as ion channels.

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this pump is moving the ions against the concentration gradients for sodium and potassium, which is why it requires energy. In fact, the pump basically maintains those concentration gradients. Ion channels are pores that allow specific charged particles to cross the membrane in response to an existing concentration gradient.

Ion channels do not always freely allow ions to diffuse across the membrane. Some are opened by certain events, meaning the channels are **gated**. So another way that channels can be categorized is on the basis of how they are gated. Although these classes of ion channels are found primarily in the cells of nervous or muscular tissue, they can also be found in the cells of epithelial and connective tissues.

A **ligand-gated channel** opens because a signalling molecule, a ligand, binds to the extracellular region of the channel. This type of channel is also known as an **ionotropic receptor** because the ligand, known as a neurotransmitter in the nervous system, binds to the protein and facilitates the ions to cross the cell membrane, which changes the protein's electric charge (Figure 12.16).

A **mechanically gated channel** opens because of a physical distortion of the cell membrane. Many channels associated with the sense of touch (somatosensation) are mechanically gated. For example, as pressure is applied to the skin, these channels open and allow ions to enter the cell. Similar to this type of channel would be the channel that opens on the basis of temperature changes, as in testing the water in the shower (Figure 12.17).

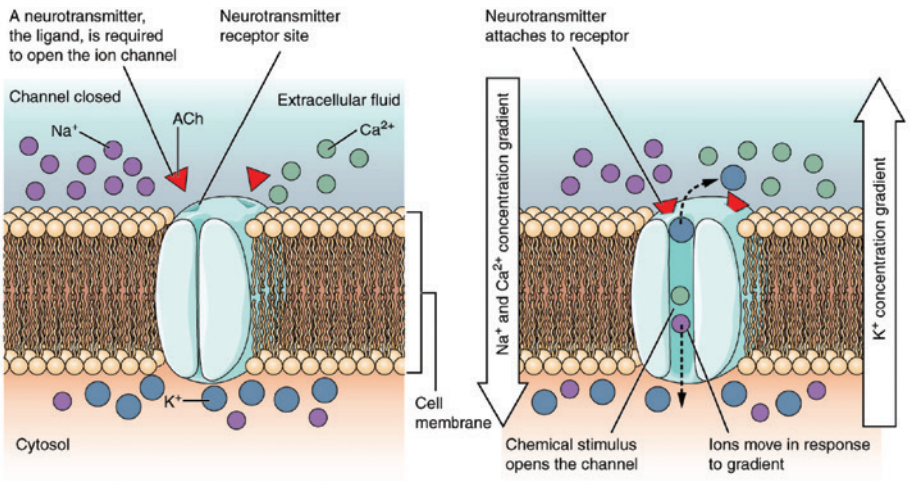


Figure 12.16 Ligand-Gated Channels. When the ligand, in this case the neurotransmitter acetylcholine, binds to a specific location on the extracellular surface of the channel protein, the pore opens to allow select ions through. The ions, in this case, are cations of sodium, calcium, and potassium.

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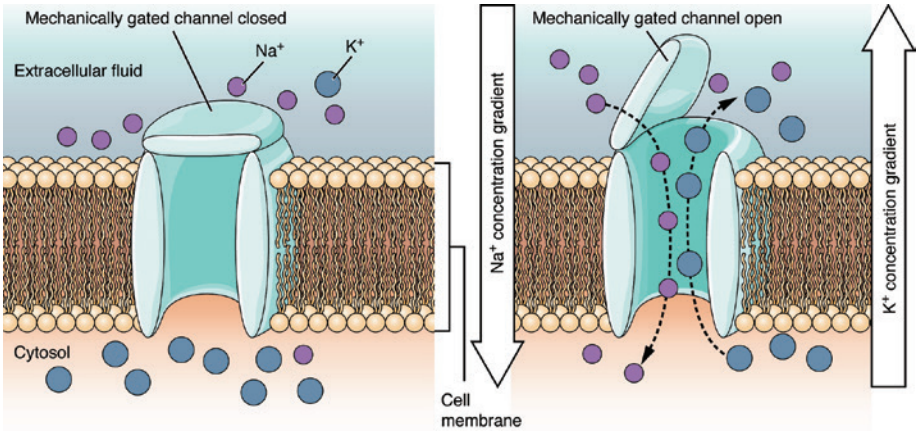


Figure 12.17 Mechanically Gated Channels. When a mechanical change occurs in the surrounding tissue, such as pressure or touch, the channel is physically opened. Thermoreceptors work on a similar principle. When the local tissue temperature changes, the protein reacts by physically opening the channel.

A **voltage-gated channel** is a channel that responds to changes in the electrical properties of the membrane in which it is embedded. Normally, the inner portion of the membrane is at a negative voltage. When that voltage becomes less negative, the channel begins to allow ions to cross the membrane (Figure 12.18).

A **leakage channel** is randomly gated, meaning that it opens and closes at random, hence the reference to leaking. There is no actual event that opens the channel; instead, it has an intrinsic rate of switching between the open and closed states. Leakage channels contribute to the resting transmembrane voltage of the excitable membrane (Figure 12.19).

The Membrane Potential

The electrical state of the cell membrane can have several variations. These are all variations in the **membrane potential**. A potential is a distribution of charge across the cell membrane, measured in millivolts (mV). The standard is to describe the inside of the cell relative to the outside, so the membrane potential is a value representing the charge on the intracellular side of the membrane based on the outside being zero, relatively speaking (Figure 12.20).

The concentration of ions in extracellular and intracellular fluids is largely balanced, with a net neutral charge. However, a slight difference in charge occurs right at the membrane surface, both internally and externally. It is the difference in this very limited region that has all the power in neurons (and muscle cells) to generate electrical signals, including action potentials.

Before these electrical signals can be described, the resting state of the membrane must be explained. When the cell is at rest and the ion channels

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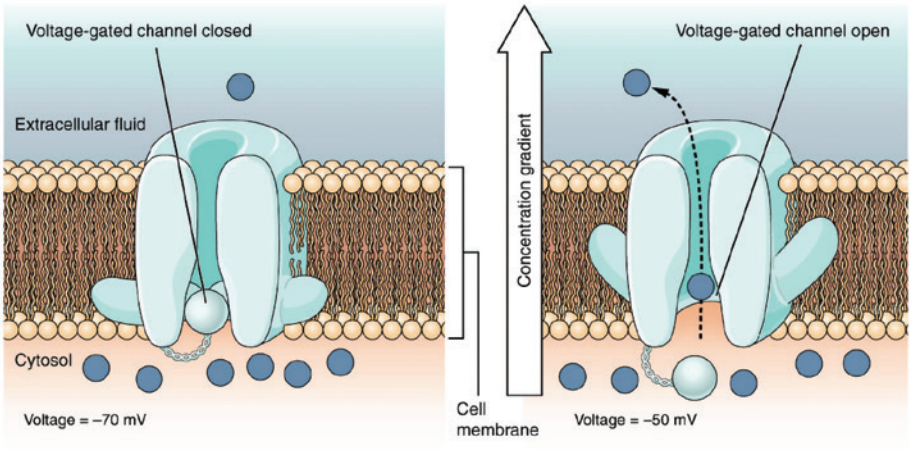


Figure 12.18 Voltage-Gated Channels. Voltage-gated channels open when the transmembrane voltage changes around them. Amino acids in the structure of the protein are sensitive to charge and cause the pore to open to the selected ion.

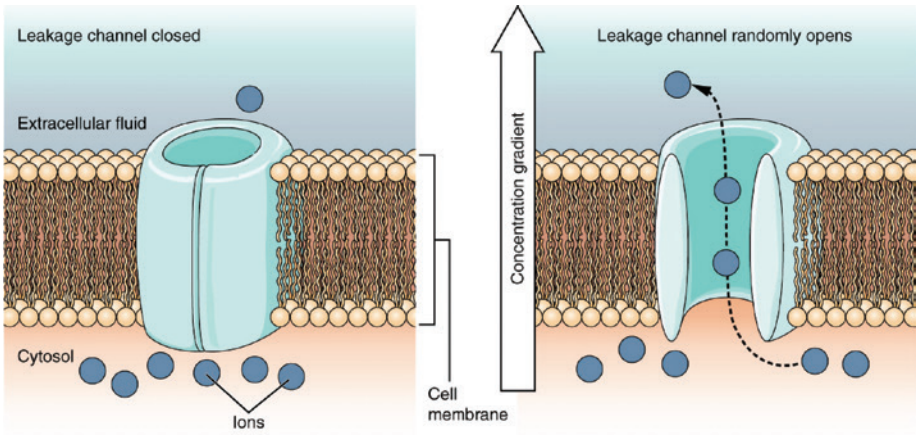


Figure 12.19 Leakage Channels. In certain situations, ions need to move across the membrane randomly. The particular electrical properties of certain cells are modified by the presence of this type of channel.

are closed (except for leakage channels, which randomly open), ions are distributed across the membrane in a very predictable way. The concentration of Na^+ outside the cell is 10 times greater than the concentration inside. Also, the concentration of K^+ inside the cell is greater than on the outside. The cytosol contains a high concentration of anions in the form of phosphate ions and negatively charged proteins.

Large anions are a component of the inner cell membrane, including specialized phospholipids and proteins associated with the inner leaflet of the

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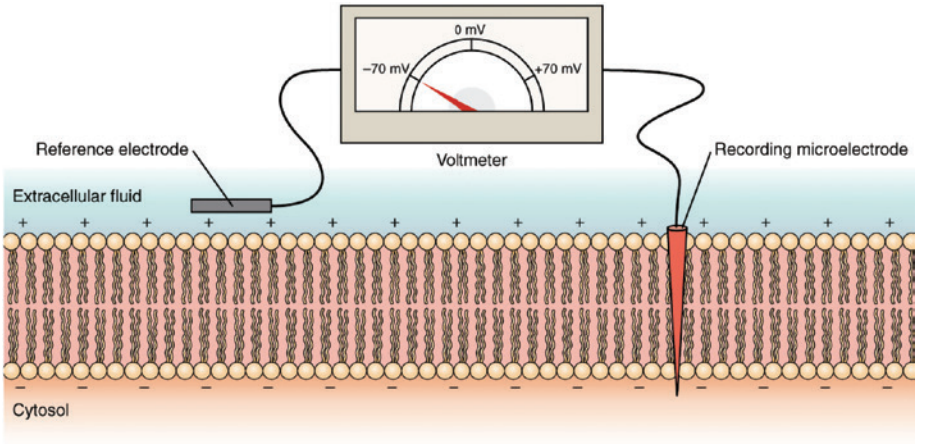


Figure 12.20 Measuring Charge Across a Membrane with a Voltmeter. A recording electrode is inserted into the cell, and a reference electrode is outside the cell. By comparing the charge measured by these two electrodes, the transmembrane voltage is determined. It is conventional to express that value for the cytosol relative to the outside.

membrane (*leaflet* is a term used for one side of the lipid bilayer membrane). The negative charge is localized in the large anions.

With the ions distributed across the membrane at these concentrations, the difference in charge is measured at −70 mV, the value described as the **resting membrane potential**. The exact value measured for the resting membrane potential varies between cells, but −70 mV is most commonly used as this value. This voltage would actually be much lower except for the contributions of some important proteins in the membrane. Leakage channels allow Na^+ to slowly move into the cell or K^+ to slowly move out, and the Na^+/K^+ pump restores them. This may appear to be a waste of energy, but each has a role in maintaining the membrane potential.

The Action Potential

Resting membrane potential describes the steady state of the cell, which is a dynamic process that is balanced by ion leakage and ion pumping. Without any outside influence, it will not change. To get an electrical signal started, the membrane potential has to change.

This starts with a channel opening for Na^+ in the membrane. Because the concentration of Na^+ is higher outside the cell than inside the cell by a factor of 10, ions will rush into the cell that are driven largely by the concentration gradient. Because sodium is a positively charged ion, it will change the relative voltage immediately inside the cell relative to immediately outside. The resting

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potential is the state of the membrane at a voltage of −70 mV, so the sodium cation entering the cell will cause it to become less negative. This is known as **depolarization**, meaning the membrane potential moves toward zero.

The concentration gradient for Na^+ is so strong that it will continue to enter the cell even after the membrane potential has become zero, so that the voltage immediately around the pore begins to become positive. The electrical gradient also plays a role, as negative proteins below the membrane attract the sodium ion. The membrane potential will reach +30 mV by the time sodium has entered the cell.

As the membrane potential reaches +30 mV, other voltage-gated channels open in the membrane. These channels are specifically for the potassium ion. A concentration gradient acts on K^+, as well. As K^+ starts to leave the cell, taking a positive charge with it, the membrane potential begins to move back toward its resting voltage. This is called **repolarization**, meaning that the membrane voltage moves back toward the −70 mV value of the resting membrane potential.

Repolarization returns the membrane potential to the −70 mV value that indicates the resting potential, but it actually overshoots that value. Potassium ions reach equilibrium when the membrane voltage is below −70 mV, so a period of **hyperpolarization** occurs while the K^+ channels are open. Those K^+ channels are slightly delayed in closing, accounting for this short overshoot.

What has been described here is the action potential, which is presented as a graph of voltage over time in Figure 12.21. It is the electrical signal that nervous tissue generates for communication. The change in the membrane voltage from −70 mV at rest to +30 mV at the end of depolarization is a 100 mV change, which can also be written as a 0.1 V change.

Example: To put that value in perspective, think about a battery. An AA battery that you might find in a television remote has a voltage of 1.5 V, and a 9 V battery (the rectangular battery with two posts on one end) is, obviously, 9 V. The change seen in the action potential is one or two orders of magnitude less than the charge in these batteries. In fact, the membrane potential can be described as a battery. A charge is stored across the membrane that can be released under the correct conditions. A battery in your remote has stored a charge that is “released” when you push a button.

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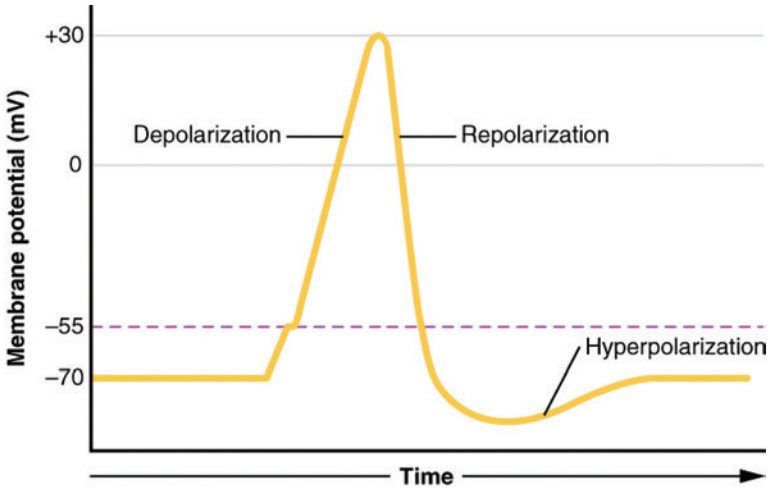


Figure 12.21 Graph of Action Potential. Plotting voltage measured across the cell membrane against time, the action potential begins with depolarization, followed by repolarization, which goes past the resting potential into hyperpolarization, and finally, the membrane returns to rest.

Interactive Link 12.2

What happens across the membrane of an electrically active cell is a dynamic process that is hard to visualize with static images or through text descriptions. View this animation (http://oer.aupress.ca/oer-202505/12.2) to learn more about this process. What is the difference between the driving forces for Na^+ and K^+? And what is similar about the movement of these two ions?

The question is, now, what initiates the action potential? The description given so far conveniently glosses over that point, but it is vital to understanding what is happening. The membrane potential will stay at the resting voltage until something changes. The description above just says that a Na^+ channel opens. Now, to say "a channel opens" does not mean that one individual transmembrane protein changes. Instead, it means that one kind of channel opens.

There are a few different types of channels that allow Na^+ to cross the membrane. A ligand-gated Na^+ channel will open when a neurotransmitter binds to it, and a mechanically gated Na^+ channel will open when a physical stimulus affects a sensory receptor (like pressure applied to the skin compresses a touch receptor). Whether it is a neurotransmitter binding to its receptor protein or a sensory stimulus activating a sensory receptor cell, some stimulus gets the

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process started. Sodium starts to enter the cell, and the membrane becomes less negative.

A third type of channel that is an important part of depolarization in the action potential is the voltage-gated Na^+ channel. The channels that start depolarizing the membrane because of a stimulus help the cell to depolarize from −70 mV to −55 mV. Once the membrane reaches that voltage, the voltage-gated Na^+ channels open. This is what is known as the **threshold**. Any depolarization that does not change the membrane potential to −55 mV or higher will not reach threshold and thus will not result in an action potential. Also, any stimulus that depolarizes the membrane to −55 mV or beyond will cause a large number of channels to open, and an action potential will be initiated.

Because of the threshold, the action potential can be likened to a digital event—it either happens or it does not. If the threshold is not reached, then no action potential occurs. If depolarization reaches −55 mV, then the action potential continues and runs all the way to +30 mV, at which K^+ causes repolarization, including the hyperpolarizing overshoot. Also, those changes are the same for every action potential, which means that once the threshold is reached, the exact same thing happens. A stronger stimulus, which might depolarize the membrane well past threshold, will not make a "bigger" action potential. Action potentials are "all-or-none." Either the membrane reaches the threshold and everything occurs as described above, or the membrane does not reach the threshold and nothing else happens. All action potentials peak at the same voltage (+30 mV), so one action potential is not bigger than another. Stronger stimuli will initiate multiple action potentials more quickly, but the individual signals are not bigger. Thus, for example, you will not feel a greater sensation of pain or have a stronger muscle contraction because of the size of the action potential, as the signals are not different sizes.

As we have seen, the depolarization and repolarization of an action potential are dependent on two types of channels (the voltage-gated Na^+ channel and the voltage-gated K^+ channel). The voltage-gated Na^+ channel actually has two gates. One is the **activation gate**, which opens when the membrane potential crosses −55 mV. The other gate is the **inactivation gate**, which closes after a specific period of time—on the order of a fraction of a millisecond. When a cell is at rest, the activation gate is closed and the inactivation gate is open. However, when the threshold is reached, the activation gate opens, allowing Na^+ to rush into the cell. Timed with the peak of depolarization, the inactivation gate closes. During repolarization, no more sodium can enter the cell. When the membrane potential passes −55 mV again, the activation gate closes. After that, the inactivation gate reopens, making the channel ready to start the whole process over again.

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The voltage-gated K^+ channel has only one gate, which is sensitive to a membrane voltage of −50 mV. However, it does not open as quickly as the voltage-gated Na^+ channel does. It might take a fraction of a millisecond for the channel to open once that voltage has been reached. The timing of this coincides exactly with when the Na^+ flow peaks, so voltage-gated K^+ channels open just as the voltage-gated Na^+ channels are being inactivated. As the membrane potential repolarizes and the voltage passes −50 mV again, the channel closes—again, with a little delay. Potassium continues to leave the cell for a short while, and the membrane potential becomes more negative, resulting in the hyperpolarizing overshoot. Then the channel closes again, and the membrane can return to the resting potential because of the ongoing activity of the nongated channels and the Na^+/K^+ pump.

All this takes place within approximately 2 ms (Figure 12.22). While an action potential is in progress, another one cannot be initiated. That effect is referred to as the **refractory period**. There are two phases of the refractory period: the **absolute refractory period** and the **relative refractory period**. During the absolute phase, another action potential will not start. This is because of the inactivation gate of the voltage-gated Na^+ channel. Once that channel is back to its resting conformation (less than −55 mV), a new action potential could be started, but only by a stronger stimulus than the one that

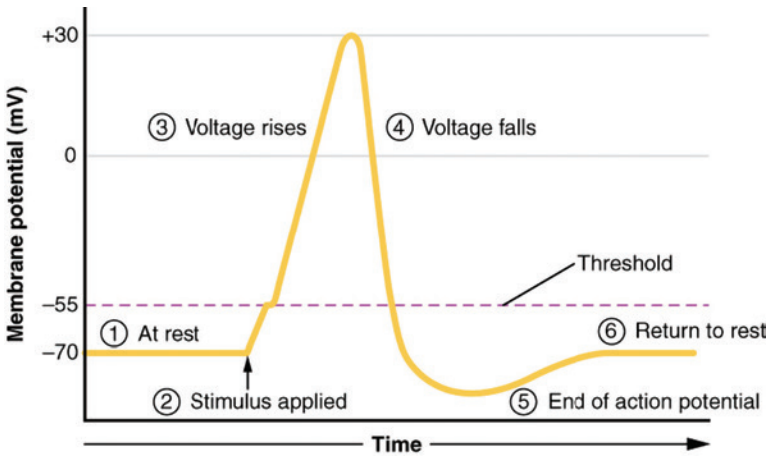


Figure 12.22 Stages of an Action Potential. Plotting voltage measured across the cell membrane against time, the events of the action potential can be related to specific changes in the membrane voltage. (1) At rest, the membrane voltage is −70 mV. (2) The membrane begins to depolarize when an external stimulus is applied. (3) The membrane voltage begins a rapid rise toward +30 mV. (4) The membrane voltage starts to return to a negative value. (5) Repolarization continues past the resting membrane voltage, resulting in hyperpolarization. (6) The membrane voltage returns to the resting value shortly after hyperpolarization.

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initiated the current action potential. This is because of the flow of K^+ out of the cell. Because that ion is rushing out, any Na^+ that tries to enter will not depolarize the cell but will only keep the cell from hyperpolarizing.

Propagation of the Action Potential

The action potential is initiated at the beginning of the axon, at what is called the initial segment. There is a high density of voltage-gated Na^+ channels so that rapid depolarization can take place here. Going down the length of the axon, the action potential is propagated because more voltage-gated Na^+ channels are opened as the depolarization spreads. This spreading occurs because Na^+ enters through the channel and moves along the inside of the cell membrane. As the Na^+ moves, or flows, a short distance along the cell membrane, its positive charge depolarizes a little more of the cell membrane. As that depolarization spreads, new voltage-gated Na^+ channels open and more ions rush into the cell, spreading the depolarization a little farther.

Because voltage-gated Na^+ channels are inactivated at the peak of the depolarization, they cannot be opened again for a brief time—the absolute refractory period. Because of this, depolarization spreading back toward previously opened channels has no effect. The action potential must propagate toward the axon terminals; as a result, the polarity of the neuron is maintained.

Propagation, as described previously, applies to unmyelinated axons. When myelination is present, the action potential propagates differently. Sodium ions that enter the cell at the initial segment start to spread along the length of the axon segment, but there are no voltage-gated Na^+ channels until the first node of Ranvier. Because there is not a constant opening of these channels along the axon segment, the depolarization spreads at an optimal speed. The distance between nodes is the optimal distance to keep the membrane still depolarized above threshold at the next node. As Na^+ spreads along the inside of the membrane of the axon segment, the charge starts to dissipate. If the node were any farther down the axon, that depolarization would have fallen off too much for voltage-gated Na^+ channels to be activated at the next node of Ranvier. If the nodes were any closer together, the speed of propagation would be slower.

Propagation along an unmyelinated axon is referred to as **continuous conduction**; along the length of a myelinated axon, it is **saltatory conduction**. Continuous conduction is slow because there are always voltage-gated Na^+ channels opening, and more and more Na^+ is rushing into the cell. Saltatory conduction is faster because the action potential basically jumps from one node to the next (*saltare* = "to leap"), and the new influx of Na^+ renews the depolarized membrane. Along with the myelination of the axon, the diameter of the axon can influence the speed of conduction. Much as water runs faster in a wide

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river than in a narrow creek, Na^+-based depolarization spreads faster down a wide axon than down a narrow one. This concept is known as **resistance** and is generally true for electrical wires or plumbing, just as it is true for axons, although the specific conditions are different at the scales of electrons or ions versus water in a river.

Interactive Link 12.3

Visit this site (http://oer.aupress.ca/oer-202505/12.3) to see a virtual neurophysiology lab and to observe electrophysiological processes in the nervous system, where scientists directly measure the electrical signals produced by neurons. Often, the action potentials occur so rapidly that watching a screen to see them occur is not helpful. A speaker is powered by the signals recorded from a neuron, and it "pops" each time the neuron fires an action potential. These action potentials are firing so fast that it sounds like static on the radio. Electrophysiologists can recognize the patterns within that static to understand what is happening. Why is the leech model used for measuring the electrical activity of neurons instead of using humans?

12.5 Communication Between Neurons

Learning Objectives

By the end of this section, you will be able to:

- Explain the differences between the types of graded potentials
- Categorize the major neurotransmitters by chemical type and effect

The electrical changes taking place within a neuron, as described in the previous section, are similar to a light switch being turned on. A stimulus starts the depolarization, but the action potential runs on its own once a threshold has been reached. The question is now, "What flips the light switch on?" Temporary changes to the cell membrane voltage can result from neurons receiving information from the environment or from the action of one neuron on another. These special types of potentials influence a neuron and determine whether an action potential will occur or not. Many of these transient signals originate at the synapse.

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Graded Potentials

Local changes in the membrane potential are called graded potentials and are usually associated with the dendrites of a neuron. The amount of change in the membrane potential is determined by the size of the stimulus that causes it. In the example of testing the temperature of the shower, slightly warm water would only initiate a small change in a thermoreceptor, whereas hot water would cause a large amount of change in the membrane potential.

Graded potentials can be of two sorts: depolarizing or hyperpolarizing (Figure 12.23). For a membrane at the resting potential, a graded potential represents a change in that voltage either above −70 mV or below −70 mV. Depolarizing graded potentials are often the result of Na^+ or Ca^{2+} entering the cell. Both of these ions have higher concentrations outside the cell than inside; because they have a positive charge, they will move into the cell, causing it to become less negative relative to the outside. Hyperpolarizing graded potentials can be caused by K^+ leaving the cell or Cl^- entering the cell. If a positive charge moves out of a cell, the cell becomes more negative; if a negative charge enters the cell, the same thing happens.

Types of Graded Potentials

For the unipolar cells of sensory neurons—both those with free nerve endings and those within encapsulations—graded potentials develop in the dendrites

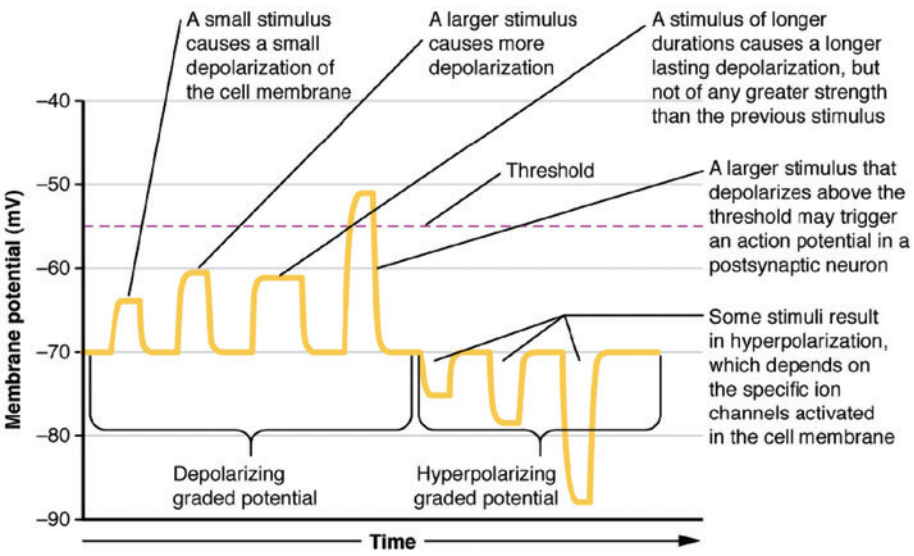


Figure 12.23 Graded Potentials. Graded potentials are temporary changes in the membrane voltage, the characteristics of which depend on the size of the stimulus. Some types of stimuli cause depolarization of the membrane, whereas others cause hyperpolarization. It depends on the specific ion channels that are activated in the cell membrane.

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that influence the generation of an action potential in the axon of the same cell. This is called a **generator potential**. For other sensory receptor cells, such as taste cells or photoreceptors of the retina, graded potentials in their membranes result in the release of neurotransmitters at synapses with sensory neurons. This is called a **receptor potential**.

A **postsynaptic potential** (**PSP**) is the graded potential in the dendrites of a neuron that is receiving synapses from other cells. Postsynaptic potentials can be depolarizing or hyperpolarizing. Depolarization in a postsynaptic potential is called an **excitatory postsynaptic potential** (**EPSP**) because it causes the membrane potential to move toward threshold. Hyperpolarization in a postsynaptic potential is an **inhibitory postsynaptic potential** (**IPSP**) because it causes the membrane potential to move away from threshold.

Summation

All types of graded potentials will result in small changes of either depolarization or hyperpolarization in the voltage of a membrane. These changes can lead to the neuron reaching threshold if the changes add together, or **summate**. The combined effects of different types of graded potentials are illustrated in Figure 12.24. If the total change in voltage in the membrane is a positive 15 mV, meaning that the membrane depolarizes from −70 mV to −55 mV, then the graded potentials will result in the membrane reaching threshold.

For receptor potentials, threshold is not a factor because the change in membrane potential for receptor cells directly causes neurotransmitter release. However, generator potentials can initiate action potentials in the sensory neuron axon, and postsynaptic potentials can initiate an action potential in the axon of other neurons. Graded potentials summate at a specific location at the beginning of the axon to initiate the action potential, namely, the initial segment. For sensory neurons, which do not have a cell body between the dendrites and the axon, the initial segment is directly adjacent to the dendritic endings. For all other neurons, the axon hillock is essentially the initial segment of the axon, and it is where summation takes place. These locations have a high density of voltage-gated Na^+ channels that initiate the depolarizing phase of the action potential.

Summation can be spatial or temporal, meaning it can be the result of multiple graded potentials at different locations on the neuron, or all at the same place but separated in time. **Spatial summation** is related to associating the activity of multiple inputs to a neuron with each other. **Temporal summation** is the relationship of multiple action potentials from a single cell, resulting in a significant change in the membrane potential. Spatial and temporal summation can act together, as well.

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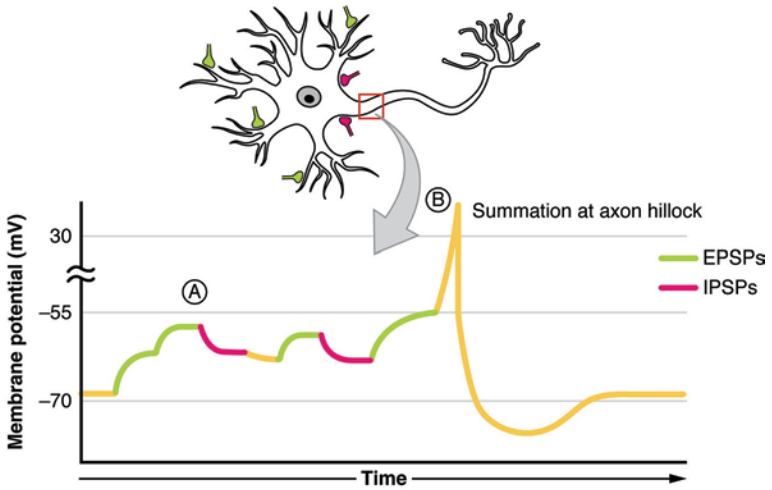


Figure 12.24 Postsynaptic Potential Summation. The result of the summation of postsynaptic potentials is the overall change in the membrane potential. At point A, several different excitatory postsynaptic potentials add up to a large depolarization. At point B, a mix of excitatory and inhibitory postsynaptic potentials results in a different end result for the membrane potential.

Interactive Link 12.4

Watch this video (http://oer.aupress.ca/oer-202505/12.4) to learn about summation. The process of converting electrical signals to chemical signals and back requires subtle changes that can result in transient increases or decreases in membrane voltage. To cause a lasting change in the target cell, multiple signals are usually added together, or summed. Does spatial summation have to happen all at once, or can the separate signals arrive on the postsynaptic neuron at slightly different times? Explain your answer.

Synapses

There are two types of connections between electrically active cells: chemical synapses and electrical synapses. In a **chemical synapse**, a chemical signal—namely, a neurotransmitter—is released from one cell and affects the other cell. In an **electrical synapse**, there is a direct connection between the two cells so that ions can pass directly from one cell to the next. If one cell is depolarized in an electrical synapse, the joined cell also depolarizes because the ions pass between the cells. Chemical synapses involve the transmission of chemical information from one cell to the next. This section will concentrate on the chemical type of synapse.

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A chemical synapse is the neuromuscular junction (NMJ) described in the chapter on muscle tissue. In the nervous system, there are many more synapses that are essentially the same as the NMJ. All synapses have common characteristics, which can be summarized in this list:

- presynaptic element
- neurotransmitter (packaged in vesicles)
- synaptic cleft
- receptor proteins
- postsynaptic element
- neurotransmitter elimination or reuptake

For the NMJ, these characteristics are as follows: the presynaptic element is the motor neuron's axon terminals, the neurotransmitter is **acetylcholine**, the synaptic cleft is the space between the cells where the neurotransmitter diffuses, the receptor protein is the nicotinic acetylcholine receptor, the postsynaptic element is the sarcolemma of the muscle cell, and the neurotransmitter is eliminated by acetylcholinesterase. Other synapses are similar to this, and the specifics are different, but they all contain the same characteristics (Figure 12.25).

Neurotransmitter Release

When an action potential reaches the axon terminals, voltage-gated Ca^{2+} channels in the membrane of the synaptic end bulb open. The concentration of Ca^{2+} increases inside the end bulb, and the Ca^{2+} ion associates with proteins in the outer surface of neurotransmitter vesicles. The Ca^{2+} facilitates the merging of the vesicle with the presynaptic membrane so that the neurotransmitter is released through exocytosis into the small gap between the cells, known as the **synaptic cleft**.

Once in the synaptic cleft, the neurotransmitter diffuses the short distance to the postsynaptic membrane and can interact with neurotransmitter receptors. Receptors are specific for the neurotransmitter, and the two fit together like a key and a lock. One neurotransmitter binds to its receptor and will not bind to receptors for other neurotransmitters, making the binding a specific chemical event.

Neurotransmitter Systems

There are several systems of neurotransmitters that are found at various synapses in the nervous system. These groups refer to the chemicals that are the neurotransmitters, and within the groups are specific systems.

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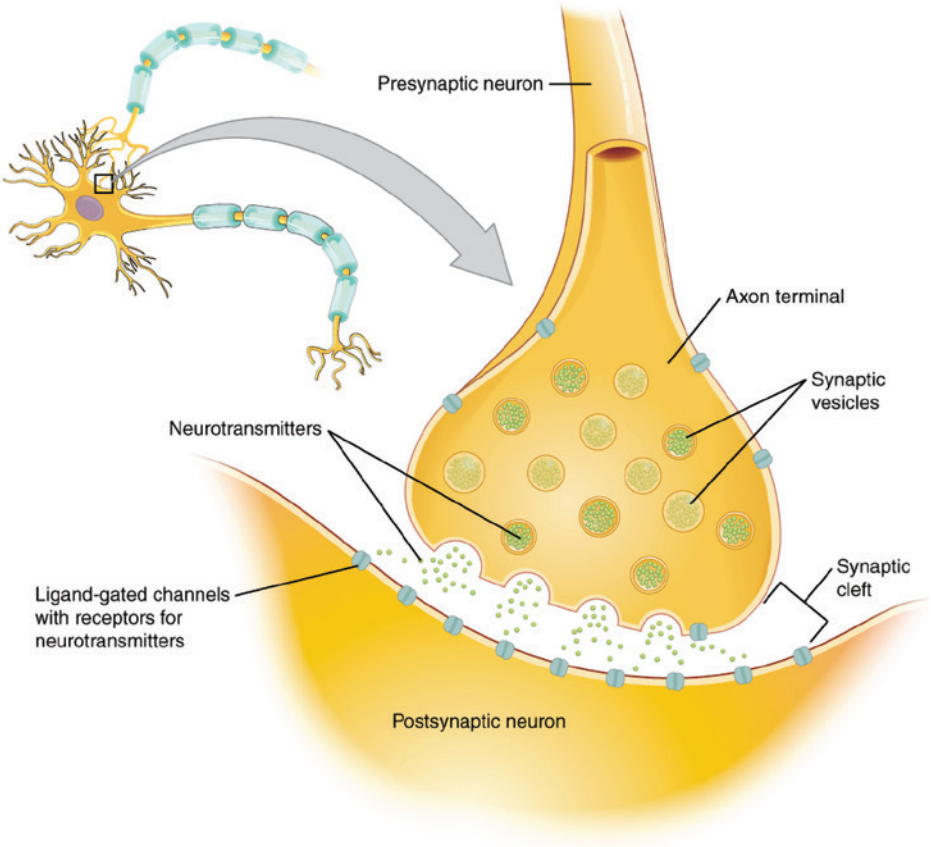


Figure 12.25 The Synapse. The synapse is a connection between a neuron and its target cell (which is not necessarily a neuron). The presynaptic element is the synaptic end bulb of the axon where Ca^{2+} enters the bulb to cause vesicle fusion and neurotransmitter release. The neurotransmitter diffuses across the synaptic cleft to bind to its receptor. The neurotransmitter is cleared from the synapse either by enzymatic degradation, neuronal reuptake, or glial reuptake.

The first group, which is a neurotransmitter system of its own, is the **cholinergic system**. It is the system based on acetylcholine. This includes the NMJ as an example of a cholinergic synapse, but cholinergic synapses are found in other parts of the nervous system. They are in the autonomic nervous system, as well as distributed throughout the brain.

The cholinergic system has two types of receptors; the **nicotinic receptor** is found in the NMJ as well as other synapses. There is also an acetylcholine receptor known as the **muscarinic receptor**. Both of these receptors are named for drugs that interact with the receptor in addition to acetylcholine. Nicotine will bind to the nicotinic receptor and activate it, similar to acetylcholine. Muscarine, a product of certain mushrooms, will bind to the muscarinic receptor. However,

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nicotine will not bind to the muscarinic receptor, and muscarine will not bind to the nicotinic receptor.

Another class of neurotransmitter is the **biogenic amine**, a group of neurotransmitters that are enzymatically made from amino acids. They have amino groups in them but no longer have carboxyl groups and are therefore no longer classified as amino acids. Serotonin is made from tryptophan. It is the basis of the serotonergic system, which has its own specific receptors. Serotonin is transported back into the presynaptic cell for repackaging.

Other biogenic amines are made from tyrosine and include dopamine, norepinephrine, and epinephrine. Dopamine is part of its own system, the dopaminergic system, which has dopamine receptors. Dopamine is removed from the synapse by transport proteins in the presynaptic cell membrane. Norepinephrine and epinephrine belong to the adrenergic neurotransmitter system. The two molecules are very similar and bind to the same receptors, which are referred to as alpha and beta receptors. Norepinephrine and epinephrine are also transported back into the presynaptic cell. The chemical epinephrine (*epi-* = "on"; *-nephrine* = kidney) is also known as adrenaline (*renal* = "kidney"), and norepinephrine is sometimes referred to as noradrenaline. The adrenal gland produces epinephrine and norepinephrine to be released into the bloodstream as hormones.

A **neuropeptide** is a neurotransmitter molecule made up of chains of amino acids connected by peptide bonds. This is what a protein is, but the term *protein* implies a certain length to the molecule. Some neuropeptides are quite short, such as met-enkephalin, which is five amino acids long. Others are long, such as beta-endorphin, which is 31 amino acids long. Neuropeptides are often released at synapses in combination with another neurotransmitter, and they often act as hormones in other systems of the body, such as vasoactive intestinal peptide (VIP) or substance P.

The effect of a neurotransmitter on the postsynaptic element is entirely dependent on the receptor protein. First, if there is no receptor protein in the membrane of the postsynaptic element, then the neurotransmitter has no effect. The depolarizing or hyperpolarizing effect is also dependent on the receptor. When acetylcholine binds to the nicotinic receptor, the postsynaptic cell is depolarized. This is because the receptor is a cation channel, and positively charged Na^+ will rush into the cell. However, when acetylcholine binds to the muscarinic receptor, of which there are several variants, it might cause depolarization or hyperpolarization of the target cell.

The amino acid neurotransmitters, glutamate, glycine, and GABA, are almost exclusively associated with just one effect. Glutamate is considered an excitatory amino acid, but only because Glu receptors in the adult cause depolarization

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of the postsynaptic cell. Glycine and GABA are considered inhibitory amino acids, again because their receptors cause hyperpolarization.

The biogenic amines have mixed effects. For example, the dopamine receptors that are classified as D1 receptors are excitatory, whereas D2-type receptors are inhibitory. Biogenic amine receptors and neuropeptide receptors can have even more complex effects because some may not directly affect the membrane potential but rather have an effect on gene transcription or other metabolic processes in the neuron. The characteristics of the various neurotransmitter systems presented in this section are organized in Table 12.3.

Table 12.3 Characteristics of Neurotransmitter Systems

System	Cholinergic	Amino acids	Biogenic amines	Neuropeptides
Neuro-transmitters	Acetylcholine	Glutamate, glycine, GABA	Serotonin (5-HT), dopamine, norepinephrine (epinephrine)	Met-enkephalin, beta-endorphin, VIP, Substance P, etc.
Receptors	Nicotinic and muscarinic receptors	Glu receptors, gly receptors, GABA receptors	5-HT receptors, D1 and D2 receptors, α-adrenergic and β-adrenergic receptors	Receptors are too numerous to list but are specific to the peptides.
Elimination	Degradation by acetylcholinesterase	Reuptake by neurons or glia	Reuptake by neurons	Degradation by enzymes called peptidases
Postsynaptic effect	Nicotinic receptor causes depolarization. Muscarinic receptors can cause both depolarization and hyperpolarization, depending on the subtype.	Glu receptors cause depolarization. Gly and GABA receptors cause hyper-polarization.	Depolarization or hyperpolarization depends on the specific receptor. For example, D1 receptors cause depolarization, and D2 receptors cause hyper-polarization.	Depolarization or hyper-polarization depends on the specific receptor.

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The important thing to remember about neurotransmitters, and signalling chemicals in general, is that the effect is entirely dependent on the receptor. Neurotransmitters bind to one of two classes of receptors at the cell surface, ionotropic or metabotropic (Figure 12.26). Ionotropic receptors are ligand-gated ion channels, such as the nicotinic receptor for acetylcholine or the glycine receptor. A **metabotropic receptor** involves a complex of proteins that result in metabolic changes within the cell. The receptor complex includes the transmembrane receptor protein, a G protein, and an effector protein. The neurotransmitter, referred to as the first messenger, binds to the receptor protein on the extracellular surface of the cell, and the intracellular side of the protein initiates activity of the G protein. The **G protein** is a guanosine triphosphate (GTP) hydrolase that physically moves from the receptor protein to the effector protein to activate the latter. An **effector protein** is an enzyme that catalyzes the generation of a new molecule, which acts as the intracellular mediator of the signal that binds to the receptor. This intracellular mediator is called the second messenger.

Different receptors use different second messengers. Two common examples of second messengers are cyclic adenosine monophosphate (cAMP) and inositol triphosphate (IP_3). The enzyme adenylate cyclase (an example of an effector protein) makes cAMP, and phospholipase C is the enzyme that makes IP_3. Second messengers, after they are produced by the effector protein, cause metabolic changes within the cell. These changes are most likely the activation of other enzymes in the cell. In neurons, they often modify ion channels, either opening or closing them. These enzymes can also cause changes in the cell, such as the activation of genes in the nucleus, and therefore the increased synthesis of proteins. In neurons, these kinds of changes are often the basis of stronger connections between cells at the synapse and may be the basis of learning and memory.

Interactive Link 12.5

Watch this video (http://oer.aupress.ca/oer-202505/12.5) to learn about the release of a neurotransmitter. The action potential reaches the end of the axon, called the axon terminal, and a chemical signal is released to tell the target cell to do something—either to initiate a new action potential, or to suppress that activity. In a very short space, the electrical signal of the action potential is changed into the chemical signal of a neurotransmitter and then back to electrical changes in the target cell membrane. What is the importance of voltage-gated calcium channels in the release of neurotransmitters?

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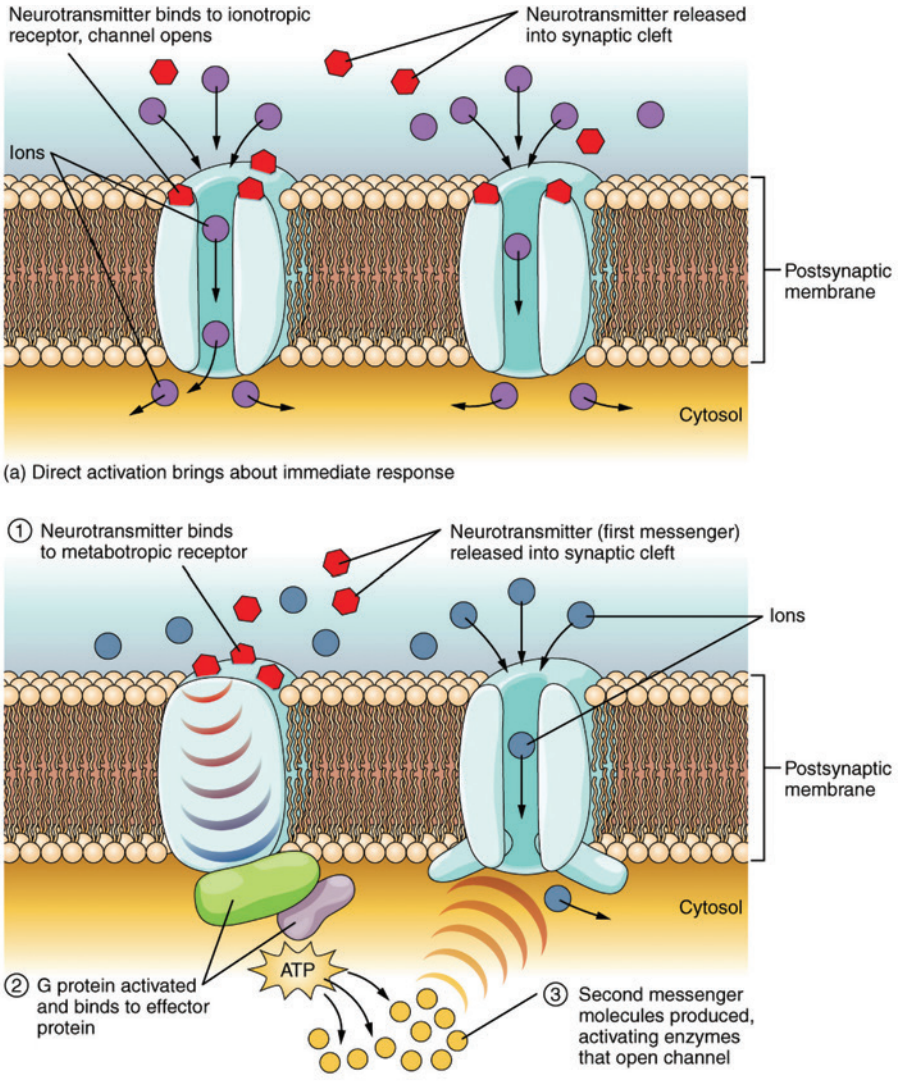


Figure 12.26 Receptor Types. (a) An ionotropic receptor is a channel that opens when the neurotransmitter binds to it. (b) A metabotropic receptor is a complex that causes metabolic changes in the cell when the neurotransmitter binds to it. (1) After binding, the G protein hydrolyzes ATP and moves to the effector protein. (2) When the G protein contacts the effector protein, the latter is activated. In the case shown, the effector protein then acts on ATP to generate a second messenger, cAMP. (3) The second messenger can then go on to cause changes in the neuron, such as opening or closing ion channels, metabolic changes, and changes in gene transcription.

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Key Terms

absolute refractory period: Time during an action period when another action potential cannot be generated because the voltage-gated Na^+ channel is inactivated.

acetylcholine: Neurotransmitter released by the presynaptic neuron's axon terminals into the synaptic cleft.

action potential: Change in voltage of a cell membrane in response to a stimulus that results in transmission of an electrical signal; unique to neurons and muscle fibres.

activation gate: Part of the voltage-gated Na^+ channel that opens when the membrane voltage reaches threshold.

astrocyte: Glial cell type of the CNS that provides support for neurons and maintains the blood-brain barrier.

autonomic nervous system (ANS): Functional division of the nervous system that is responsible for homeostatic reflexes that coordinate control of cardiac and smooth muscle, as well as glandular tissue.

axon: Single process of the neuron that carries an electrical signal (action potential) away from the cell body toward a target cell.

axon hillock: Tapering of the neuron cell body that gives rise to the axon.

axon segment: Single stretch of the axon insulated by myelin and bounded by nodes of Ranvier at either end (except for the first, which is after the initial segment, and the last, which is followed by the axon terminal).

axon terminal: End of the axon, where there are usually several branches extending toward the target cell.

axoplasm: Cytoplasm of an axon, which is different in composition than the cytoplasm of the neuronal cell body.

biogenic amine: Class of neurotransmitters that are enzymatically derived from amino acids but no longer contain a carboxyl group.

bipolar: Shape of a neuron with two processes extending from the neuron cell body—the axon and one dendrite.

blood-brain barrier (BBB): Physiological barrier between the circulatory system and the central nervous system that establishes a privileged blood supply, restricting the flow of substances into the CNS.

brain: The large organ of the central nervous system composed of white and grey matter, contained within the cranium, and continuous with the spinal cord.

central nervous system (CNS): Anatomical division of the nervous system located within the cranial and vertebral cavities, namely, the brain and spinal cord.

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cerebral cortex: Outermost layer of grey matter in the brain, where conscious perception takes place.

cerebrospinal fluid (CSF): Circulatory medium within the CNS that is produced by ependymal cells in the choroid plexus filtering the blood.

chemical synapse: Connection between two neurons, or between a neuron and its target, where a neurotransmitter diffuses across a very short distance.

cholinergic system: Neurotransmitter system of acetylcholine, which includes its receptors and the enzyme acetylcholinesterase.

choroid plexus: Specialized structure containing ependymal cells that line blood capillaries and filter blood to produce CSF in the four ventricles of the brain.

continuous conduction: Slow propagation of an action potential along an unmyelinated axon owing to voltage-gated Na^+ channels located along the entire length of the cell membrane.

dendrite: One of many branchlike processes that extends from the neuron cell body and functions as a contact for incoming signals (synapses) from other neurons or sensory cells.

depolarization: Change in a cell membrane potential from rest toward zero.

effector protein: Enzyme that catalyzes the generation of a new molecule, which acts as the intracellular mediator of the signal that binds to the receptor.

electrical synapse: Connection between two neurons, or any two electrically active cells, where ions flow directly through channels spanning their adjacent cell membranes.

enteric nervous system (ENS): Neural tissue associated with the digestive system that is responsible for nervous control through autonomic connections.

ependymal cell: Glial cell type in the CNS responsible for producing cerebrospinal fluid.

excitable membrane: Cell membrane that regulates the movement of ions so that an electrical signal can be generated.

excitatory postsynaptic potential (EPSP): Graded potential in the postsynaptic membrane that is the result of depolarization and makes an action potential more likely to occur.

G protein: Guanosine triphosphate (GTP) hydrolase that physically moves from the receptor protein to the effector protein to activate the latter.

ganglion: Localized collection of neuron cell bodies in the peripheral nervous system.

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gated: Property of a channel that determines how it opens under specific conditions, such as voltage change or physical deformation.

generator potential: Graded potential from dendrites of a unipolar cell that generates the action potential in the initial segment of that cell's axon.

glial cell: One of the various types of neural tissue cells responsible for maintenance of the tissue and largely responsible for supporting neurons.

graded potential: Change in the membrane potential that varies in size, depending on the size of the stimulus that elicits it.

grey matter: Regions of the nervous system containing cell bodies of neurons with few or no myelinated axons; actually may be more pink or tan in colour but called grey in contrast to white matter.

hyperpolarization: Period of the action potential when the membrane voltage is below −70 mV with K^+ channels open and potassium ions reach equilibrium.

inactivation gate: Part of a voltage-gated Na^+ channel that closes when the membrane potential reaches +30 mV.

inhibitory postsynaptic potential (IPSP): Graded potential in the postsynaptic membrane that is the result of hyperpolarization and makes an action potential less likely to occur.

initial segment: First part of the axon as it emerges from the axon hillock, where the electrical signals known as action potentials are generated.

integration (association areas): Nervous system function that combines sensory perceptions and higher cognitive functions (memories, learning, emotion, etc.) to produce a response.

ionotropic receptor: Neurotransmitter receptor that acts as an ion channel gate and opens by the binding of the neurotransmitter.

leakage channel: Ion channel that opens randomly and is not gated to a specific event, also known as a nongated channel.

ligand-gated channels: Another name for an ionotropic receptor for which a neurotransmitter is the ligand.

lower motor neuron: Second neuron in the motor command pathway that is directly connected to the skeletal muscle.

mechanically gated channel: Ion channel that opens when a physical event directly affects the structure of the protein.

membrane potential: Distribution of charge across the cell membrane, based on the charges of ions.

metabotropic receptor: Neurotransmitter receptor that involves a complex of proteins that cause metabolic changes in a cell.

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microglia: Glial cell type in the CNS that serves as the resident component of the immune system.

multipolar: Shape of a neuron that has multiple processes—the axon and two or more dendrites.

muscarinic receptor: Type of acetylcholine receptor protein that is characterized by also binding to muscarine and is a metabotropic receptor.

myelin: Lipid-rich insulating substance surrounding the axons of many neurons, allowing for faster transmission of electrical signals.

myelin sheath: Lipid-rich layer of insulation that surrounds an axon, formed by oligodendrocytes in the CNS and Schwann cells in the PNS; facilitates the transmission of electrical signals.

nerve: Cordlike bundle of axons located in the peripheral nervous system that transmits sensory input and response output to and from the central nervous system.

neuron: Neural tissue cell that is primarily responsible for generating and propagating electrical signals into, within, and out of the nervous system.

neuropeptide: Neurotransmitter type that includes protein molecules and shorter chains of amino acids.

neurotransmitter: Chemical signal that is released from the synaptic end bulb of a neuron to cause a change in the target cell.

nicotinic receptor: Type of acetylcholine receptor protein that is characterized by also binding to nicotine and is an ionotropic receptor.

node of Ranvier: Gap between two myelinated regions of an axon, allowing for the strengthening of the electrical signal as it propagates down the axon.

nucleus: In the nervous system, a localized collection of neuron cell bodies that are functionally related; a "centre" of neural function.

oligodendrocyte: Glial cell type in the CNS that provides the myelin insulation for axons in tracts.

peripheral nervous system (PNS): Anatomical division of the nervous system that is largely outside the cranial and vertebral cavities, namely, all parts except the brain and spinal cord.

postsynaptic potential (PSP): Graded potential in the postsynaptic membrane caused by the binding of neurotransmitter to protein receptors.

process: In cells, an extension of a cell body; in the case of neurons, this includes the axon and dendrites.

propagation: Movement of an action potential along the length of an axon.

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Purkinje cell: A multipolar neuron that has a very important role to play in the cerebellum.

receptor potential: Graded potential in a specialized sensory cell that directly causes the release of neurotransmitter without an intervening action potential.

refractory period: Time after the initiation of an action potential when another action potential cannot be generated.

relative refractory period: Time during the refractory period when a new action potential can only be initiated by a stronger stimulus than the current action potential because voltage-gated K^+ channels are not closed.

repolarization: Return of the membrane potential to its normally negative voltage at the end of the action potential.

resistance: Property of an axon that relates to the ability of particles to diffuse through the cytoplasm; this is inversely proportional to the fibre diameter.

response: Nervous system function that causes a target tissue (muscle or gland) to produce an event as a consequence to stimuli.

resting membrane potential: The difference in voltage measured across a cell membrane under steady-state conditions, typically −70 mV.

saltatory conduction: Quick propagation of the action potential along a myelinated axon owing to voltage-gated Na^+ channels being present only at the nodes of Ranvier.

satellite cell: Glial cell type in the PNS that provides support for neurons in the ganglia.

Schwann cell: Glial cell type in the PNS that provides the myelin insulation for axons in nerves.

sensation: Nervous system function that receives information from the environment and translates it into the electrical signals of nervous tissue.

sensory receptor: Nervous structures specialized for detection of temperature, touch, pain, and so on.

sodium-potassium pump (ATPase): Cell membrane proteins specialized in moving sodium ions (Na^+) out of a cell and potassium ions (K^+) into a cell, thus regulating ion concentration on both sides of the cell membrane.

soma (cell body): In neurons, that portion of the cell that contains the nucleus; the cell body, as opposed to the cell processes (axons and dendrites).

somatic nervous system (SNS): Functional division of the nervous system that is concerned with conscious perception, voluntary movement, and skeletal muscle reflexes.

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spatial summation: Combination of graded potentials across the neuronal cell membrane caused by signals from separate presynaptic elements that add up to initiate an action potential.

spinal cord: Organ of the central nervous system found within the vertebral cavity and connected with the periphery through spinal nerves; mediates reflex behaviours.

stimulus: An event in the external or internal environment that registers as activity in a sensory neuron.

summate: To add together, as in the cumulative change in postsynaptic potentials toward reaching threshold in the membrane, either across a span of the membrane or over a certain amount of time.

synapse: Narrow junction across which a chemical signal passes from one neuron to the next, initiating a new electrical signal in the target cell.

synaptic cleft: Small gap between cells in a chemical synapse where a neurotransmitter diffuses from the presynaptic element to the postsynaptic element.

synaptic end bulb: Swelling at the end of an axon where neurotransmitter molecules are released onto a target cell across a synapse.

temporal summation: Combination of graded potentials at the same location on a neuron, resulting in a strong signal from one input.

thalamus: Region of the central nervous system that acts as a relay for sensory pathways.

thermoreceptor: Type of sensory receptor capable of transducing temperature stimuli into neural action potentials.

threshold: Membrane voltage at which an action potential is initiated.

tract: Bundle of axons in the central nervous system having the same function and point of origin.

unipolar: Shape of a neuron that has only one process that includes both the axon and dendrite.

upper motor neuron: First neuron in the motor command pathway with its cell body in the cerebral cortex; synapses on the lower motor neuron in the spinal cord.

ventricle: Central cavity within the brain where CSF is produced and circulates.

voltage-gated channel: Ion channel that opens because of a change in the charge distributed across the membrane where it is located.

white matter: Regions of the nervous system containing mostly myelinated axons, making the tissue appear white because of the high lipid content of myelin.

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Chapter Review

12.1 Basic Structure and Function of the Nervous System

The nervous system can be separated into divisions on the basis of anatomy and physiology. The anatomical divisions are the central and peripheral nervous systems. The CNS is the brain and spinal cord. The PNS is everything else. Functionally, the nervous system can be divided into those regions that are responsible for sensation, those that are responsible for integration, and those that are responsible for generating responses. All these functional areas are found in both the central and peripheral anatomy.

Considering the anatomical regions of the nervous system, there are specific names for the structures within each division. A localized collection of neuron cell bodies is referred to as a nucleus in the CNS and as a ganglion in the PNS. A bundle of axons is referred to as a tract in the CNS and as a nerve in the PNS. Whereas nuclei and ganglia are specifically in the central or peripheral divisions, axons can cross the boundary between the two. A single axon can be part of a nerve and a tract. The name for that specific structure depends on its location.

Nervous tissue can also be described as grey matter and white matter on the basis of its appearance in unstained tissue. These descriptions are more often used in the CNS. Grey matter is where nuclei are found, and white matter is where tracts are found. In the PNS, ganglia are basically grey matter, and nerves are white matter.

The nervous system can also be divided on the basis of how it controls the body. The somatic nervous system (SNS) is responsible for functions that result in moving skeletal muscles. Any sensory or integrative functions that result in the movement of skeletal muscle would be considered somatic. The autonomic nervous system (ANS) is responsible for functions that affect cardiac or smooth muscle tissue or that cause glands to produce their secretions. Autonomic functions are distributed between the central and peripheral regions of the nervous system. The sensations that lead to autonomic functions can be the same sensations that are part of initiating somatic responses. Somatic and autonomic integrative functions may overlap as well.

A special division of the nervous system is the enteric nervous system, which is responsible for controlling the digestive organs. Parts of the autonomic nervous system overlap with the enteric nervous system. The enteric nervous system is exclusively found in the periphery because it is the nervous tissue in the organs of the digestive system.

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12.2 Nervous Tissue

Nervous tissue contains two major cell types, neurons and glial cells. Neurons are the cells responsible for communication through electrical signals. Glial cells are supporting cells, maintaining the environment around the neurons.

Neurons are polarized cells, based on the flow of electrical signals along their membrane. Signals are received at the dendrites, are passed along the cell body, and propagate along the axon toward the target, which may be another neuron, muscle tissue, or a gland. Many axons are insulated by a lipid-rich substance called myelin. Specific types of glial cells provide this insulation.

Several types of glial cells are found in the nervous system, and they can be categorized by the anatomical division in which they are found. In the CNS, astrocytes, oligodendrocytes, microglia, and ependymal cells are found. Astrocytes are important for maintaining the chemical environment around the neuron and are crucial for regulating the blood-brain barrier. Oligodendrocytes are the myelinating glia in the CNS. Microglia act as phagocytes and play a role in immune surveillance. Ependymal cells are responsible for filtering the blood to produce cerebrospinal fluid, which is a circulatory fluid that performs some of the functions of blood in the brain and spinal cord because of the BBB. In the PNS, satellite cells are supporting cells for the neurons, and Schwann cells insulate peripheral axons.

12.3 The Functions of Nervous Tissue

Sensation starts with the activation of a sensory ending, such as the thermoreceptor in the skin sensing the temperature of the water. The sensory endings in the skin initiate an electrical signal that travels along the sensory axon within a nerve into the spinal cord, where it synapses with a neuron in the grey matter of the spinal cord. The temperature information represented in that electrical signal is passed to the next neuron by a chemical signal that diffuses across the small gap of the synapse and initiates a new electrical signal in the target cell. That signal travels through the sensory pathway to the brain, passing through the thalamus, where conscious perception of the water temperature is made possible by the cerebral cortex. Following integration of that information with other cognitive processes and sensory information, the brain sends a command back down to the spinal cord to initiate a motor response by controlling a skeletal muscle. The motor pathway is composed of two cells, the upper motor neuron and the lower motor neuron. The upper motor neuron has its cell body in the cerebral cortex and synapses on a cell in the grey matter of the spinal cord. The lower motor neuron is that cell in the grey matter of the spinal cord, and its axon extends into the periphery, where it synapses with a skeletal muscle in a neuromuscular junction.

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12.4 The Action Potential

The nervous system is characterized by electrical signals that are sent from one area to another. Whether those areas are close or very far apart, the signal must travel along an axon. The basis of the electrical signal is the controlled distribution of ions across the membrane. Transmembrane ion channels regulate when ions can move in or out of the cell, so that a precise signal is generated. This signal is the action potential, which has a very characteristic shape based on voltage changes across the membrane in a given time period.

The membrane is normally at rest with established Na^+ and K^+ concentrations on either side. A stimulus will start the depolarization of the membrane, and voltage-gated channels will result in further depolarization, followed by repolarization of the membrane. A slight overshoot of hyperpolarization marks the end of the action potential. While an action potential is in progress, another cannot be generated under the same conditions. While the voltage-gated Na^+ channel is inactivated, absolutely no action potentials can be generated. Once that channel has returned to its resting state, a new action potential is possible, but it must be started by a relatively stronger stimulus to overcome the K^+ leaving the cell.

The action potential travels down the axon as voltage-gated ion channels are opened by the spreading depolarization. In unmyelinated axons, this happens in a continuous fashion because there are voltage-gated channels throughout the membrane. In myelinated axons, propagation is described as saltatory because voltage-gated channels are only found at the nodes of Ranvier, and the electrical events seem to "jump" from one node to the next. Saltatory conduction is faster than continuous conduction, meaning that myelinated axons propagate their signals faster. The diameter of the axon also makes a difference, as ions diffusing within the cell have less resistance in a wider space.

12.5 Communication Between Neurons

The basis of the electrical signal within a neuron is the action potential that propagates down the axon. For a neuron to generate an action potential, it needs to receive input from another source, either another neuron or a sensory stimulus. That input will result in opening ion channels in the neuron, resulting in a graded potential based on the strength of the stimulus. Graded potentials can be depolarizing or hyperpolarizing and can summate to affect the probability of the neuron reaching threshold.

Graded potentials can be the result of sensory stimuli. If the sensory stimulus is received by the dendrites of a unipolar sensory neuron, such as the sensory neuron ending in the skin, the graded potential is called a generator

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potential because it can directly generate the action potential in the initial segment of the axon. If the sensory stimulus is received by a specialized sensory receptor cell, the graded potential is called a receptor potential. Graded potentials produced by interactions between neurons at synapses are called postsynaptic potentials (PSPs). A depolarizing graded potential at a synapse is called an excitatory PSP, and a hyperpolarizing graded potential at a synapse is called an inhibitory PSP.

Synapses are the contacts between neurons, which can either be chemical or electrical in nature. Chemical synapses are far more common. At a chemical synapse, a neurotransmitter is released from the presynaptic element and diffuses across the synaptic cleft. The neurotransmitter binds to a receptor protein and causes a change in the postsynaptic membrane (the PSP). The neurotransmitter must be inactivated or removed from the synaptic cleft so that the stimulus is limited in time.

The particular characteristics of a synapse vary based on the neurotransmitter system produced by that neuron. The cholinergic system is found at the neuromuscular junction and in certain places within the nervous system. Amino acids such as glutamate, glycine, and gamma-aminobutyric acid (GABA) are used as neurotransmitters. Other neurotransmitters are the result of amino acids being enzymatically changed, as in the biogenic amines, or being covalently bonded together, as in the neuropeptides.

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13

Anatomy of the Nervous System

Chapter Objectives

After studying this chapter, you will be able to:

- Name the major regions of the adult nervous system
- Locate regions of the cerebral cortex on the basis of anatomical landmarks common to all human brains
- Describe the regions of the spinal cord in cross-section
- List the cranial nerves in order of anatomical location and provide the central and peripheral connections
- List the spinal nerves by vertebral region and by which nerve plexus each supplies

The nervous system is responsible for controlling much of the body, through both somatic (voluntary) and autonomic (involuntary) functions. The structures of the nervous system must be described in detail to understand how many of these functions are possible.

13.1 The Central Nervous System

Learning Objectives

By the end of this section, you will be able to:

- Name the major regions of the adult brain

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- Describe the connections between the cerebrum and brain stem through the diencephalon and from those regions into the spinal cord
- Recognize the complex connections within the subcortical structures of the basal nuclei
- Explain the arrangement of grey and white matter in the spinal cord

The **brain** and the **spinal cord** are the **central nervous system**, and they represent the main organs of the nervous system. The spinal cord is a single structure, whereas the adult brain is described in terms of four major regions: the cerebrum, the diencephalon, the brain stem, and the cerebellum. A person's conscious experiences are based on neural activity in the brain. The regulation of homeostasis is governed by a specialized region in the brain. The coordination of reflexes depends on the integration of sensory and motor pathways in the spinal cord.

The Cerebrum

The iconic grey mantle of the human brain, which appears to make up most of the mass of the brain, is the **cerebrum** (Figure 13.1). The wrinkled portion is the **cerebral cortex**, and the rest of the structure is beneath that outer covering. There is a large separation between the two sides of the cerebrum called the **longitudinal fissure**. It separates the cerebrum into two distinct halves, a right and a left **cerebral hemisphere**. Deep within the cerebrum, the white matter of the **corpus callosum** provides the major pathway for communication between the two hemispheres of the cerebral cortex.

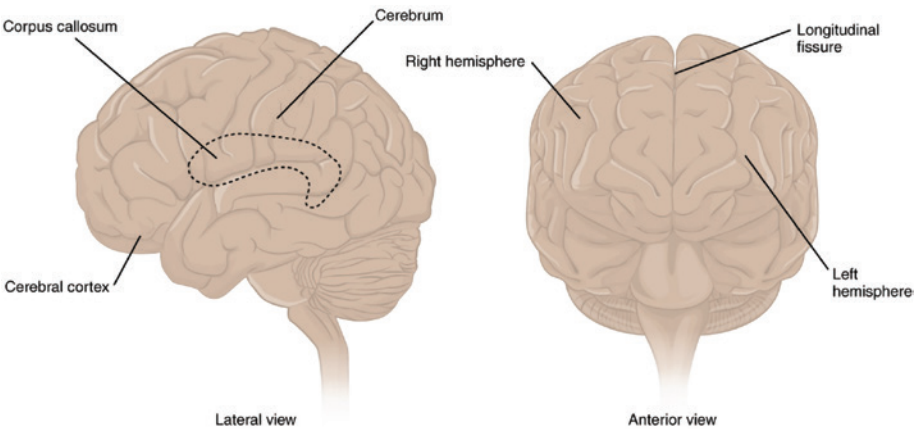


Figure 13.1 The Cerebrum. The cerebrum is a large component of the CNS in humans, and the most obvious aspect of it is the folded surface called the cerebral cortex.

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Many of the higher neurological functions, such as memory, emotion, and consciousness, are the result of cerebral function. The complexity of the cerebrum is different across vertebrate species. The cerebrum of the most primitive vertebrates is not much more than the connection for the sense of smell. In mammals, the cerebrum comprises the outer grey matter that is the cortex and several deep nuclei that belong to three important functional groups. The **basal nuclei** are responsible for cognitive processing, the most important function being that associated with planning movements. The basal forebrain contains nuclei that are important in learning and memory. The **limbic cortex** is the region of the cerebral cortex that is part of the **limbic system**, a collection of structures involved in emotion, memory, and behaviour.

Cerebral Cortex

The cerebrum is covered by a continuous layer of grey matter that wraps around either side of the forebrain—the cerebral cortex. This thin, extensive region of wrinkled grey matter is responsible for the higher functions of the nervous system. A **gyrus** (plural = gyri) is the ridge of one of those wrinkles, and a **sulcus** (plural = sulci) is the groove between two gyri. The pattern of these folds of tissue indicates specific regions of the cerebral cortex.

The head is limited by the size of the birth canal, and the brain must fit inside the cranial cavity of the skull. Extensive folding in the cerebral cortex enables more grey matter to fit into this limited space. If the grey matter of the cortex were peeled off the cerebrum and laid out flat, its surface area would be roughly equal to one square metre.

The folding of the cortex maximizes the amount of grey matter in the cranial cavity. The surface of the brain can be mapped on the basis of the locations of large gyri and sulci. Using these landmarks, the cortex can be separated into four major regions, or lobes (Figure 13.2). The **lateral sulcus** that separates the **temporal lobe** from the other regions is one such landmark.

Superior to the lateral sulcus are the **parietal lobe** and the **frontal lobe**, which are separated from each other by the **central sulcus**. The posterior region of the cortex is the **occipital lobe**, which has no obvious anatomical border between it and the parietal or temporal lobes on the lateral surface of the brain. From the medial surface, an obvious landmark separating the parietal and occipital lobes is called the **parieto-occipital sulcus**. The fact that there is no obvious anatomical border between these lobes is consistent with the functions of these regions being interrelated.

The main sensation associated with the parietal lobe is **somatosensation**, meaning the general sensations associated with the body. Posterior to the central sulcus is the **postcentral gyrus**, the primary somatosensory cortex. All

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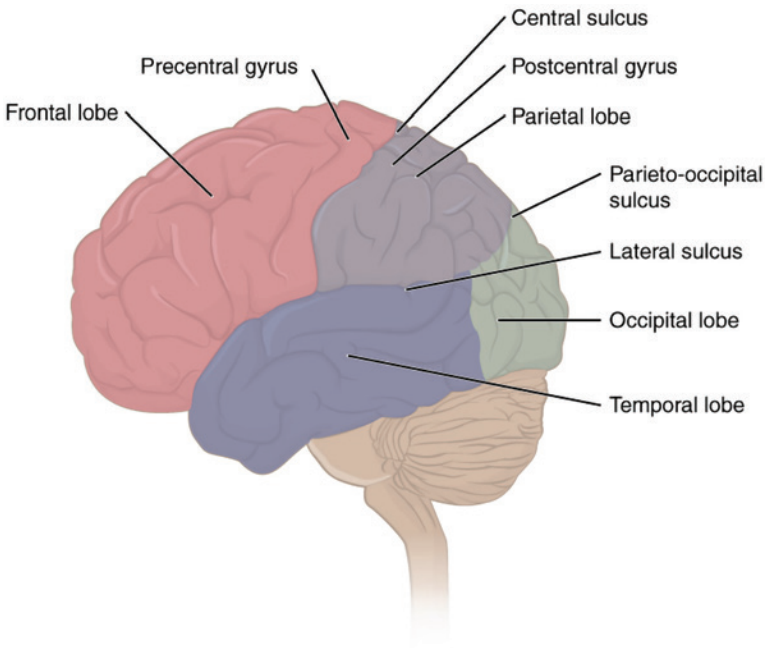


Figure 13.2 Lobes of the Cerebral Cortex. The cerebral cortex is divided into four lobes. Extensive folding increases the surface area available for cerebral functions.

the tactile senses are processed in this area, including touch, pressure, tickle, pain, itch, and vibration, as well as more general senses of the body such as **proprioception** and **kinesthesia**, which are the senses of body position and movement, respectively.

Anterior to the central sulcus is the **frontal lobe**, which is primarily associated with motor functions. The **precentral gyrus** is the primary motor cortex. Cells from this region of the cerebral cortex are the upper motor neurons that instruct cells in the spinal cord to move skeletal muscles. Anterior to this region are a few areas that are associated with planned movements. The **premotor area** is responsible for thinking of a movement to be made. The **frontal eye fields** are important in eliciting eye movements and in attending to visual stimuli. **Broca's area** is responsible for the production of language or controlling movements responsible for speech; in the vast majority of people, it is located only on the left side. Anterior to these regions is the **prefrontal lobe**, which serves cognitive functions that can be the basis of personality, short-term memory, and consciousness. The prefrontal lobotomy is an outdated mode of treatment for personality disorders (psychiatric conditions) that profoundly affected the personality of the patient.

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Subcortical Structures

Beneath the cerebral cortex are sets of nuclei known as **subcortical nuclei** that augment cortical processes. The nuclei of the basal **forebrain** serve as the primary location for acetylcholine production, which modulates the overall activity of the cortex, possibly leading to greater attention to sensory stimuli. Alzheimer's disease is associated with a loss of neurons in the basal forebrain. The **hippocampus** and **amygdala** are medial-lobe structures that, along with the adjacent cortex, are involved in long-term memory formation and emotional responses. The basal nuclei are a set of nuclei in the cerebrum responsible for comparing cortical processing with the general state of activity in the nervous system to influence the likelihood of movement taking place. For example, while a student is sitting in a classroom listening to a lecture, the basal nuclei will keep the urge to jump up and scream from actually happening. (The basal nuclei are also referred to as the basal ganglia, although that is potentially confusing because the term *ganglia* is typically used for peripheral structures.)

The basal nuclei in the cerebrum are connected with a few more nuclei in the brain stem that together act as a functional group that forms a motor pathway. Two streams of information processing take place in the basal nuclei, the direct pathway, and the indirect pathway. The **direct pathway** causes the disinhibition of the thalamus (inhibition of one cell on a target cell that then inhibits the first cell), whereas the **indirect pathway** causes, or reinforces, the normal inhibition of the thalamus. The thalamus can then either excite the cortex (as a result of the direct pathway) or fail to excite the cortex (as a result of the indirect pathway).

Interactive Link 13.1

Watch this video (http://oer.aupress.ca/oer-202505/13.1) to learn about the basal nuclei (also known as the basal ganglia), which have two pathways that process information within the cerebrum. As shown in this video, the direct pathway is the shorter pathway through the system that results in increased activity in the cerebral cortex and increased motor activity. The direct pathway is described as resulting in "disinhibition" of the thalamus. What does disinhibition mean? What are the two neurons doing individually to cause this?

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Interactive Link 13.2

Watch this video (http://oer.aupress.ca/oer-202505/13.2) to learn about the basal nuclei (also known as the basal ganglia), which have two pathways that process information within the cerebrum. As shown in this video, the indirect pathway is the longer pathway through the system that results in decreased activity in the cerebral cortex, and therefore less motor activity. The indirect pathway has an extra couple of connections in it, including disinhibition of the subthalamic nucleus. What is the end result on the thalamus, and therefore on movement initiated by the cerebral cortex?

The Diencephalon

The **diencephalon** is the one region of the adult brain that retains its name from embryologic development. It is the connection between the cerebrum and the rest of the nervous system, with one exception. The rest of the brain, the spinal cord, and the PNS all send information to the cerebrum through the diencephalon. Output from the cerebrum passes through the diencephalon. The single exception is the system associated with **olfaction**, or the sense of smell, which connects directly with the cerebrum. In the earliest vertebrate species, the cerebrum was not much more than olfactory bulbs that received peripheral information about the chemical environment (to call it smell in these organisms is imprecise because they lived in the ocean).

The diencephalon is deep beneath the cerebrum and constitutes the walls of the third ventricle. The diencephalon can be described as any region of the brain with "thalamus" in its name. The two major regions of the diencephalon are the thalamus itself and the hypothalamus (Figure 13.3). There are other structures, such as the **epithalamus**, which contains the pineal gland, or the **subthalamus**, which includes the subthalamic nucleus that is part of the basal nuclei.

Thalamus

The **thalamus** is a collection of nuclei that relay information between the cerebral cortex and the periphery, spinal cord, or brain stem. All sensory information, except for the sense of smell, passes through the thalamus before being processed by the cortex. Axons from the peripheral sensory organs, or intermediate nuclei, synapse in the thalamus, and thalamic neurons project directly to the cerebrum. It is a requisite synapse in any sensory pathway, except for olfaction. The thalamus does not just pass the information on; it also processes that information. For example, the portion of the thalamus that

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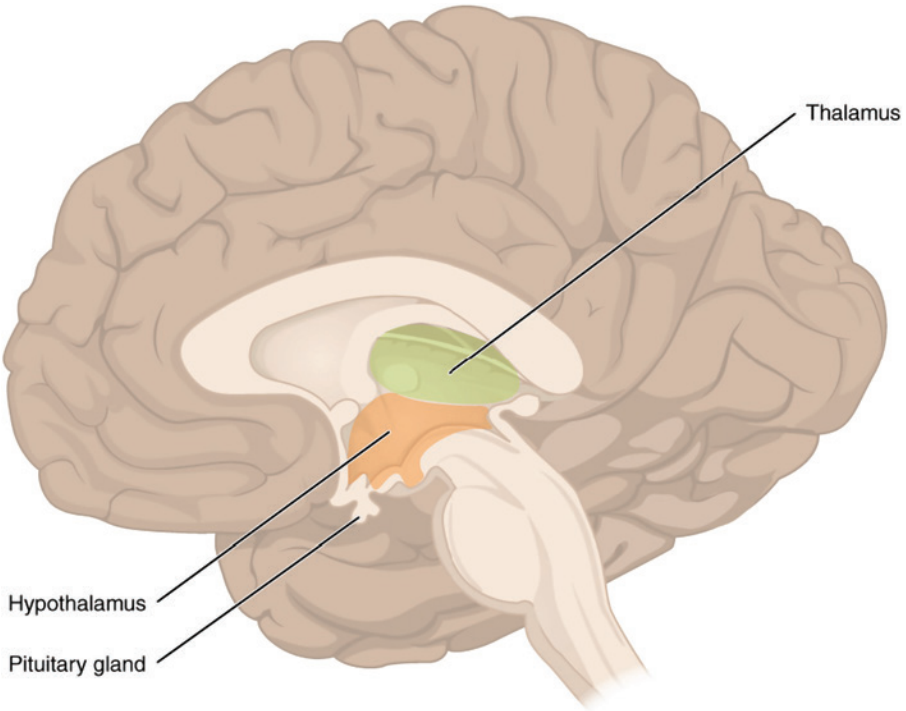


Figure 13.3 The Diencephalon. The diencephalon is composed primarily of the thalamus and hypothalamus, which together define the walls of the third ventricle. The thalami are two elongated, ovoid structures on either side of the midline that make contact in the middle. The hypothalamus is inferior and anterior to the thalamus, culminating in a sharp angle to which the pituitary gland is attached.

receives visual information will influence what visual stimuli are important or what receives attention.

The cerebrum also sends information down to the thalamus, which usually communicates motor commands. This involves interactions with the cerebellum and other nuclei in the brain stem. The cerebrum interacts with the basal nuclei, which involves connections with the thalamus. The primary output of the basal nuclei is to the thalamus, which relays that output to the cerebral cortex. The cortex also sends information to the thalamus that will then influence the effects of the basal nuclei.

Hypothalamus

Inferior and slightly anterior to the thalamus is the **hypothalamus**, the other major region of the diencephalon. The hypothalamus is a collection of nuclei that are largely involved in regulating homeostasis, like body temperature. The hypothalamus is the executive region in charge of the autonomic nervous system and the endocrine system through its regulation of the anterior pituitary

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gland. Other parts of the hypothalamus are involved in memory and emotion as part of the limbic system.

Brain Stem

The **midbrain** and **hindbrain** (composed of the pons and the medulla) are collectively referred to as the **brain stem** (Figure 13.4). The structure emerges from the ventral surface of the forebrain as a tapering cone that connects the brain to the spinal cord. Attached to the brain stem, but considered a separate region of the adult brain, is the cerebellum. The midbrain coordinates sensory representations of the visual, auditory, and somatosensory perceptual spaces. The pons is the main connection with the cerebellum. The pons and the medulla regulate several crucial functions, including the cardiovascular and respiratory systems and rates.

The cranial nerves connect through the brain stem and provide the brain with the sensory input and motor output associated with the head and neck, including most of the special senses. The major ascending and descending pathways between the spinal cord and brain, specifically the cerebrum, pass through the brain stem.

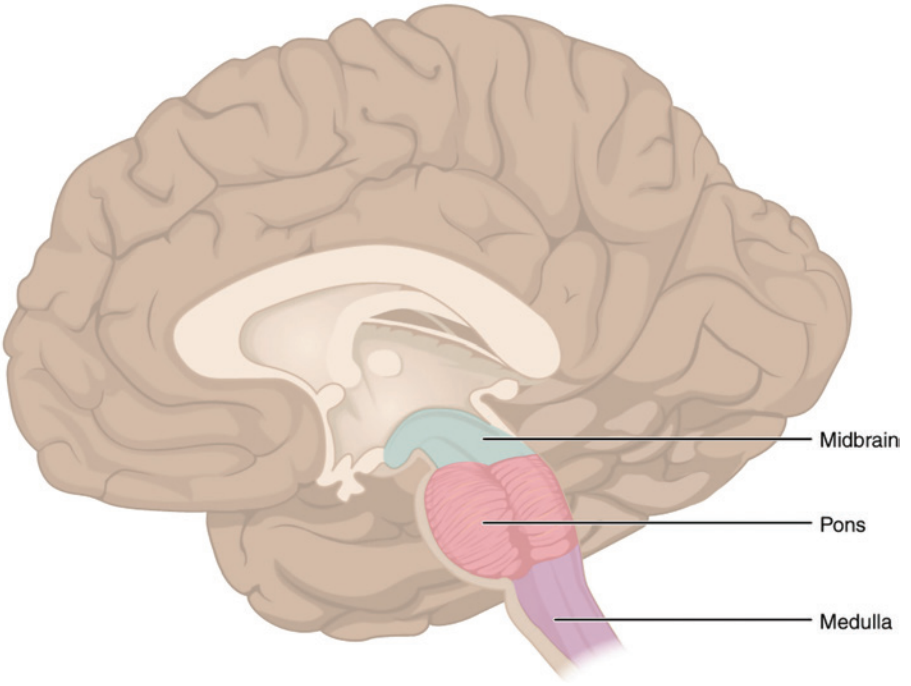


Figure 13.4 The Brain Stem. The brain stem comprises three regions: the midbrain, the pons, and the medulla.

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Midbrain

The cerebral aqueduct passes through the centre of the midbrain, such that these regions are the roof and floor of that canal.

The tectum is composed of four bumps known as the colliculi (singular = colliculus), which means "little hill" in Latin. The **inferior colliculus** is the inferior pair of these enlargements and is part of the auditory brain stem pathway. Neurons of the inferior colliculus project to the thalamus, which then sends auditory information to the cerebrum for the conscious perception of sound. The **superior colliculus** is the superior pair and combines sensory information about visual space, auditory space, and somatosensory space. Activity in the superior colliculus is related to orienting the eyes to a sound or touch stimulus.

Pons

The word **pons** comes from the Latin word for bridge. It is visible on the anterior surface of the brain stem as the thick bundle of white matter attached to the cerebellum. The pons is the main connection between the cerebellum and the brain stem. The bridgelike white matter is only the anterior surface of the pons; the grey matter beneath that is a continuation of the floor of the cerebral aqueduct from the midbrain. Grey matter in the floor of the cerebral aqueduct region of the pons contains neurons receiving descending input from the forebrain that is sent to the cerebellum.

Medulla

The **medulla** (also called the **medulla oblongata**) is the region known as the myelencephalon in the embryonic brain. The initial portion of the name, *myel*, refers to the significant white matter found in this region—especially on its exterior, which is continuous with the white matter of the spinal cord. The floor of the cerebral aqueduct of the midbrain and pons continues into the medulla because this grey matter is responsible for processing cranial nerve information. A diffuse region of grey matter throughout the brain stem, known as the **reticular formation**, is related to sleep and wakefulness, such as general brain activity and attention.

The Cerebellum

The **cerebellum**, as the name suggests, is the "little brain." It is covered in gyri and sulci like the cerebrum and looks like a miniature version of that part of the brain (Figure 13.5). The cerebellum is largely responsible for comparing information from the cerebrum with sensory feedback from the periphery through the spinal cord. It accounts for approximately 10 percent of the mass of the brain. The cerebellum's major functions include coordination of movements and balance.

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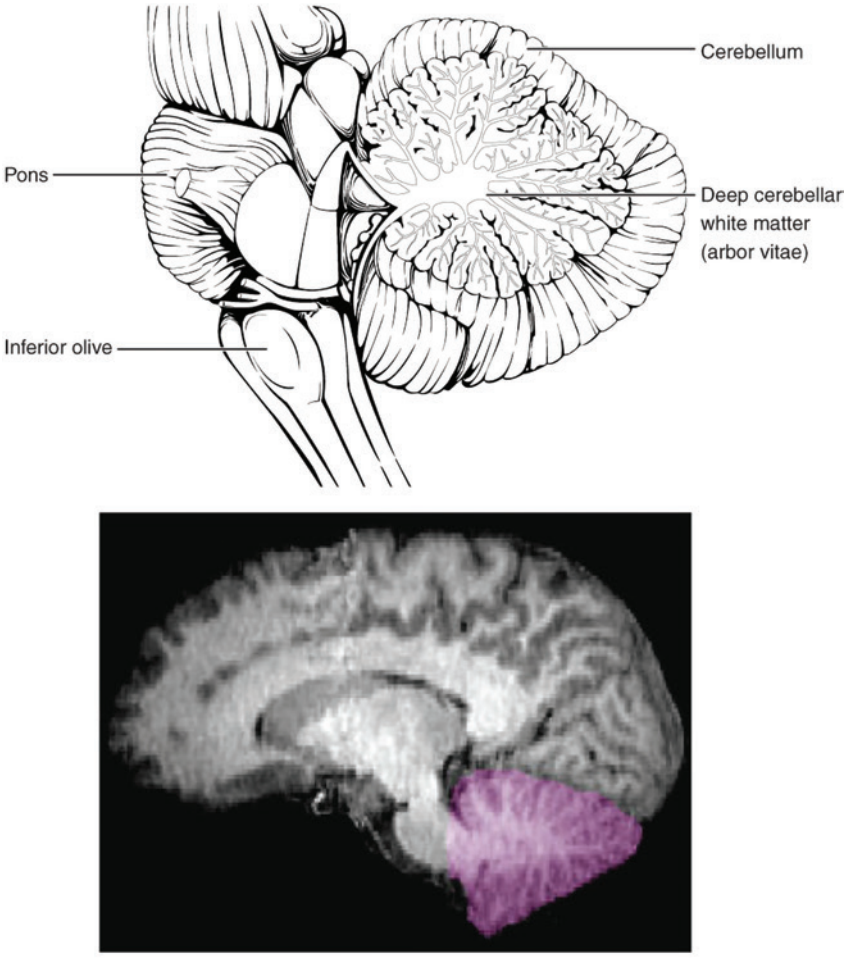


Figure 13.5 The Cerebellum. The cerebellum is situated on the posterior surface of the brain stem (bottom image). Descending input from the cerebellum enters through the large white matter structure of the pons. Ascending input from the periphery and spinal cord enters through the fibres of the inferior olive. Output goes to the midbrain, which sends a descending signal to the spinal cord.

The Spinal Cord

The description of the CNS is concentrated on the structures of the brain, but the **spinal cord** is another major organ of the system. Whereas the brain develops out of expansions of the neural tube into primary and then secondary vesicles, the spinal cord maintains the tube structure and is only specialized into certain regions. As the spinal cord continues to develop in the newborn, anatomical features mark its surface. The anterior midline is marked by the **anterior median fissure**, and the posterior midline is marked by the **posterior**

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median sulcus. On the whole, the posterior regions are responsible for sensory functions, and the anterior regions are associated with motor functions.

The length of the spinal cord is divided into regions that correspond to the regions of the vertebral column. The name of a spinal cord region corresponds to the level at which spinal nerves pass through the intervertebral foramina. Immediately adjacent to the brain stem is the cervical region, followed by the thoracic, then the lumbar, and finally the sacral region. The spinal cord is not the full length of the vertebral column because the spinal cord does not grow significantly longer after the first or second year, but the skeleton continues to grow. The nerves that emerge from the spinal cord pass through the intervertebral foramina at the respective levels. As the vertebral column grows, these nerves grow with it and result in a long bundle of nerves that resembles a horse's tail and is named the **cauda equina**. The sacral spinal cord is at the level of the upper lumbar vertebral bones. The spinal nerves extend from their various levels to the proper level of the vertebral column.

Grey Horns

In cross-section, the grey matter of the spinal cord has the appearance of an ink-blot test, with the spread of the grey matter on one side replicated on the other—a shape reminiscent of a bulbous capital "H." As shown in Figure 13.6, the grey matter is subdivided into regions that are referred to as horns. The **posterior horn** is responsible for sensory processing. The **anterior horn** sends out motor signals to the skeletal muscles. The **lateral horn**, which is only found in the thoracic, upper lumbar, and sacral regions, contains cell bodies of motor neurons of the autonomic nervous system. In the centre of the grey matter is a small space called the **central canal**; it extends the entire length of the spinal cord and is filled with cerebrospinal fluid. At its superior end, the central canal is continuous with the fourth ventricle (a space that contains cerebrospinal fluid) in the medulla oblongata of the brain.

Some of the largest neurons of the spinal cord are the multipolar motor neurons in the anterior horn. The fibres that cause contraction of skeletal muscles are the axons of these neurons. The motor neuron that causes contraction of the big toe, for example, is located in the sacral spinal cord. The axon that has to reach all the way to the belly of that muscle may be a metre in length. The neuronal cell body that maintains that long fibre must be quite large, possibly several hundred micrometres in diameter, making it one of the largest cells in the body.

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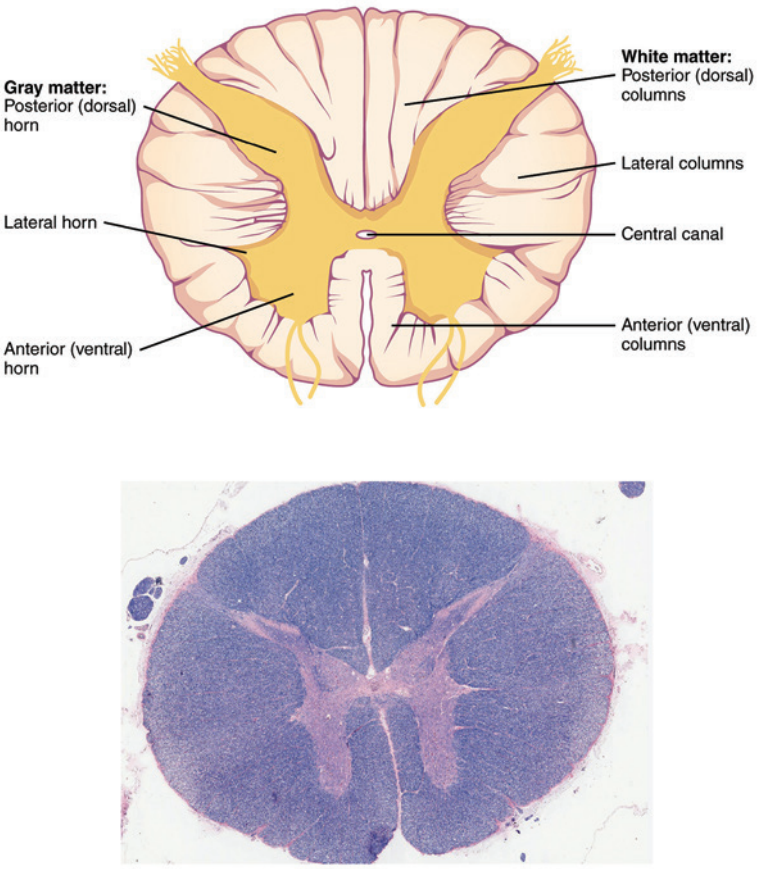


Figure 13.6 Cross-Section of Spinal Cord. The schematic and histology (bottom) view cross-section of a thoracic spinal cord segment shows the posterior, anterior, and lateral horns of grey matter, as well as the posterior, anterior, and lateral columns of white matter. LM × 40. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

White Columns

Just as the grey matter is separated into horns, the white matter of the spinal cord is separated into columns. **Ascending tracts** of nervous system fibres in these columns carry sensory information up to the brain, whereas **descending tracts** carry motor commands from the brain. Looking at the spinal cord longitudinally, the columns extend along its length as continuous bands of white matter. Between the two posterior horns of grey matter are the **posterior columns.** Between the two anterior horns and bounded by the axons of motor neurons emerging from that grey matter area are the **anterior columns.** The areas of white matter on either side of the spinal cord, between the posterior horn and the axons of the anterior horn neurons, are the **lateral**

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columns. The posterior columns are composed of axons of ascending tracts. The anterior and lateral columns are composed of many different groups of axons of both ascending and descending tracts—the latter carrying motor commands down from the brain to the spinal cord to control output to the periphery.

Interactive Link 13.3

Watch this video (http://oer.aupress.ca/oer-202505/13.3) to learn about the grey matter of the spinal cord that receives input from fibres of the dorsal (posterior) root and sends information out through the fibres of the ventral (anterior) root. As discussed in this video, these connections represent the interactions of the CNS with peripheral structures for both sensory and motor functions. The cervical and lumbar spinal cords have enlargements as a result of larger populations of neurons. What are these enlargements responsible for?

Interactive Link 13.4

Compared with the nearest evolutionary relative, the chimpanzee, the human has a huge brain. At a point in the past, a common ancestor gave rise to the two species of humans and chimpanzees. That evolutionary history is long and is still an area of intense study. But something happened to increase the size of the human brain relative to the chimpanzee. Read this article (http://oer.aupress.ca/oer-202505/13.4) in which the author explores the current understanding of why this happened.

According to one hypothesis about the expansion of brain size, what tissue might have been sacrificed so energy was available to grow our larger brain? Based on what you know about that tissue and nervous tissue, why would there be a trade-off between them in terms of energy use?

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13.2 Circulation and the Central Nervous System

Learning Objectives

By the end of this section, you will be able to:

- Describe the vessels that supply the CNS with blood
- Name the components of the ventricular system and the regions of the brain in which each is located
- Explain the production of cerebrospinal fluid and its flow through the ventricles

The CNS is crucial to the operation of the body, and any compromise in the brain and spinal cord can lead to severe difficulties. The CNS has a privileged blood supply, as suggested by the blood-brain barrier. The function of the tissue in the CNS is crucial to the survival of the organism, so the contents of the blood cannot simply pass into the central nervous tissue. To protect this region from the toxins and pathogens that may be travelling through the bloodstream, there is strict control over what can move out of the general systems and into the brain and spinal cord.

Because of this privilege, the CNS needs specialized structures for the maintenance of circulation. This begins with a unique arrangement of blood vessels carrying fresh blood into the CNS. Beyond the supply of blood, the CNS filters that blood into cerebrospinal fluid (CSF), which is then circulated through the cavities of the brain and spinal cord, called ventricles.

Blood Supply to the Brain

A lack of oxygen to the CNS can be devastating, and the cardiovascular system has specific regulatory reflexes to ensure that the blood supply is not interrupted. There are multiple routes for blood to get into the CNS, with specializations to protect that blood supply and to maximize the ability of the brain to get an uninterrupted perfusion.

Arterial Supply

The major artery carrying recently oxygenated blood away from the heart is the aorta. The very first branches off the aorta supply the heart with nutrients and oxygen. The next branches give rise to the **common carotid arteries**, which further branch into the **internal carotid arteries**. The external carotid arteries supply blood to the tissues on the surface of the cranium (Figure 13.7).

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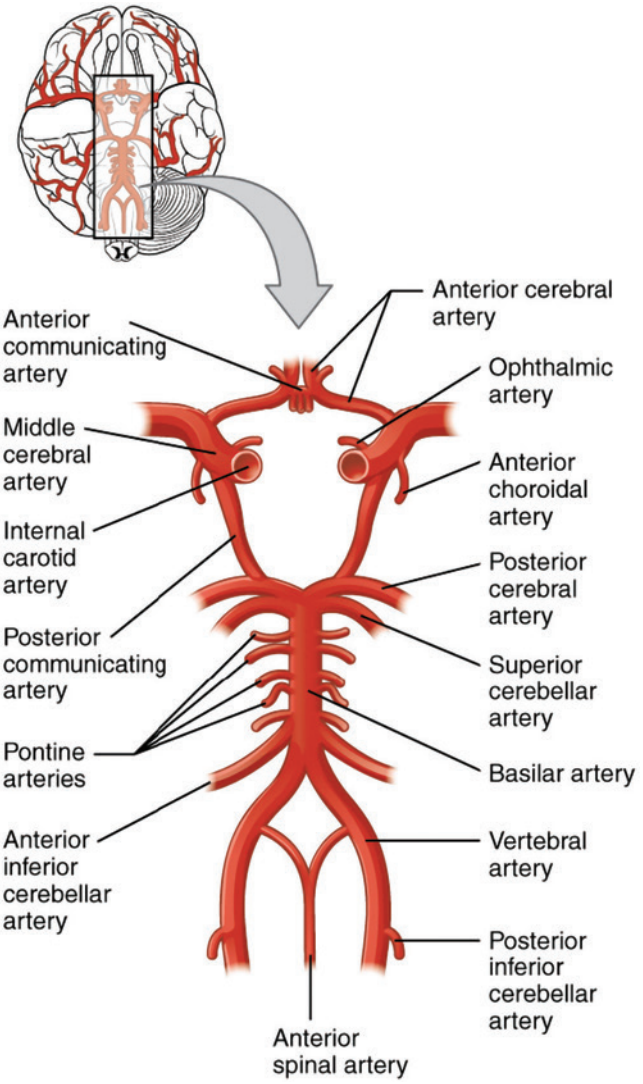


Figure 13.7 Circle of Willis. The blood supply to the brain enters through the internal carotid arteries and the vertebral arteries, eventually giving rise to the circle of Willis.

The bases of the common carotids contain stretch receptors that immediately respond to the drop in blood pressure upon standing. The **orthostatic reflex** is a reaction to this change in body position, so that blood pressure is maintained against the increasing effect of gravity. Heart rate increases—a reflex of the sympathetic division of the autonomic nervous system—and this raises blood pressure. The internal carotid artery enters the cranium through the carotid canal in the temporal bone. A second set of vessels that supply the CNS are the **vertebral arteries**, which are protected as they pass through the neck region by the transverse foramina of the cervical vertebrae. The left and right internal

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carotid arteries and branches of the basilar artery all become the **circle of Willis**, a confluence of arteries that can maintain perfusion of the brain even if narrowing or a blockage limits flow through one part.

Interactive Link 13.5

Watch this animation (http://oer.aupress.ca/oer-202505/13.5) to see how blood flows to the brain and passes through the circle of Willis before being distributed through the cerebrum. The circle of Willis is a specialized arrangement of arteries that ensures constant perfusion of the cerebrum even in the event of a blockage of one of the arteries in the circle. The animation shows the normal direction of flow through the circle of Willis to the middle cerebral artery.

Where would the blood come from if there were a blockage just posterior to the middle cerebral artery on the left?

Venous Return

After passing through the CNS, blood returns to the circulation through a series of **dural sinuses** and veins (Figure 13.8). The **superior sagittal sinus** runs in the groove of the longitudinal fissure, where it absorbs CSF from the meninges. The superior sagittal sinus drains to the confluence of sinuses, along with the occipital sinuses and straight sinus, to then drain into the transverse sinuses. The transverse sinuses connect to the sigmoid sinuses, which then connect to the **jugular veins**. From there, the blood continues toward the heart to be pumped to the lungs for reoxygenation.

Protective Coverings of the Brain and Spinal Cord

The outer surface of the CNS is covered by a series of membranes composed of connective tissue called the **meninges**, which protect the brain. The **dura mater** is a thick fibrous layer and a strong protective sheath over the entire brain and spinal cord. It is anchored to the inner surface of the cranium and vertebral cavity. The **arachnoid mater** is a membrane of thin fibrous tissue that forms a loose sac around the CNS. Beneath the arachnoid is a thin, filamentous mesh called the arachnoid trabeculae, which looks like a spider web, giving this layer its name. Directly adjacent to the surface of the CNS is the **pia mater**, a thin fibrous membrane that follows the convolutions of gyri and sulci in the cerebral cortex and fits into other grooves and indentations (Figure 13.9).

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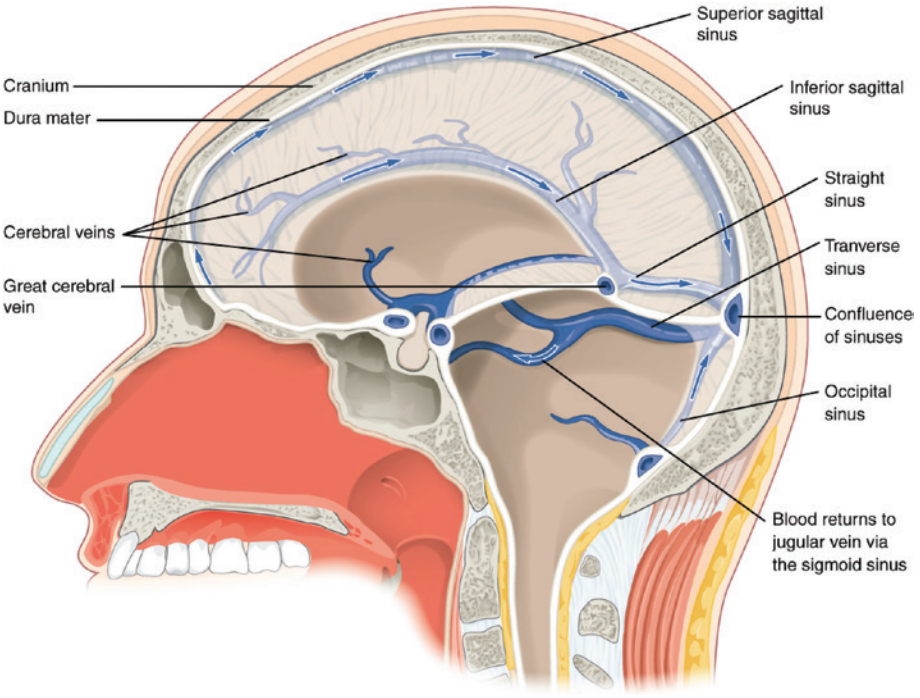


Figure 13.8 Dural Sinuses and Veins. Blood drains from the brain through a series of sinuses that connect to the jugular veins.

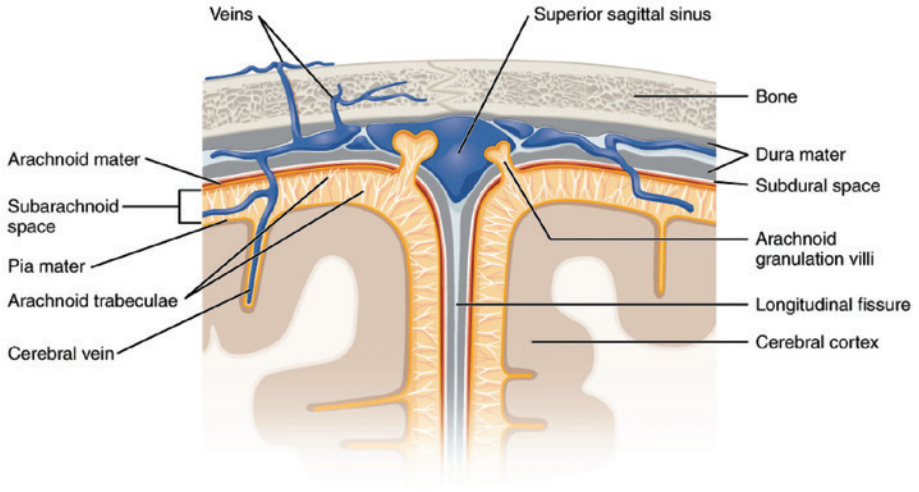


Figure 13.9 Meningeal Layers of the Superior Sagittal Sinus. The layers of the meninges in the longitudinal fissure of the superior sagittal sinus are shown, with the dura mater adjacent to the inner surface of the cranium, the pia mater adjacent to the surface of the brain, and the arachnoid and subarachnoid space between them. An arachnoid villus is shown emerging into the dural sinus to allow CSF to filter back into the blood for drainage.

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Dura Mater

Like a thick cap covering the brain, the **dura mater** is a tough outer covering. The name comes from the Latin for "tough mother" to represent its physically protective role. It encloses the entire CNS and the major blood vessels that enter the cranium and vertebral cavity. It is directly attached to the inner surface of the bones of the cranium and to the very end of the vertebral cavity.

There are infoldings of the dura that fit into large crevasses of the brain. Two infoldings go through the midline separations of the cerebrum and cerebellum; one forms a shelflike tent between the occipital lobes of the cerebrum and the cerebellum, and the other surrounds the pituitary gland. The dura also surrounds and supports the venous sinuses.

Arachnoid Mater

The middle layer of the meninges is the arachnoid, named for the spiderweb-like trabeculae between it and the pia mater. The arachnoid defines a saclike enclosure around the CNS. The trabeculae are found in the **subarachnoid space**, which is filled with circulating cerebrospinal fluid (CSF).

The subarachnoid space is filled with circulating CSF, which also provides a liquid cushion to the brain and spinal cord. Similar to clinical blood work, a sample of CSF can be withdrawn to find chemical evidence of neuropathology or metabolic traces of the biochemical functions of nervous tissue.

Pia Mater

The outer surface of the CNS is covered by the thin fibrous membrane of the pia mater. It is thought to have a continuous layer of cells providing a fluid-impermeable membrane. The pia extends into every convolution of the CNS, lining the inside of the sulci in the cerebral and cerebellar cortices. At the end of the spinal cord, a thin filament extends from the inferior end of the CNS at the upper lumbar region of the vertebral column to the sacral end of the vertebral column. Because the spinal cord does not extend through the lower lumbar region of the vertebral column, a needle can be inserted through the dura and arachnoid layers to withdraw CSF. This procedure is called a **lumbar puncture** and avoids the risk of damaging the central tissue of the spinal cord. Blood vessels that nourish the central nervous tissue are between the pia mater and the nervous tissue.

Interactive Link 13.6

Watch this video (http://oer.aupress.ca/oer-202505/13.6) that describes the procedure known as the lumbar puncture, a medical

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procedure used to sample the CSF. Because of the anatomy of the CNS, it is a relatively safe location to insert a needle. Why is the lumbar puncture performed in the lower lumbar area of the vertebral column?

The Ventricular System

Cerebrospinal fluid (**CSF**) circulates throughout and around the CNS. In other tissues, water and small molecules are filtered through capillaries as the major contributors to the interstitial fluid. In the brain, CSF is produced in special structures to perfuse through the nervous tissue of the CNS and is continuous with the interstitial fluid. Specifically, CSF circulates to remove metabolic wastes from the interstitial fluids of nervous tissues and return them to the bloodstream. The **ventricles** are the open spaces within the brain where CSF circulates. In some of these spaces, CSF is produced by filtering the blood, which is performed by a specialized membrane known as a choroid plexus. The CSF circulates through all the ventricles to eventually emerge into the subarachnoid space, where it will be reabsorbed into the blood.

The Ventricles

There are four ventricles within the brain, all of which developed from the original hollow space within the neural tube, the **central canal**. The first two are named the right and left **lateral ventricles** and are deep within the cerebrum. These ventricles are connected to the **third ventricle** by two openings called the **interventricular foramina**. The third ventricle is the space between the left and right sides of the diencephalon, which opens into the **cerebral aqueduct** that passes through the midbrain. The aqueduct opens into the **fourth ventricle**, which is the space between the cerebellum and the pons and upper medulla (Figure 13.10). The two ventricles are in the left and right sides and were at one time referred to as the first and second ventricles. The interventricular foramina connect the frontal region of the lateral ventricles with the third ventricle. The third ventricle is the space bounded by the medial walls of the hypothalamus and thalamus. The two thalami touch in the centre of most brains as the massa intermedia, which is surrounded by the third ventricle. The cerebral aqueduct opens just inferior to the epithalamus and passes through the midbrain. The aqueduct opens up into the fourth ventricle. The floor of the fourth ventricle is the dorsal surface of the pons and upper medulla. The fourth ventricle then narrows into the central canal of the spinal cord.

The ventricular system opens up to the subarachnoid space from the fourth ventricle. The single **median aperture** and the pair of **lateral apertures** connect

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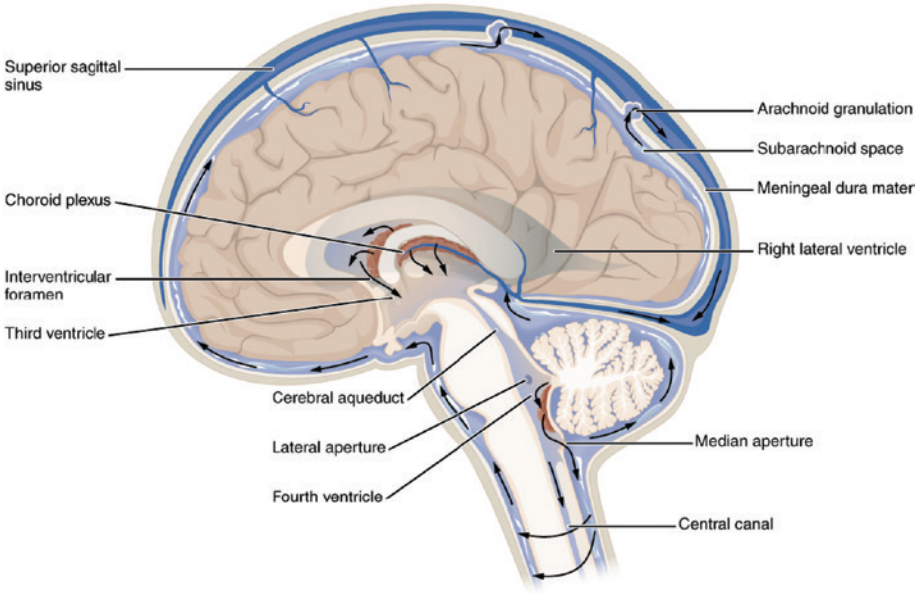


Figure 13.10 Cerebrospinal Fluid Circulation. The choroid plexus in the four ventricles produces CSF, which is circulated through the ventricular system and then enters the subarachnoid space through the median and lateral apertures. The CSF is then reabsorbed into the blood at the arachnoid granulations, where the arachnoid membrane emerges into the dural sinuses.

to the subarachnoid space so that CSF can flow through the ventricles and around the outside of the CNS. Cerebrospinal fluid is produced within the ventricles by a type of specialized membrane called a **choroid plexus**. Ependymal cells (one of the types of glial cells described in the introduction to the nervous system) surround blood capillaries and filter the blood to make CSF. The fluid is a clear solution with a limited amount of the constituents of blood. It is essentially water, small molecules, and electrolytes. Oxygen and carbon dioxide are dissolved into the CSF, as they are in blood, and can diffuse between the fluid and the nervous tissue.

Cerebrospinal Fluid Circulation

The choroid plexuses are found in all four ventricles. Observed in dissection, they appear as soft, fuzzy structures that may still be pink, depending on how well the circulatory system is cleared in preparation of the tissue. The CSF is produced from components extracted from the blood, so its flow out of the ventricles is tied to the pulse of cardiovascular circulation.

From the lateral ventricles, the CSF flows into the third ventricle, where more CSF is produced, and then through the cerebral aqueduct into the fourth ventricle, where even more CSF is produced. A very small amount of CSF is

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filtered at any one of the plexuses, for a total of about 500 millilitres daily, but it is continuously made and pulses through the ventricular system, keeping the fluid moving. From the fourth ventricle, CSF can continue down the central canal of the spinal cord, but this is essentially a cul-de-sac, so more of the fluid leaves the ventricular system and moves into the subarachnoid space through the median and lateral apertures.

Within the subarachnoid space, the CSF flows around all of the CNS, providing two important functions. As with elsewhere in its circulation, the CSF picks up metabolic wastes from the nervous tissue and moves them out of the CNS. It also acts as a liquid cushion for the brain and spinal cord. By surrounding the entire system in the subarachnoid space, it provides a thin buffer around the organs within the strong, protective dura mater. The arachnoid granulations are outpocketings of the arachnoid membrane into the dural sinuses so that CSF can be reabsorbed into the blood, along with the metabolic wastes. From the dural sinuses, blood drains out of the head and neck through the jugular veins, along with the rest of the circulation for blood, to be reoxygenated by the lungs and wastes to be filtered out by the kidneys (Table 13.1).

Interactive Link 13.7

Watch this animation (http://oer.aupress.ca/oer-202505/13.7) that shows the flow of CSF through the brain and spinal cord, and how it originates from the ventricles and then spreads into the space within the meninges, where the fluids then move into the venous sinuses to return to the cardiovascular circulation. What are the structures that produce CSF, and where are they found? How are the structures indicated in this animation?

Table 13.1 Components of CSF Circulation

	Lateral ventricles	Third ventricle	Cerebral aqueduct	Fourth ventricle	Central canal	Subarachnoid space
Location in CNS	Cerebrum	Diencephalon	Midbrain	Between pons / upper medulla and cerebellum	Spinal cord	External to entire CNS
Blood vessel structure	Choroid plexus	Choroid plexus	None	Choroid plexus	None	Arachnoid granulations

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13.3 The Peripheral Nervous System

Learning Objectives

By the end of this section, you will be able to:

- Describe the structures found in the PNS
- Distinguish between somatic and autonomic structures, including the special peripheral structures of the enteric nervous system
- Name the twelve cranial nerves and explain the functions associated with each
- Describe the sensory and motor components of spinal nerves and the plexuses that they pass through

The PNS is not as contained as the CNS because it is defined as everything that is not the CNS. Some peripheral structures are incorporated into the other organs of the body. In describing the anatomy of the PNS, it is necessary to describe the common structures, the nerves and the ganglia, as they are found in various parts of the body. Many of the neural structures that are incorporated into other organs are features of the digestive system; these structures are known as the **enteric nervous system** and are a special subset of the PNS.

Ganglia

A ganglion (plural—ganglia) is a group of neuron cell bodies in the periphery. Ganglia can be categorized, for the most part, as either **sensory ganglia** or **autonomic ganglia**, referring to their primary functions. The most common type of sensory ganglion is a **dorsal** (**posterior**) **root ganglion**. These ganglia are the cell bodies of neurons with axons that are sensory endings in the periphery, such as in the skin, and that extend into the CNS through the dorsal nerve root. The ganglion is an enlargement of the nerve root. Under microscopic inspection, it can be seen to include the cell bodies of the neurons, as well as bundles of fibres that are the posterior nerve root. The cells of the dorsal root ganglion are unipolar cells, classified by shape. Also, the small round nuclei of satellite cells can be seen surrounding—as if they were orbiting—the neuron cell bodies.

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Interactive Link 13.8

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/13.8) to explore the tissue sample in greater detail. If you zoom in on the dorsal root ganglion, you can see smaller satellite glial cells surrounding the large cell bodies of the sensory neurons. From what structure do satellite cells derive during embryologic development?

Another type of sensory ganglion is a **cranial nerve ganglion**. This is analogous to the dorsal root ganglion, except that it is associated with a **cranial nerve** instead of a **spinal nerve**. The roots of cranial nerves are within the cranium, whereas the ganglia are outside the skull.

The other major category of ganglia is **autonomic ganglia**, related to the **autonomic nervous system**, which is divided into the **sympathetic nervous system** and the **parasympathetic nervous system**. The **sympathetic chain ganglia** constitute a row of ganglia along the vertebral column that receive central input from the lateral horn of the thoracic and upper lumbar spinal cord. Superior to the chain ganglia are three **paravertebral ganglia** in the cervical region. Three other autonomic ganglia that are related to the sympathetic chain are the **prevertebral ganglia**, which are located outside of the chain but have similar functions. They are referred to as prevertebral because they are anterior to the vertebral column. The neurons of these autonomic ganglia are multipolar in shape, with dendrites radiating out around the cell body, where synapses from the spinal cord neurons are made. The neurons of the chain, paravertebral, and prevertebral ganglia then project to organs in the head and neck, thoracic, abdominal, and pelvic cavities to regulate the sympathetic aspect of homeostatic mechanisms.

Another group of **autonomic ganglia** is the **terminal ganglia**, which receive input from cranial nerves or sacral spinal nerves and are responsible for regulating the parasympathetic aspect of homeostatic mechanisms. These two sets of ganglia, sympathetic and parasympathetic, often project to the same organs—one input from the chain ganglia and one input from a terminal ganglion—to regulate the overall function of an organ. For example, the heart receives two inputs such as these: One increases heart rate, and the other decreases it. The terminal ganglia that receive input from cranial nerves are found in the head and neck, as well as the thoracic and upper abdominal cavities, whereas the terminal ganglia that receive sacral input are in the lower abdominal and pelvic cavities.

Terminal ganglia below the head and neck are often incorporated into the wall of the target organ as a **plexus**. A plexus, in a general sense, is a network

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of fibres or vessels. This can apply to nervous tissue (as in this instance) or structures containing blood vessels (such as a choroid plexus). For example, the **enteric plexus** is the extensive network of axons and neurons in the wall of the small and large intestines. The enteric plexus is actually part of the enteric nervous system, along with the **gastric plexuses** and the **esophageal plexus**. Though the enteric nervous system receives input originating from central neurons of the autonomic nervous system, it does not require CNS input to function. In fact, it operates independently to regulate the digestive system.

Nerves

Bundles of axons in the PNS are referred to as nerves. These structures in the periphery are different than the central counterpart, called a tract. Nerves are composed of more than just nervous tissue. They have connective tissues invested in their structure as well as blood vessels supplying the tissues with nourishment. The outer surface of a nerve is a surrounding layer of fibrous connective tissue called the **epineurium**. Within the nerve, axons are further bundled into **fascicles**, which are each surrounded by their own layer of fibrous connective tissue called **perineurium**. Finally, individual axons are surrounded by loose connective tissue called the **endoneurium** (Figure 13.11). These three layers are similar to the connective tissue sheaths for muscles. Nerves are associated with the region of the CNS to which they are connected, either as cranial nerves connected to the brain or as spinal nerves connected to the spinal cord.

Interactive Link 13.9

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/13.9) to explore the tissue sample in greater detail. With what structures in a skeletal muscle are the endoneurium, perineurium, and epineurium comparable?

Cranial Nerves

The nerves attached to the brain are the cranial nerves, which are primarily responsible for the sensory and motor functions of the head and neck (one of these nerves targets organs in the thoracic and abdominal cavities as part of the parasympathetic nervous system). There are twelve cranial nerves, which are designated CNI through CNXII for “cranial nerve,” using Roman numerals for 1 through 12. They can be classified as sensory nerves, motor nerves, or a combination of both, meaning that the axons in these nerves

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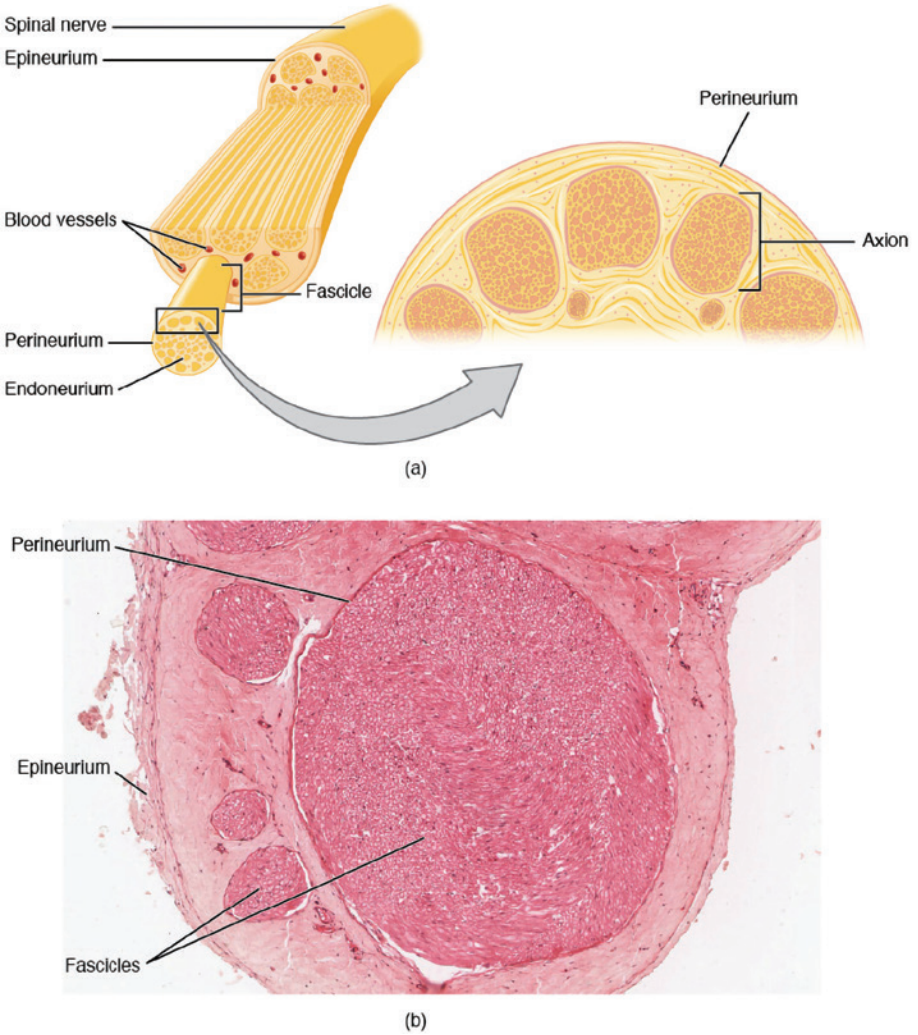


Figure 13.11 Nerve Structure. The structure of a nerve is organized by the layers of connective tissue on the outside, around each fascicle, and surrounding the individual nerve fibres (tissue source: simian). LM × 40. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

originate from sensory ganglia external to the cranium or motor nuclei within the brain stem. Sensory axons enter the brain to synapse in a nucleus. Motor axons connect to skeletal muscles of the head or neck. Three of the nerves are solely composed of sensory fibres; five are strictly motor; and the remaining four are mixed nerves.

The names of the cranial nerves are listed in Table 13.2 along with a brief description of their function, their source (sensory ganglion or motor nucleus), and their target (sensory nucleus or skeletal muscle). They are listed here with a brief explanation of each nerve (Figure 13.13).

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Figure 13.12 Close-Up of Nerve Trunk. Zoom in on this slide of a nerve trunk to examine the endoneurium, perineurium, and epineurium in greater detail (tissue source: simian). LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

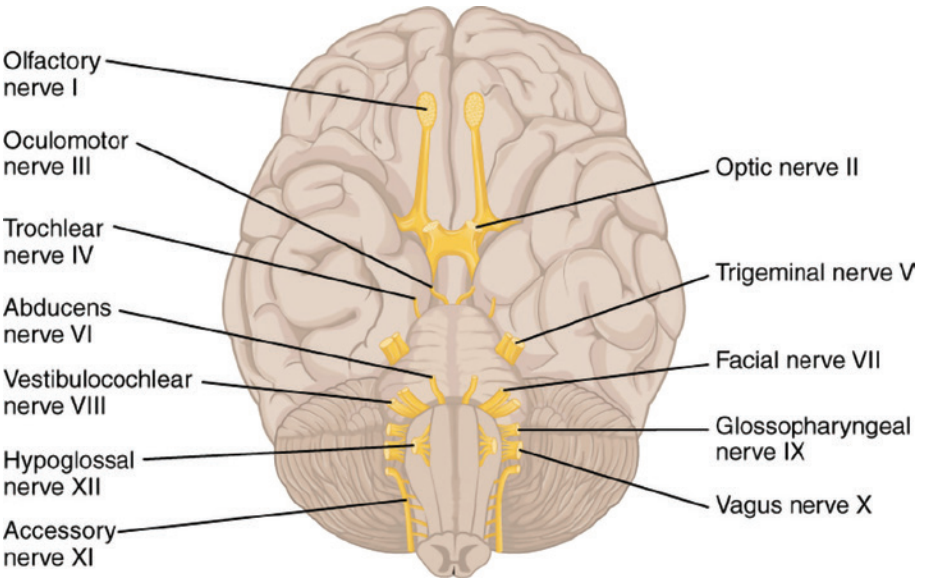


Figure 13.13 The Cranial Nerves. The anatomical arrangement of the roots of the cranial nerves is observed from an inferior view of the brain.

The **olfactory nerve** and **optic nerve** are responsible for the sense of smell and vision, respectively. The **oculomotor nerve** is responsible for eye movements by controlling four of the **extraocular muscles**. It is also responsible for lifting the upper eyelid when the eyes point up, and for pupillary constriction. The **trochlear nerve** and the **abducens nerve** are both responsible for eye movement but do so by controlling different extraocular muscles. The

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trigeminal nerve is responsible for cutaneous sensations of the face and controls the muscles of mastication.

The **facial nerve** is responsible for the muscles involved in facial expressions, as well as part of the sense of taste and the production of saliva. The **vestibulocochlear nerve** (**auditory**) is responsible for the senses of hearing and balance. The **glossopharyngeal nerve** is responsible for controlling muscles in the oral cavity and upper throat, as well as part of the sense of taste and the production of saliva. The **vagus nerve** is responsible for contributing to homeostatic control of the organs of the thoracic and upper abdominal cavities. The **spinal accessory nerve** is responsible for controlling the muscles of the neck, along with cervical spinal nerves. The **hypoglossal nerve** is responsible for controlling the muscles of the lower throat and tongue.

Three of the cranial nerves also contain autonomic fibres, and a fourth is almost purely a component of the autonomic system. The oculomotor, facial, and glossopharyngeal nerves contain fibres that contact autonomic ganglia. The oculomotor fibres initiate pupillary constriction, whereas the facial and glossopharyngeal fibres both initiate salivation. The vagus nerve primarily targets autonomic ganglia in the thoracic and upper abdominal cavities.

Interactive Link 13.10

Visit this site (http://oer.aupress.ca/oer-202505/13.10) to read about a man who wakes with a headache and a loss of vision. His regular doctor sends him to an ophthalmologist to address the vision loss. The ophthalmologist recognizes a greater problem and immediately sends him to the emergency room. Once there, the patient undergoes a large battery of tests, but a definite cause cannot be found. A specialist recognizes the problem as meningitis, but the question is what caused it originally. How can that be cured? The loss of vision comes from swelling around the optic nerve, which probably presented as a bulge on the inside of the eye. Why is swelling related to meningitis going to push on the optic nerve?

Another important aspect of the cranial nerves that lends itself to a mnemonic is the functional role each nerve plays. The nerves fall into one of three basic groups: They are sensory, motor, or both (see Table 13.2). The first, second, and eighth nerves are purely sensory: the olfactory (CNI), optic (CNII), and vestibulocochlear (CNVIII) nerves. The three eye-movement nerves are all motor: the oculomotor (CNIII), trochlear (CNIV), and abducens (CNVI). The

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Table 13.2 Cranial Nerves

#	Name	Type: sensory, motor, both	Function
I	Olfactory	Sensory (S)	S—controls the sense of smell
II	Optic	Sensory (S)	S—controls the sense of vision
III	Oculomotor	Motor (M)	M—controls movement of the eye
IV	Trochlear	Motor (M)	M—controls movement of the eye
V	Trigeminal	Sensory/motor (B)	S—responsible for cutaneous sensations of the face: touch, pain, thermal from skin, head, mouth M—controls the muscles of mastication
VI	Abducens	Motor (M)	M—controls movement of the eye
VII	Facial	Sensory/motor (B)	S—controls the senses of taste, touch, pain, thermal from skin and external ear canal, and the production of saliva M—controls muscles involved in facial expressions
VIII	Vestibulocochlear (auditory)	Sensory (S)	S—controls the earing and balance
IX	Glossopharyngeal	Sensory/motor (B)	S—controls sense of taste, deep sensation in some swallowing muscles, touch, pain, thermal from skin and external ear canal and upper pharynx, and the production of saliva M—controls muscles in the oral cavity and upper throat
X	Vagus	Sensory/motor (B)	S—contributes to homeostatic control of the organs of the thoracic and upper abdominal cavities, taste, deep sensation from pharynx and larynx; touch, pain, thermal from skin and external ear canal; sensations from thoracic and abdominal organs M—stimulates muscles in the pharynx, larynx, and the soft palate, the muscles in the heart, involuntary contractions in the digestive tract
XI	Spinal accessory	Motor (M)	M—controls movement of the head and neck
XII	Hypoglossal	Motor (M)	M—controls movement of the lower throat

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spinal accessory (CNXI) and hypoglossal (CNXII) nerves are also strictly motor. The remainder of the nerves contain both sensory and motor fibres. They are the trigeminal (CNV), facial (CNVII), glossopharyngeal (CNIX), and vagus (CNX) nerves.

The nerves that convey both are often related to one another. The trigeminal and facial nerves both concern the face; one concerns the sensations, and the other concerns the muscle movements. The facial and glossopharyngeal nerves are both responsible for conveying gustatory, or taste, sensations as well as controlling salivary glands. The vagus nerve is involved in visceral responses to taste, namely, the gag reflex. This is not an exhaustive list of what these combination nerves do, but there is a thread of relation between them.

Spinal Nerves

The nerves connected to the spinal cord are the **spinal nerves**. The arrangement of these nerves is much more regular than that of the cranial nerves. All the spinal nerves are combined sensory and motor axons that separate into two nerve roots. The sensory axons enter the spinal cord as the dorsal nerve root. The motor fibres, both somatic and autonomic, emerge as the ventral nerve root. The dorsal root ganglion for each nerve is an enlargement of the spinal nerve.

There are 31 spinal nerves, named for the level of the spinal cord at which each one emerges. There are 8 pairs of cervical nerves designated C1 to C8, 12 thoracic nerves designated T1 to T12, 5 pairs of lumbar nerves designated L1 to L5, 5 pairs of sacral nerves designated S1 to S5, and 1 pair of coccygeal nerves.

The nerves are numbered from the superior to inferior positions, and each emerges from the vertebral column through the intervertebral foramen at its level. The first nerve, C1, emerges between the first cervical vertebra and the occipital bone. The second nerve, C2, emerges between the first and second cervical vertebrae. The same occurs for C3 to C7, but C8 emerges between the seventh cervical vertebra and the first thoracic vertebra. For the thoracic and lumbar nerves, each one emerges between the vertebra that has the same designation and the next vertebra in the column. The sacral nerves emerge from the sacral foramina along the length of that unique vertebra.

Spinal nerves extend outward from the vertebral column to innervate the periphery. The nerves in the periphery are not straight continuations of the spinal nerves, but rather the reorganization of the axons in those nerves to follow different courses. Axons from different spinal nerves will come together into a **systemic nerve**. This occurs at four places along the length of the vertebral column, each identified as a **nerve plexus**, whereas the other spinal nerves

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directly correspond to nerves at their respective levels. In this instance, the word *plexus* is used to describe networks of nerve fibres with no associated cell bodies.

Of the four nerve plexuses, two are found at the cervical level, one at the lumbar level, and one at the sacral level (Figure 13.14). The **cervical plexus** is composed of axons from spinal nerves C1 through C5 and branches into nerves in the posterior neck and head, as well as the **phrenic nerve**, which connects to the diaphragm at the base of the thoracic cavity. The other plexus from the cervical level is the **brachial plexus**. Spinal nerves C4 through T1 reorganize through this plexus to give rise to the nerves of the arms, as the name brachial suggests. A large nerve from this plexus is the **radial nerve**, from which the **axillary nerve** branches to go to the armpit region. The radial nerve continues through the arm and is paralleled by the **ulnar nerve** and the **median nerve**. The **lumbar plexus** arises from all the lumbar spinal nerves and gives rise to nerves enervating the pelvic region and the anterior leg.

The **femoral nerve** is one of the major nerves from this plexus, which gives rise to the **saphenous nerve** as a branch that extends through the anterior lower leg. The **sacral plexus** comes from the lower lumbar nerves L4 and L5 and the sacral nerves S1 to S4. The most significant systemic nerve to come from this plexus is the **sciatic nerve**, which is a combination of the **tibial nerve** and the **fibular nerve**.

These plexuses are described as arising from spinal nerves and giving rise to certain systemic nerves, but they contain fibres that serve sensory functions or fibres that serve motor functions. This means that some fibres extend from cutaneous or other peripheral sensory surfaces and send action potentials into the CNS. Those are axons of sensory neurons in the dorsal root ganglia that enter the spinal cord through the dorsal nerve root. Other fibres are the axons of motor neurons of the anterior horn of the spinal cord, which emerge in the ventral nerve root and send action potentials to cause skeletal muscles to contract in their target regions. For example, the radial nerve contains fibres of cutaneous sensation in the arm, as well as motor fibres that move muscles in the arm.

Spinal nerves of the thoracic region, T2 through T11, are not part of the plexuses but rather emerge and give rise to the **intercostal nerves** found between the ribs, which articulate with the vertebrae surrounding the spinal nerve.

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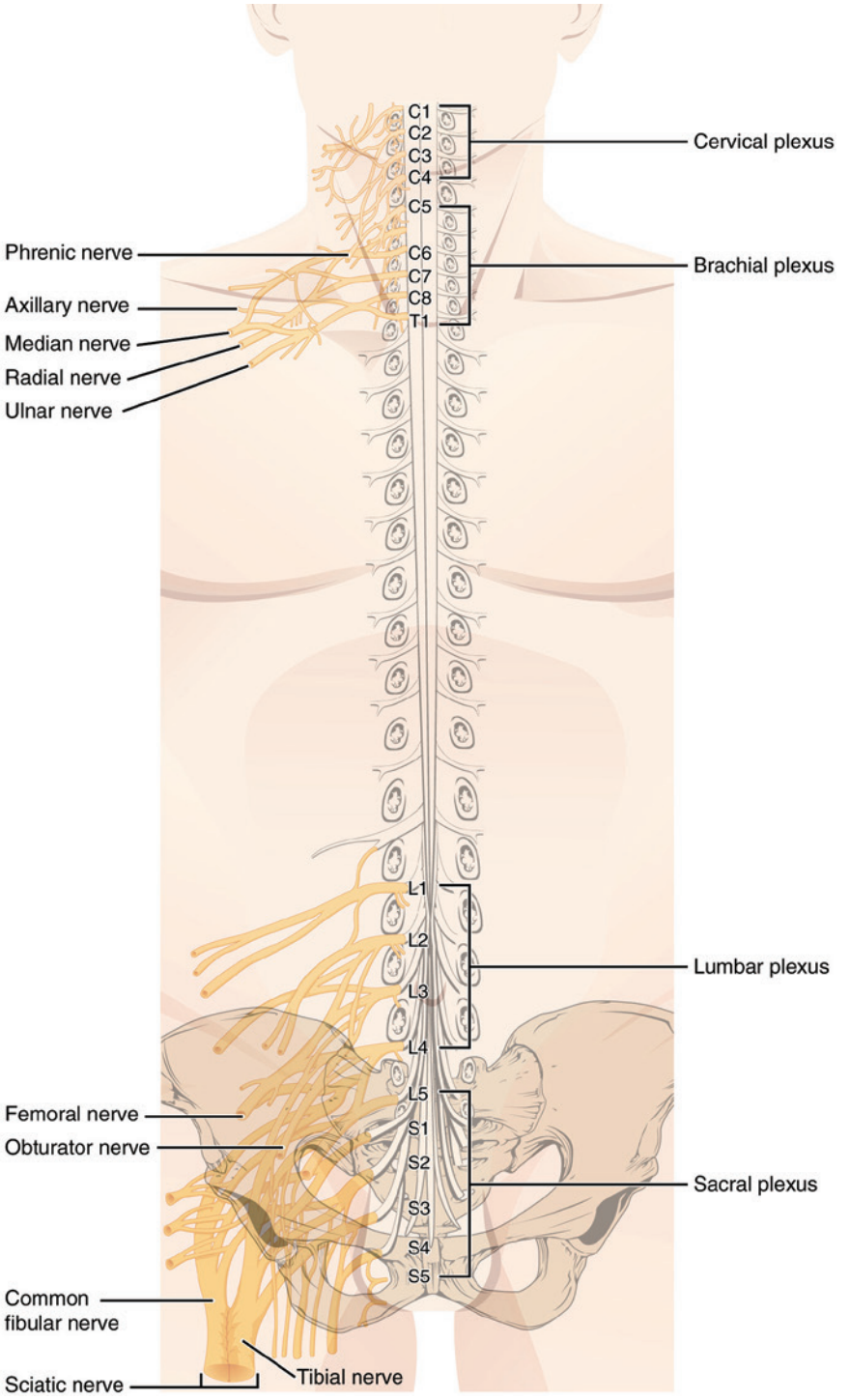


Figure 13.14 Nerve Plexuses of the Body. There are four main nerve plexuses in the human body. The cervical plexus supplies nerves to the posterior head and neck, as well as to the diaphragm. The brachial plexus supplies nerves to the arm. The lumbar plexus supplies nerves to the anterior leg. The sacral plexus supplies nerves to the posterior leg.

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Key Terms

abducens nerve: Sixth cranial nerve; responsible for contraction of one of the extraocular muscles.

amygdala: Nucleus deep in the temporal lobe of the cerebrum that is related to memory and emotional behaviour.

anterior column: White matter between the anterior horns of the spinal cord composed of many different groups of axons of both ascending and descending tracts.

anterior horn: Grey matter of the spinal cord containing multipolar motor neurons, sometimes referred to as the ventral horn.

anterior median fissure: Deep midline feature of the anterior spinal cord, marking the separation between the right and left sides of the cord.

arachnoid mater: Middle layer of the meninges named for the spider-web–like trabeculae that extend between it and the pia mater.

ascending tract: Central nervous system fibres carrying sensory information from the spinal cord or periphery to the brain.

autonomic ganglia: Related to the autonomic nervous system, which is divided into the sympathetic and parasympathetic nervous systems.

axillary nerve: Systemic nerve of the arm that arises from the brachial plexus.

basal nuclei: Nuclei of the cerebrum (with a few components in the upper brain stem and diencephalon) that are responsible for assessing cortical movement commands and comparing them with the general state of the individual through broad modulatory activity of dopamine neurons; largely related to motor function.

brachial plexus: Nerve plexus associated with the lower cervical spinal nerves and the first thoracic spinal nerve.

brain stem: Region of the adult brain that includes the midbrain, pons, and medulla oblongata and develops from the mesencephalon, metencephalon, and myelencephalon of the embryonic brain.

Broca's area: Region of the frontal lobe associated with the motor commands necessary for speech production and located only in the cerebral hemisphere responsible for language production, which is the left side in approximately 95 percent of the population.

cauda equina: Bundle of spinal nerve roots that descend from the lower spinal cord below the first lumbar vertebra and lie within the vertebral cavity; has the appearance of a horse's tail.

central canal: Hollow space within the spinal cord that is the remnant of the centre of the neural tube.

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central sulcus: Surface landmark of the cerebral cortex that marks the boundary between the frontal and parietal lobes.

cerebellum: Region of the adult brain connected primarily to the pons, which developed from the metencephalon (along with the pons), and is largely responsible for comparing information from the cerebrum with sensory feedback from the periphery through the spinal cord.

cerebral aqueduct: Connection of the ventricular system between the third and fourth ventricles located in the midbrain.

cerebral cortex: Outer grey matter covering the forebrain, marked by wrinkles and folds known as gyri and sulci.

cerebral hemisphere: One-half of the bilaterally symmetrical cerebrum.

cerebrum: Region of the adult brain that develops from the telencephalon and is responsible for higher neurological functions such as memory, emotion, and consciousness.

Cerebrospinal fluid (CSF): Circulates throughout and around the CNS; it is produced in special structures to perfuse through the nervous tissue of the CNS to remove metabolic wastes from the interstitial fluids of nervous tissues and return them to the bloodstream.

cervical plexus: Nerve plexus associated with the upper cervical spinal nerves.

choroid plexus: Specialized structure containing ependymal cells lining blood capillaries that filter blood to produce CSF in the four ventricles of the brain.

circle of Willis: Unique anatomical arrangement of blood vessels around the base of the brain that maintains perfusion of blood into the brain, even if one component of the structure is blocked or narrowed.

common carotid artery: Blood vessel that branches off the aorta (or the brachiocephalic artery on the right) and supplies blood to the head and neck.

corpus callosum: Large white matter structure that connects the right and left cerebral hemispheres.

cranial nerve: One of twelve nerves connected to the brain that are responsible for sensory or motor functions of the head and neck.

cranial nerve ganglion: Sensory ganglion of cranial nerves.

descending tract: Central nervous system fibres carrying motor commands from the brain to the spinal cord or periphery.

diencephalon: Region of the adult brain that retains its name from embryonic development and includes the thalamus and hypothalamus.

direct pathway: Connections within the basal nuclei from the striatum to the globus pallidus internal segment and substantia nigra pars reticulata that disinhibit the thalamus to increase cortical control of movement.

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dorsal (posterior) root ganglion: Sensory ganglion attached to the posterior nerve root of a spinal nerve.

dura mater: Tough, fibrous, outer layer of the meninges that is attached to the inner surface of the cranium and vertebral column and surrounds the entire CNS.

dural sinus: Any of the venous structures surrounding the brain, enclosed within the dura mater, which drain blood from the CNS to the common venous return of the jugular veins.

endoneurium: Innermost layer of connective tissue that surrounds individual axons within a nerve.

enteric nervous system: Peripheral structures, namely, ganglia and nerves, that are incorporated into the digestive system organs.

enteric plexus: Neuronal plexus in the wall of the intestines, which is part of the enteric nervous system.

epineurium: Outermost layer of connective tissue that surrounds an entire nerve.

epithalamus: Region of the diencephalon containing the pineal gland.

esophageal plexus: Neuronal plexus in the wall of the esophagus that is part of the enteric nervous system.

extraocular muscles: Six skeletal muscles that control eye movement within the orbit.

facial nerve: Seventh cranial nerve; responsible for contraction of the facial muscles and for part of the sense of taste, as well as causing saliva production.

fascicle: Small bundles of nerve or muscle fibres enclosed by connective tissue.

femoral nerve: Systemic nerve of the anterior leg that arises from the lumbar plexus.

fibular nerve: Systemic nerve of the posterior leg that begins as part of the sciatic nerve.

forebrain: Anterior region of the adult brain that develops from the prosencephalon and includes the cerebrum and diencephalon.

fourth ventricle: The portion of the ventricular system that is in the region of the brain stem and opens into the subarachnoid space through the median and lateral apertures.

frontal eye field: Region of the frontal lobe associated with motor commands to orient the eyes toward an object of visual attention.

frontal lobe: Region of the cerebral cortex directly beneath the frontal bone of the cranium.

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gastric plexuses: Neuronal networks in the wall of the stomach that are part of the enteric nervous system.

glossopharyngeal nerve: Ninth cranial nerve; responsible for the contraction of muscles in the tongue and throat and for part of the sense of taste as well as causing saliva production.

gyrus: Ridge formed by convolutions on the surface of the cerebrum or cerebellum.

hindbrain: Posterior region of the adult brain that develops from the rhombencephalon and includes the pons, medulla oblongata, and cerebellum.

hippocampus: Grey matter deep in the temporal lobe that is very important for long-term memory formation.

hypoglossal nerve: 12th cranial nerve; responsible for the contraction of muscles of the tongue.

hypothalamus: Major region of the diencephalon that is responsible for coordinating autonomic and endocrine control of homeostasis.

indirect pathway: Connections within the basal nuclei from the striatum through the globus pallidus external segment and subthalamic nucleus to the globus pallidus internal segment/substantia nigra pars compacta that result in inhibition of the thalamus to decrease cortical control of movement.

inferior colliculus: Half of the midbrain tectum that is part of the brain stem auditory pathway.

intercostal nerve: Systemic nerve in the thoracic cavity that is found between two ribs.

internal carotid artery: Branch from the common carotid artery that enters the cranium and supplies blood to the brain.

interventricular foramina: Openings between the lateral ventricles and the third ventricle, allowing for the passage of CSF.

jugular veins: Blood vessels that return "used" blood from the head and neck.

kinesthesia: General sensory perception of movement of the body.

lateral apertures: Pair of openings from the fourth ventricle to the subarachnoid space on either side and between the medulla and cerebellum.

lateral column: White matter of the spinal cord between the posterior horn on one side and the axons from the anterior horn on the same side; composed of many different groups of axons, of both ascending and descending tracts, carrying motor commands to and from the brain.

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lateral horn: Region of the spinal cord grey matter in the thoracic, upper lumbar, and sacral regions that is the central component of the sympathetic division of the autonomic nervous system.

lateral sulcus: Surface landmark of the cerebral cortex that marks the boundary between the temporal lobe and the frontal and parietal lobes.

lateral ventricles: Portions of the ventricular system that are in the region of the cerebrum.

limbic cortex: Collection of structures of the cerebral cortex that are involved in emotion, memory, and behaviour and are part of the larger limbic system.

limbic system: Structures at the edge (limit) of the boundary between the forebrain and hindbrain that are most associated with emotional behaviour and memory formation.

longitudinal fissure: Large separation along the midline between the two cerebral hemispheres.

lumbar plexus: Nerve plexus associated with the lumbar spinal nerves.

lumbar puncture: Procedure used to withdraw CSF from the lower lumbar region of the vertebral column that avoids the risk of damaging CNS tissue because the spinal cord ends at the upper lumbar vertebrae.

median aperture: Singular opening from the fourth ventricle into the subarachnoid space at the midline between the medulla and cerebellum.

median nerve: Systemic nerve of the arm, located between the ulnar and radial nerves.

medulla (medulla oblongata): White matter region in the brain that is continuous with the white matter of the spinal cord.

meninges: Protective outer coverings of the CNS composed of connective tissue.

midbrain: Middle region of the adult brain that develops from the mesencephalon.

nerve plexus: Network of nerves without neuronal cell bodies included.

occipital lobe: Region of the cerebral cortex directly beneath the occipital bone of the cranium.

oculomotor nerve: Third cranial nerve; responsible for contraction of four of the extraocular muscles, the muscle in the upper eyelid, and pupillary constriction.

olfaction: Special sense responsible for smell, which has a unique, direct connection to the cerebrum.

olfactory nerve: First cranial nerve; responsible for the sense of smell.

optic nerve: Second cranial nerve; responsible for visual sensation.

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orthostatic reflex: Sympathetic function that maintains blood pressure when standing to offset the increased effect of gravity.

parasympathetic nervous system: Branch of the autonomic nervous system that conserves energy and calms the body after stress.

paravertebral ganglia: Autonomic ganglia superior to the sympathetic chain ganglia.

parietal lobe: Region of the cerebral cortex directly beneath the parietal bone of the cranium.

parieto-occipital sulcus: Groove in the cerebral cortex representing the border between the parietal and occipital cortices.

perineurium: Layer of connective tissue surrounding fascicles within a nerve.

phrenic nerve: Systemic nerve from the cervical plexus that innervates the diaphragm.

pia mater: Thin, innermost membrane of the meninges that directly covers the surface of the CNS.

plexus: Network of nerves or nervous tissue.

postcentral gyrus: Primary motor cortex located in the frontal lobe of the cerebral cortex.

posterior columns: White matter of the spinal cord that lies between the posterior horns of the grey matter, sometimes referred to as the dorsal column; composed of axons of ascending tracts that carry sensory information up to the brain.

posterior horn: Grey matter region of the spinal cord in which sensory input arrives, sometimes referred to as the dorsal horn.

posterior median sulcus: Midline feature of the posterior spinal cord, marking the separation between right and left sides of the cord.

precentral gyrus: Ridge just posterior to the central sulcus, in the parietal lobe, where somatosensory processing initially takes place in the cerebrum.

prefrontal lobe: Specific region of the frontal lobe anterior to the more specific motor function areas, which can be related to the early planning of movements and intentions to the point of being personality-type functions.

premotor area: Region of the frontal lobe responsible for planning movements that will be executed through the primary motor cortex.

prevertebral ganglia: Autonomic ganglia that are anterior to the vertebral column and functionally related to the sympathetic chain ganglia.

proprioception: General sensory perceptions providing information about the location and movement of body parts; the "sense of the self."

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radial nerve: Systemic nerve of the arm, the distal component of which is located near the radial bone.

reticular formation: Diffuse region of grey matter throughout the brain stem that regulates sleep, wakefulness, and states of consciousness.

sacral plexus: Nerve plexus associated with the lower lumbar and sacral spinal nerves.

saphenous nerve: Systemic nerve of the lower anterior leg that is a branch from the femoral nerve.

sciatic nerve: Systemic nerve from the sacral plexus that is a combination of the tibial and fibular nerves and extends across the hip joint and gluteal region into the upper posterior leg.

sensory ganglia: Clusters of nerve cell bodies located outside the central nervous system that relay sensory information.

somatosensation: General senses related to the body, usually thought of as the senses of touch, which would include pain, temperature, and proprioception.

spinal accessory nerve: 11th cranial nerve; responsible for contraction of neck muscles.

spinal nerve: One of 31 nerves connected to the spinal cord.

subarachnoid space: Space between the arachnoid mater and pia mater that contains CSF and the fibrous connections of the arachnoid trabeculae.

subcortical nucleus: All the nuclei beneath the cerebral cortex, including the basal nuclei and the basal forebrain.

substantia nigra pars reticulata: Nuclei within the basal nuclei that serve as an output centre of the nuclei; part of the motor pathway.

subthalamus: Nucleus within the basal nuclei that is part of the indirect pathway.

sulcus: Groove formed by convolutions in the surface of the cerebral cortex.

superior colliculus: Half of the midbrain tectum that is responsible for aligning visual, auditory, and somatosensory spatial perceptions.

superior sagittal sinus: Dural sinus that runs along the top of the longitudinal fissure and drains blood from the majority of the outer cerebrum.

sympathetic chain ganglia: Autonomic ganglia in a chain along the anterolateral aspect of the vertebral column that are responsible for contributing to homeostatic mechanisms of the autonomic nervous system.

sympathetic nervous system: Branch of the autonomic nervous system that mediates the body's involuntary response to stress, danger, or intense physical activity.

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systemic nerve: Nerve in the periphery distal to a nerve plexus or spinal nerve.

temporal lobe: Region of the cerebral cortex directly beneath the temporal bone of the cranium.

terminal ganglion: Autonomic ganglia that are near or within the walls of organs and are responsible for contributing to homeostatic mechanisms of the autonomic nervous system.

thalamus: Major region of the diencephalon that is responsible for relaying information between the cerebrum and the hindbrain, spinal cord, and periphery.

third ventricle: Portion of the ventricular system that is in the region of the diencephalon.

tibial nerve: Systemic nerve of the posterior leg that begins as part of the sciatic nerve.

trigeminal nerve: Fifth cranial nerve; responsible for cutaneous sensation of the face and contraction of the muscles of mastication.

trochlear nerve: Fourth cranial nerve; responsible for contraction of one of the extraocular muscles.

ulnar nerve: Systemic nerve of the arm located close to the ulna, a bone of the forearm.

vagus nerve: 10th cranial nerve; responsible for the autonomic control of organs in the thoracic and upper abdominal cavities.

ventricles: Remnants of the hollow centre of the neural tube that are spaces for cerebrospinal fluid to circulate through the brain.

vertebral arteries: Arteries that ascend along either side of the vertebral column through the transverse foramina of the cervical vertebrae and enter the cranium through the foramen magnum.

vestibulocochlear nerve (auditory): Eighth cranial nerve; responsible for the sensations of hearing and balance.

Chapter Review

13.1 The Central Nervous System

The adult brain is separated into four major regions: the cerebrum, the diencephalon, the brain stem, and the cerebellum. The cerebrum is the largest portion and contains the cerebral cortex and subcortical nuclei. It is divided into two halves by the longitudinal fissure.

The cortex is separated into the frontal, parietal, temporal, and occipital lobes. The frontal lobe is responsible for motor functions, from planning

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movements through executing commands to be sent to the spinal cord and periphery. The most anterior portion of the frontal lobe is the prefrontal cortex, which is associated with aspects of personality through its influence on motor responses in decision-making.

The other lobes are responsible for sensory functions. The parietal lobe is where somatosensation is processed. The occipital lobe is where visual processing begins, although the other parts of the brain can contribute to visual function. The temporal lobe contains the cortical area for auditory processing but also has regions crucial for memory formation.

Nuclei beneath the cerebral cortex, known as the subcortical nuclei, are responsible for augmenting cortical functions. The basal nuclei receive input from cortical areas and compare it with the general state of the individual through the activity of a dopamine-releasing nucleus. The output influences the activity of part of the thalamus that can then increase or decrease cortical activity, which often results in changes to motor commands. The basal forebrain is responsible for modulating cortical activity in attention and memory.

The limbic system includes deep cerebral nuclei that are responsible for emotion and memory.

The diencephalon includes the thalamus and the hypothalamus, along with some other structures. The thalamus is a relay between the cerebrum and the rest of the nervous system. The hypothalamus coordinates homeostatic functions through the autonomic and endocrine systems.

The brain stem is composed of the midbrain, pons, and medulla. It controls the head and neck region of the body through the cranial nerves. There are control centres in the brain stem that regulate the cardiovascular and respiratory systems.

The cerebellum is connected to the brain stem, primarily at the pons, where it receives a copy of the descending input from the cerebrum to the spinal cord. It can compare this with sensory feedback input through the medulla and send output through the midbrain that can correct motor commands for coordination.

13.2 Circulation and the Central Nervous System

The CNS has a privileged blood supply established by the blood-brain barrier. Establishing this barrier are anatomical structures that help protect and isolate the CNS. The arterial blood to the brain comes from the internal carotid and vertebral arteries, which both contribute to the unique circle of Willis that provides constant perfusion of the brain even if one of the blood vessels is blocked or narrowed. That blood is eventually filtered to make a separate medium, the CSF, that circulates within the spaces of the brain and then into

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the surrounding space defined by the meninges, the protective covering of the brain and spinal cord.

The blood that nourishes the brain and spinal cord is behind the glial cell–enforced blood-brain barrier, which limits the exchange of material from blood vessels with the interstitial fluid of the nervous tissue. Thus, metabolic wastes are collected in cerebrospinal fluid that circulates through the CNS. This fluid is produced by filtering blood at the choroid plexuses in the four ventricles of the brain. It then circulates through the ventricles and into the subarachnoid space, between the pia mater and the arachnoid mater.

The blood, now with the reabsorbed CSF, drains out of the cranium through the dural sinuses. The dura mater is the tough outer covering of the CNS, which is anchored to the inner surface of the cranial and vertebral cavities. It surrounds the venous space known as the dural sinuses, which connect to the jugular veins, where blood drains from the head and neck.

13.3 The Peripheral Nervous System

The PNS is composed of the groups of neurons (ganglia) and bundles of axons (nerves) that are outside of the brain and spinal cord. Ganglia are of two types: sensory or autonomic. Sensory ganglia contain unipolar sensory neurons and are found on the dorsal root of all spinal nerves as well as associated with many of the cranial nerves. Autonomic ganglia are in the sympathetic chain, the associated paravertebral or prevertebral ganglia, or terminal ganglia near or within the organs controlled by the autonomic nervous system.

Nerves are classified as cranial nerves or spinal nerves on the basis of their connection to the brain or spinal cord, respectively. The twelve cranial nerves can be strictly sensory in function, strictly motor in function, or a combination of the two functions. Sensory fibres are axons of sensory ganglia that carry sensory information into the brain and target sensory nuclei. Motor fibres are axons of motor neurons in motor nuclei of the brain stem and target skeletal muscles of the head and neck. Spinal nerves are all mixed nerves with both sensory and motor fibres. Spinal nerves emerge from the spinal cord and reorganize through plexuses, which then give rise to systemic nerves. Thoracic spinal nerves are not part of any plexus but give rise to the intercostal nerves directly.

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14

The Somatic Nervous System

Chapter Objectives

After studying this chapter, you will be able to:

- Describe the components of the somatic nervous system
- Name the modalities and submodalities of the sensory systems
- Distinguish between general and special senses
- Describe regions of the central nervous system that contribute to somatic functions
- Explain the stimulus-response motor pathway

The somatic nervous system is traditionally considered a division within the peripheral nervous system. However, this misses an important point: somatic refers to a functional division, whereas peripheral refers to an anatomic division. The somatic nervous system is responsible for our conscious perception of the environment and for our voluntary responses to that perception by means of skeletal muscles. Peripheral sensory neurons receive input from environmental stimuli, but the neurons that produce motor responses originate in the central nervous system. The distinction between the structures (i.e., anatomy) of the peripheral and central nervous systems and functions (i.e., physiology) of the somatic and autonomic systems can most easily be demonstrated through a simple reflex action.

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14.1 Sensory Perception

Learning Objectives

By the end of this section, you will be able to:

- Describe different types of sensory receptors
- Describe the structures responsible for the special senses of taste, smell, hearing, balance, and vision
- Distinguish how different tastes are transduced
- Describe the means of mechanoreception for hearing and balance
- List the supporting structures around the eye and describe the structure of the eyeball
- Describe the processes of phototransduction

A major role of sensory receptors is to help us learn about the environment around us, or about the state of our internal environment. Stimuli from varying sources, and of different types, are received and changed into the electrochemical signals of the nervous system. This occurs when a stimulus changes the cell membrane potential of a sensory neuron. The stimulus causes the sensory cell to produce an action potential that is relayed into the central nervous system (CNS), where it is integrated with other sensory information—or sometimes higher cognitive functions—to become a conscious perception of that stimulus. The central integration may then lead to a motor response.

Describing sensory function with the term *sensation* or *perception* is a deliberate distinction. Sensation is the activation of sensory receptor cells at the level of the stimulus. Perception is the central processing of sensory stimuli into a meaningful pattern. Perception is dependent on sensation, but not all sensations are perceived. Receptors are the cells or structures that detect sensations. A receptor cell is changed directly by a stimulus. A transmembrane protein receptor is a protein in the cell membrane that mediates a physiological change in a neuron, most often through the opening of ion channels or changes in the cell signalling processes. Transmembrane receptors are activated by chemicals called ligands. For example, a molecule in food can serve as a ligand for taste receptors. Other transmembrane proteins, which are not accurately called receptors, are sensitive to mechanical or thermal changes. Physical changes in these proteins increase ion flow across the membrane and can generate an action potential or a graded potential in the sensory neurons.

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Sensory Receptors

Stimuli in the environment activate specialized receptor cells in the peripheral nervous system. Different types of stimuli are sensed by different types of receptor cells. Receptor cells can be classified into types on the basis of three different criteria: cell type, position, and function. Receptors can be classified structurally on the basis of cell type and their position in relation to the stimuli they sense. They can also be classified functionally on the basis of the **transduction** of stimuli, or how the mechanical stimulus, light, or chemical changed the cell membrane potential.

Structural Receptor Types

The cells that interpret information about the environment can be either (1) a neuron that has a **free nerve ending**, with dendrites embedded in tissue that would receive a sensation; (2) a neuron that has an **encapsulated ending** in which the sensory nerve endings are encapsulated in connective tissue that enhances their sensitivity; or (3) a **specialized receptor cell**, which has distinct structural components that interpret a specific type of stimulus (Figure 14.1). The pain and temperature receptors in the dermis of the skin are examples of neurons that have free nerve endings. Also located in the dermis of the skin are lamellated corpuscles, neurons with encapsulated nerve endings that respond to pressure and touch. The cells in the retina that respond to light stimuli are an example of a specialized receptor, a **photoreceptor**.

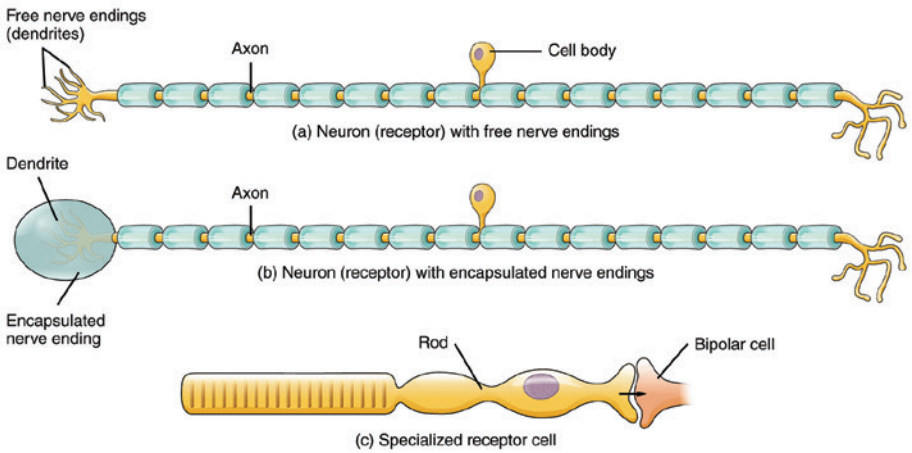


Figure 14.1 Receptor Classification by Cell Type. Receptor cell types can be classified on the basis of their structure. Sensory neurons can have either (a) free nerve endings or (b) encapsulated endings. Photoreceptors in the eyes, such as rod cells, are examples of (c) specialized receptor cells. These cells release neurotransmitters onto a bipolar cell, which then synapses with the optic nerve neurons.

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Another way that receptors can be classified is based on their location relative to the stimuli. An **exteroceptor** is a receptor that is located near a stimulus in the external environment, such as the somatosensory receptors that are located in the skin. An **interoceptor** is one that interprets stimuli from internal organs and tissues, such as the receptors that sense the increase in blood pressure in the aorta or carotid sinus. Finally, a **proprioceptor** is a receptor located near a moving part of the body, such as a muscle and tendons, that interprets the positions of the tissues as they move.

Functional Receptor Types

A third classification of receptors is by how the receptor transduces stimuli into membrane potential changes. Stimuli are of three general types. Some stimuli are ions and macromolecules that affect transmembrane receptor proteins when these chemicals diffuse across the cell membrane. Some stimuli are physical variations in the environment that affect receptor cell membrane potentials. Other stimuli include the electromagnetic radiation from visible light. For humans, the only electromagnetic energy that is perceived by our eyes is visible light. Some other organisms have receptors that humans lack, such as the heat sensors of snakes, the ultraviolet light sensors of bees, or magnetic receptors in migratory birds.

Receptor cells can be further categorized on the basis of the type of stimuli they transduce. Chemical stimuli can be interpreted by a **chemoreceptor** that interprets chemical stimuli, such as an object's taste or smell. **Osmoreceptors** respond to solute concentrations of body fluids. Additionally, pain is primarily a chemical sense that interprets the presence of chemicals from tissue damage or similar intense stimuli through a **nociceptor**. Physical stimuli, such as pressure and vibration, as well as the sensation of sound and body position (balance), are interpreted through a **mechanoreceptor**. Another physical stimulus that has its own type of receptor is temperature, which is sensed through a **thermoreceptor** that is sensitive to temperatures either above (heat) or below (cold) normal body temperature. **Photoreceptors** are located in the eyes, and they detect light.

Sensory Modalities

Ask anyone what the senses are, and they are likely to list the five major senses—taste, smell, touch, hearing, and sight. However, these are not all the senses. The most obvious omission from this list is balance. Also, what is referred to simply as touch can be further subdivided into pressure, vibration, stretch, and hair-follicle position, on the basis of the type of mechanoreceptors that perceive these touch sensations. Other overlooked senses include temperature perception by thermoreceptors and pain perception by nociceptors.

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Within the realm of physiology, senses can be classified as either general or specific. A **general sense** is one that is distributed throughout the body and has receptor cells within the structures of other organs. Mechanoreceptors in the skin, muscles, or the walls of blood vessels or the walls of the urinary bladder are examples of this type. General senses often contribute to the sense of touch, to **proprioception** (body movement) and **kinesthesia** (body movement), or to a **visceral sense**, which is most important to autonomic functions. A **special sense** is one that has a specific organ devoted to it, namely, the eye, inner ear, tongue, or nose.

Each of the senses is referred to as a **sensory modality**. Modality refers to the way that information is encoded, which is similar to the idea of transduction. The main sensory modalities can be described on the basis of how each is transduced. The chemical senses are taste and smell. The general sense that is usually referred to as touch includes chemical sensation in the form of nociception, or pain. Pressure, vibration, muscle stretch, and the movement of hair by an external stimulus are all sensed by mechanoreceptors. Hearing and balance are also sensed by mechanoreceptors. Finally, vision involves the activation of photoreceptors.

Listing all the different sensory modalities involves separating the five major senses into more specific categories, or **submodalities**, of the larger sense. An individual sensory modality represents the sensation of a specific type of stimulus. For example, the general sense of touch, which is known as **somatosensation**, can be separated into light pressure, deep pressure, vibration, itch, pain, temperature, or hair movement.

Gustation (Taste)

Only a few recognized submodalities exist within the sense of taste, or **gustation**. Until recently, only four tastes were recognized: sweet, salty, sour, and bitter. Umami is a Japanese word that means "delicious taste," and is often translated to mean savory. Very recent research has suggested that there may also be a sixth taste for fats, or lipids.

Gustation is the special sense associated with the tongue. The surface of the tongue, along with the rest of the oral cavity, is lined by a stratified squamous epithelium. Raised bumps called **papillae** (singular = papilla) contain the structures for gustatory transduction. There are four types of papillae, based on their appearance: circumvallate, foliate, filiform, and fungiform (Figure 14.2). Within the structure of the papillae are **taste buds** that contain specialized **gustatory receptor cells** for the transduction of taste stimuli. These receptor cells are sensitive to the chemicals contained within foods that are ingested, and they release neurotransmitters based on the amount of the chemical in the food. Neurotransmitters from the gustatory cells can activate sensory neurons in the facial, glossopharyngeal, and vagus cranial nerves.

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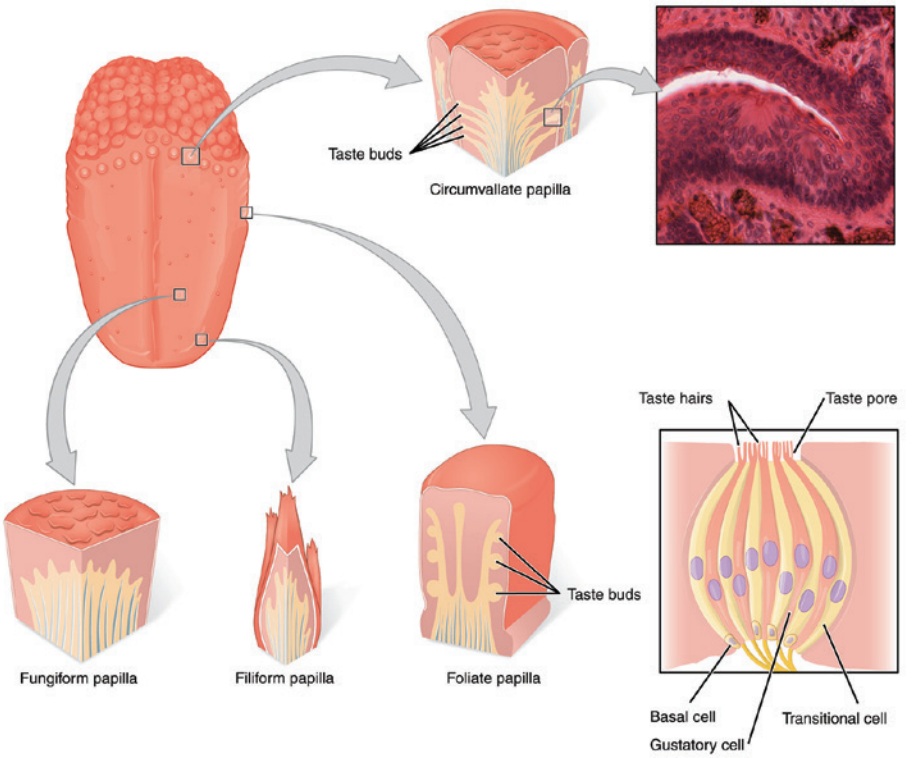


Figure 14.2 The Tongue. The tongue is covered with small bumps, called papillae, which contain taste buds that are sensitive to chemicals in ingested food or drink. Different types of papillae are found in different regions of the tongue. The taste buds contain specialized gustatory receptor cells that respond to chemical stimuli dissolved in the saliva. These receptor cells activate sensory neurons that are part of the facial and glossopharyngeal nerves. LM × 1600. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Salty taste is simply the perception of sodium ions (Na^+) in the saliva. When you eat something salty, the salt crystals dissociate into the component ions Na^+ and Cl^-, which dissolve into the saliva in your mouth. The Na^+ concentration becomes high outside the gustatory cells, creating a strong concentration gradient that drives the diffusion of the ion into the cells. The entry of Na^+ into these cells results in the depolarization of the cell membrane and the generation of a receptor potential.

Sour taste is the perception of H^+ concentration. Just as with sodium ions in salty flavors, these hydrogen ions enter the cell and trigger depolarization. Sour flavors are, essentially, the perception of acids in our food. Increasing hydrogen-ion concentrations in the saliva (lowering saliva pH) triggers progressively stronger graded potentials in the gustatory cells. For example, orange juice—which contains citric acid—will taste sour because it has a pH value of

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approximately 3. Of course, it is often sweetened so that the sour taste is masked. These two tastes (salty and sour) are triggered by the cations Na^+ and H^+.

The other tastes result from food molecules binding to a G protein–coupled receptor. A G protein signal transduction system ultimately leads to depolarization of the gustatory cell. The sweet taste is the sensitivity of gustatory cells to the presence of glucose dissolved in the saliva. Other monosaccharides, such as fructose, and artificial sweeteners such as aspartame (NutraSweet™), saccharine, or sucralose (Splenda™) also activate the sweet receptors. The affinity for each of these molecules varies, and some will taste sweeter than glucose because they bind to the G protein–coupled receptor differently.

Bitter taste is similar to sweet in that food molecules bind to G protein–coupled receptors. However, there are a number of different ways in which this can happen because there is a large diversity of bitter-tasting molecules. Some bitter molecules depolarize gustatory cells, whereas others hyperpolarize gustatory cells. Likewise, some bitter molecules increase G protein activation within the gustatory cells, whereas other bitter molecules decrease G protein activation. The specific response depends on which molecule is binding to the receptor.

One major group of bitter-tasting molecules is alkaloids. **Alkaloids** are nitrogen-containing molecules that are commonly found in bitter-tasting plant products, such as coffee, hops (in beer), tannins (in wine), tea, and aspirin. By containing toxic alkaloids, the plant is less susceptible to microbial infection and less attractive to herbivores.

Therefore, the function of bitter taste may primarily be related to stimulating the gag reflex to avoid ingesting poisons. Because of this, many bitter foods that are normally ingested are often combined with a sweet component to make them more palatable (cream and sugar in coffee, for example). The highest concentration of bitter receptors appears to be in the posterior tongue, where a gag reflex could still spit out poisonous food.

The taste known as umami is often referred to as the savory taste. Like sweet and bitter, it is based on the activation of G protein–coupled receptors by a specific molecule. The molecule that activates this receptor is the amino acid L-glutamate. Therefore, the umami flavor is often perceived while eating protein-rich foods. Not surprisingly, dishes that contain meat are often described as savory.

Once the gustatory cells are activated by the taste molecules, they release neurotransmitters onto the dendrites of sensory neurons. These neurons are part of the facial and glossopharyngeal cranial nerves, as well as a component within the vagus nerve dedicated to the gag reflex. The facial nerve connects to taste buds in the anterior third of the tongue. The glossopharyngeal

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nerve connects to taste buds in the posterior two-thirds of the tongue. The vagus nerve connects to taste buds in the extreme posterior of the tongue, verging on the pharynx, which are more sensitive to noxious stimuli such as bitterness.

Interactive Link 14.1

Watch this video (http://oer.aupress.ca/oer-202505/14.1) to learn about Dr. Danielle Reed of the Monell Chemical Senses Centre in Philadelphia, Pennsylvania, who became interested in science at an early age because of her sensory experiences. She recognized that her sense of taste was unique compared with other people she knew. Now she studies the genetic differences between people and their sensitivities to taste stimuli. In the video, there is a brief image of a person sticking out their tongue, which has been covered with a coloured dye. This is how Dr. Reed is able to visualize and count papillae on the surface of the tongue. People fall into two groups known as "tasters" and "nontasters" based on the density of papillae on their tongue, which also indicates the number of taste buds.

Nontasters can taste food, but they are not as sensitive to certain tastes, such as bitterness. Dr. Reed discovered that she is a nontaster, which explains why she perceived bitterness differently from other people she knew. Are you very sensitive to tastes? Can you see any similarities among the members of your family?

Olfaction (Smell)

Like taste, the sense of smell, or **olfaction**, is also responsive to chemical stimuli. The olfactory receptor neurons are located in a small region within the superior nasal cavity (Figure 14.3). This region is referred to as the **olfactory epithelium** and contains bipolar sensory neurons. Each **olfactory sensory neuron** has dendrites called **olfactory hairs** that extend from the apical surface of the epithelium into the mucus lining the cavity. As airborne molecules are inhaled through the nose, they pass over the olfactory epithelial region and dissolve into the mucus. These **odorant molecules** bind to proteins that keep them dissolved in the mucus and help transport them to the olfactory dendrites. The odorant-protein complex binds to a receptor protein within the cell membrane of an olfactory dendrite. These receptors are G protein–coupled and will produce a graded membrane potential in the olfactory neurons.

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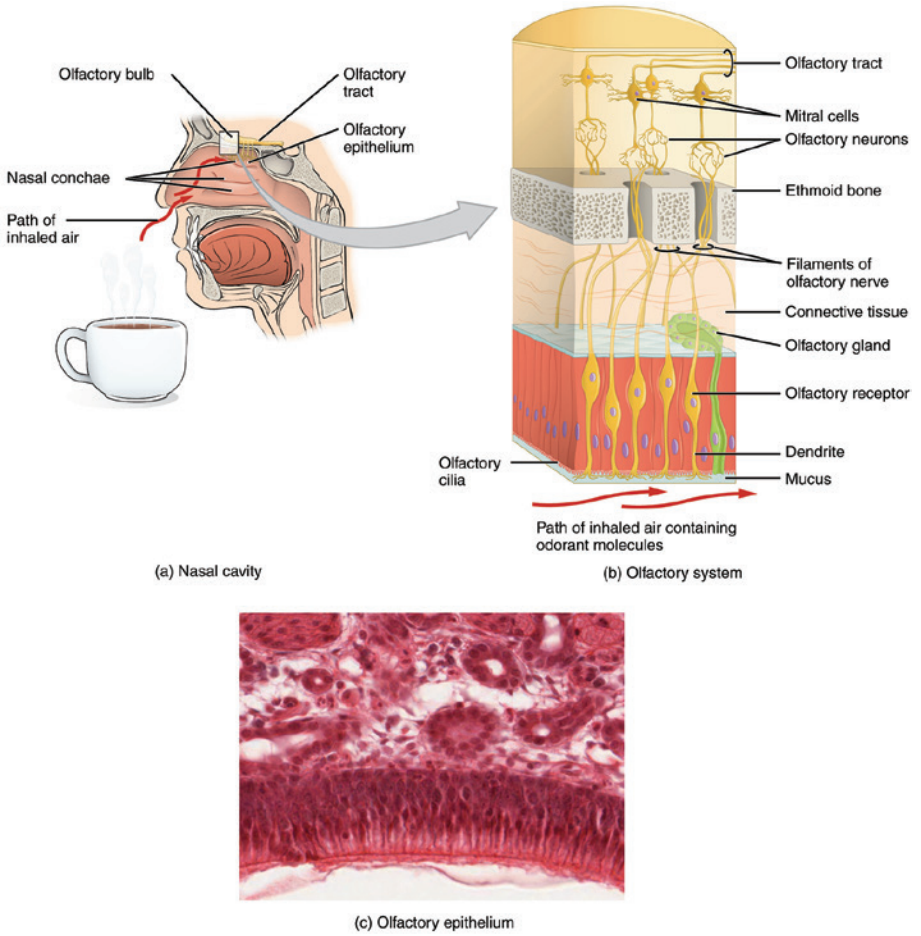


Figure 14.3 The Olfactory System. (a) The olfactory system begins in the peripheral structures of the nasal cavity. (b) The olfactory receptor neurons are within the olfactory epithelium. (c) Axons of the olfactory receptor neurons project through the cribriform plate of the ethmoid bone and synapse with the neurons of the olfactory bulb (tissue source: simian). LM × 812. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

The axon of an olfactory neuron extends from the basal surface of the epithelium, through an olfactory foramen in the cribriform plate of the ethmoid bone, and into the brain. The axons of the group called the **olfactory nerves** connect to the **olfactory bulb** on the ventral surface of the frontal lobe. From there, the axons form the **olfactory tract** and then split to travel to several brain regions. Some travel to the cerebrum, specifically to the primary **olfactory cortex** that is located in the inferior and medial areas of the temporal lobe. Others project to structures within the limbic system and hypothalamus, where smells become associated with long-term memory and emotional responses. This is how certain smells trigger emotional memories, such as the smell of

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food associated with one's birthplace. Smell is the one sensory modality that does not synapse in the thalamus before connecting to the cerebral cortex. This intimate connection between the olfactory system and the cerebral cortex is one reason why smell can be a potent trigger of memories and emotion.

The nasal epithelium, including the olfactory cells, can be harmed by airborne toxic chemicals. Therefore, the olfactory neurons are regularly replaced within the nasal epithelium, after which the axons of the new neurons must find their appropriate connections in the olfactory bulb. These new axons grow along the axons that are already in place in the cranial nerve.

Audition (Hearing)

Hearing, or **audition**, is the transduction of sound waves into a neural signal that is made possible by the structures of the ear (Figure 14.4). The large, fleshy structure on the lateral aspect of the head is known as the **auricle**. Some sources will also refer to this structure as the pinna, though that term is more appropriate for a structure that can be moved, such as the external ear of a cat. The C-shaped curves of the auricle direct sound waves toward the auditory canal. The canal enters the skull through the external auditory meatus of the temporal bone. At the end of the auditory canal is the **tympanic membrane**, or eardrum, which vibrates after it is struck by sound waves. The auricle, ear canal, and tympanic membrane are often referred to as the **external ear**. The **middle ear** consists of

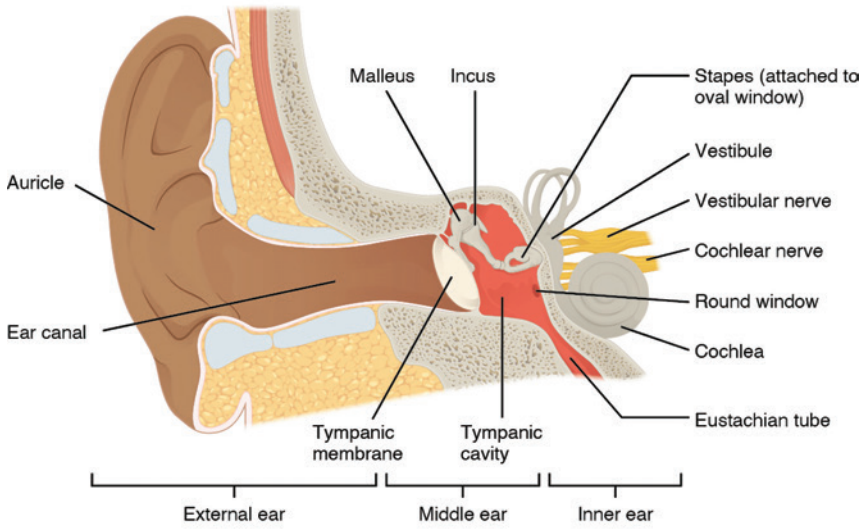


Figure 14.4 Structures of the Ear. The external ear contains the auricle, ear canal, and tympanic membrane. The middle ear contains the ossicles and is connected to the pharynx by the Eustachian tube. The inner ear contains the cochlea and vestibule, which are responsible for audition and equilibrium, respectively.

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a space spanned by three small bones called the **ossicles**. The three ossicles are the **malleus**, **incus**, and **stapes**, which are Latin names that roughly translate to hammer, anvil, and stirrup. The malleus is attached to the tympanic membrane and articulates with the incus. The incus, in turn, articulates with the stapes. The stapes is then attached to the **inner ear**, where the sound waves will be transduced into a neural signal. The middle ear is connected to the pharynx through the **Eustachian tube**, which helps equilibrate air pressure across the tympanic membrane. The tube is normally closed but will pop open when the muscles of the pharynx contract during swallowing or yawning.

The inner ear is often described as a bony labyrinth, as it is composed of a series of canals embedded within the temporal bone. It has two separate regions, the **cochlea** and the **vestibule**, which are responsible for hearing and balance, respectively. The neural signals from these two regions are relayed to the brain stem through separate fibre bundles. However, these two distinct bundles travel together from the inner ear to the brain stem as the vestibulocochlear nerve. Sound is transduced into neural signals within the cochlear region of the inner ear, which contains the sensory neurons of the **spiral ganglia**. These ganglia are located within the spiral-shaped cochlea of the inner ear. The cochlea is attached to the stapes through the **oval window**.

The oval window is located at the beginning of a fluid-filled tube within the cochlea called the **scala vestibuli**. The scala vestibuli extends from the oval window, travelling alongside the **cochlear duct**, which is the central cavity of the cochlea that contains the sound-transducing neurons. At the uppermost tip of the cochlea, the scala vestibuli curves alongside the cochlear duct. The fluid-filled tube, now called the **scala tympani**, returns to the base of the cochlea, this time travelling under the cochlear duct (Figure 14.5). The scala tympani ends at the **round window**, which is covered by a membrane that contains the fluid within the scala.

As vibrations of the ossicles travel through the oval window, the fluid of the scala vestibuli and scala tympani moves in a wavelike motion. The frequencies of the fluid waves match the frequencies of the sound waves. The membrane covering the round window will bulge out or pucker in with the movement of the fluid within the scala tympani.

A cross-sectional view of the cochlea shows that the scala vestibuli and scala tympani run along both sides of the cochlear duct (Figure 14.6 and Figure 14.7). The cochlear duct contains the **organ of Corti**, which transduces the wave motion of the two scalae into neural signals. The organ of Corti lies on top of the **basilar membrane**, which is the side of the cochlear duct located between the organ of Corti and the scala tympani. As the fluid waves move through the scala vestibuli and scala tympani, the basilar membrane moves at a specific spot, depending

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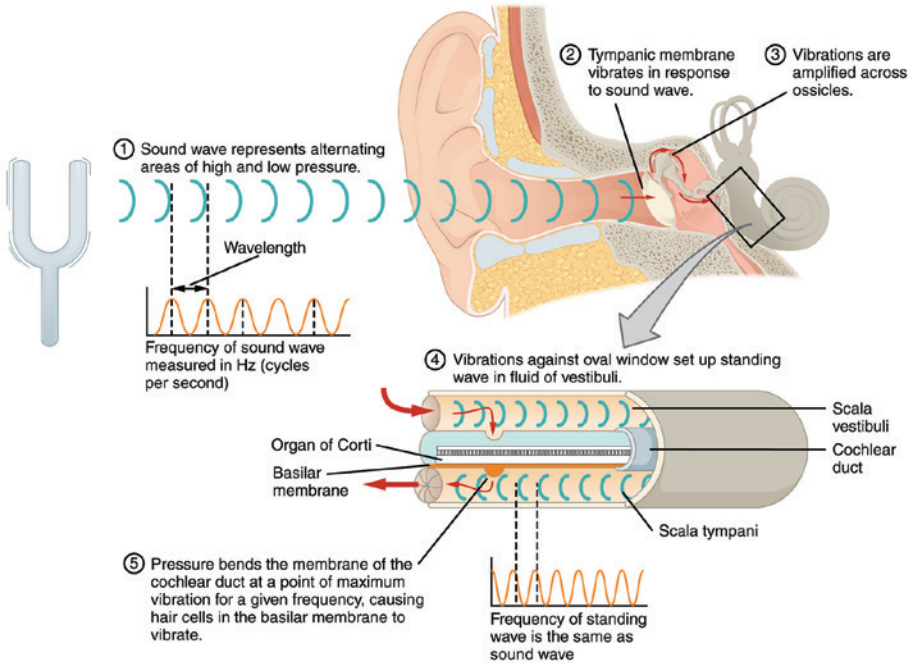


Figure 14.5 Transmission of Sound Waves to Cochlea. A sound wave causes the tympanic membrane to vibrate. This vibration is amplified as it moves across the malleus, incus, and stapes. The amplified vibration is picked up by the oval window, causing pressure waves in the fluid of the scala vestibuli and scala tympani. The complexity of the pressure waves is determined by the changes in amplitude and frequency of the sound waves entering the ear.

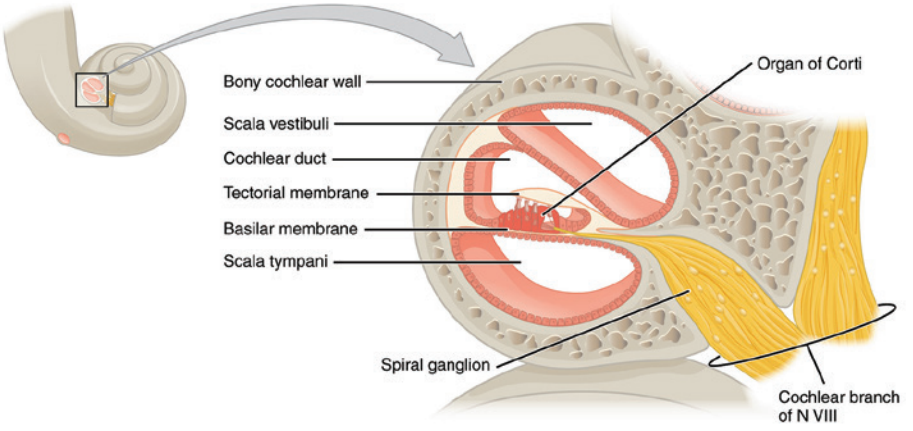


Figure 14.6 Cross Section of the Cochlea. The three major spaces within the cochlea are highlighted. The scala tympani and scala vestibuli lie on either side of the cochlear duct. The organ of Corti, containing the mechanoreceptor hair cells, is adjacent to the scala tympani, where it sits atop the basilar membrane.

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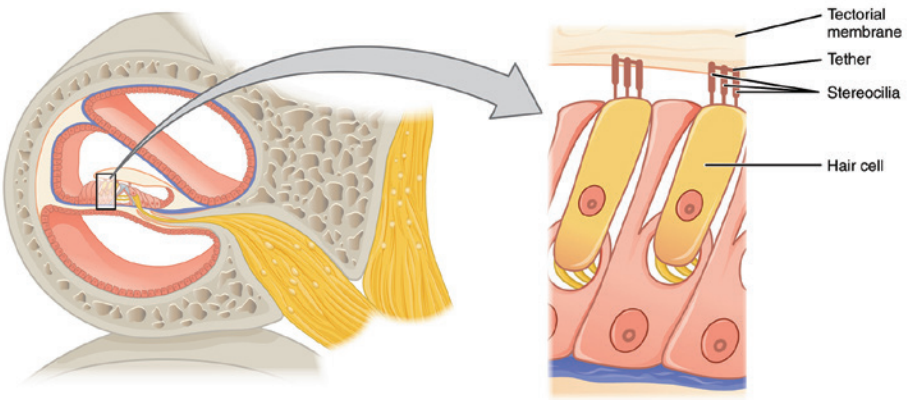


Figure 14.7 Hair Cell. The hair cell is a mechanoreceptor with an array of stereocilia emerging from its apical surface. The stereocilia are tethered together by proteins that open ion channels when the array is bent toward the tallest member of their array and close when the array is bent toward the shortest member of their array.

on the frequency of the waves. Higher frequency waves move the region of the basilar membrane that is close to the base of the cochlea.

Lower frequency waves move the region of the basilar membrane that is near the tip of the cochlea.

The organ of Corti contains **hair cells**, which are named for the hairlike **stereocilia** extending from the cell's apical surfaces (Figure 14.7). The stereocilia are an array of microvilli-like structures arranged from tallest to shortest.

Protein fibres tether adjacent stereocilia together within each array, such that the array will bend in response to movements of the basilar membrane.

The stereocilia extend up from the hair cells to the overlying **tectorial membrane**, which is attached medially to the organ of Corti. When the pressure waves from the scala move the basilar membrane, the stereocilia are bent against the overhanging tectorial membrane. This bends the stereocilia either toward or away from the tallest member of each array. When the stereocilia bend toward the tallest member of their array, tension in the protein tethers opens ion channels in the hair cell membrane. This will depolarize the hair cell membrane, triggering impulses that travel down the afferent cochlear branch of the vestibulocochlear nerve fibres attached to the hair cells. When the stereocilia bend toward the shortest member of their array, the tension on the tethers slackens and the ion channels close. When no sound is present, and the stereocilia are standing straight, a small amount of tension still exists on the tethers, keeping the membrane potential of the hair cell slightly depolarized (Figure 14.7).

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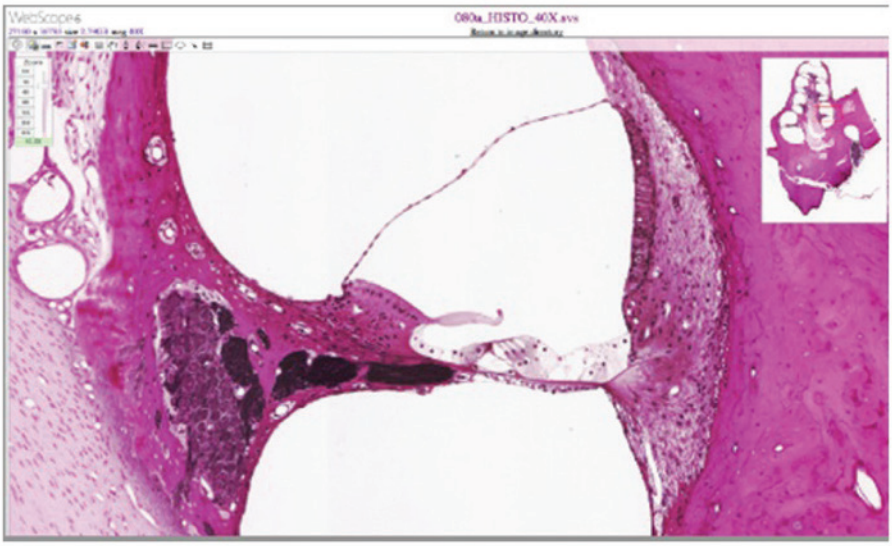


Figure 14.8 Cochlea and Organ of Corti. LM × 412. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Interactive Link 14.2

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/14.2) to explore the tissue sample in greater detail. The basilar membrane is the thin membrane that extends from the central core of the cochlea to the edge. What are anchored to this membrane so that they can be activated by the movement of the fluids within the cochlea?

As discussed, a given region of the basilar membrane will only move if the incoming sound is at a specific frequency. Because the tectorial membrane only moves where the basilar membrane moves, the hair cells in this region will also only respond to sounds of this specific frequency. Therefore, as the frequency of a sound changes, different hair cells are activated all along the basilar membrane. The cochlea encodes auditory stimuli for frequencies between 20 and 20,000 Hz, which is the range of sound that human ears can detect. The unit of Hertz measures the frequency of sound waves in terms of cycles produced per second. Frequencies as low as 20 Hz are detected by hair cells at the apex, or tip, of the cochlea. Frequencies in the higher ranges of 20 KHz are encoded by hair cells at the base of the cochlea, close to the round and oval windows (Figure 14.9). Most auditory stimuli contain a mixture of

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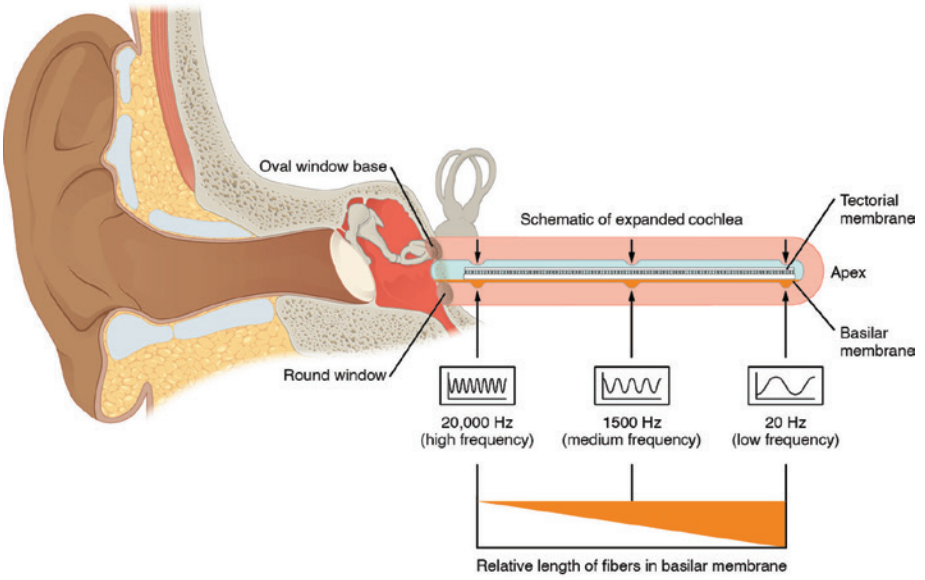


Figure 14.9 Frequency Coding in the Cochlea. The standing sound wave generated in the cochlea by the movement of the oval window deflects the basilar membrane on the basis of the frequency of sound. Therefore, hair cells at the base of the cochlea are activated only by high frequencies, whereas those at the apex of the cochlea are activated only by low frequencies.

sounds at a variety of frequencies and intensities (represented by the amplitude of the sound wave). The hair cells along the length of the cochlear duct, which are each sensitive to a particular frequency, allow the cochlea to separate auditory stimuli by frequency, just as a prism separates visible light into its component colours.

Interactive Link 14.3

Watch this video (http://oer.aupress.ca/oer-202505/14.3) to learn more about how the structures of the ear convert sound waves into a neural signal by moving the "hairs," or stereocilia, of the cochlear duct. Specific locations along the length of the duct encode specific frequencies, or pitches. The brain interprets the meaning of the sounds we hear as music, speech, noise, and so on. Which ear structures are responsible for the amplification and transfer of sound from the external ear to the inner ear?

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Interactive Link 14.4

Watch this animation (http://oer.aupress.ca/oer-202505/14.4) to learn more about the inner ear and to see the cochlea unroll, with the base at the back of the image and the apex at the front. Specific wavelengths of sound cause specific regions of the basilar membrane to vibrate, much like the keys of a piano produce sound at different frequencies. Based on the animation, where do frequencies—from high to low pitches—cause activity in the hair cells within the cochlear duct?

Equilibrium (Balance)

Along with audition, the inner ear is responsible for encoding information about **equilibrium**, the sense of balance. A similar mechanoreceptor—a hair cell with stereocilia—senses head position, head movement, and whether our bodies are in motion. These cells are located within the **vestibular apparatus** of the inner ear. Head position is sensed by the **utricle** and **saccule**, whereas rotational movements of the head are sensed by the **semicircular canals**. The neural signals generated in the **vestibular ganglion** are transmitted through the vestibular branch of the vestibulocochlear nerve to the brain stem and cerebellum.

The utricle and saccule are both largely composed of **macula** tissue (plural = maculae). The macula is composed of hair cells surrounded by support cells. The stereocilia of the hair cells extend into a viscous gel called the **otolithic membrane** (Figure 14.10). On top of the otolithic membrane is a layer of calcium carbonate crystals, called **otoliths**. The otoliths essentially make the otolithic membrane top-heavy. The otolithic membrane moves separately from the macula in response to head movements. Tilting the head causes the otolithic membrane to slide over the macula in the direction of gravity. The moving otolithic membrane, in turn, bends the stereocilia, causing some hair cells to depolarize as others hyperpolarize. The exact position of the head as well as linear acceleration and linear deceleration are interpreted by the brain based on the pattern of hair-cell depolarization.

The semicircular canals are three ringlike extensions of the vestibule. One is oriented in the horizontal plane, whereas the other two are oriented in the vertical plane. The anterior and posterior vertical canals are oriented at approximately 45 degrees relative to the sagittal plane (Figure 14.11). The base of each semicircular canal, where it meets with the vestibule, connects to an enlarged region known as the **ampulla**. The ampulla contains the hair cells that respond to rotational movement, such as turning the head while saying "no."

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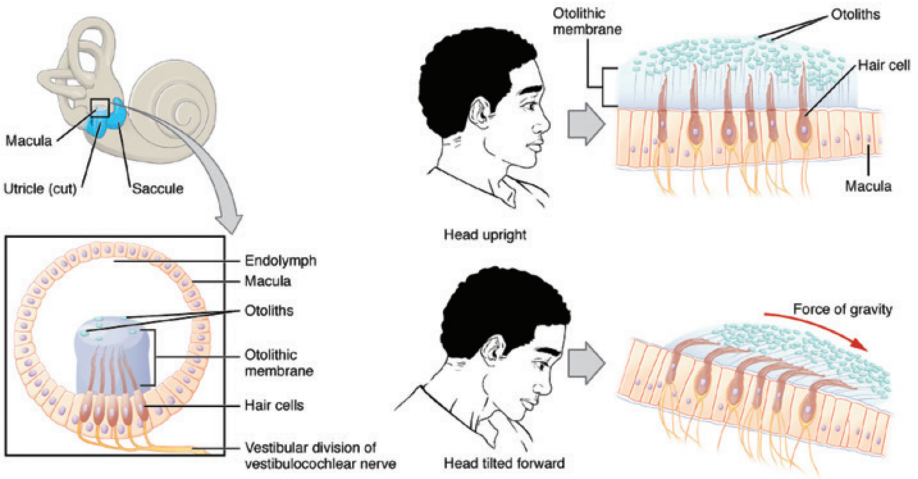


Figure 14.10 Linear Acceleration and Deceleration by Maculae. The maculae are specialized for sensing linear acceleration and deceleration, such as when gravity acts on the tilting head, or if the head starts moving in a straight line. The difference in inertia between the hair cell stereocilia and the otolithic membrane in which they are embedded leads to a shearing force that causes the stereocilia to bend in the direction of that linear acceleration or deceleration.

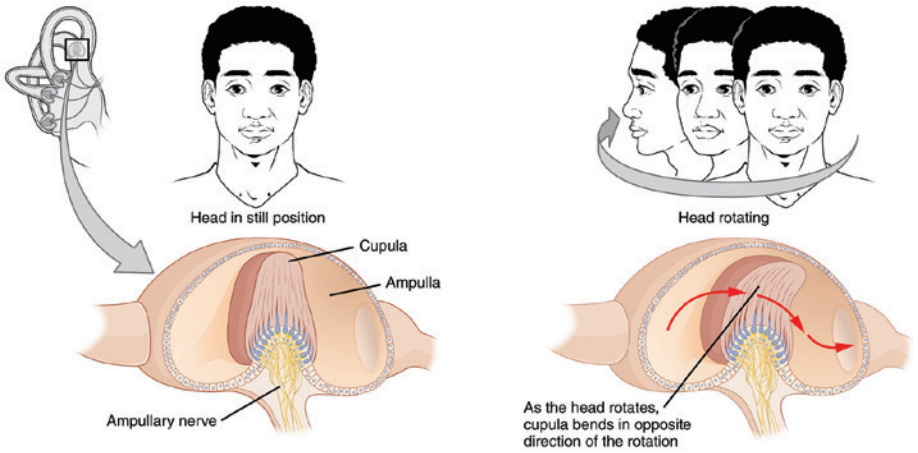


Figure 14.11 Rotational Coding by Semicircular Canals. Rotational movement of the head is encoded by the hair cells in the base of the semicircular canals. As one of the canals moves in an arc with the head, the internal fluid moves in the opposite direction, causing the cupula and stereocilia to bend. The movement of two canals within a plane results in information about the direction in which the head is moving, and activation of all six canals can give a very precise indication of head movement in three dimensions.

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The stereocilia of these hair cells extend into the **cupula**, a membrane that projects toward the top of the ampulla. As the head rotates in a plane parallel to the semicircular canal, the fluid lags, deflecting the cupula in the direction opposite to the head movement. The semicircular canals contain several ampullae, with some oriented horizontally and others oriented vertically. By comparing the relative movements of both the horizontal and vertical ampullae, the vestibular system can detect the direction of most head movements within three-dimensional (3-D) space.

Somatosensation (Touch)

Somatosensation is considered a general sense, as opposed to the special senses discussed in this section. Somatosensation is the group of sensory modalities that are associated with touch, proprioception, and interoception. These modalities include pressure, vibration, light touch, tickle, itch, temperature, pain, proprioception, and kinesthesia. This means that its receptors are not associated with a specialized organ but are instead spread throughout the body in a variety of organs. Many of the somatosensory receptors are located in the skin, but receptors are also found in muscles, tendons, joint capsules, ligaments, and in the walls of visceral organs.

Two types of somatosensory signals that are transduced by **free nerve endings** are pain and temperature. These two modalities use thermoreceptors and nociceptors to transduce temperature and pain stimuli, respectively.

Temperature receptors are stimulated when local temperatures differ from body temperature. Some thermoreceptors are sensitive to just cold and others to just heat. Nociception is the sensation of potentially damaging stimuli. Mechanical, chemical, or thermal stimuli beyond a set threshold will elicit painful sensations. Stressed or damaged tissues release chemicals that activate receptor proteins in the nociceptors.

For example, the sensation of heat associated with spicy foods involves capsaicin (a molecule that activates nociceptors by interacting with a temperature-sensitive ion channel and is the basis for “hot” sensations in spicy food), the active molecule in hot peppers. Capsaicin molecules bind to a transmembrane ion channel in nociceptors that is sensitive to temperatures above 37°C. The dynamics of capsaicin binding with this transmembrane ion channel are unusual in that the molecule remains bound for a long time. Because of this, it will decrease the ability of other stimuli to elicit pain sensations through the activated nociceptor. For this reason, capsaicin can be used as a topical analgesic, such as in products such as Icy Hot.

If you drag your finger across a textured surface, the skin of your finger will vibrate. Such low-frequency vibrations are sensed by **mechanoreceptors**

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called Merkel cells, also known as type I cutaneous mechanoreceptors. Merkel cells are located in the stratum basale of the epidermis. Deep pressure and vibration are transduced by **lamellated** (**Pacinian**) **corpuscles**, which are receptors with encapsulated endings found deep in the dermis, or subcutaneous tissue. Light touch is transduced by the **encapsulated corpuscle endings** known as tactile (Meissner) corpuscles. Follicles are also wrapped in a plexus of nerve endings known as the **hair follicle plexus**. These nerve endings detect the movement of hair at the surface of the skin, such as when an insect may be walking along the skin. Stretching of the skin is transduced by stretch receptors known as bulbous corpuscles. **Bulbous corpuscles** are also known as Ruffini corpuscles, or type II cutaneous mechanoreceptors.

Other somatosensory receptors are found in the joints and muscles. **Stretch receptors** monitor the stretching of tendons, muscles, and the components of joints. For example, have you ever stretched your muscles before or after exercise and noticed that you can only stretch so far before your muscles spasm back to a less stretched state? This spasm is a reflex that is initiated by stretch receptors to avoid muscle tearing. Such stretch receptors can also prevent overcontraction of a muscle. In skeletal muscle tissue, these stretch receptors are called **muscle spindles**. Golgi tendon organs similarly transduce the stretch levels of tendons called **tendon stretch organs**. Bulbous corpuscles are also present in joint capsules, where they measure stretch in the components of the skeletal system within the joint. The types of nerve endings, their locations, and the stimuli they transduce are presented in Table 14.1.

Vision

Vision is the special sense of sight that is based on the transduction of light stimuli received through the eyes. The eyes are located within either orbit in the skull. The bony orbits surround the eyeballs, protecting them and anchoring the soft tissues of the eye. **Lacrimal glands** are lateral to the orbit that produces tears to wash across the surface of the eye (Figure 14.12).

The eye itself is a hollow sphere composed of three layers of tissue. The outermost layer is the **fibrous tunic**, which includes the white **sclera** and clear **cornea**. The sclera accounts for five-sixths of the surface of the eye, most of which is not visible, though humans are unique compared with many other species in having so much of the "white of the eye" visible (Figure 14.13). The transparent cornea covers the anterior area of the eye and allows light to enter the eye. The middle layer of the eye is the **vascular tunic**, which is mostly composed of the choroid, ciliary body, and iris. The **choroid** is a layer of highly vascularized connective tissue that provides a blood supply to the eyeball. The choroid is posterior to the **ciliary body**, a muscular structure

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Table 14.1 Mechanoreceptors of Somatosensation

Name	Historical (eponymous) name	Location(s)	Stimuli
Free nerve endings	*	Dermis, cornea, tongue, joint capsules, visceral organs	Pain, temperature, mechanical deformation
Mechanoreceptors	Merkel's discs	Epidermal-dermal junction, mucosal membranes	Low frequency vibration (5–15 Hz)
Bulbous corpuscle	Ruffini's corpuscle	Dermis, joint capsules	Stretch
Encapsulated corpuscle	Meissner's corpuscle	Papillary dermis, especially in the fingertips and lips	Light touch, vibrations below 50 Hz
Lamellated corpuscle	Pacinian corpuscle	Deep dermis, subcutaneous tissue	Deep pressure, high-frequency vibration (around 250 Hz)
Hair follicle plexus	*	Wrapped around hair follicles in the dermis	Movement of hair
Muscle spindle	*	In line with skeletal muscle fibres	Muscle contraction and stretch
Tendon stretch organ	Golgi tendon organ	In line with tendons	Stretch of tendons

* No corresponding eponymous name.

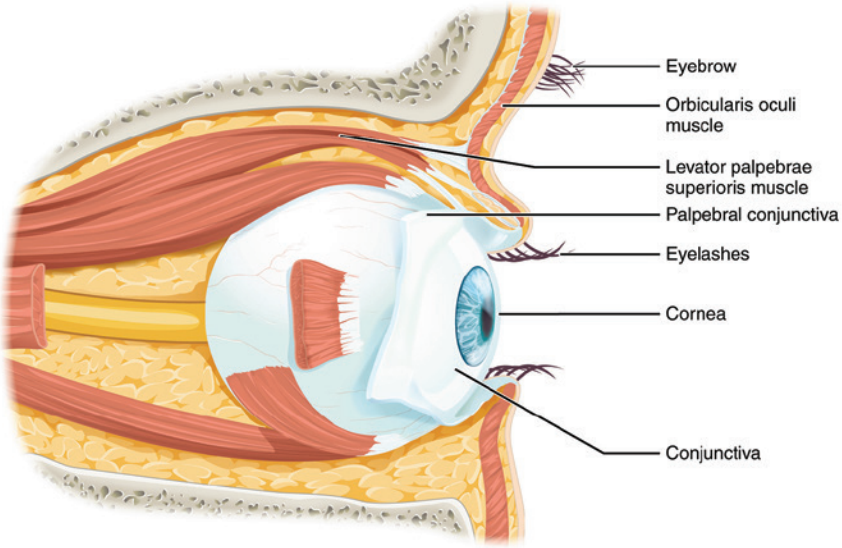


Figure 14.12 The Eye in the Orbit. The eye is located within the orbit and surrounded by soft tissues that protect and support its function. The orbit is surrounded by the cranial bones of the skull.

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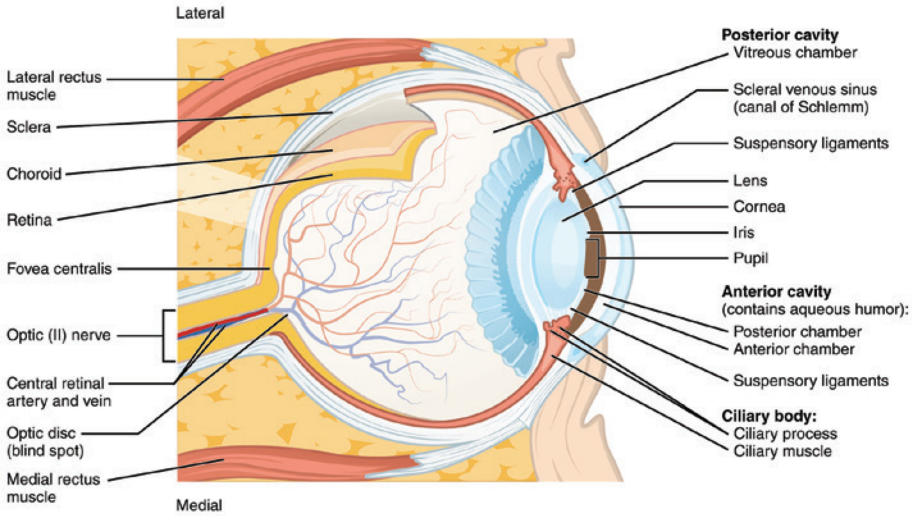


Figure 14.13 Structure of the Eye. The sphere of the eye can be divided into anterior and posterior cavities. The wall of the eye is composed of three layers: the fibrous tunic, vascular tunic, and neural tunic. Within the neural tunic is the retina, with three layers of cells and two synaptic layers in between. The centre of the retina has a small indentation known as the fovea.

that is attached to the **lens** by suspensory ligaments, or **zonule fibres**. These two structures adjust the shape of the lens, allowing it to focus light on the back of the eye. Overlaying the ciliary body, and visible in the anterior eye, is the **iris**—the coloured part of the eye. The iris is a smooth muscle that opens or closes the **pupil**, which is the hole at the centre of the iris that allows light to enter. The iris constricts the pupil in response to bright light and dilates the pupil in response to dim light. The innermost layer of the eye is the **neural tunic**, or **retina**, which contains the nervous tissue responsible for photoreception.

The eye is also divided into two cavities: the anterior cavity and the posterior cavity. The anterior cavity is the space between the cornea and lens, including the iris and ciliary body. It is filled with a watery fluid called the **aqueous humour**. The posterior cavity is the space behind the lens that extends to the posterior side of the interior eyeball, where the retina is located. The posterior cavity is filled with a more viscous fluid called the **vitreous humour**.

The retina is composed of several layers and contains specialized cells for the initial processing of visual stimuli. The photoreceptors (rods and cones) change their membrane potential when stimulated by light energy. The change in membrane potential alters the amount of neurotransmitter that the photoreceptor cells release onto **bipolar cells** in the outer synaptic layer. It is the bipolar cell in the retina that connects a photoreceptor to a **retinal ganglion cell** (**RGC**) in the inner synaptic layer. There, **amacrine cells** additionally contribute

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to retinal processing before an action potential is produced by the RGC. The axons of RGCs, which lie at the innermost layer of the retina, collect at the **optic disc** and leave the eye as the **optic nerve** (see Figure 14.13). Because these axons pass through the retina, there are no photoreceptors at the very back of the eye, where the optic nerve begins. This creates a "blind spot" in the retina, and a corresponding blind spot in our visual field.

Note that the photoreceptors in the retina, **rods** and **cones**, are located behind the axons, RGCs, bipolar cells, and retinal blood vessels. A significant amount of light is absorbed by these structures before the light reaches the photoreceptor cells. However, at the exact centre of the retina is a small area known as the **fovea**. At the fovea, the retina lacks the supporting cells and blood vessels and only contains photoreceptors. Therefore, **visual acuity**, or the sharpness of vision, is greatest at the fovea. This is because the fovea is where the least amount of incoming light is absorbed by other retinal structures (see Figure 14.13). As one moves in every direction from this central point of the retina, visual acuity drops significantly. In addition, each photoreceptor cell of the fovea is connected to a single RGC. Therefore, this RGC does not have to integrate inputs from multiple photoreceptors, which reduces the accuracy of visual transduction. Toward the edges of the retina, several photoreceptors converge on RGCs (through the bipolar cells) up to a ratio of 50 to 1. The difference in visual acuity between the fovea and peripheral retina is easily evidenced by looking directly at a word in the middle of this paragraph. The visual stimulus in the middle of the field of view falls on the fovea and is in the sharpest focus. Without moving your eyes off that word, notice that words at the beginning or end of the paragraph are not in focus. The images in your peripheral vision are focused onto the peripheral retina and have vague, blurry edges and words that are not as clearly identified. As a result, a large part of the neural function of the eyes is concerned with moving the eyes and head so that important visual stimuli are centred on the fovea.

Light falling on the retina causes chemical changes to pigment molecules in the photoreceptors, ultimately leading to a change in the activity of the RGCs. Photoreceptor cells have two parts, the inner segment and the outer segment (Figure 14.14). The **inner segment** contains the nucleus and other common organelles of a cell, whereas the **outer segment** is a specialized region in which photoreception takes place. There are two types of photoreceptors—rods and cones—which differ in the shape of their outer segment. The rod-shaped outer segments of the **rod photoreceptors** (**rods**) contain a stack of membrane-bound discs that contain the photosensitive pigment **rhodopsin**. The cone-shaped outer segments of the **cone photoreceptors** (**cones**) contain their photosensitive pigments in infoldings of the cell membrane. There are three cone photopigments, called **opsins**, which are each sensitive to a particular wavelength of light. The

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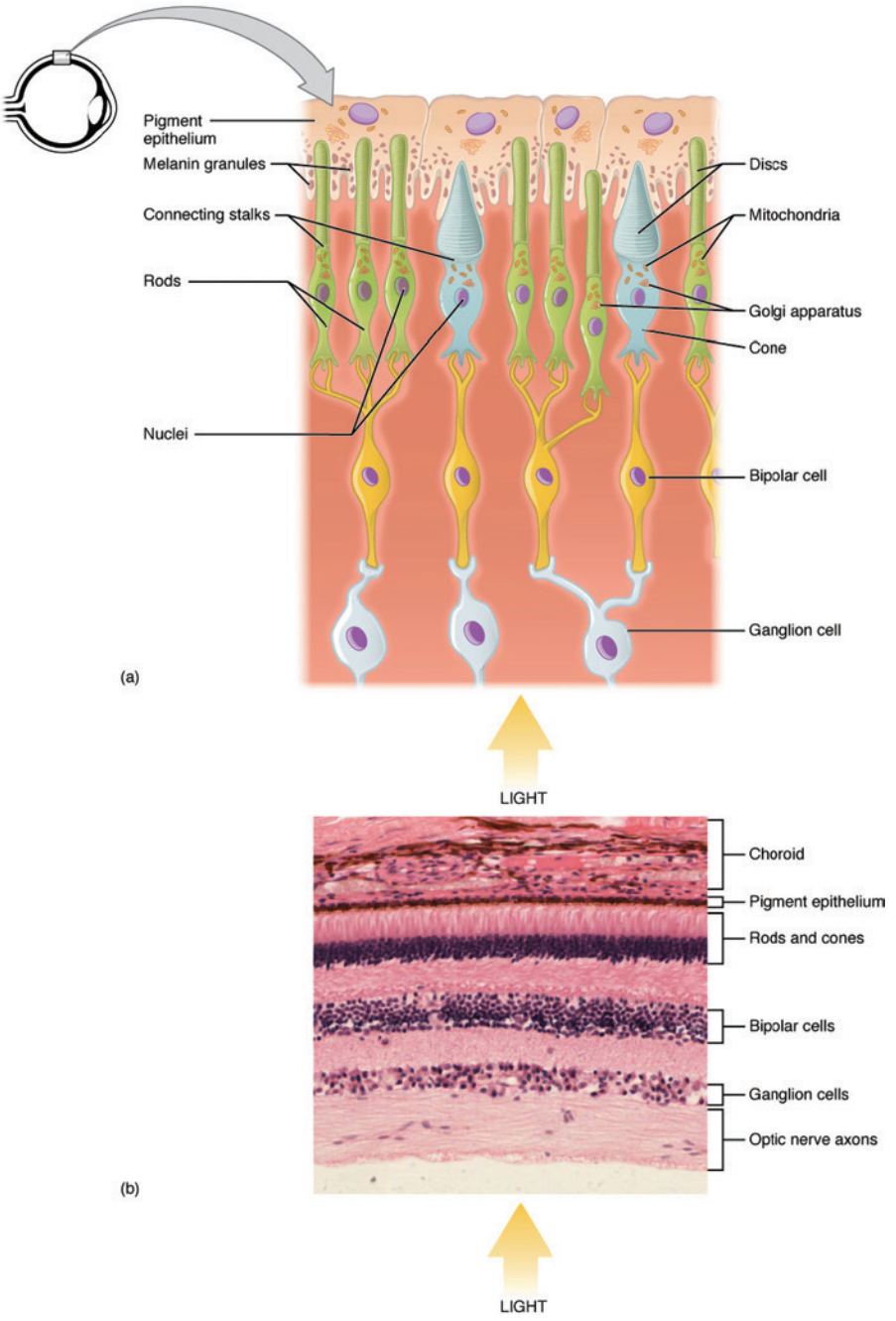


Figure 14.14 Photoreceptor. (a) All photoreceptors have inner segments containing the nucleus and other important organelles and outer segments with membrane arrays containing the photosensitive opsin molecules. Rod outer segments are long columnar shapes with stacks of membrane-bound discs that contain the rhodopsin pigment. Cone outer segments are short, tapered shapes with folds of membrane in place of the discs in the rods. (b) The tissue of the retina shows a dense layer of nuclei of the rods and cones. LM × 800. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

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wavelength of visible light determines its colour. The pigments in human eyes are specialized in perceiving three different primary colours: red, green, and blue.

At the molecular level, visual stimuli cause changes in the photopigment molecule that lead to changes in the membrane potential of the photoreceptor cell.

Interactive Link 14.5

Watch this video (http://oer.aupress.ca/oer-202505/14.5) to learn more about a transverse section through the brain that depicts the visual pathway from the eye to the occipital cortex. The first half of the pathway is the projection from the RGCs through the optic nerve to the lateral geniculate nucleus in the thalamus on either side. This first fibre in the pathway synapses on a thalamic cell that then projects to the visual cortex in the occipital lobe, where "seeing," or visual perception, takes place. This video gives an abbreviated overview of the visual system by concentrating on the pathway from the eyes to the occipital lobe. The video makes the statement (at 0:45) that "specialized cells in the retina called ganglion cells convert the light rays into electrical signals." What aspect of retinal processing is simplified by that statement? Explain your answer.

Sensory Nerves

Once any sensory cell transduces a stimulus into a nerve impulse, that impulse has to travel along axons to reach the CNS. In many of the special senses, the axons leaving the sensory receptors have a **topographical** arrangement, meaning that the location of the sensory receptor relates to the location of the axon in the nerve. For example, in the retina, axons from RGCs in the fovea are located at the centre of the optic nerve, where they are surrounded by axons from the more peripheral RGCs.

Spinal Nerves

Generally, spinal nerves contain afferent axons from sensory receptors in the periphery, such as from the skin, mixed with efferent axons travelling to the muscles or other effector organs. As the spinal nerve nears the spinal cord, it splits into dorsal and ventral roots. The dorsal root contains only the axons of sensory neurons, whereas the ventral roots contain only the axons of the motor neurons. Some of the branches will synapse with local neurons in the dorsal root ganglion, posterior (dorsal) horn, or even the anterior (ventral) horn, at the level of the spinal cord where they enter. Other branches will travel a short distance

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up or down the spine to interact with neurons at other levels of the spinal cord. A branch may also turn into the posterior (dorsal) column of the white matter to connect with the brain. For the sake of convenience, we will use the terms *ventral* and *dorsal* in reference to structures within the spinal cord that are part of these pathways. This will help underscore the relationships between the different components. Typically, spinal nerve systems that connect to the brain are **contralateral**, in that the right side of the body is connected to the left side of the brain and the left side of the body to the right side of the brain.

Cranial Nerves

Cranial nerves convey specific sensory information from the head and neck directly to the brain. Whereas spinal information is contralateral, cranial nerve systems, with some exceptions, are mostly **ipsilateral**, meaning that a cranial nerve on the right side of the head is connected to the right side of the brain. Some cranial nerves contain only sensory axons, such as the olfactory, optic, and vestibulocochlear nerves. Other cranial nerves contain both sensory and motor axons, including the trigeminal, facial, glossopharyngeal, and vagus nerves (however, the vagus nerve is not associated with the somatic nervous system). The general senses of somatosensation for the face travel through the trigeminal system.

14.2 Central Processing

Learning Objectives

By the end of this section, you will be able to:

- Describe the pathways that sensory systems follow into the central nervous system
- Differentiate between the two major ascending pathways in the spinal cord
- Describe the pathway of somatosensory input from the face and compare it to the ascending pathways in the spinal cord
- Explain topographical representations of sensory information in at least two systems
- Describe two pathways of visual processing and the functions associated with each

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Sensory Pathways

Specific regions of the CNS coordinate different somatic processes using sensory inputs and motor outputs of peripheral nerves. A simple case is a reflex caused by a synapse between a dorsal sensory neuron axon and a motor neuron in the ventral horn. More complex arrangements are possible to integrate peripheral sensory information with higher processes. The important regions of the CNS that play a role in somatic processes can be separated into the spinal cord, brain stem, diencephalon, cerebral cortex, and subcortical structures.

Spinal Cord and Brain Stem

A sensory pathway that carries peripheral sensations to the brain is referred to as an **ascending pathway**, or ascending tract. The various sensory modalities each follow specific pathways through the CNS. Tactile and other somatosensory stimuli activate receptors in the skin, muscles, tendons, and joints throughout the entire body.

However, the somatosensory pathways are divided into two separate systems on the basis of the location of the receptor neurons. Somatosensory stimuli from below the neck pass along the sensory pathways of the spinal cord, whereas somatosensory stimuli from the head and neck travel through the cranial nerves—specifically, the trigeminal system.

The **dorsal column system** (sometimes referred to as the dorsal column–medial lemniscus) and the **spinothalamic tract** are two major pathways that bring sensory information to the brain (Figure 14.15). The sensory pathways in each of these systems are composed of three successive neurons.

The dorsal column system begins with the axon of a dorsal root ganglion neuron entering the dorsal root and joining the dorsal column white matter in the spinal cord. As axons of this pathway enter the dorsal column, they take on a positional arrangement so that axons from lower levels of the body position themselves medially, whereas axons from upper levels of the body position themselves laterally. The dorsal column is separated into two component tracts that contain axons from the legs and lower body, and axons from the upper body and arms.

The spinothalamic tract also begins with neurons in a dorsal root ganglion. These neurons extend their axons to the dorsal horn, where they synapse with the second neuron in their respective pathway. The name "spinothalamic" comes from this second neuron, which has its cell body in the spinal cord grey matter and connects to the thalamus. Axons from these second neurons then decussate (i.e., cross over to the opposite side) within the spinal cord and ascend to the brain and enter the thalamus, where each synapses with the third neuron in its respective pathway. The neurons in the thalamus then project their axons to the spinothalamic tract, which synapses in the postcentral gyrus of the cerebral cortex.

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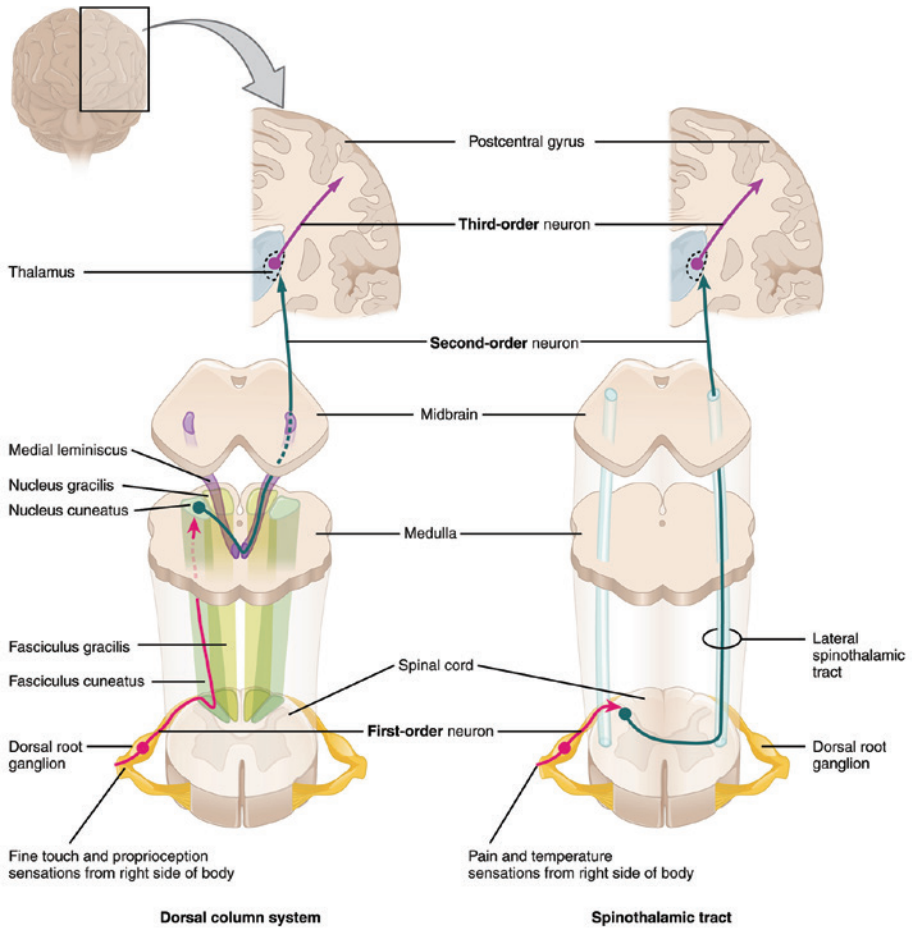


Figure 14.15 Anterior View of Ascending Sensory Pathways of the Spinal Cord. The dorsal column system and spinothalamic tract are the major ascending pathways that connect the periphery with the brain.

These two systems are similar in that they both begin with dorsal root ganglion cells, as with most general sensory information. The dorsal column system is primarily responsible for touch sensations and proprioception, whereas the spinothalamic tract pathway is primarily responsible for pain and temperature sensations. Another similarity is that the second neurons in both of these pathways are contralateral, because they project across the midline to the other side of the brain or spinal cord. In the dorsal column system, this decussation takes place in the brain stem; in the spinothalamic pathway, it takes place in the spinal cord at the same spinal cord level at which the information entered. The third neurons in the two pathways are essentially the same. In both, the second neuron synapses in the thalamus, and the thalamic neuron projects to the somatosensory cortex.

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The trigeminal pathway carries somatosensory information from the face, head, mouth, and nasal cavity. As with the previously discussed tracts, the sensory pathways of the trigeminal pathway each involve three successive neurons. First, axons from the trigeminal ganglion enter the brain stem at the level of the pons. The sensory pathway for gustation travels along the facial and glossopharyngeal cranial nerves, which synapse with neurons of the **solitary nucleus** in the brain stem.

The sensory pathway for audition travels along the vestibulocochlear nerve, which synapses with neurons in the cochlear nuclei of the superior medulla. Within the brain stem, input from either ear is combined to extract location information from the auditory stimuli. Whereas the initial auditory stimuli received at the cochlea strictly represent the frequency—or pitch—of the stimuli, the locations of sounds can be determined by comparing information arriving at both ears. Sound localization is a feature of central processing in the auditory nuclei of the brain stem.

Balance is coordinated through the vestibular system, the nerves of which are composed of axons from the vestibular ganglion that carries information from the utricle, saccule, and semicircular canals. The system contributes to controlling head and neck movements in response to vestibular signals. An important function of the vestibular system is coordinating eye and head movements to maintain visual attention. Most of the axons terminate in the **vestibular nuclei** of the medulla. Some axons project from the vestibular ganglion directly to the cerebellum, with no intervening synapse in the vestibular nuclei. The cerebellum is primarily responsible for initiating movements on the basis of equilibrium information (Figure 14.16).

To assist the visual system, fibres of the vestibular nuclei project to the oculomotor, trochlear, and abducens nuclei to influence signals sent along the cranial nerves. These connections constitute the pathway of the **vestibulo-ocular reflex** (**VOR**), which compensates for head and body movement by stabilizing images on the retina (Figure 14.16). Finally, the vestibular nuclei project to the thalamus to join the proprioceptive pathway of the dorsal column system, allowing conscious perception of equilibrium.

The connections of the optic nerve are more complicated than those of other cranial nerves. Instead of the connections being between each eye and the brain, visual information is segregated between the left and right sides of the visual field. In addition, some of the information from one side of the visual field projects to the opposite side of the brain. Within each eye, the axons projecting from the medial side of the retina decussate at the **optic chiasm**. For example, the axons from the medial retina of the left eye cross over to the right side of the brain at the optic chiasm. However, within each eye, the axons projecting from

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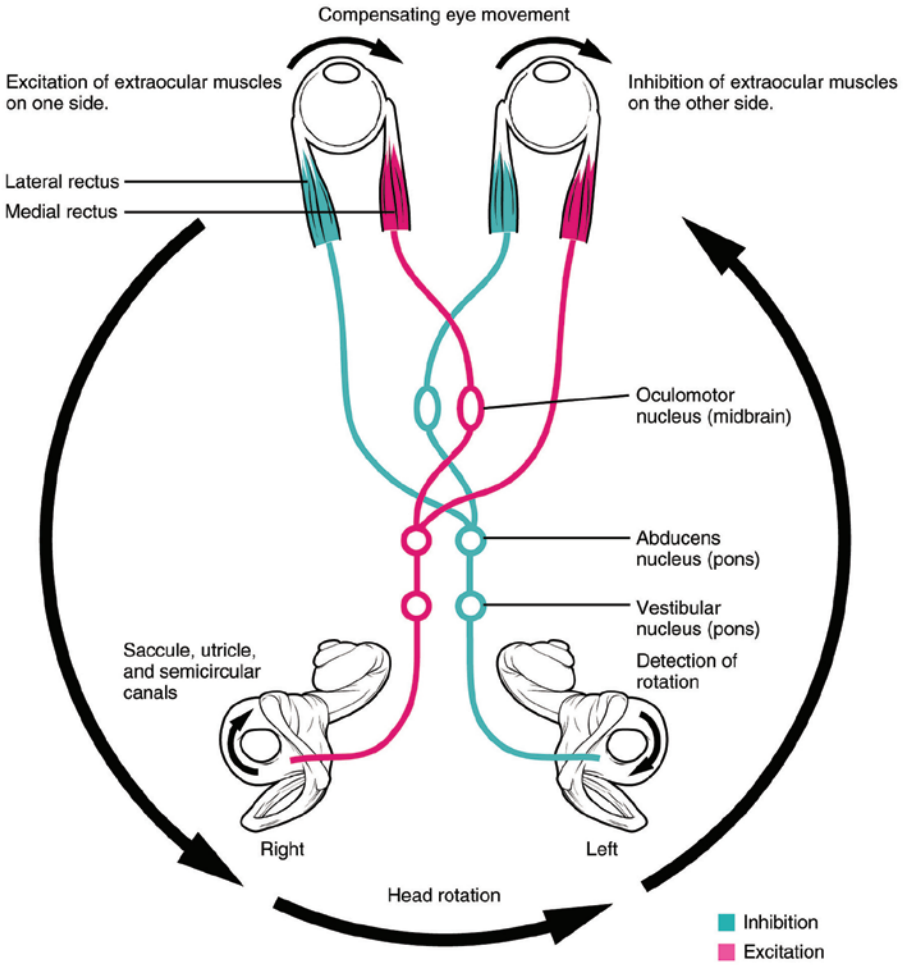


Figure 14.16 Vestibulo-Ocular Reflex. Connections between the vestibular system and the cranial nerves controlling eye movement keep the eyes centred on a visual stimulus, even though the head is moving. During head movement, the eye muscles move the eyes in the opposite direction to the head movement, keeping the visual stimulus centred in the field of view.

the lateral side of the retina do not decussate. For example, the axons from the lateral retina of the right eye project back to the right side of the brain.

Therefore, the left field of view of each eye is processed on the right side of the brain, whereas the right field of view of each eye is processed on the left side of the brain (Figure 14.17).

Unlike the photoreceptors, however, these photosensitive RGCs cannot be used to perceive images. By simply responding to the absence or presence of light, these RGCs can send information about day length. The perceived proportion of sunlight to darkness establishes the **circadian rhythm** of our bodies, allowing certain physiological events to occur at approximately the same time every day.

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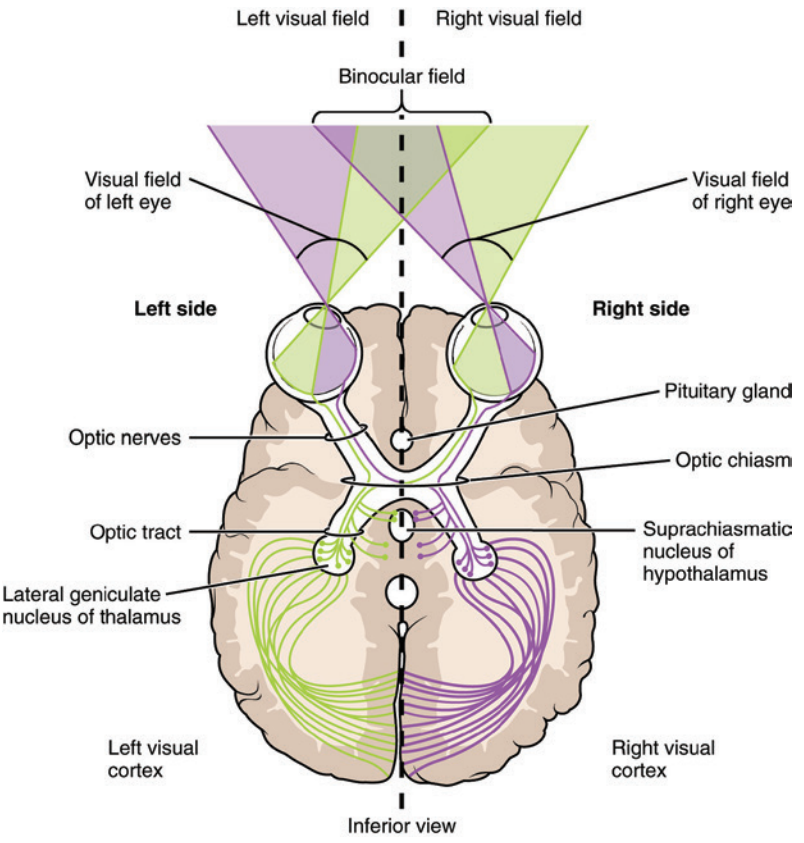


Figure 14.17 Segregation of Visual Field Information at the Optic Chiasm. Contralateral visual field information from the lateral retina projects to the ipsilateral brain, whereas ipsilateral visual field information has to decussate at the optic chiasm to reach the opposite side of the brain. (Note that this is an inferior view.)

Diencephalon

The diencephalon is beneath the cerebrum and includes the thalamus and hypothalamus. In the somatic nervous system, the thalamus is an important relay for communication between the cerebrum and the rest of the nervous system. The hypothalamus has both somatic and autonomic functions. In addition, the hypothalamus communicates with the limbic system, which controls emotions and memory functions.

Sensory input to the thalamus comes from most of the special senses and ascending somatosensory tracts. Each sensory system is relayed through a particular nucleus in the thalamus. The thalamus is a required transfer point for most sensory tracts that reach the cerebral cortex, where conscious sensory perception begins. The one exception to this rule is the olfactory system. The

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olfactory tract axons from the olfactory bulb project directly to the cerebral cortex, along with the limbic system and hypothalamus.

The thalamus is a collection of several nuclei that can be categorized into three anatomical groups. White matter running through the thalamus defines the three major regions of the thalamus, which are an anterior nucleus, a medial nucleus, and a lateral group of nuclei. The anterior nucleus serves as a relay between the hypothalamus and the emotion and memory-producing limbic system. The medial nuclei serve as a relay for information from the limbic system and basal ganglia to the cerebral cortex. This allows memory creation during learning but also determines alertness. The special and somatic senses connect to the lateral nuclei, where their information is relayed to the appropriate sensory cortex of the cerebrum.

Cortical Processing

As described earlier, many of the sensory axons are positioned in the same way as their corresponding receptor cells in the body. This allows identification of the position of a stimulus on the basis of which receptor cells are sending information. The cerebral cortex also maintains this sensory topography in the particular areas of the cortex that correspond to the position of the receptor cells. The somatosensory cortex provides an example in which, in essence, the locations of the somatosensory receptors in the body are mapped onto the somatosensory cortex, which is located in the postcentral gyrus. This mapping is often depicted using a **sensory homunculus** (Figure 14.18).

The term *homunculus* refers to a map of the human body that is laid across a portion of the cerebral cortex. In the somatosensory cortex, the external genitals, feet, and lower legs are represented on the medial face of the gyrus within the longitudinal fissure. As the gyrus curves out of the fissure and along the surface of the parietal lobe, the body map continues through the thighs, hips, trunk, shoulders, arms, and hands. The head and face are just lateral to the fingers as the gyrus approaches the lateral sulcus.

The cortex has been described as having specific regions that are responsible for processing specific information; there is the visual cortex, somatosensory cortex, gustatory cortex, and so on. However, our experience of these senses is not divided. Instead, we experience what can be referred to as a seamless percept. Our perceptions of the various sensory modalities—though distinct in their content—are integrated by the brain so that we experience the world as a continuous whole.

In the cerebral cortex, sensory processing begins at the **primary sensory cortex**, then proceeds to an **association area**, and finally moves into a

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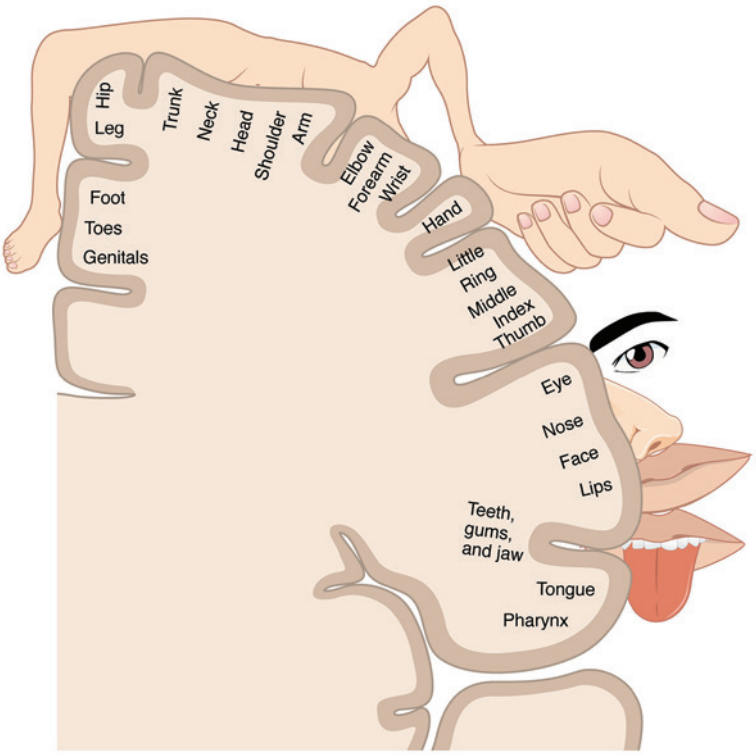


Figure 14.18 The Sensory Homunculus. A cartoon representation of the sensory homunculus is arranged adjacent to the cortical region in which the processing takes place.

multimodal integration area. For example, the visual pathway projects from the retinae through the thalamus to the primary visual cortex in the occipital lobe. This area is primarily in the medial wall within the longitudinal fissure. Here, visual stimuli begin to be recognized as basic shapes. Edges of objects are recognized and built into more complex shapes. Also, inputs from both eyes are compared to extract depth information.

Because of the overlapping field of view between the two eyes, the brain can begin to estimate the distance of stimuli based on **binocular vision**.

Interactive Link 14.6

Watch this video (http://oer.aupress.ca/oer-202505/14.6) to learn more about how the brain perceives 3-D motion. Similar to how retinal disparity offers 3-D moviegoers a way to extract 3-D information from the two-dimensional visual field projected onto the retina, the brain can extract information about movement in space by comparing what

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the two eyes see. If the movement of a visual stimulus is leftward in one eye and rightward in the opposite eye, the brain interprets this as movement toward (or away) from the face along the midline. If both eyes see an object moving in the same direction, but at different rates, what would that mean for spatial movement?

There are two main regions that surround the primary cortex that are usually referred to as areas V2 and V3 (the primary visual cortex is area V1). These surrounding areas are the visual association cortex. The visual association regions develop more complex visual perceptions by adding colour and motion information. The information processed in these areas is then sent to regions of the temporal and parietal lobes. Visual processing has two separate streams of processing: one into the temporal lobe and one into the parietal lobe. These are the ventral and dorsal streams, respectively (Figure 14.19).

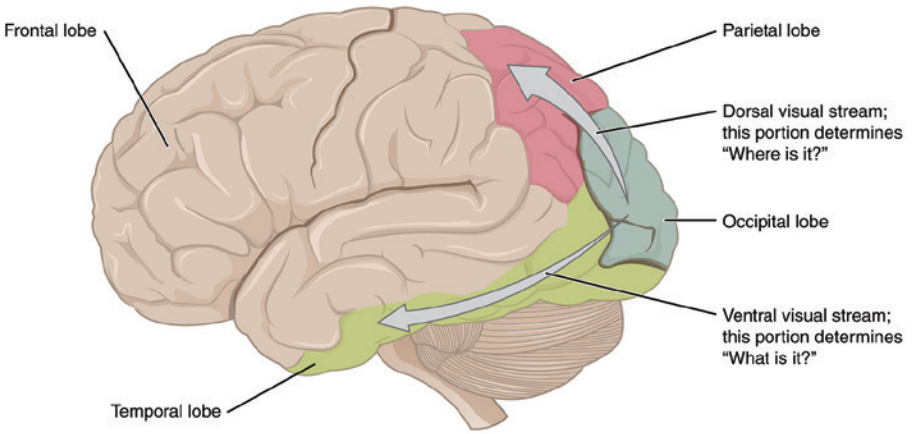


Figure 14.19 Ventral and Dorsal Visual Streams. From the primary visual cortex in the occipital lobe, visual processing continues in two streams—one into the temporal lobe and one into the parietal lobe.

The **ventral stream** identifies visual stimuli and their significance. Because the ventral stream uses temporal lobe structures, it begins to interact with the nonvisual cortex and may be important in visual stimuli becoming part of memories. The **dorsal stream** locates objects in space and helps in guiding movements of the body in response to visual inputs. The dorsal stream enters the parietal lobe, where it interacts with somatosensory cortical areas that are important for our perception of the body and its movements. The dorsal stream can then influence frontal lobe activity, where motor functions originate.

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Interactive Link 14.7

The inability to recognize people by their faces is a troublesome problem. It can be caused by trauma, or it may be inborn. Watch this video (http://oer.aupress.ca/oer-202505/14.7) to learn more about a person who lost the ability to recognize faces as a result of an injury. She cannot recognize the faces of close family members or herself. What other information can a person suffering from prosopagnosia use to figure out who they are seeing?

14.3 Motor Responses

Learning Objectives

By the end of this section, you will be able to:

- List the components of the basic processing stream for the motor system
- Describe the pathway of descending motor commands from the cortex to the skeletal muscles
- Compare different descending pathways by both structure and function
- Explain the initiation of movement from the neurological connections
- Describe several reflex arcs and their functional roles

The defining characteristic of the somatic nervous system is that it controls skeletal muscles. Somatic senses inform the nervous system about the external environment, but the response to that is through voluntary muscle movement. The term *voluntary* suggests that there is a conscious decision to make a movement. However, some aspects of the somatic system use voluntary muscles without conscious control. One example is the ability of our breathing to switch to unconscious control while we are focused on another task. However, the muscles that are responsible for the basic process of breathing are also utilized for speech, which is entirely voluntary.

Cortical Responses

Let's start with sensory stimuli that have been registered through receptor cells and the information relayed to the CNS along ascending pathways. In the cerebral cortex, the initial processing of sensory perception progresses to

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associative processing and then integration in multimodal areas of the cortex. These levels of processing can lead to the incorporation of sensory perceptions into memory, but more importantly, they lead to a response. The completion of cortical processing through the primary, associative, and integrative sensory areas initiates a similar progression of motor processing, usually in different cortical areas.

Whereas the sensory cortical areas are located in the occipital, temporal, and parietal lobes, motor functions are largely controlled by the frontal lobe (see Figure 13.2). The most anterior regions of the frontal lobe—the prefrontal areas—are important for **executive functions**, which are those cognitive functions that lead to goal-directed behaviours. These higher cognitive processes include **working memory**, which has been called a "mental scratch pad," that can help organize and represent information that is not in the immediate environment. The prefrontal lobe is responsible for aspects of attention, such as inhibiting distracting thoughts and actions so that a person can focus on a goal and direct behaviour toward achieving that goal.

The functions of the prefrontal cortex are integral to the personality of an individual because it is largely responsible for what a person intends to do and how they accomplish those plans. A famous case of damage to the prefrontal cortex is that of Phineas Gage, dating back to 1848. He was a railroad worker who had a metal spike impale his prefrontal cortex (Figure 14.20). He survived the accident, but according to secondhand accounts, his personality changed drastically. Friends described him as no longer acting like himself. Whereas he was a hardworking, amiable man before the accident, he turned into an irritable, temperamental, and lazy man after the accident. Many of the accounts of his change may have been inflated in the retelling, and some behaviour was likely attributable to alcohol used as a pain medication. However, the accounts suggest that some aspects of his personality did change. Also, there is new evidence that, though his life changed dramatically, he was able to become a functioning stagecoach driver, suggesting that the brain has the ability to recover even from major trauma such as this.

Secondary Motor Cortices

In generating motor responses, the executive functions of the prefrontal cortex will need to initiate actual movements. One way to define the prefrontal area is any region of the frontal lobe that does not elicit movement when electrically stimulated. These are primarily in the anterior part of the frontal lobe. The regions of the frontal lobe that remain are the regions of the cortex that produce movement. The prefrontal areas project into the secondary motor cortices, which include the **premotor cortex** and the **supplemental motor area**.

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(a)



(b)

Figure 14.20 Phineas Gage. The victim of an accident while working on a railroad in 1848, Phineas Gage had a large iron rod impaled through the prefrontal cortex of his frontal lobe. After the accident, his personality appeared to change, but he eventually learned to cope with the trauma and lived as a coach driver even after such a traumatic event. (Illustration (b) by John M. Harlow, MD.)

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Two important regions that assist in planning and coordinating movements are located adjacent to the primary motor cortex. The premotor cortex is more lateral, whereas the supplemental motor area is more medial and superior. The premotor area aids in controlling movements of the core muscles to maintain posture during movement, whereas the supplemental motor area is hypothesized to be responsible for planning and coordinating movement. The supplemental motor area also manages sequential movements that are based on prior experience (i.e., learned movements). Neurons in these areas are most active leading up to the initiation of movement. For example, these areas might prepare the body for the movements necessary to drive a car in anticipation of a traffic light changing.

Adjacent to these two regions are two specialized motor planning centres. The **frontal eye fields** are responsible for moving the eyes in response to visual stimuli. There are direct connections between the frontal eye fields and the **superior colliculus**. Also, anterior to the premotor cortex and primary motor cortex is **Broca's area** (which is found only in the left hemisphere in most people). This area is responsible for controlling movement of the structures of speech production. The area is named after a French surgeon and anatomist who studied patients who could not produce speech. They did not have impairments to understanding speech, only to producing speech sounds, suggesting a damaged or underdeveloped Broca's area.

Primary Motor Cortex

The primary motor cortex is located in the precentral gyrus of the frontal lobe. This cortex receives input from several areas that aid in planning movement, and its principal output stimulates spinal cord neurons to stimulate skeletal muscle contraction.

The primary motor cortex is arranged in a similar fashion to the primary somatosensory cortex, in that it has a topographical map of the body, creating a motor homunculus. The neurons responsible for musculature in the feet and lower legs are in the medial wall of the precentral gyrus, with the thighs, trunk, and shoulder at the crest of the longitudinal fissure. The hand and face are in the lateral face of the gyrus. Also, the relative space allotted for the different regions is exaggerated in muscles that have greater innervation. The greatest amount of cortical space is given to muscles that perform fine, agile movements, such as the muscles of the fingers and the lower face. The "power muscles" that perform coarser movements, such as the buttock and back muscles, occupy much less space on the motor cortex.

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Descending Pathways

The motor output from the cortex descends into the brain stem and to the spinal cord to control the musculature through motor neurons. Neurons located in the primary motor cortex, named **Betz cells**, are large cortical neurons that synapse with lower motor neurons in the brain stem or in the spinal cord. The two descending pathways travelled by the axons of Betz cells are the **corticobulbar tract** and the **corticospinal tract**, respectively. Both tracts are named for their origin in the cortex and their targets—either the brain stem (the term *bulbar* refers to the brain stem as the bulb, or enlargement, at the top of the spinal cord) or the spinal cord.

These two descending pathways are responsible for the conscious or voluntary movements of skeletal muscles. Any motor command from the primary motor cortex is sent down the axons of the Betz cells to activate lower motor neurons in either the cranial motor nuclei or in the ventral horn of the spinal cord. The axons of the corticobulbar tract are ipsilateral, meaning they project from the cortex to the motor nucleus on the same side of the nervous system. Conversely, the axons of the corticospinal tract are largely contralateral, meaning that they cross the midline of the brain stem or spinal cord and synapse on the opposite side of the body. Therefore, the right motor cortex of the cerebrum controls muscles on the left side of the body and vice versa.

The corticospinal tract descends from the cortex through the deep white matter of the cerebrum. It then passes between the caudate nucleus and putamen of the basal nuclei as a bundle called the **internal capsule**. The tract then passes through the midbrain as the **cerebral peduncles**, after which it burrows through the pons. Upon entering the medulla, the tracts make up the large white matter tract referred to as the **pyramids** (Figure 14.21). The defining landmark of the medullary-spinal border is the **pyramidal decussation**, which is where most of the fibres in the corticospinal tract cross over to the opposite side of the brain. At this point, the tract separates into two parts, which have control over different domains of the musculature.

Appendicular Control

The **lateral corticospinal tract** is composed of the fibres that cross the midline at the pyramidal decussation (see Figure 14.21). The axons cross over from the anterior position of the pyramids in the medulla to the lateral column of the spinal cord. These axons are responsible for controlling appendicular muscles.

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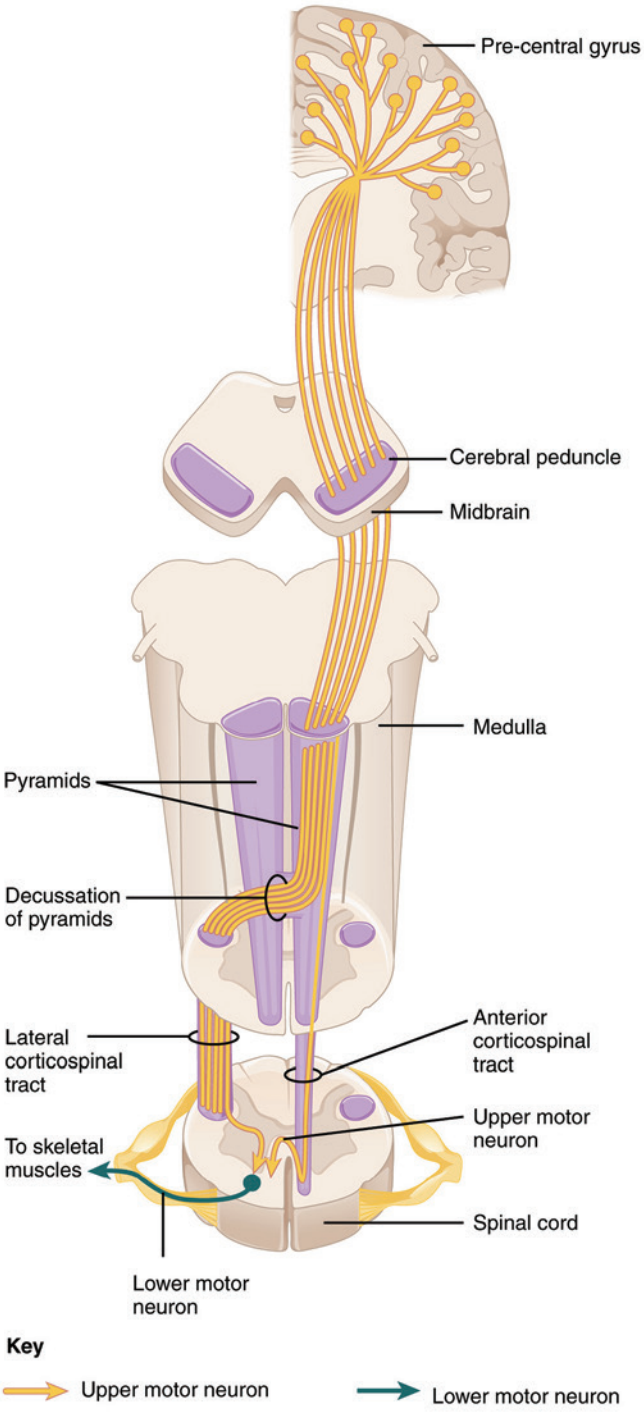


Figure 14.21 Corticospinal Tract. The major descending tract that controls skeletal muscle movements is the corticospinal tract. It is composed of two neurons, the upper motor neuron and the lower motor neuron. The upper motor neuron has its cell body in the primary motor cortex of the frontal lobe and synapses on the lower motor neuron, which is in the ventral horn of the spinal cord and projects to the skeletal muscle in the periphery.

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Axial Control

The **anterior corticospinal tract** is responsible for controlling the muscles of the trunk (see Figure 14.21). These axons do not decussate in the medulla. Instead, they remain in an anterior position as they descend the brain stem and enter the spinal cord. These axons then travel to the spinal cord level, where they synapse with a lower motor neuron. Upon reaching the appropriate level, the axons decussate, entering the ventral horn on the opposite side of the spinal cord from which they entered. In the ventral horn, these axons synapse with their corresponding lower motor neurons. The lower motor neurons are located in the medial regions of the ventral horn, as they control the axial muscles of the trunk.

Because movements of the trunk involve both sides of the body, the anterior corticospinal tract is not entirely contralateral. Some collateral branches of the tract will project into the ipsilateral ventral horn to control synergistic muscles on that side of the body or to inhibit antagonistic muscles through interneurons within the ventral horn.

Through the influence of both sides of the body, the anterior corticospinal tract can coordinate postural muscles in broad movements of the body. These coordinating axons in the anterior corticospinal tract are often considered bilateral, as they are both ipsilateral and contralateral.

Interactive Link 14.8

Watch this video (http://oer.aupress.ca/oer-202505/14.8) to learn more about the descending motor pathway for the somatic nervous system. The autonomic connections are mentioned, which are covered in another chapter. From this brief video, only some of the descending motor pathway of the somatic nervous system is described. Which division of the pathway is described, and which division is left out?

Extrapyramidal Controls

Other descending connections between the brain and the spinal cord are called the **extrapyramidal system**. The name comes from the fact that this system is outside the corticospinal pathway, which includes the pyramids in the medulla. A few pathways originating from the brain stem contribute to this system.

The **tectospinal tract** projects from the midbrain to the spinal cord and is important for postural movements that are driven by the superior colliculus. The name of the tract comes from an alternate name for the superior

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colliculus, which is the tectum. The **reticulospinal tract** connects the reticular system, a diffuse region of grey matter in the brain stem, with the spinal cord. This tract influences trunk and proximal limb muscles related to posture and locomotion. The reticulospinal tract also contributes to muscle tone and influences autonomic functions. The **vestibulospinal tract** connects the brain stem nuclei of the vestibular system with the spinal cord. This allows posture, movement, and balance to be modulated on the basis of equilibrium information provided by the vestibular system.

The pathways of the extrapyramidal system are influenced by subcortical structures. For example, connections between the secondary motor cortices and the extrapyramidal system modulate spine and cranium movements. The basal nuclei, which are important for regulating movement initiated by the CNS, influence the extrapyramidal system as well as its thalamic feedback to the motor cortex.

The conscious movement of our muscles is more complicated than simply sending a single command from the precentral gyrus down to the proper motor neurons. During the movement of any body part, our muscles relay information back to the brain, and the brain is constantly sending "revised" instructions back to the muscles. The cerebellum is important in contributing to the motor system because it compares cerebral motor commands with proprioceptive feedback. The corticospinal fibres that project to the ventral horn of the spinal cord have branches that also synapse in the pons, which project to the cerebellum. Also, the proprioceptive sensations of the dorsal column system have a collateral projection to the medulla that projects to the cerebellum. These two streams of information are compared in the cerebellar cortex. Conflicts between the motor commands sent by the cerebrum and body position information provided by the proprioceptors cause the cerebellum to stimulate the **red nucleus** of the midbrain. The red nucleus then sends corrective commands to the spinal cord along the **rubrospinal tract**. The name of this tract comes from the word for "red" that is seen in the English word "ruby."

A good example of how the cerebellum corrects cerebral motor commands can be illustrated by walking in water. An original motor command from the cerebrum to walk will result in a highly coordinated set of learned movements.

However, in water, the body cannot actually perform a typical walking movement as instructed. The cerebellum can alter the motor command, stimulating the leg muscles to take larger steps to overcome the water resistance.

The cerebellum can make the necessary changes through the rubrospinal tract. Modulating the basic command to walk also relies on spinal reflexes, but the cerebellum is responsible for calculating the appropriate response. When the cerebellum does not work properly, coordination and balance are severely affected. The most dramatic example of this is during the

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overconsumption of alcohol. Alcohol inhibits the ability of the cerebellum to interpret proprioceptive feedback, making it more difficult to coordinate body movements, such as walking a straight line or guiding the hand to touch the tip of the nose.

Interactive Link 14.9

Visit this site (http://oer.aupress.ca/oer-202505/14.9) to read about an elderly woman who starts to lose the ability to control fine movements, such as speech and the movement of limbs. Many of the usual causes were ruled out. It was not a stroke, Parkinson's disease, diabetes, or thyroid dysfunction. The next most obvious cause was medication, so her pharmacist had to be consulted. The side effect of a drug meant to help her sleep had resulted in changes in motor control. What regions of the nervous system are likely to be the focus of haloperidol side effects?

Ventral Horn Output

The somatic nervous system provides output strictly to skeletal muscles. The **lower motor neurons**, which are responsible for the contraction of these muscles (lack of this is called paresis), are found in the ventral horn of the spinal cord. These large, multipolar neurons have a corona of dendrites surrounding the cell body and an axon that extends out of the ventral horn. This axon travels through the ventral nerve root to join the emerging spinal nerve. The axon is relatively long because it needs to reach muscles in the periphery of the body. The diameters of cell bodies may be on the order of hundreds of micrometres to support the long axon; some axons are a metre in length, such as the lumbar motor neurons that innervate muscles in the first digits of the feet.

The axons will also branch to innervate multiple muscle fibres. Together, the motor neuron and all the muscle fibres that it controls make up a motor unit. Motor units vary in size. Some may contain up to 1,000 muscle fibres, such as in the quadriceps, or they may only have 10 fibres, such as in an extraocular muscle. The number of muscle fibres that are part of a motor unit corresponds to the precision of control of that muscle. Also, muscles that have finer motor control have more motor units connecting to them, and this requires a larger topographical field in the primary motor cortex.

Motor neuron axons connect to muscle fibres at a neuromuscular junction. This is a specialized synaptic structure at which multiple axon terminals synapse with the muscle fibre sarcolemma. The synaptic end bulbs of the motor neurons

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secrete acetylcholine, which binds to receptors on the sarcolemma. The binding of acetylcholine opens ligand-gated ion channels, increasing the movement of cations across the sarcolemma. This depolarizes the sarcolemma, initiating muscle contraction. Whereas other synapses result in graded potentials that must reach a threshold in the postsynaptic target, activity at the neuromuscular junction reliably leads to muscle fibre contraction with every nerve impulse received from a motor neuron. However, the strength of contraction and the number of fibres that contract can be affected by the frequency of the motor neuron impulses.

Reflexes

This chapter began by introducing reflexes as an example of the basic elements of the somatic nervous system. Simple somatic reflexes do not include the higher centres discussed for conscious or voluntary aspects of movement. Reflexes can be spinal or cranial, depending on the nerves and central components that are involved. The example described at the beginning of the chapter involved heat and pain sensations from a hot stove, causing withdrawal of the arm through a connection in the spinal cord that leads to contraction of the biceps brachii. The description of this **withdrawal reflex** was simplified, for the sake of the introduction, to emphasize the parts of the somatic nervous system. But to consider reflexes fully, more attention needs to be given to this example.

As you withdraw your hand from the stove, you do not want to slow that reflex down. As the biceps brachii contracts, the antagonistic triceps brachii needs to relax. Because the neuromuscular junction is strictly excitatory, the biceps will contract when the motor nerve is active. Skeletal muscles do not actively relax. Instead, the motor neuron needs to "quiet down," or be inhibited. In the hot-stove-withdrawal reflex, this occurs through an interneuron in the spinal cord. The interneuron's cell body is located in the dorsal horn of the spinal cord. The interneuron receives a synapse from the axon of the sensory neuron that detects that the hand is being burned. In response to this stimulation from the sensory neuron, the interneuron then inhibits the motor neuron that controls the triceps brachii. This is done by releasing a neurotransmitter or other signal that hyperpolarizes the motor neuron connected to the triceps brachii, making it less likely to initiate an action potential. With this motor neuron being inhibited, the triceps brachii relaxes. Without the antagonistic contraction, withdrawal from the hot stove is faster and prevents further tissue damage from occurring.

Another example of a withdrawal reflex occurs when you step on a painful stimulus, like a tack or a sharp rock. The nociceptors that are activated by the painful stimulus activate the motor neurons responsible for contraction of the tibialis anterior muscle. This causes dorsiflexion of the foot. An inhibitory interneuron, activated by a collateral branch of the nociceptor fibre, will inhibit

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the motor neurons of the gastrocnemius and soleus muscles to cancel plantar flexion. An important difference in this reflex is that plantar flexion is most likely in progress as the foot is pressing down onto the tack. Contraction of the tibialis anterior is not the most important aspect of the reflex, as continuation of plantar flexion will result in further damage from stepping onto the tack.

Another type of reflex is a **stretch reflex**. In this reflex, when a skeletal muscle is stretched, a muscle spindle receptor is activated. The axon from this receptor structure will cause direct contraction of the muscle. A collateral of the muscle spindle fibre will also inhibit the motor neuron of the antagonist muscles. The reflex helps maintain muscles at a constant length. A common example of this reflex is the knee jerk that is elicited by a rubber hammer struck against the patellar ligament in a physical exam.

A specialized reflex to protect the surface of the eye is the **corneal reflex**, or the eye blink reflex. When the cornea is stimulated by a tactile stimulus, or even by bright light in a related reflex, blinking is initiated. The sensory component travels through the trigeminal nerve, which carries somatosensory information from the face, or through the optic nerve, if the stimulus is bright light. The motor response travels through the facial nerve and innervates the orbicularis oculi on the same side. This reflex is commonly tested during a physical exam using an air puff or a gentle touch of a cotton-tipped applicator.

Interactive Link 14.10

Watch this video (http://oer.aupress.ca/oer-202505/14.10) to learn more about the reflex arc of the corneal reflex. When the right cornea senses a tactile stimulus, what happens to the left eye? Explain your answer.

Interactive Link 14.11

Watch this video (http://oer.aupress.ca/oer-202505/14.11) to learn more about newborn reflexes. Newborns have a set of reflexes that are expected to have been crucial to survival before the modern age. These reflexes disappear as the baby grows, as some of them may be unnecessary as they age. The video demonstrates a reflex called the Babinski reflex, in which the foot flexes dorsally and the toes splay out when the sole of the foot is lightly scratched. This is normal for newborns, but it is a sign of reduced myelination of the spinal tract in adults. Why would this reflex be a problem for an adult?

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Key Terms

alkaloid: Substance, usually from a plant source, that is chemically basic with respect to pH and will stimulate bitter receptors.

amacrine cell: Type of cell in the retina that connects to the bipolar cells near the outer synaptic layer and provides the basis for early image processing within the retina.

ampulla: In the ear, the structure at the base of a semicircular canal that contains the hair cells and cupula for transduction of rotational movement of the head.

anterior corticospinal tract: Division of the corticospinal pathway that travels through the ventral (anterior) column of the spinal cord and controls axial musculature through the medial motor neurons in the ventral (anterior) horn.

aqueous humour: Watery fluid that fills the anterior chamber containing the cornea, iris, ciliary body, and lens of the eye.

ascending pathway: Fibre structure that relays sensory information from the periphery through the spinal cord and brain stem to other structures of the brain.

association area: Region of cortex connected to a primary sensory cortical area that further processes the information to generate more complex sensory perceptions.

audition: Sense of hearing.

auricle: Fleshy external structure of the ear.

basilar membrane: In the ear, the floor of the cochlear duct on which the organ of Corti sits.

Betz cells: Output cells of the primary motor cortex that cause musculature to move through synapses on cranial and spinal motor neurons.

binocular vision: Indications of the distance of visual stimuli on the basis of slight differences in the images projected onto either retina.

bipolar cell: Cell type in the retina that connects the photoreceptors to the RGCs.

Broca's area: Region of the frontal lobe associated with the motor commands necessary for speech production.

bulbous (Ruffini) corpuscles: Responsible for the detection of stretching of the skin, known as type II cutaneous mechanoreceptors.

cerebral peduncles: Segments of the descending motor pathway that make up the white matter of the ventral midbrain.

chemoreceptor: Sensory receptor cell that is sensitive to chemical stimuli, such as in taste, smell, or pain.

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choroid: Highly vascular tissue in the wall of the eye that supplies the outer retina with blood.

ciliary body: Smooth muscle structure on the interior surface of the iris that controls the shape of the lens through the zonule fibres.

circadian rhythm: Internal perception of the daily cycle of light and dark based on retinal activity related to sunlight.

cochlea: Auditory portion of the inner ear containing structures to transduce sound stimuli.

cochlear duct: Space within the auditory portion of the inner ear that contains the organ of Corti and is adjacent to the scala tympani and scala vestibuli on either side.

cone photoreceptor: One of the two types of retinal receptor cell that is specialized for colour vision through the use of three photopigments distributed through three separate populations of cells.

contralateral: Word meaning "on the opposite side," as in axons that cross the midline in a fibre tract.

cornea: Fibrous covering of the anterior region of the eye that is transparent so that light can pass through it.

corneal reflex: Protective response to stimulation of the cornea that causes contraction of the orbicularis oculi muscle, resulting in blinking of the eye.

corticobulbar tract: Connection between the cortex and the brain stem responsible for generating movement.

corticospinal tract: Connection between the cortex and the spinal cord responsible for generating movement.

cupula: Specialized structure within the base of a semicircular canal that bends the stereocilia of hair cells when the head rotates by way of the relative movement of the enclosed fluid.

dorsal column system: Ascending tract of the spinal cord associated with fine touch and proprioceptive sensations.

dorsal stream: Connections between cortical areas from the occipital to parietal lobes that are responsible for the perception of visual motion and guiding movement of the body in relation to that motion.

encapsulated corpuscle ending: Configuration of a sensory receptor neuron with dendrites surrounded by specialized structures to aid in transduction of a particular type of sensation, such as the lamellated corpuscles in the deep dermis and subcutaneous tissue.

equilibrium: Sense of balance that includes sensations of position and movement of the head.

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Eustachian tube: Tube connecting the pharynx with the middle ear, which helps equilibrate air pressure across the tympanic membrane; it is normally closed but will pop open when the muscles of the pharynx contract during swallowing or yawning.

executive functions: Cognitive processes of the prefrontal cortex that lead to directing goal-directed behaviour, which is a precursor to executing motor commands.

external ear: Structures on the lateral surface of the head, including the auricle and the ear canal up to the tympanic membrane.

exteroceptor: Sensory receptor that is positioned to interpret stimuli from the external environment, such as photoreceptors in the eye or somatosensory receptors in the skin.

extrapyramidal system: Pathways between the brain and spinal cord that are separate from the corticospinal tract and are responsible for modulating the movements generated through that primary pathway.

fibrous tunic: Outer layer of the eye primarily composed of connective tissue known as the sclera and cornea.

fovea: Exact centre of the retina at which visual stimuli are focused for maximal acuity, where the retina is thinnest and there is nothing but photoreceptors.

free nerve ending: Configuration of a sensory receptor neuron with dendrites in the connective tissue of the organ, such as in the dermis of the skin, that are most often sensitive to chemical, thermal, and mechanical stimuli.

frontal eye fields: Area of the prefrontal cortex responsible for moving the eyes to attend to visual stimuli.

general sense: Any sensory system that is distributed throughout the body and incorporated into organs of multiple other systems, such as the walls of the digestive organs or the skin.

gustation: Sense of taste.

gustatory receptor cells: Sensory cells in the taste bud that transduce the chemical stimuli of gustation.

hair cells: Mechanoreceptor cells found in the inner ear that transduce stimuli for the senses of hearing and balance.

hair follicle plexus: Follicles are also wrapped in a plexus of nerve endings—detect the movement of hair at the surface of the skin, such as when an insect may be walking along the skin.

incus (also anvil): Ossicle of the middle ear that connects the malleus to the stapes.

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inner ear: Structure within the temporal bone that contains the sensory apparati of hearing and balance.

inner segment: In the eye, the section of a photoreceptor that contains the nucleus and other major organelles for normal cellular functions.

internal capsule: Segment of the descending motor pathway that passes between the caudate nucleus and the putamen.

interoceptor: Sensory receptor that is positioned to interpret stimuli from internal organs, such as stretch receptors in the wall of blood vessels.

ipsilateral: Word meaning on the same side, as in axons that do not cross the midline in a fibre tract.

iris: Coloured portion of the anterior eye that surrounds the pupil.

kinesthesia: Sense of body movement based on sensations in skeletal muscles, tendons, joints, and the skin.

lacrimal glands: Are lateral to the orbit that produces tears to wash across the surface of the eye.

lamellated (Pacinian) corpuscles: Responsible for the detection of deep pressure and vibration.

lateral corticospinal tract: Division of the corticospinal pathway that travels through the lateral column of the spinal cord and controls appendicular musculature through the lateral motor neurons in the ventral (anterior) horn.

lens: Component of the eye that focuses light on the retina.

lower motor neurons: Found in the ventral horn of the spinal cord and are responsible for the contraction of these muscles.

macula: Enlargement at the base of a semicircular canal at which transduction of equilibrium stimuli takes place within the ampulla.

malleus (also hammer): Ossicle that is directly attached to the tympanic membrane.

mechanoreceptor: Receptor cell that transduces mechanical stimuli into an electrochemical signal.

middle ear: Space within the temporal bone between the ear canal and bony labyrinth where the ossicles amplify sound waves from the tympanic membrane to the oval window.

multimodal integration area: Region of the cerebral cortex in which information from more than one sensory modality is processed to arrive at higher-level cortical functions such as memory, learning, or cognition.

muscle spindles: Stretch receptors in the skeletal muscle tissue.

neural tunic: Layer of the eye that contains nervous tissue, namely, the retina.

nociceptor: Receptor cell that senses pain stimuli.

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odorant molecules: Volatile chemicals that bind to receptor proteins in olfactory neurons to stimulate the sense of smell.
olfaction: Sense of smell.
olfactory bulb: Central target of the first cranial nerve; located on the ventral surface of the frontal lobe in the cerebrum.
olfactory cortex: That is located in the inferior and medial areas of the temporal lobe.
olfactory epithelium: Region of the nasal epithelium where olfactory neurons are located.
olfactory hairs: Dendrites of the olfactory sensory neuron located in the apical surface of the epithelium into the mucus lining the cavity with role in detection of odorant molecules dissolved in the mucus.
olfactory nerves: Group of axons that connect to the olfactory bulb.
olfactory sensory neuron: Receptor cell of the olfactory system, sensitive to the chemical stimuli of smell, the axons of which compose the first cranial nerve.
olfactory tract: Narrow band of nerve fibres in the brain that connects the olfactory bulb to the primary olfactory cortex.
opsin: Protein that contains the photosensitive cofactor retinal for phototransduction.
optic chiasm: Decussation point in the visual system at which medial retina fibres cross to the other side of the brain.
optic disc: Spot on the retina at which RGC axons leave the eye and blood vessels of the inner retina pass.
optic nerve: Second cranial nerve, which is responsible for visual sensation.
organ of Corti: Structure in the cochlea in which hair cells transduce movements from sound waves into electrochemical signals.
osmoreceptor: Receptor cell that senses differences in the concentrations of body fluids on the basis of osmotic pressure.
ossicles: Three small bones in the middle ear.
otolith: Layer of calcium carbonate crystals located on top of the otolithic membrane.
otolithic membrane: Gelatinous substance in the utricle and saccule of the inner ear that contains calcium carbonate crystals and into which the stereocilia of hair cells are embedded.
outer segment: In the eye, the section of a photoreceptor that contains opsin molecules that transduce light stimuli.
oval window: Membrane at the base of the cochlea where the stapes attaches, marking the beginning of the scala vestibuli.

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papilla: For gustation, a bumplike projection on the surface of the tongue that contains taste buds.

photoreceptor: Receptor cell specialized to respond to light stimuli.

premotor cortex: Cortical area anterior to the primary motor cortex that is responsible for planning movements.

primary sensory cortex: Region of the cerebral cortex that initially receives sensory input from an ascending pathway from the thalamus and begins the processing that will result in conscious perception of that modality.

proprioception: Sense of position and movement of the body.

proprioceptor: Receptor cell that senses changes in the position and kinesthetic aspects of the body.

pupil: Open hole at the centre of the iris that light passes through into the eye.

pyramidal decussation: Location at which corticospinal tract fibres cross the midline and segregate into the anterior and lateral divisions of the pathway.

pyramids: Segment of the descending motor pathway that travels in the anterior position of the medulla.

red nucleus: Midbrain nucleus that sends corrective commands to the spinal cord along the rubrospinal tract, based on the disparity between an original command and the sensory feedback from movement.

reticulospinal tract: Extrapyramidal connections between the brain stem and spinal cord that modulate movement, contribute to posture, and regulate muscle tone.

retina: Nervous tissue of the eye at which phototransduction takes place.

retinal ganglion cell (RGC): Neuron of the retina that projects along the second cranial nerve.

rhodopsin: Photopigment molecule found in the rod photoreceptors.

rod photoreceptor: One of the two types of retinal receptor cell that is specialized for low-light vision.

round window: Membrane that marks the end of the scala tympani.

rubrospinal tract: Descending motor control pathway, originating in the red nucleus, that mediates control of the limbs on the basis of cerebellar processing.

saccule: Structure of the inner ear responsible for transducing linear acceleration in the vertical plane.

scala tympani: Portion of the cochlea that extends from the apex to the round window.

scala vestibuli: Portion of the cochlea that extends from the oval window to the apex.

sclera: White of the eye.

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semicircular canals: Structures within the inner ear responsible for transducing rotational movement information.

sensory homunculus: Topographic representation of the body within the somatosensory cortex demonstrating the correspondence between neurons processing stimuli and sensitivity.

sensory modality: A particular system for interpreting and perceiving environmental stimuli by the nervous system.

solitary nucleus: Medullar nucleus that receives taste information from the facial and glossopharyngeal nerves.

somatosensation: General sense associated with modalities lumped together as touch.

specialized receptor cell: Cell that transduces environmental stimuli into neural signals.

special sense: Any sensory system associated with a specific organ structure, namely, smell, taste, sight, hearing, and balance.

spinothalamic tract: Ascending tract of the spinal cord associated with pain and temperature sensations.

spiral ganglion: Location of neuronal cell bodies that transmit auditory information along the eighth cranial nerve.

stapes (also stirrup): Ossicle of the middle ear that is attached to the inner ear.

stereocilia: Array of apical membrane extensions in a hair cell that transduce movements when they are bent.

stretch receptors: Monitor the stretching of tendons, muscles, and the components of joints.

stretch reflex: Response to activation of the muscle spindle stretch receptor that causes contraction of the muscle to maintain a constant length.

submodality: Specific sense within a broader major sense, such as sweet as a part of the sense of taste or colour as a part of vision.

superior colliculus: Structure in the midbrain that combines visual, auditory, and somatosensory input to coordinate spatial and topographic representations of the three sensory systems.

supplemental motor area: Cortical area anterior to the primary motor cortex that is responsible for planning movements.

taste buds: Structures within a papilla on the tongue that contain gustatory receptor cells.

tectorial membrane: Component of the organ of Corti that lies over the hair cells, into which the stereocilia are embedded.

tectospinal tract: Extrapyramidal connections between the superior colliculus and spinal cord.

tendon (Golgi) stretch organs: Transduce the stretch levels of tendons.

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thermoreceptor: Sensory receptor specialized for temperature stimuli.
topographical: Relating to positional information.
transduction: Process of changing an environmental stimulus into the electrochemical signals of the nervous system.
tympanic membrane: Ear drum.
utricle: Structure of the inner ear responsible for transducing linear acceleration in the horizontal plane.
vascular tunic: Middle layer of the eye primarily composed of connective tissue with a rich blood supply.
ventral stream: Connections between cortical areas from the occipital lobe to the temporal lobe that are responsible for the identification of visual stimuli.
vestibular apparatus: Component of the vestibular system that contains the hair cell with stereocilia responsible for senses, head position, head movement, and whether our bodies are in motion.
vestibular ganglion: Location of neuronal cell bodies that transmit equilibrium information along the eighth cranial nerve.
vestibular nuclei: Targets of the vestibular component of the eighth cranial nerve.
vestibule: In the ear, the portion of the inner ear responsible for the sense of equilibrium.
vestibulo-ocular reflex (VOR): Reflex based on connections between the vestibular system and the cranial nerves of eye movements that ensures images are stabilized on the retina as the head and body move.
vestibulospinal tract: Extrapyramidal connections between the vestibular nuclei in the brain stem and spinal cord that modulate movement and contribute to balance on the basis of the sense of equilibrium.
visceral sense: Sense associated with the internal organs.
vision: Special sense of sight based on the transduction of light stimuli.
visual acuity: Property of vision related to the sharpness of focus, which varies in relation to retinal position.
vitreous humour: Viscous fluid that fills the posterior chamber of the eye.
withdrawal reflex: From a painful stimulus only requires the sensory fibre that enters the spinal cord and the motor neuron that projects to a muscle.
working memory: Function of the prefrontal cortex to maintain a representation of information that is not in the immediate environment.
zonule fibres: Fibrous connections between the ciliary body and the lens.

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Chapter Review

14.1 Sensory Perception

The senses are olfaction (smell), gustation (taste), somatosensation (sensations associated with the skin and body), audition (hearing), equilibrium (balance), and vision. With the exception of somatosensation, this list represents the special senses, or those systems of the body that are associated with specific organs such as the tongue or eye. Somatosensation belongs to the general senses, which are those sensory structures that are distributed throughout the body and in the walls of various organs. The special senses are all primarily part of the somatic nervous system in that they are consciously perceived through cerebral processes, though some special senses contribute to autonomic function. The general senses can be divided into somatosensation, which is commonly considered touch, but includes tactile, pressure, vibration, temperature, and pain perception. The general senses also include the visceral senses, which are separate from the somatic nervous system function in that they do not normally rise to the level of conscious perception.

The cells that transduce sensory stimuli into the electrochemical signals of the nervous system are classified on the basis of structural or functional aspects of the cells. The structural classifications are based on either the anatomy of the cell that is interacting with the stimulus (free nerve endings, encapsulated endings, or specialized receptor cells) or where the cell is located relative to the stimulus (interoceptor, exteroceptor, or proprioceptor). Third, the functional classification is based on how the cell transduces the stimulus into a neural signal.

Chemoreceptors respond to chemical stimuli and are the basis for olfaction and gustation. Related to chemoreceptors are osmoreceptors and nociceptors for fluid balance and pain reception, respectively. Mechanoreceptors respond to mechanical stimuli and are the basis for most aspects of somatosensation, as well as being the basis of audition and equilibrium in the inner ear. Thermoreceptors are sensitive to temperature changes, and photoreceptors are sensitive to light energy.

The nerves that convey sensory information from the periphery to the CNS are either spinal nerves, connected to the spinal cord, or cranial nerves, connected to the brain. Spinal nerves have mixed populations of fibres; some are motor fibres and some are sensory. The sensory fibres connect to the spinal cord through the dorsal root, which is attached to the dorsal root ganglion. Sensory information from the body that is conveyed through spinal nerves will project to the opposite side of the brain to be processed by the cerebral cortex. The cranial nerves can be strictly sensory fibres, such as the olfactory, optic,

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and vestibulocochlear nerves, or mixed sensory and motor nerves, such as the trigeminal, facial, glossopharyngeal, and vagus nerves. The cranial nerves are connected to the same side of the brain from which the sensory information originates.

14.2 Central Processing

Sensory input to the brain enters through pathways that travel through either the spinal cord (for somatosensory input from the body) or the brain stem (for everything else, except the visual and olfactory systems) to reach the diencephalon. In the diencephalon, sensory pathways reach the thalamus. This is necessary for all sensory systems to reach the cerebral cortex, except for the olfactory system, which is directly connected to the frontal and temporal lobes.

The two major tracts in the spinal cord, originating from sensory neurons in the dorsal root ganglia, are the dorsal column system and the spinothalamic tract. The major differences between the two are in the type of information that is relayed to the brain and where the tracts decussate. The dorsal column system primarily carries information about touch and proprioception and crosses the midline in the medulla. The spinothalamic tract is primarily responsible for pain and temperature sensation and crosses the midline in the spinal cord at the level at which it enters. The trigeminal nerve adds similar sensation information from the head to these pathways.

The auditory pathway passes through multiple nuclei in the brain stem, in which additional information is extracted from the basic frequency stimuli processed by the cochlea. Sound localization is made possible through the activity of these brain stem structures. The vestibular system enters the brain stem and influences activity in the cerebellum, spinal cord, and cerebral cortex.

The visual pathway segregates information from the two eyes so that one-half of the visual field projects to the other side of the brain. Within visual cortical areas, the perception of the stimuli and their location is passed along two streams, one ventral and one dorsal. The ventral visual stream connects to structures in the temporal lobe that are important for long-term memory formation. The dorsal visual stream interacts with the somatosensory cortex in the parietal lobe, and together they can influence the activity in the frontal lobe to generate movements of the body in relation to visual information.

14.3 Motor Responses

The motor components of the somatic nervous system begin with the frontal lobe of the brain, where the prefrontal cortex is responsible for higher functions such as working memory. The integrative and associate functions of the prefrontal lobe feed into the secondary motor areas, which help plan movements.

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The premotor cortex and supplemental motor area then feed into the primary motor cortex, which initiates movements. Large Betz cells project through the corticobulbar and corticospinal tracts to synapse on lower motor neurons in the brain stem and ventral horn of the spinal cord, respectively. These connections are responsible for generating movements of skeletal muscles.

The extrapyramidal system includes projections from the brain stem and higher centres that influence movement, mostly to maintain balance and posture, as well as to maintain muscle tone. The superior colliculus and red nucleus in the midbrain, the vestibular nuclei in the medulla, and the reticular formation throughout the brain stem each have tracts projecting to the spinal cord in this system. Descending inputs from the secondary motor cortices, basal nuclei, and cerebellum connect to the origins of these tracts in the brain stem.

All these motor pathways project to the spinal cord to synapse with motor neurons in the ventral horn of the spinal cord. These lower motor neurons are the cells that connect to skeletal muscle and cause contractions. These neurons project through the spinal nerves to connect to the muscles at neuromuscular junctions. One motor neuron connects to multiple muscle fibres within a target muscle. The number of fibres that are innervated by a single motor neuron varies on the basis of the precision necessary for that muscle and the amount of force necessary for that motor unit. The quadriceps, for example, have many fibres controlled by single motor neurons for powerful contractions that do not need to be precise.

Reflexes are the simplest circuits within the somatic nervous system. A withdrawal reflex from a painful stimulus only requires the sensory fibre that enters the spinal cord and the motor neuron that projects to a muscle. Antagonist and postural muscles can be coordinated with the withdrawal, making the connections more complex. The simple, single neuronal connection is the basis of somatic reflexes. The corneal reflex is a contraction of the orbicularis oculi muscle to blink the eyelid when something touches the surface of the eye. Stretch reflexes maintain a constant length of muscles by causing a contraction of a muscle to compensate for a stretch that can be sensed by a specialized receptor called a muscle spindle.

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15

The Autonomic Nervous System

Chapter Objectives

After studying this chapter, you will be able to:

- Describe the components of the autonomic nervous system
- Differentiate between the structures of the sympathetic and parasympathetic divisions in the autonomic nervous system
- Name the components of a visceral reflex specific to the autonomic division to which it belongs
- Predict the response of a target effector to autonomic input on the basis of the released signalling molecule
- Describe how the central nervous system coordinates and contributes to autonomic functions

The autonomic nervous system is often associated with the "fight-or-flight response," which refers to the preparation of the body to either run away from a threat or to stand and fight in the face of that threat. The autonomic nervous system is not just about responding to threats. Besides the fight-or-flight response, there are the responses referred to as "rest and digest." If that lioness is successful in her hunting, then she is going to rest from the exertion. Her heart rate will slow. Breathing will return to normal. The digestive system has a big job to do. Much of the function of the autonomic system is based on the connections within an autonomic, or visceral, reflex.

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15.1 Divisions of the Autonomic Nervous System

Learning Objectives

By the end of this section, you will be able to:

- Name the components that generate the sympathetic and parasympathetic responses of the autonomic nervous system
- Explain the differences in output connections within the two divisions of the autonomic nervous system
- Describe the signalling molecules and receptor proteins involved in communication within the two divisions of the autonomic nervous system

The nervous system can be divided into two functional parts: the somatic nervous system and the autonomic nervous system. The major differences between the two systems are evident in the responses that each produces. The somatic nervous system causes contraction of skeletal muscles. The autonomic nervous system controls cardiac and smooth muscle, as well as glandular tissue. The somatic nervous system is associated with voluntary responses (though many can happen without conscious awareness, like breathing), and the autonomic nervous system is associated with involuntary responses, such as those related to homeostasis.

The autonomic nervous system regulates many of the internal organs through a balance of two aspects, or divisions. In addition to the endocrine system, the autonomic nervous system is instrumental in homeostatic mechanisms in the body. The two divisions of the autonomic nervous system are the **sympathetic division** and the **parasympathetic division**. The sympathetic system is associated with the **fight-or-flight response**, and parasympathetic activity is referred to by the epithet of **rest and digest**. Homeostasis is the balance between the two systems. At each target effector, dual innervation determines activity. For example, the heart receives connections from both the sympathetic and parasympathetic divisions. One causes heart rate to increase, whereas the other causes heart rate to decrease.

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Interactive Link 15.1

Watch this video (http://oer.aupress.ca/oer-202505/15.1) to learn more about adrenaline and the fight-or-flight response. When someone is said to have a rush of adrenaline, the image of bungee jumpers or skydivers usually comes to mind. But adrenaline, also known as epinephrine, is an important chemical in coordinating the body's fight-or-flight response. In this video, you look inside the physiology of the fight-or-flight response, as envisioned for a firefighter. His body's reaction is the result of the sympathetic division of the autonomic nervous system causing system-wide changes as it prepares for extreme responses. What two changes does adrenaline bring about to help the skeletal muscle response?

Sympathetic Division of the Autonomic Nervous System

To respond to a threat—to fight or to run away—the sympathetic system causes divergent effects as many different effector organs are activated together for a common purpose. More oxygen needs to be inhaled and delivered to skeletal muscle. The respiratory, cardiovascular, and musculoskeletal systems are all activated together.

Additionally, sweating keeps the excess heat that comes from muscle contraction from causing the body to overheat. The digestive system slows down so that blood is not absorbing nutrients when it should be delivering oxygen to skeletal muscles. To coordinate all these responses, the connections in the sympathetic system diverge from a limited region of the central nervous system (CNS) to a wide array of ganglia that project to the many effector organs simultaneously. The complex set of structures that compose the output of the sympathetic system makes it possible for these disparate effectors to come together in a coordinated, systemic change.

The sympathetic division of the autonomic nervous system influences the various organ systems of the body through connections emerging from the thoracic and upper lumbar spinal cord. It is referred to as the **thoracolumbar system** to reflect this anatomical basis. A **central neuron** in the lateral horn of any of these spinal regions projects to ganglia adjacent to the vertebral column through the ventral spinal roots. The majority of ganglia of the sympathetic system belong to a network of **sympathetic chain ganglia** that runs alongside the vertebral column.

The ganglia appear as a series of clusters of neurons linked by axonal bridges. There are typically 23 ganglia in the chain on either side of the spinal column. Three correspond to the cervical region, 12 are in the thoracic region, four are

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in the lumbar region, and four correspond to the sacral region. The cervical and sacral levels are not connected to the spinal cord directly through the spinal roots, but through ascending or descending connections through the bridges within the chain.

A diagram that shows the connections of the sympathetic system is somewhat like a circuit diagram that shows the electrical connections between different receptacles and devices. In Figure 15.1, the "circuits" of the sympathetic system are intentionally simplified.

To continue with the analogy of the circuit diagram, there are three different types of "junctions" that operate within the sympathetic system (Figure 15.2). The first type is most direct: the sympathetic nerve projects to the chain ganglion at the same level as the **target effector** (the organ, tissue, or gland to be innervated). An example of this type is spinal nerve T1 that synapses with the T1 chain ganglion to innervate the trachea. The fibres of this branch are called **white rami communicantes** (singular = ramus communicans); they are myelinated and therefore referred to as white (see Figure 15.2a). The axon from the central neuron (the preganglionic fibre shown as a solid line) synapses with the **ganglionic neuron** (with the postganglionic fibre shown as a dashed line). This neuron then projects to a target effector—in this case, the trachea—via **grey rami communicantes**, which are unmyelinated axons.

In some cases, the target effectors are located superior or inferior to the spinal segment at which the preganglionic fibre emerges. With respect to the "wiring" involved, the synapse with the ganglionic neuron occurs at chain ganglia superior or inferior to the location of the central neuron. An example of this is spinal nerve T1, which innervates the eye. The spinal nerve tracks up through the chain until it reaches the **superior cervical ganglion**, where it synapses with the postganglionic neuron (see Figure 15.2b). The cervical ganglia are referred to as **paravertebral ganglia**, given their location adjacent to prevertebral ganglia in the sympathetic chain.

Not all axons from the central neurons terminate in the chain ganglia. Additional branches from the ventral nerve root continue through the chain and on to one of the collateral ganglia as the **greater splanchnic nerve** or **lesser splanchnic nerve**. For example, the greater splanchnic nerve at the level of T5 synapses with a collateral ganglion outside the chain before making the connection to the postganglionic nerves that innervate the stomach (see Figure 15.2c).

Collateral ganglia, also called **prevertebral ganglia**, are situated anterior to the vertebral column and receive inputs from splanchnic nerves as well as central sympathetic neurons. They are associated with controlling organs in the abdominal cavity and are also considered part of the enteric nervous system. The three collateral ganglia are the **celiac ganglion**, the **superior**

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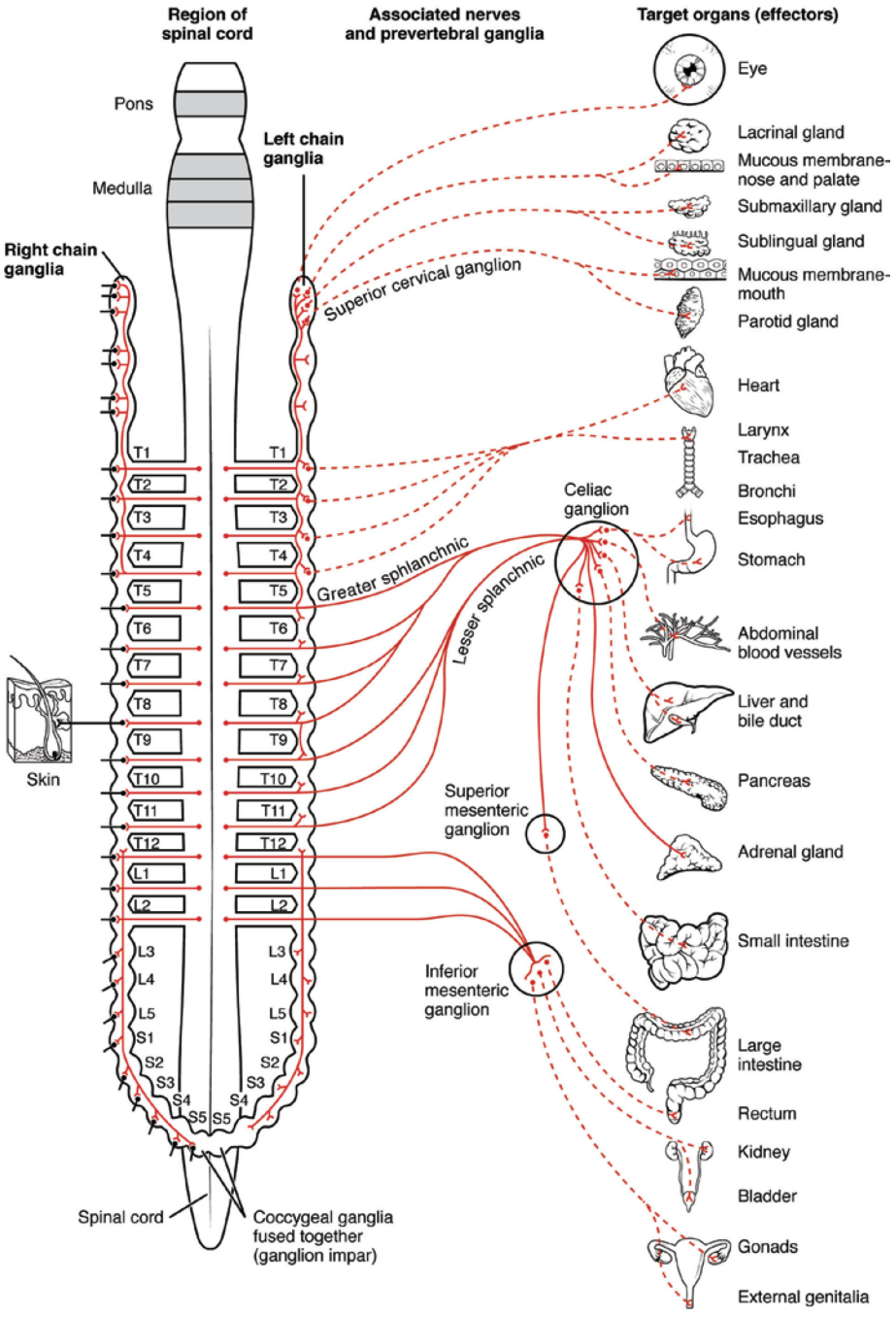


Figure 15.1 Connections of the Sympathetic Division of the Autonomic Nervous System. Neurons from the lateral horn of the spinal cord (preganglionic nerve fibres—solid lines) project to the chain ganglia on either side of the vertebral column or to collateral (prevertebral) ganglia that are anterior to the vertebral column in the abdominal cavity. Axons from these ganglionic neurons (postganglionic nerve fibres—dotted lines) then project to target effectors throughout the body.

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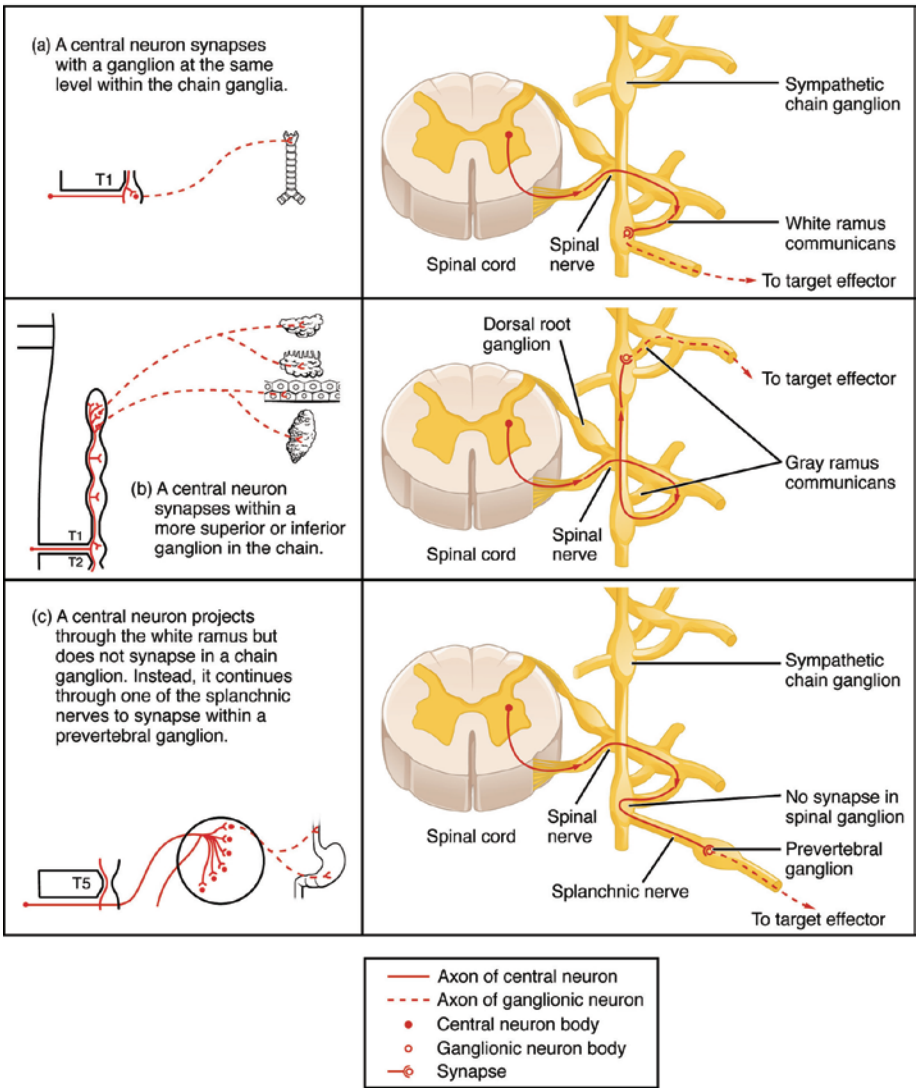


Figure 15.2 Sympathetic Connections and Chain Ganglia. The axon from a central sympathetic neuron in the spinal cord can project to the periphery in a number of different ways. (a) The fibre can project out to the ganglion at the same level and synapse on a ganglionic neuron. (b) A branch can project to a more superior or inferior ganglion in the chain. (c) A branch can project through the white ramus communicans but cannot terminate on a ganglionic neuron in the chain. Instead, it projects through one of the splanchnic nerves to a collateral ganglion or the adrenal medulla (not pictured).

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mesenteric ganglion, and the **inferior mesenteric ganglion** (see Figure 15.1). The word *celiac* refers to a body cavity (in this case, the abdominal cavity), and the word *mesenteric* refers to the digestive system.

An axon from the central neuron that projects to a sympathetic ganglion is referred to as a **preganglionic fibre** or neuron and represents the output from the CNS to the ganglion. Because the sympathetic ganglia are adjacent to the vertebral column, preganglionic sympathetic fibres are relatively short, and they are myelinated. A **postganglionic fibre**—the axon from a ganglionic neuron that projects to the target effector—represents the output of a ganglion that directly influences the organ. Compared with the preganglionic fibres, postganglionic sympathetic fibres are long because of the relatively greater distance from the ganglion to the target effector. These fibres are unmyelinated. (Note that the term *postganglionic neuron* may be used to describe the projection from a ganglion to the target. The problem with that usage is that the cell body is in the ganglion, and only the fibre is postganglionic. Typically, the term *neuron* applies to the entire cell.)

One type of preganglionic sympathetic fibre does not terminate in a ganglion. These are the axons from central sympathetic neurons that project to the **adrenal medulla**, the interior portion of the adrenal gland. These axons are still referred to as preganglionic fibres, but the target is not a ganglion. The adrenal medulla releases signalling molecules into the bloodstream, rather than using axons to communicate with target structures. The cells in the adrenal medulla that are contacted by the preganglionic fibres are called **chromaffin cells**. These cells are neurosecretory cells that develop from the neural crest along with the sympathetic ganglia, reinforcing the idea that the gland is, functionally, a sympathetic ganglion.

The projections of the sympathetic division of the autonomic nervous system diverge widely, resulting in a broad influence of the system throughout the body. As a response to a threat, the sympathetic system would increase heart rate and breathing rate, cause blood flow to the skeletal muscle to increase, and cause blood flow to the digestive system to decrease. Sweat gland secretion should also increase as part of an integrated response. All those physiological changes are going to be required to occur together to run away from the hunting lioness, or the modern equivalent. This divergence is seen in the branching patterns of preganglionic sympathetic neurons—a single preganglionic sympathetic neuron may have 10–20 targets. An axon that leaves a central neuron of the lateral horn in the thoracolumbar spinal cord will pass through the white ramus communicans and enter the sympathetic chain, where it will branch toward a variety of targets. At the level of the spinal cord at which the preganglionic sympathetic fibre exits the spinal cord, a branch will synapse on a neuron in the adjacent chain ganglion. Some branches will extend up or down to a different level of the chain ganglia.

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Other branches will pass through the chain ganglia and project through one of the splanchnic nerves to a collateral ganglion. Finally, some branches may project through the splanchnic nerves to the adrenal medulla. All these branches mean that one preganglionic neuron can influence different regions of the sympathetic system very broadly, by acting on widely distributed organs.

Parasympathetic Division of the Autonomic Nervous System

The parasympathetic system can also be referred to as the **craniosacral system** (or outflow) because the preganglionic neurons are located in nuclei of the brain stem and the lateral horn of the sacral spinal cord.

The connections, or "circuits," of the parasympathetic division are similar to the general layout of the sympathetic division, with a few specific differences (Figure 15.3). The preganglionic fibres from the cranial region travel in cranial nerves, whereas the preganglionic fibres from the sacral region travel in spinal nerves. The targets of these fibres are **terminal ganglia**, which are located near—or even within—the target effector. These ganglia are often referred to as **intramural ganglia** when they are found within the walls of the target organ. The postganglionic fibre projects from the terminal ganglia a short distance to the target effector, or to the specific target tissue within the organ.

Comparing the relative lengths of axons in the parasympathetic system, the preganglionic fibres are long and the postganglionic fibres are short because the ganglia are close to—and sometimes within—the target effectors.

Chemical Signalling in the Autonomic Nervous System

Where an autonomic neuron connects with a target, there is a synapse. The electrical signal of the action potential causes the release of a signalling molecule, which will bind to receptor proteins on the target cell. Synapses of the autonomic system are classified as either **cholinergic**, meaning that **acetylcholine** (**ACh**) is released, or **adrenergic**, meaning that **norepinephrine** is released. The terms *cholinergic* and *adrenergic* refer not only to the signalling molecule that is released but also to the class of receptors that each binds.

The cholinergic system includes two classes of receptors: the **nicotinic receptor** and the **muscarinic receptor**. Both receptor types bind to ACh and cause changes in the target cell. The receptors are named for, and differentiated by, other molecules that bind to them. Whereas nicotine will bind to the nicotinic receptor, and muscarine will bind to the muscarinic receptor, there is no cross-reactivity between the receptors. These molecules are **exogenous**, meaning that they are made outside of the human body, so a researcher can use them without any confounding **endogenous** results (results caused by the molecules produced in the body).

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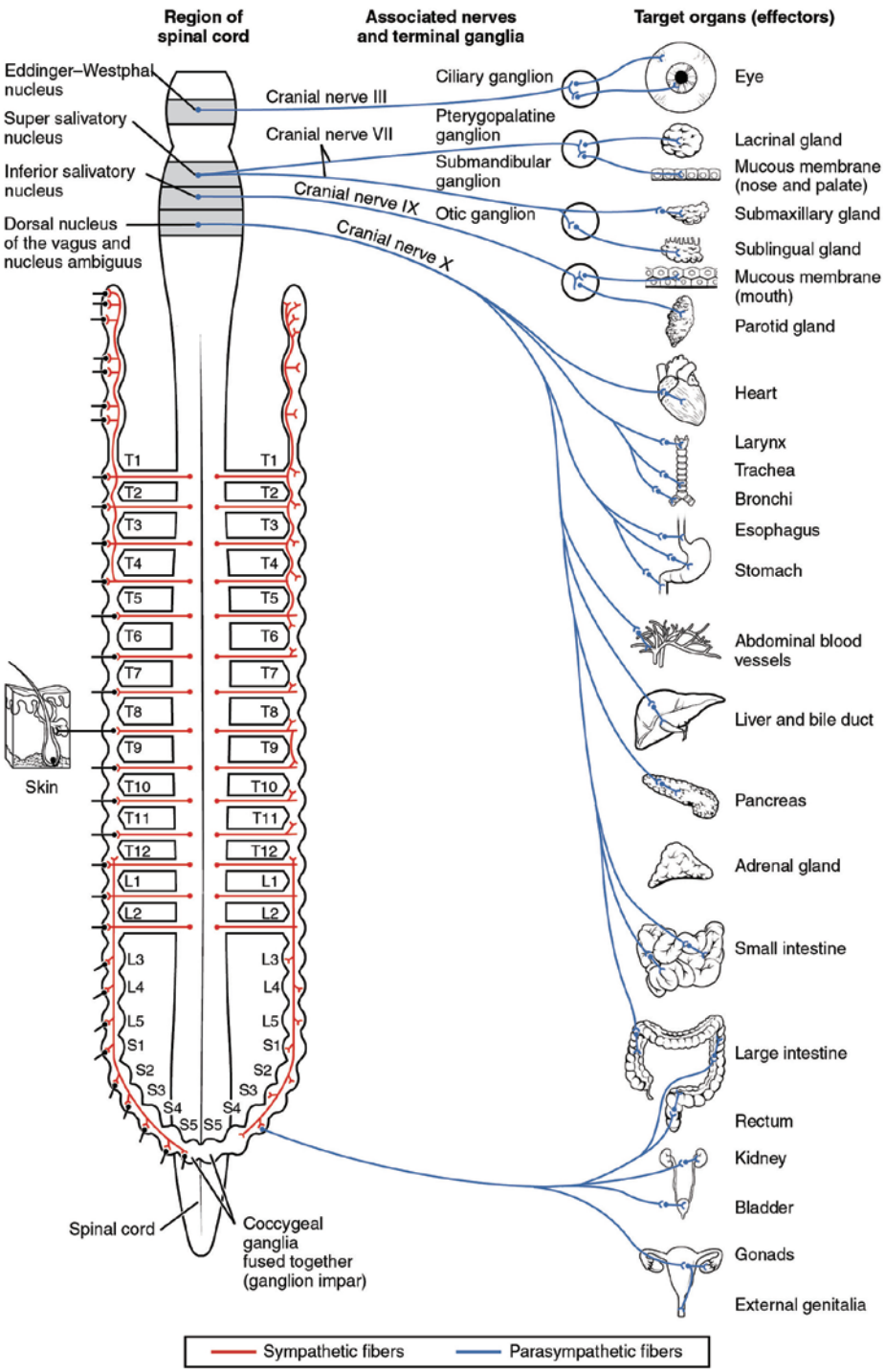


Figure 15.3 Connections of the Parasympathetic Division of the Autonomic Nervous System. Neurons from brain stem nuclei, or from the lateral horn of the sacral spinal cord, project to terminal ganglia near or within the various organs of the body. Axons from these ganglionic neurons then project short distances to those target effectors.

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The adrenergic system also has two types of receptors, named the **alpha-adrenergic** (**α-adrenergic**) **receptor** and **beta-adrenergic** (**β-adrenergic**) **receptor**. Unlike cholinergic receptors, these receptor types are not classified by which drugs can bind to them. All of them are G protein–coupled receptors. There are two types of α-adrenergic receptors, termed α_1 and α_2, and there are three types of β-adrenergic receptors, termed β_1, β_2, and β_3. An additional aspect of the adrenergic system is that there is a second signalling molecule called **epinephrine**. The chemical difference between norepinephrine and epinephrine is the addition of a methyl group (CH_3) in epinephrine.

The term *adrenergic* should remind you of the word *adrenaline*, which is associated with the fight-or-flight response described at the beginning of the chapter. Adrenaline and epinephrine are two names for the same molecule. The adrenal gland secretes adrenaline. Similarly, norepinephrine and noradrenaline are two names for the same molecule.

Having understood the cholinergic and adrenergic systems, their role in the autonomic system is relatively simple to understand. All preganglionic fibres, both sympathetic and parasympathetic, release ACh. All ganglionic neurons—the targets of these preganglionic fibres—have nicotinic receptors in their cell membranes. The nicotinic receptor is a ligand-gated cation channel that results in depolarization of the postsynaptic membrane. The postganglionic parasympathetic fibres also release ACh, but the receptors on their targets are muscarinic receptors, which are G protein–coupled receptors and do not exclusively cause depolarization of the postsynaptic membrane. Postganglionic sympathetic fibres release norepinephrine, except for fibres that project to sweat glands and to blood vessels associated with skeletal muscles, which release ACh (Table 15.1).

Table 15.1 Autonomic System Signalling Molecules

	Sympathetic	Parasympathetic
Preganglionic	Acetylcholine → nicotinic receptor	Acetylcholine → nicotinic receptor
Postganglionic	Norepinephrine → α- or β-adrenergic receptors Acetylcholine → muscarinic receptor (associated with sweat glands and the blood vessels within skeletal muscles)	Acetylcholine → muscarinic receptor

Signalling molecules can belong to two broad groups. Neurotransmitters are released at synapses, whereas hormones are released into the bloodstream. These are simplistic definitions, but they can help clarify this point. Acetylcholine can be considered a neurotransmitter because it is released by axons at

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synapses. The adrenergic system, however, presents a challenge. Postganglionic sympathetic fibres release norepinephrine, which can be considered a neurotransmitter. But the adrenal medulla releases epinephrine and norepinephrine into circulation, so they should be considered hormones.

What are referred to here as synapses may not fit the strictest definition of a synapse. Some sources will refer to the connection between a postganglionic fibre and a target effector as neuroeffector junctions; neurotransmitters, as defined above, would be called neuromodulators. The structure of postganglionic connections is not the typical synaptic end bulb that is found at the neuromuscular junction; rather, they are chains of swellings along the length of a postganglionic fibre called a **varicosity** (Figure 15.4).

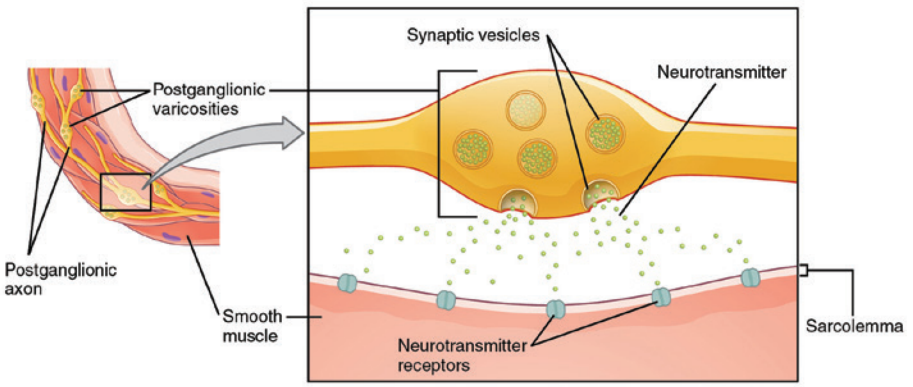


Figure 15.4 Autonomic Varicosities. The connection between autonomic fibres and target effectors is not the same as the typical synapse, such as the neuromuscular junction. Instead of a synaptic end bulb, a neurotransmitter is released from swellings along the length of a fibre that makes an extended network of connections in the target effector.

Interactive Link 15.2

Watch this video (https://oer.aupress.ca/oer-202505/15.2) to learn more about the nervous system. As described in this video, the nervous system has a way to deal with threats and stress that is separate from the conscious control of the somatic nervous system. The system comes from a time when threats were about survival, but in the modern age, these responses become part of stress and anxiety. This video describes how the autonomic system is only part of the response to threats or stressors. What other organ system gets involved, and what part of the brain coordinates the two systems for the entire response, including epinephrine (adrenaline) and cortisol?

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15.2 Autonomic Reflexes and Homeostasis

Learning Objectives

By the end of this section, you will be able to:

- Compare the structure of somatic and autonomic reflex arcs
- Explain the differences in sympathetic and parasympathetic reflexes
- Differentiate between short and long reflexes
- Determine the effect of the autonomic nervous system on the regulation of the various organ systems on the basis of the signalling molecules involved

The autonomic nervous system regulates organ systems through circuits that resemble the reflexes described in the somatic nervous system. The main difference between the somatic and autonomic systems is which target tissues are the effectors. Somatic responses are solely based on skeletal muscle contraction. The autonomic system, however, targets cardiac and smooth muscle, as well as glandular tissue. Whereas the basic circuit is a **reflex arc**, there are differences in the structure of those reflexes for the somatic and autonomic systems.

The Structure of Reflexes

One difference between a **somatic reflex**, such as the withdrawal reflex, and a **visceral reflex**, which is an autonomic reflex, is in the **efferent branch**. The output of a somatic reflex is the lower motor neuron in the ventral horn of the spinal cord that projects directly to a skeletal muscle to cause its contraction. The output of a visceral reflex is a two-step pathway starting with the preganglionic fibre emerging from a lateral horn neuron in the spinal cord, or a cranial nucleus neuron in the brain stem, to a ganglion—followed by the postganglionic fibre projecting to a target effector. The other part of a reflex, the **afferent branch**, is often the same between the two systems. Sensory neurons receiving input from the periphery—with cell bodies in the sensory ganglia, of either a cranial nerve or a dorsal root ganglion adjacent to the spinal cord—project into the CNS to initiate the reflex (Figure 15.5).

Afferent Branch

The afferent branch of a reflex arc differs between somatic and visceral reflexes in some instances. Many of the inputs to visceral reflexes are from special or somatic senses, but particular senses are associated with the viscera that are

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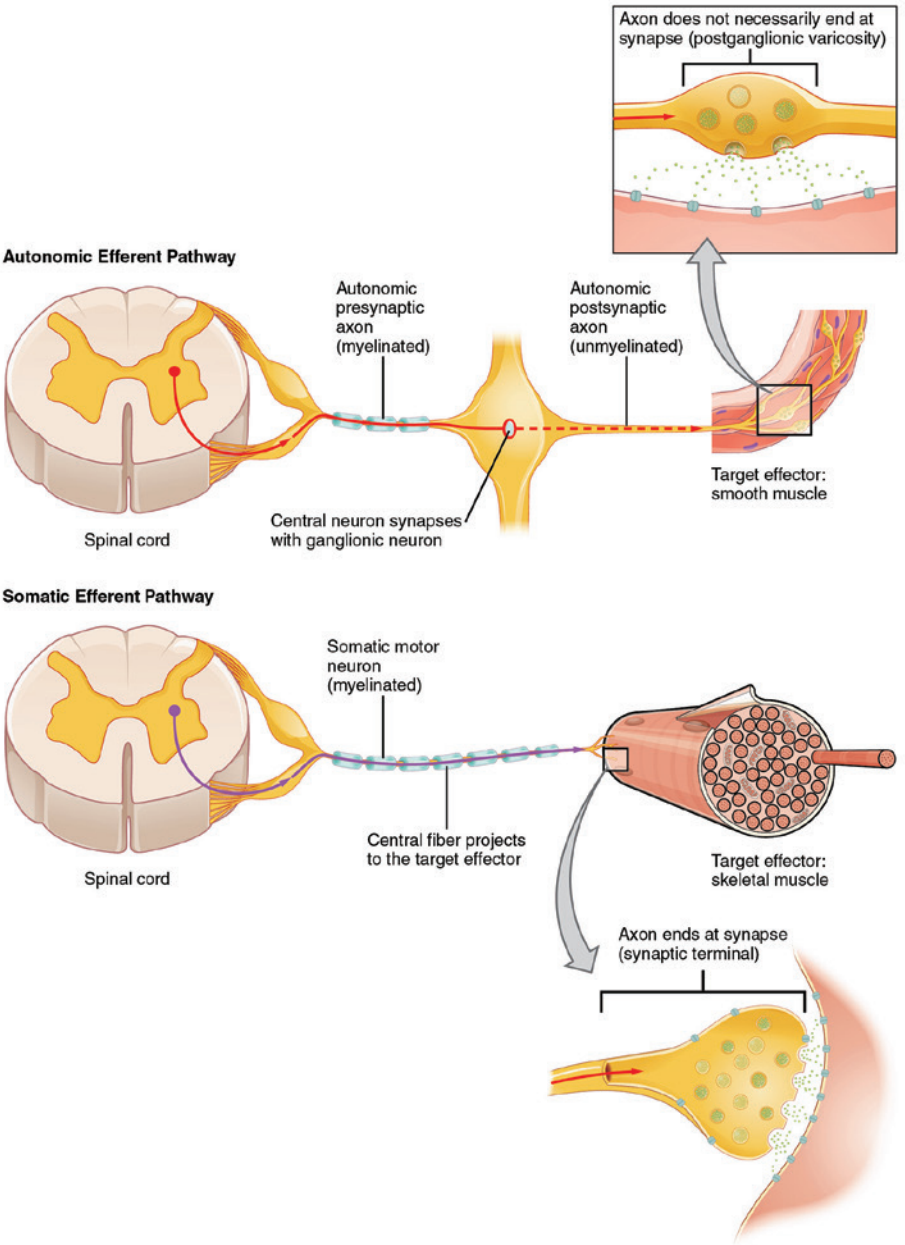


Figure 15.5 Comparison of Somatic and Visceral Reflexes. The afferent inputs to somatic and visceral reflexes are essentially the same, whereas the efferent branches are different. Somatic reflexes, for instance, involve a direct connection from the ventral horn of the spinal cord to the skeletal muscle. Visceral reflexes involve a projection from the central neuron to a ganglion, followed by a second projection from the ganglion to the target effector.

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not part of the conscious perception of the environment through the somatic nervous system. For example, there is a specific type of mechanoreceptor, called a **baroreceptor**, in the walls of the aorta and carotid sinuses that senses the stretch of those organs when blood volume or pressure increases. You do not have a conscious perception of having high blood pressure, but that is an important afferent branch of the cardiovascular and, particularly, vasomotor reflexes. The sensory neuron is essentially the same as any other general sensory neuron. The baroreceptor apparatus is part of the ending of a unipolar neuron that has a cell body in a sensory ganglion. The baroreceptors from the carotid arteries have axons in the glossopharyngeal nerve, and those from the aorta have axons in the vagus nerve.

Though visceral senses are not primarily a part of conscious perception, those sensations sometimes make it to conscious awareness. If a visceral sense is strong enough, it will be perceived. The sensory homunculus—the representation of the body in the primary somatosensory cortex—only has a small region allotted for the perception of internal stimuli. If you swallow a large bolus of food, for instance, you will probably feel the lump of that food as it pushes through your esophagus, or even if your stomach is distended after a large meal. If you inhale especially cold air, you can feel it as it enters your larynx and trachea. These sensations are not the same as feeling high blood pressure or high blood sugar levels.

When particularly strong visceral sensations rise to the level of conscious perception, the sensations are often felt in unexpected places. For example, strong visceral sensations of the heart will be felt as pain in the left shoulder and left arm. This irregular pattern of projection of conscious perception of visceral sensations is called **referred pain**.

Depending on the organ system affected, the referred pain will project to different areas of the body (Figure 15.6). The location of referred pain is not random, but a definitive explanation of the mechanism has not been established. The most broadly accepted theory for this phenomenon is that the visceral sensory fibres enter into the same level of the spinal cord as the somatosensory fibres of the referred pain location. By this explanation, the visceral sensory fibres from the mediastinal region, where the heart is located, would enter the spinal cord at the same level as the spinal nerves from the shoulder and arm, so the brain misinterprets the sensations from the mediastinal region as being from the axillary and brachial regions. Projections from the medial and inferior divisions of the cervical ganglia do enter the spinal cord at the middle to lower cervical levels, which is where the somatosensory fibres enter.

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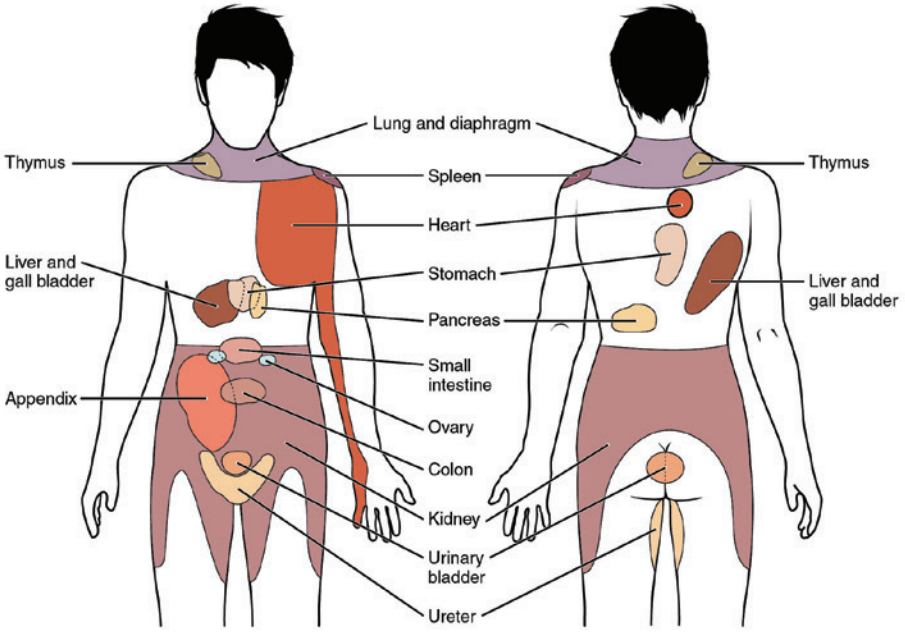


Figure 15.6 Referred Pain Chart. Conscious perception of visceral sensations maps to specific regions of the body, as shown in this chart. Some sensations are felt locally, whereas others are perceived as affecting areas that are quite distant from the involved organ.

Efferent Branch

The efferent branch of the visceral reflex arc begins with the projection from the central neuron along the preganglionic fibre. This fibre then makes a synapse on the ganglionic neuron that projects to the target effector.

The effector organs that are the targets of the autonomic system range from the iris and ciliary body of the eye to the urinary bladder and reproductive organs. The thoracolumbar output, through the various sympathetic ganglia, reaches all these organs. The cranial component of the parasympathetic system projects from the eye to part of the intestines. The sacral component reaches the majority of the large intestine and the pelvic organs of the urinary and reproductive systems.

Short and Long Reflexes

Somatic reflexes involve sensory neurons that connect sensory receptors to the CNS and motor neurons that project back out to the skeletal muscles. Visceral reflexes that involve the thoracolumbar or craniosacral systems share similar connections. However, there are reflexes that do not need to involve any CNS components. A **long reflex** has afferent branches that enter the spinal cord or brain and involve the efferent branches, as previously explained. A **short reflex**

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is completely peripheral and only involves the local integration of sensory input with motor output (Figure 15.7).

The difference between short and long reflexes is in the involvement of the CNS. Somatic reflexes always involve the CNS, even in a monosynaptic reflex in which the sensory neuron directly activates the motor neuron. That synapse is in the spinal cord or brain stem, so it has to involve the CNS. However, in the autonomic system, there is the possibility that the CNS is not involved. Because the efferent branch of a visceral reflex involves two neurons—the central neuron and the ganglionic neuron—a "short circuit" can be possible. If a sensory neuron projects directly to the ganglionic neuron and causes it to activate the effector target, then the CNS is not involved.

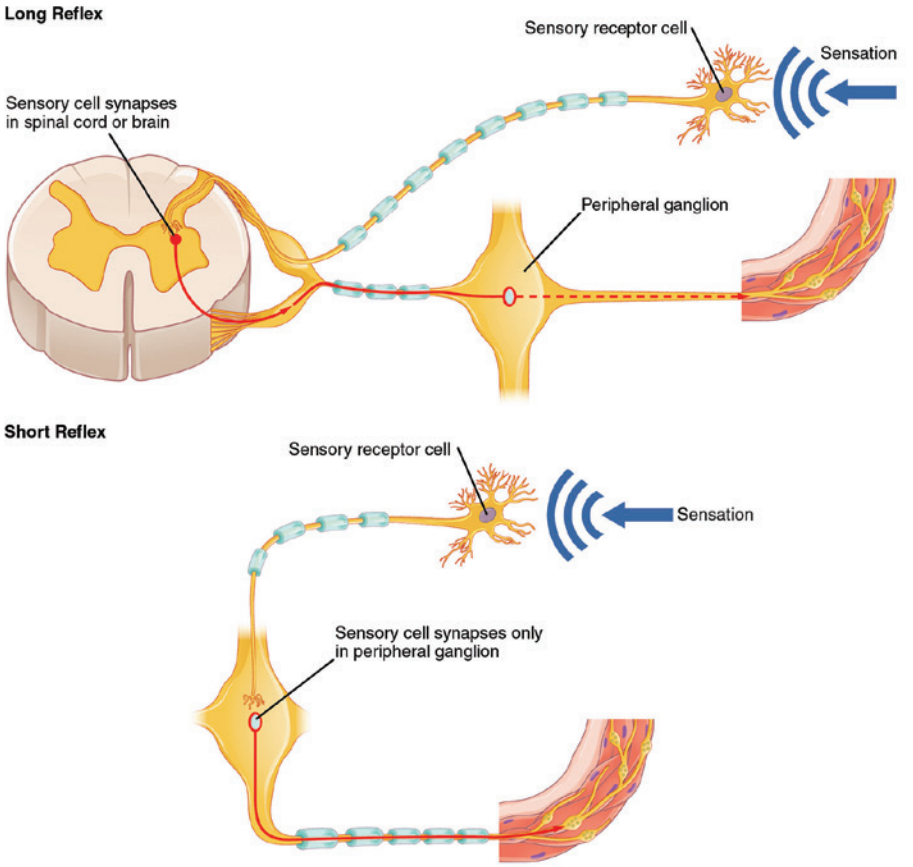


Figure 15.7 Short and Long Reflexes. Sensory input can stimulate either a short or a long reflex. A sensory neuron can project to the CNS or to an autonomic ganglion. The short reflex involves the direct stimulation of a postganglionic fibre by the sensory neuron, whereas the long reflex involves integration in the spinal cord or brain.

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A division of the nervous system that is related to the autonomic nervous system is the enteric nervous system. The word *enteric* refers to the digestive organs, so this represents the nervous tissue that is part of the digestive system. There are a few **myenteric plexuses** in which the nervous tissue in the wall of the digestive tract organs can directly influence digestive function. If stretch receptors in the stomach are activated by the filling and distension of the stomach, a short reflex will directly activate the smooth muscle fibres of the stomach wall to increase motility to digest the excessive food in the stomach. No CNS involvement is needed because the stretch receptor is directly activating a neuron in the wall of the stomach that causes the smooth muscle to contract. That neuron, connected to the smooth muscle, is a postganglionic parasympathetic neuron that can be controlled by a fibre found in the vagus nerve.

Interactive Link 15.3

Read this article (http://oer.aupress.ca/oer-202505/15.3) to learn about a teenager who experiences a series of spells that suggest a stroke. He undergoes endless tests and seeks input from multiple doctors. In the end, one expert, one question, and a simple blood pressure cuff answers the question. Why would the heart have to beat faster when the teenager changes his body position from lying down to sitting, and then to standing?

Balance in Competing Autonomic Reflex Arcs

The autonomic nervous system is important for homeostasis because its two divisions compete at the target effector. The balance of homeostasis is attributable to the competing inputs from the sympathetic and parasympathetic divisions (dual innervation). At the level of the target effector, the signal of which system is sending the message is strictly chemical. A signalling molecule binds to a receptor that causes changes in the target cell, which in turn causes the tissue or organ to respond to the changing conditions of the body.

Competing Neurotransmitters

The postganglionic fibres of the sympathetic and parasympathetic divisions both release neurotransmitters that bind to receptors on their targets. Postganglionic sympathetic fibres release norepinephrine, with a minor exception, whereas postganglionic parasympathetic fibres release ACh. For any given target, the difference in which division of the autonomic nervous system is

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exerting control is just in which chemical binds to its receptors. The target cells will have adrenergic and muscarinic receptors. If norepinephrine is released, it will bind to the adrenergic receptors present on the target cell, and if ACh is released, it will bind to the muscarinic receptors on the target cell.

In the sympathetic system, there are exceptions to this pattern of dual innervation. The postganglionic sympathetic fibres that contact the blood vessels within skeletal muscle and that contact sweat glands do not release norepinephrine; they release ACh. This does not create any problem because there is no parasympathetic input to the sweat glands. Sweat glands have muscarinic receptors and produce and secrete sweat in response to the presence of ACh.

At most of the other targets of the autonomic system, the effector response is based on which neurotransmitter is released and what receptor is present. For example, regions of the heart that establish heart rate are contacted by postganglionic fibres from both systems. If norepinephrine is released onto those cells, it binds to an adrenergic receptor that causes the cells to depolarize faster, and the heart rate increases. If ACh is released onto those cells, it binds to a muscarinic receptor that causes the cells to hyperpolarize so that they cannot reach threshold as easily, and the heart rate slows. Without this parasympathetic input, the heart would work at a rate of approximately 100 beats per minute (bpm). The sympathetic system speeds that up, as it would during exercise, to 120–140 bpm, for example. The parasympathetic system slows it down to the resting heart rate of 60–80 bpm.

Another example is in the control of pupillary size (Figure 15.8). The afferent branch responds to light hitting the retina. Photoreceptors are activated, and the signal is transferred to the retinal ganglion cells that send an action potential along the optic nerve into the diencephalon. If light levels are low, the sympathetic system sends a signal out through the upper thoracic spinal cord to the superior cervical ganglion of the sympathetic chain.

The postganglionic fibre then projects to the iris, where it releases norepinephrine onto the radial fibres of the iris (a smooth muscle). When those fibres contract, the pupil dilates—increasing the amount of light hitting the retina. If light levels are too high, the parasympathetic system sends a signal out from the Edinger-Westphal nucleus through the oculomotor nerve. This fibre synapses in the ciliary ganglion in the posterior orbit. The postganglionic fibre then projects to the iris, where it releases ACh onto the circular fibres of the iris—another smooth muscle. When those fibres contract, the pupil constricts to limit the amount of light hitting the retina.

In this example, the autonomic system is controlling how much light hits the retina. It is a homeostatic reflex mechanism that keeps the activation of photoreceptors within certain limits. In the context of avoiding a threat like

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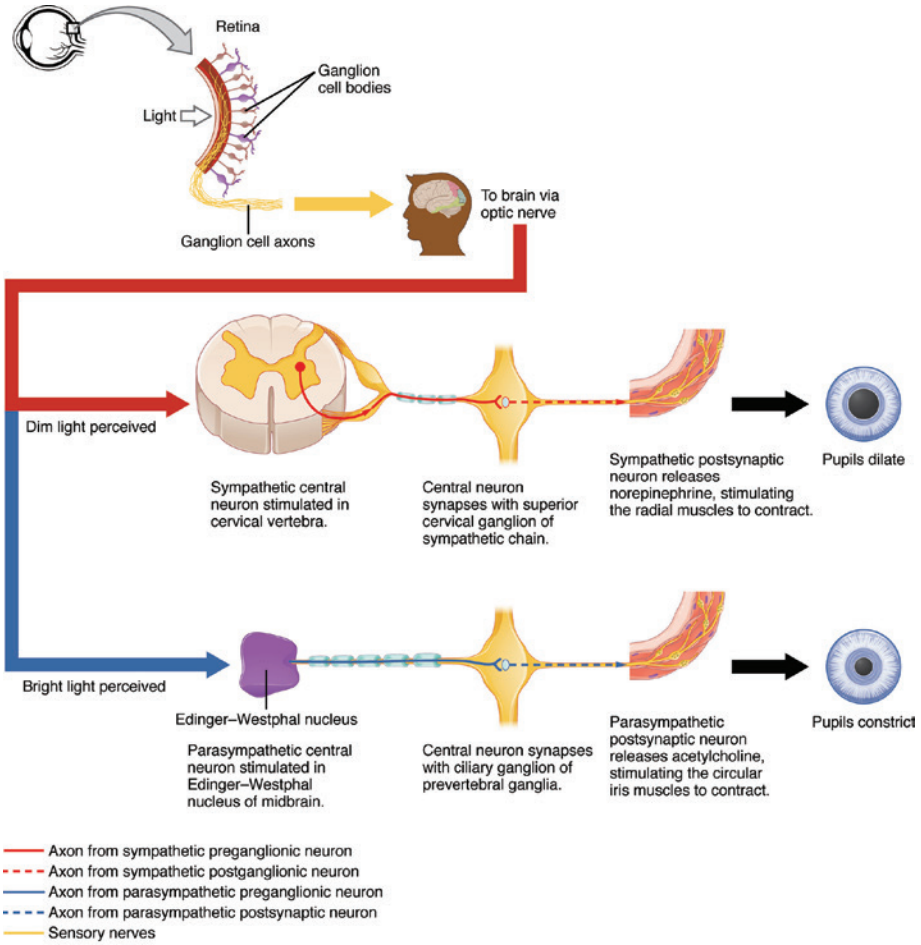


Figure 15.8 Autonomic Control of Pupillary Size. Activation of the pupillary reflex comes from the amount of light activating the retinal ganglion cells, as sent along the optic nerve. The output of the sympathetic system projects through the superior cervical ganglion, whereas the parasympathetic system originates in the midbrain and projects through the oculomotor nerve to the ciliary ganglion, which then projects to the iris. The postganglionic fibres of either division release neurotransmitters onto the smooth muscles of the iris to cause changes in the pupillary size. Norepinephrine results in dilation, and ACh results in constriction.

the lioness on the savannah, the sympathetic response for fight or flight will increase pupillary diameter so that more light hits the retina and more visual information is available for running away. Likewise, the parasympathetic response of rest reduces the amount of light reaching the retina, allowing the photoreceptors to cycle through bleaching and be regenerated for further visual perception; this is what the homeostatic process is attempting to maintain.

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Interactive Link 15.4

Watch this video (http://oer.aupress.ca/oer-202505/15.4) to learn about the pupillary reflexes. The pupillary light reflex involves sensory input through the optic nerve and motor response through the oculomotor nerve to the ciliary ganglion, which projects to the circular fibres of the iris. As shown in this short animation, pupils will constrict to limit the amount of light falling on the retina under bright lighting conditions. What constitutes the afferent and efferent branches of the competing reflex (dilation)?

Autonomic Tone

Organ systems are balanced between the input from the sympathetic and parasympathetic divisions. When something upsets that balance, the homeostatic mechanisms strive to return it to its regular state. For each organ system, there may be more of a sympathetic or parasympathetic tendency to the resting state, which is known as the **autonomic tone** of the system. For example, the heart rate was described in the Competing Neurotransmitters section. Because the resting heart rate is the result of the parasympathetic system slowing the heart down from its intrinsic rate of 100 bpm, the heart can be said to be in parasympathetic tone.

In a similar fashion, another aspect of the cardiovascular system is primarily under sympathetic control. Blood pressure is partially determined by the contraction of smooth muscle in the walls of blood vessels. These tissues have adrenergic receptors that respond to the release of norepinephrine from postganglionic sympathetic fibres by constricting and increasing blood pressure. The hormones released from the adrenal medulla—epinephrine and norepinephrine—will also bind to these receptors. Those hormones travel through the bloodstream, where they can easily interact with the receptors in the vessel walls. The parasympathetic system has no significant input to the systemic blood vessels, so the sympathetic system determines their tone.

There is a limited number of blood vessels that respond to sympathetic input in a different fashion. Blood vessels in skeletal muscle, particularly those in the lower limbs, are more likely to dilate. It does not have an overall effect on blood pressure to alter the tone of the vessels but rather allows for blood flow to increase for those skeletal muscles that will be active in the fight-or-flight response. The blood vessels that have a parasympathetic projection are limited to those in the erectile tissue of the reproductive organs. Acetylcholine released by these postganglionic parasympathetic fibres causes the vessels to dilate, leading to the engorgement of the erectile tissue.

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15.3 Central Control

Learning Objectives

By the end of this section, you will be able to:

- Describe the role of higher centres of the brain in autonomic regulation
- Explain the connection of the hypothalamus to homeostasis
- Describe the regions of the CNS that link the autonomic system with emotion
- Describe the pathways important to descending control of the autonomic system

The pupillary light reflex (Figure 15.9) begins when light hits the retina and causes a signal to travel along the optic nerve. This is visual sensation, because the afferent branch of this reflex is simply sharing the special sense pathway. Bright light hitting the retina leads to the parasympathetic response, through the oculomotor nerve, followed by the postganglionic fibre from the ciliary ganglion, which stimulates the circular fibres of the iris to contract and constrict the pupil. When light hits the retina in one eye, both pupils constrict. When that light is removed, both pupils dilate again back to the resting position. When

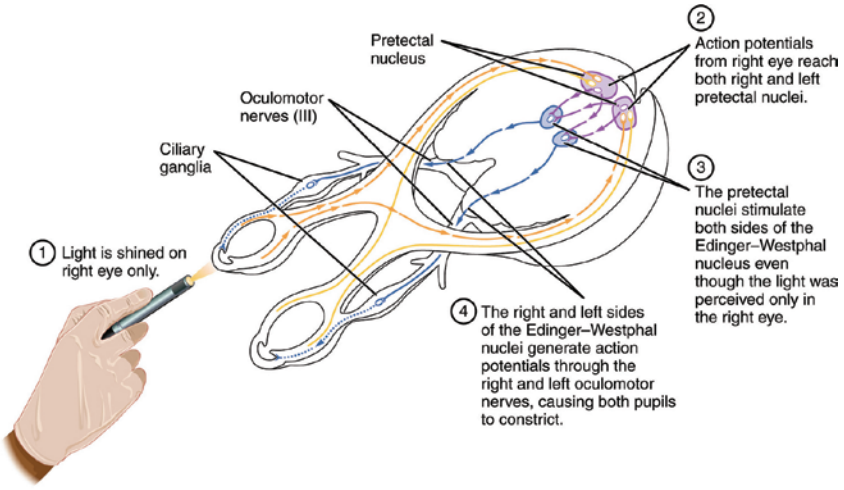


Figure 15.9 Pupillary Reflex Pathways. The pupil is under competing autonomic control in response to light levels hitting the retina. The sympathetic system will dilate the pupil when the retina is not receiving enough light, and the parasympathetic system will constrict the pupil when too much light hits the retina.

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the stimulus is unilateral (presented to only one eye), the response is bilateral (both eyes). The same is not true for somatic reflexes. If you touch a hot radiator, you only pull that arm back, not both. Central control of autonomic reflexes is different from that of somatic reflexes. The hypothalamus, along with other CNS locations, controls the autonomic system.

Forebrain Structures

Autonomic control is based on the visceral reflexes, composed of the afferent and efferent branches. These homeostatic mechanisms are based on the balance between the two divisions of the autonomic system, which results in tone for various organs that is based on the predominant input from the sympathetic or parasympathetic systems. Coordinating that balance requires integration that begins with forebrain structures like the hypothalamus and continues into the brain stem and spinal cord.

The Hypothalamus

The hypothalamus is the control centre for many homeostatic mechanisms. It regulates both autonomic function and endocrine function. The roles it plays in the pupillary reflexes demonstrate the importance of this control centre. The optic nerve projects primarily to the thalamus, which is the necessary relay to the occipital cortex for conscious visual perception. Another projection of the optic nerve, however, goes to the hypothalamus.

The Amygdala

The amygdala is a group of nuclei in the medial region of the temporal lobe that is part of the **limbic lobe**. The limbic lobe includes structures that are involved in emotional responses, as well as structures that contribute to memory function. The limbic lobe has strong connections with the hypothalamus and influences the state of its activity on the basis of emotional state. For example, when you are anxious or scared, the amygdala will send signals to the hypothalamus along the medial forebrain bundle that will stimulate the sympathetic fight-or-flight response. The hypothalamus will also stimulate the release of stress hormones through its control of the endocrine system in response to amygdala input.

The Medulla

The medulla contains nuclei referred to as the **cardiovascular centre**, which controls the smooth and cardiac muscle of the cardiovascular system through autonomic connections. When the homeostasis of the cardiovascular system

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shifts, such as when blood pressure changes, the coordination of the autonomic system can be accomplished within this region. Furthermore, when descending inputs from the hypothalamus stimulate this area, the sympathetic system can increase activity in the cardiovascular system, such as in response to anxiety or stress. The preganglionic sympathetic fibres that are responsible for increasing heart rate are referred to as the **cardiac accelerator nerves**, whereas the preganglionic sympathetic fibres responsible for constricting blood vessels compose the **vasomotor nerves**.

Several brain stem nuclei are important for the visceral control of major organ systems. One brain stem nucleus involved in cardiovascular function is the solitary nucleus. It receives sensory input about blood pressure and cardiac function from the glossopharyngeal and vagus nerves, and its output will activate sympathetic stimulation of the heart or blood vessels through the upper thoracic lateral horn. Another brain stem nucleus important for visceral control is the dorsal motor nucleus of the vagus nerve, which is the motor nucleus for the parasympathetic functions ascribed to the vagus nerve, including decreasing the heart rate, relaxing bronchial tubes in the lungs, and activating digestive function through the enteric nervous system. The nucleus ambiguus, which is named for its ambiguous histology, also contributes to the parasympathetic output of the vagus nerve and targets muscles in the pharynx and larynx for swallowing and speech, as well as contributing to the parasympathetic tone of the heart along with the dorsal motor nucleus of the vagus.

Interactive Link 15.5

Watch this video (http://oer.aupress.ca/oer-202505/15.5) to learn about physical responses to emotion. The autonomic system, which is important for regulating the homeostasis of the organ systems, is also responsible for our physiological responses to emotions such as fear. The video summarizes the extent of the body's reactions and describes several effects of the autonomic system in response to fear. On the basis of what you have already studied about autonomic function, which effect would you expect to be associated with parasympathetic, rather than sympathetic, activity?

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Interactive Link 15.6

Watch this video (http://oer.aupress.ca/oer-202505/15.6) to learn about the side effects of 3-D movies. As discussed in this video, movies that are shot in 3-D can cause motion sickness, which elicits the autonomic symptoms of nausea and sweating. The disconnection between the perceived motion on the screen and the lack of any change in equilibrium stimulates these symptoms. Why do you think sitting close to the screen or right in the middle of the theatre makes motion sickness during a 3-D movie worse?

Key Terms

acetylcholine (ACh): Neurotransmitter that binds at a motor end-plate to trigger depolarization.

adrenal medulla: Interior portion of the adrenal (or suprarenal) gland that releases epinephrine and norepinephrine into the bloodstream as hormones.

adrenergic: Synapse where norepinephrine is released, which binds to α- or β-adrenergic receptors.

afferent branch: Component of a reflex arc that represents the input from a sensory neuron, for either a special or general sense.

alpha (α)-adrenergic receptor: One of the receptors to which epinephrine and norepinephrine bind, which comes in two subtypes: α_1 and α_2.

autonomic tone: Tendency of an organ system to be governed by one division of the autonomic nervous system over the other, such as heart rate being lowered by parasympathetic input at rest.

baroreceptor: Mechanoreceptor that senses the stretch of blood vessels to indicate changes in blood pressure.

beta (β)-adrenergic receptor: One of the receptors to which epinephrine and norepinephrine bind, which comes in three subtypes: β_1, β_2, and β_3.

cardiac accelerator nerves: Preganglionic sympathetic fibres that cause the heart rate to increase when the cardiovascular centre in the medulla initiates a signal.

cardiovascular centre: Region in the medulla that controls the cardiovascular system through cardiac accelerator nerves and vasomotor nerves, which are components of the sympathetic division of the autonomic nervous system.

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celiac ganglion: One of the collateral ganglia of the sympathetic system that projects to the digestive system.

central neuron: The cell body of a neuron in the autonomic system that is located in the central nervous system, specifically the lateral horn of the spinal cord or a brain stem nucleus.

cholinergic: Synapse at which acetylcholine is released and binds to the nicotinic or muscarinic receptor.

chromaffin cells: Neuroendocrine cells of the adrenal medulla that release epinephrine and norepinephrine into the bloodstream as part of sympathetic system activity.

collateral ganglia: Ganglia outside of the sympathetic chain that are targets of sympathetic preganglionic fibres, which are the celiac, inferior mesenteric, and superior mesenteric ganglia.

craniosacral system: Alternate name for the parasympathetic division of the autonomic nervous system that is based on the anatomical location of central neurons in brain stem nuclei and the lateral horn of the sacral spinal cord; also referred to as craniosacral outflow.

efferent branch: Component of a reflex arc that represents the output, with the target being an effector, such as muscle or glandular tissue.

endogenous: Describes a substance made in the human body.

epinephrine: Signalling molecule released from the adrenal medulla into the bloodstream as part of the sympathetic response.

exogenous: Describes a substance made outside of the human body.

fight-or-flight response: Set of responses induced by sympathetic activity that lead to either fleeing a threat or standing up to it, which in the modern world is often associated with anxious feelings.

ganglionic neuron: Specifically refers to the cell body of a neuron in the autonomic system that is located in a ganglion.

greater splanchnic nerve: Nerve that contains fibres of the central sympathetic neurons that do not synapse in the chain ganglia but project onto the celiac ganglion.

grey rami communicantes (singular = ramus communicans): Unmyelinated structures that provide a short connection from a sympathetic chain ganglion to the spinal nerve that contains the postganglionic sympathetic fibre.

inferior mesenteric ganglion: One of the collateral ganglia of the sympathetic system that projects to the digestive system.

intramural ganglia: Terminal ganglia of the parasympathetic system that are found within the walls of the target effector.

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lesser splanchnic nerve: Nerve that contains fibres of the central sympathetic neurons that do not synapse in the chain ganglia but project onto the inferior mesenteric ganglion.

limbic lobe: Structures arranged around the edges of the cerebrum that are involved in memory and emotion.

long reflex: Reflex arc that includes the central nervous system.

muscarinic receptor: Type of acetylcholine receptor protein that is characterized by also binding to muscarine and is a metabotropic receptor.

myenteric plexuses: Nervous tissue in the wall of the digestive tract organs that can directly influence digestive function.

nicotinic receptor: Type of acetylcholine receptor protein that is characterized by also binding to nicotine and is an ionotropic receptor.

norepinephrine: Signalling molecule released as a neurotransmitter by most postganglionic sympathetic fibres as part of the sympathetic response, or as a hormone into the bloodstream from the adrenal medulla.

parasympathetic division: Division of the autonomic nervous system responsible for restful and digestive functions.

paravertebral ganglia: Autonomic ganglia superior to the sympathetic chain ganglia.

postganglionic fibre: Axon from a ganglionic neuron in the autonomic nervous system that projects to and synapses with the target effector; sometimes referred to as a postganglionic neuron.

preganglionic fibre: Axon from a central neuron in the autonomic nervous system that projects to and synapses with a ganglionic neuron; sometimes referred to as a preganglionic neuron.

prevertebral ganglia: Autonomic ganglia that are anterior to the vertebral column and functionally related to the sympathetic chain ganglia.

referred pain: The conscious perception of visceral sensation projected to a different region of the body, such as the left shoulder and arm pain as a sign of a heart attack.

reflex arc: Circuit of a reflex that involves a sensory input and motor output, or an afferent branch and an efferent branch, and an integrating centre to connect the two branches.

rest and digest: Set of functions associated with the parasympathetic system that lead to restful actions and digestion.

short reflex: Reflex arc that does not include any components of the central nervous system.

somatic reflex: Reflex involving skeletal muscle as the effector, under the control of the somatic nervous system.

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superior cervical ganglion: One of the paravertebral ganglia of the sympathetic system that projects to the head.

superior mesenteric ganglion: One of the collateral ganglia of the sympathetic system that projects to the digestive system.

sympathetic chain ganglia: Series of ganglia adjacent to the vertebral column that receive input from central sympathetic neurons.

sympathetic division: Division of the autonomic nervous system associated with the fight-or-flight response.

target effector: Organ, tissue, or gland that will respond to the control of an autonomic or somatic or endocrine signal.

terminal ganglia: Ganglia of the parasympathetic division of the autonomic system, which are located near or within the target effector, the latter also known as intramural ganglia.

thoracolumbar system: Alternate name for the sympathetic division of the autonomic nervous system that is based on the anatomical location of central neurons in the lateral horn of the thoracic.

varicosity: Structure of some autonomic connections that is not a typical synaptic end bulb, but a string of swellings along the length of a fibre that makes a network of connections with the target effector.

vasomotor nerves: Preganglionic sympathetic fibres that cause the constriction of blood vessels in response to signals from the cardiovascular centre.

visceral reflex: Reflex involving an internal organ as the effector, under the control of the autonomic nervous system.

white rami communicantes (singular = ramus communicans): Myelinated structures that provide a short connection from a sympathetic chain ganglion to the spinal nerve that contains the preganglionic sympathetic fibre.

Chapter Review

15.1 Divisions of the Autonomic Nervous System

The primary responsibilities of the autonomic nervous system are to regulate homeostatic mechanisms in the body, which is also part of what the endocrine system does. The key to understanding the autonomic system is to explore the response pathways—the output of the nervous system. The way we respond to the world around us, to manage the internal environment on the basis of the external environment, is divided between two parts of the autonomic nervous system. The sympathetic division responds to threats and produces a readiness to confront the threat or to run away: the fight-or-flight response. The

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parasympathetic division plays the opposite role. When the external environment does not present any immediate danger, a restful mode descends on the body, and the digestive system is more active.

The sympathetic output of the nervous system originates from the lateral horn of the thoracolumbar spinal cord. An axon from one of these central neurons projects by way of the ventral spinal nerve root and spinal nerve to a sympathetic ganglion, either in the sympathetic chain ganglia or one of the collateral locations, where it synapses on a ganglionic neuron.

These preganglionic fibres release ACh, which excites the ganglionic neuron through the nicotinic receptor. The axon from the ganglionic neuron—the postganglionic fibre—then projects to a target effector where it will release norepinephrine to bind to an adrenergic receptor, causing a change in the physiology of that organ in keeping with the broad, divergent sympathetic response. The postganglionic connections to sweat glands in the skin and blood vessels supplying and upper lumbar spinal cord skeletal muscle are, however, exceptions; those fibres release ACh onto muscarinic receptors. The sympathetic system has a specialized preganglionic connection to the adrenal medulla that causes epinephrine and norepinephrine to be released into the bloodstream rather than exciting a neuron that contacts an organ directly. This hormonal component means that the sympathetic chemical signal can spread throughout the body very quickly and affect many organ systems at once.

The parasympathetic output is based in the brain stem and sacral spinal cord. Neurons from particular nuclei in the brain stem or from the lateral horn of the sacral spinal cord (preganglionic neurons) project to terminal (intramural) ganglia located close to or within the wall of target effectors. These preganglionic fibres also release ACh onto nicotinic receptors to excite the ganglionic neurons. The postganglionic fibres then contact the target tissues within the organ to release ACh, which binds to muscarinic receptors to induce rest-and-digest responses.

Signalling molecules utilized by the autonomic nervous system are released from axons and can be considered as either neurotransmitters (when they directly interact with the effector) or as hormones (when they are released into the bloodstream). The same molecule, such as norepinephrine, could be considered either a neurotransmitter or a hormone on the basis of whether it is released from a postganglionic sympathetic axon or from the adrenal gland. The synapses in the autonomic system are not always the typical type of connection first described in the neuromuscular junction. Instead of having synaptic end bulbs at the very end of an axonal fibre, they may have swellings—called varicosities—along the length of a fibre so that it makes a network of connections within the target tissue.

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15.2 Autonomic Reflexes and Homeostasis

Autonomic nervous system function is based on the visceral reflex. This reflex is similar to the somatic reflex, but the efferent branch is composed of two neurons. The central neuron projects from the spinal cord or brain stem to synapse on the ganglionic neuron that projects to the effector. The afferent branch of the somatic and visceral reflexes is very similar, as many somatic and special senses activate autonomic responses. However, there are visceral senses that do not form part of conscious perception. If a visceral sensation, such as cardiac pain, is strong enough, it will rise to the level of consciousness. However, the sensory homunculus does not provide a representation of the internal structures to the same degree as the surface of the body, so visceral sensations are often experienced as referred pain, such as feelings of pain in the left shoulder and arm in connection with a heart attack.

The role of visceral reflexes is to maintain a balance of function in the organ systems of the body. The two divisions of the autonomic system each play a role in effecting change, usually in competing directions. The sympathetic system increases heart rate, whereas the parasympathetic system decreases heart rate. The sympathetic system dilates the pupil of the eye, whereas the parasympathetic system constricts the pupil. The competing inputs can contribute to the resting tone of the organ system. Heart rate is normally under parasympathetic tone, whereas blood pressure is normally under sympathetic tone. The heart rate is slowed by the autonomic system at rest, whereas blood vessels retain a slight constriction at rest.

In a few systems of the body, the competing input from the two divisions is not the norm. The sympathetic tone of blood vessels is caused by the lack of parasympathetic input to the systemic circulatory system. Only certain regions receive parasympathetic input that relaxes the smooth muscle wall of the blood vessels. Sweat glands are another example, which only receive input from the sympathetic system.

15.3 Central Control

The autonomic system integrates sensory information and higher cognitive processes to generate output, which balances homeostatic mechanisms. The central autonomic structure is the hypothalamus, which coordinates sympathetic and parasympathetic efferent pathways to regulate activities of the organ systems of the body. The majority of hypothalamic output travels through the medial forebrain bundle and the dorsal longitudinal fasciculus to influence the brain stem and spinal components of the autonomic nervous system. The medial forebrain bundle also connects the hypothalamus with higher centres of

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the limbic system, where emotion can influence visceral responses. The amygdala is a structure within the limbic system that influences the hypothalamus in the regulation of the autonomic system as well as the endocrine system.

These higher centres have descending control of the autonomic system through brain stem centres, primarily in the medulla, such as the cardiovascular centre. This collection of medullary nuclei regulates cardiac function, as well as blood pressure. Sensory inputs from the heart, aorta, and carotid sinuses project to these regions of the medulla. The solitary nucleus increases sympathetic tone of the cardiovascular system through the cardiac accelerator and vasomotor nerves. The nucleus ambiguus and the dorsal motor nucleus both contribute fibres to the vagus nerve, which exerts parasympathetic control of the heart by decreasing heart rate.

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16

The Endocrine System

Chapter Objectives

After studying this chapter, you will be able to:

- Identify the contributions of the endocrine system to homeostasis
- Discuss the chemical composition of hormones and the mechanisms of hormone action
- Summarize the site of production, regulation, and effects of the hormones of the pituitary, thyroid, parathyroid, adrenal, and pineal glands
- Discuss the hormonal regulation of the reproductive system
- Explain the role of the pancreatic endocrine cells in the regulation of blood glucose
- Identify the hormones released by the heart, kidneys, and other organs with secondary endocrine functions
- Discuss several common diseases associated with endocrine system dysfunction

You may never have thought of it this way, but when you send a text message to two friends to meet you at the dining hall at six, you're sending digital signals that (you hope) will affect their behaviour—even though they are some distance away. Similarly, certain cells send chemical signals to other cells in the body that influence their behaviour. This long-distance intercellular communication, coordination, and control is critical for homeostasis, and it is the fundamental function of the endocrine system.

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16.1 An Overview of the Endocrine System

Learning Objectives

By the end of this section, you will be able to:

- Distinguish the types of intercellular communication, their importance, mechanisms, and effects of hormones
- Identify the major organs and tissues of the endocrine system and their location in the body

Communication is a process in which a sender transmits signals to one or more receivers to control and coordinate actions. In the human body, two major organ systems participate in relatively "long-distance" communication: the nervous system and the endocrine system. Together, these two systems are primarily responsible for maintaining homeostasis in the body.

Neural and Endocrine Signalling

The nervous system uses two types of intercellular communication—electrical and chemical signalling—either by the direct action of an electrical potential or, in the latter case, through the action of chemical neurotransmitters such as serotonin or norepinephrine. Neurotransmitters act locally and rapidly. When an electrical signal in the form of an action potential arrives at the synaptic terminal, it diffuses across the synaptic cleft (the gap between a sending neuron and a receiving neuron or muscle cell). Once the neurotransmitters interact (bind) with receptors on the receiving (postsynaptic) cell, the receptor stimulation is transduced into a response such as continued electrical signalling or modification of cellular response. The target cell responds within milliseconds of receiving the chemical "message"; this response then ceases very quickly once the neural signalling ends. In this way, neural communication enables body functions that involve quick, brief actions, such as movement, sensation, and cognition. In contrast, the **endocrine system** uses just one method of communication: chemical signalling. These signals are sent by the endocrine organs, which secrete chemicals—the **hormone**—into the extracellular fluid.

Hormones are transported primarily via the bloodstream throughout the body, where they bind to receptors on target cells, inducing a characteristic response. As a result, endocrine signalling requires more time than neural signalling to prompt a response in target cells, though the precise amount of time varies with different hormones. For example, when you are confronted with a dangerous

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or frightening situation, the fight-or-flight response is initiated, triggering the release of adrenal hormones—epinephrine and norepinephrine—within seconds. In contrast, it may take up to 48 hours for target cells to respond to certain reproductive hormones.

Interactive Link 16.1

Visit this link (http://oer.aupress.ca/oer-202505/16.1) to watch an animation of the events that occur when a hormone binds to a cell membrane receptor. What is the secondary messenger made by adenylyl cyclase during the activation of liver cells by epinephrine?

In addition, endocrine signalling is typically less specific than neural signalling. The same hormone may play a role in a variety of different physiological processes depending on the target cells involved. For example, the hormone oxytocin promotes uterine contractions in people in labour. It is also important in breastfeeding and may be involved in the sexual response and in feelings of emotional attachment in humans.

In general, the nervous system involves quick responses to rapid changes in the external environment, and the endocrine system is usually slower acting—taking care of the internal environment of the body, maintaining homeostasis, and controlling reproduction (Table 16.1).

Table 16.1 Endocrine and Nervous Systems

	Endocrine system	Nervous system
Signalling mechanism(s)	Chemical	Chemical/electrical
Primary chemical signal	Hormones	Neurotransmitters
Distance travelled	Long or short	Always short
Response time	Fast or slow	Always fast
Environment targeted	Internal	Internal and external

Structures of the Endocrine System

The endocrine system consists of cells, tissues, and organs that secrete hormones as a primary or secondary function. The **endocrine gland** is the major player in this system. The primary function of these ductless glands is to secrete their hormones directly into the surrounding fluid. The interstitial fluid and the

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blood vessels then transport the hormones throughout the body. The endocrine system includes the pituitary, thyroid, parathyroid, adrenal, and pineal glands (Figure 16.1). Some of these glands have both endocrine and nonendocrine functions. For example, the pancreas contains cells that function in digestion (nonendocrine) as well as cells that secrete the hormones insulin and glucagon, which regulate blood glucose levels. The hypothalamus, thymus, heart, kidneys, stomach, small intestine, liver, skin, ovaries, and testes are other organs that contain cells with endocrine functions. Moreover, adipose tissue has long been known to produce hormones, and recent research has revealed that even bone tissue has endocrine functions.

The ductless endocrine glands are not to be confused with the body's **exocrine system**, whose glands release their secretions through ducts that deliver the secretions to specific destinations (e.g., to the surface of the skin). Examples of exocrine glands include the sebaceous and sweat glands of the skin. As just noted, the pancreas also has an exocrine function: Most of its cells secrete pancreatic juice through the pancreatic and accessory ducts to the lumen of the small intestine.

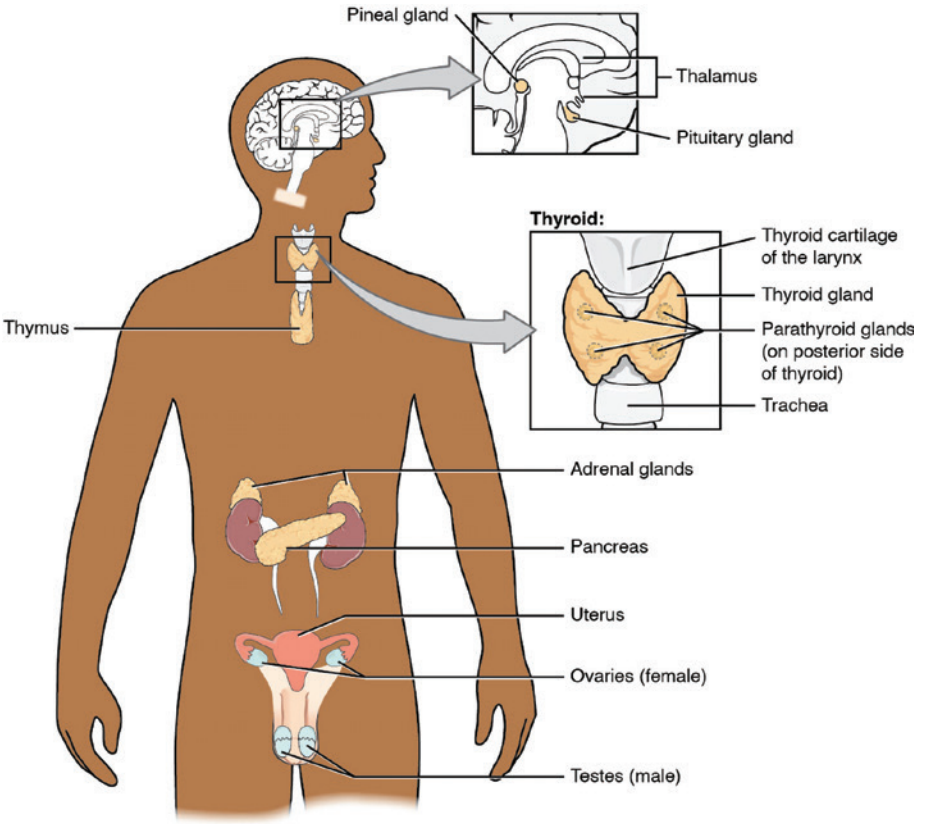


Figure 16.1 Endocrine System. Endocrine glands and cells are located throughout the body and play an important role in homeostasis.

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Other Types of Chemical Signalling

In endocrine signalling, hormones secreted into the extracellular fluid diffuse into the blood or lymph and can then travel great distances throughout the body. In contrast, autocrine signalling takes place within the same cell. An **autocrine** is a chemical that elicits a response in the same cell that secreted it. Interleukin-1, or IL-1, is a signalling molecule that plays an important role in inflammatory response. The cells that secrete IL-1 have receptors on their cell surface that bind these molecules, resulting in autocrine signalling.

Local intercellular communication is the province of the **paracrine**, also called a paracrine factor, which is a chemical that induces a response in neighbouring cells. Although paracrines may enter the bloodstream, their concentration is generally too low to elicit a response from distant tissues. A familiar example to those with asthma is histamine, a paracrine that is released by immune cells in the bronchial tree. Histamine causes the smooth muscle cells of the bronchi to constrict, narrowing the airways. Another example is the neurotransmitters of the nervous system, which act only locally within the synaptic cleft.

16.2 Hormones

Learning Objectives

By the end of this section, you will be able to:

- Identify the three major classes of hormones on the basis of chemical structure
- Compare and contrast intracellular and cell membrane hormone receptors
- Describe signalling pathways that involve cAMP and IP3
- Identify several factors that influence a target cell's response
- Discuss the role of feedback loops and humoral, hormonal, and neural stimuli in hormone control

Although a given hormone may travel throughout the body in the bloodstream, it will affect the activity only of its target cells—that is, cells with receptors for that particular hormone. Once the hormone binds to the receptor, a chain of events is initiated that leads to the target cell's response. Hormones play a critical role in the regulation of physiological processes because of the target cell responses they regulate. These responses contribute to human reproduction, growth and

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development of body tissues, metabolism, fluid and electrolyte balance, sleep, and many other body functions. The major hormones of the human body and their effects are identified in Table 16.2.

Types of Hormones

The hormones of the human body can be divided into two major groups on the basis of their chemical structure. Hormones derived from amino acids include amines, peptides, and proteins. Those derived from lipids include steroids (Figure 16.2). These chemical groups affect a hormone's distribution, the type of receptors it binds to, and other aspects of its function.

Amine Hormones

Hormones derived from the modification of amino acids are referred to as amine hormones. Amine hormones are synthesized from the amino acids tryptophan or tyrosine. An example of a hormone derived from tryptophan is melatonin, which is secreted by the pineal gland and helps regulate circadian rhythm. Tyrosine derivatives include the metabolism-regulating thyroid hormones, as well as the catecholamines, such as epinephrine, norepinephrine, and dopamine. Epinephrine and norepinephrine are secreted by the adrenal medulla and play a role in the fight-or-flight response, whereas dopamine is secreted by the hypothalamus and inhibits the release of certain anterior pituitary hormones.

Peptide and Protein Hormones

Whereas the amine hormones are derived from a single amino acid, peptide and protein hormones consist of multiple amino acids that link to form an amino acid chain. Peptide hormones consist of short chains of amino acids, whereas protein hormones are longer polypeptides. Both types are synthesized like other body proteins: DNA is transcribed into mRNA, which is translated into an amino acid chain. Examples of peptide hormones include antidiuretic hormone (ADH), a pituitary hormone important in fluid balance, and atrial natriuretic peptide, which is produced by the heart and helps decrease blood pressure. Some examples of protein hormones include growth hormone, which is produced by the pituitary gland, and follicle-stimulating hormone (FSH), which has an attached carbohydrate group and is thus classified as a glycoprotein. FSH helps stimulate the maturation of eggs in the ovaries and sperm in the testes.

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Table 16.2 Endocrine Glands and Their Major Hormones

Endocrine gland	Associated hormones	Chemical class	Effect
Pituitary (anterior)	Growth hormone (GH)	Protein	Promotes growth of body tissues
Pituitary (anterior)	Prolactin (PRL)	Peptide	Promotes milk production
Pituitary (anterior)	Thyroid-stimulating hormone (TSH)	Glycoprotein	Stimulates thyroid hormone release
Pituitary (anterior)	Adrenocorticotropic hormone (ACTH)	Peptide	Stimulates hormone release by adrenal cortex
Pituitary (anterior)	Follicle-stimulating hormone (FSH)	Glycoprotein	Stimulates gamete production
Pituitary (anterior)	Luteinizing hormone (LH)	Glycoprotein	Stimulates androgen production by gonads
Pituitary (posterior)	Antidiuretic hormone (ADH)	Peptide	Stimulates water reabsorption by kidneys
Pituitary (posterior)	Oxytocin	Peptide	Stimulates uterine contractions during childbirth
Thyroid	Thyroxine (T_4), triiodothyronine (T_3)	Amine	Stimulates basal metabolic rate
Thyroid	Calcitonin	Peptide	Reduces blood Ca^{2+} levels
Parathyroid	Parathyroid hormone (PTH)	Peptide	Increases blood Ca^{2+} levels
Adrenal (cortex)	Aldosterone	Steroid	Increases blood Na^{+} levels
Adrenal (cortex)	Cortisol, corticosterone, cortisone	Steroid	Increases blood glucose levels
Adrenal (medulla)	Epinephrine, norepinephrine	Amine	Stimulates fight-or-flight response
Pineal	Melatonin	Amine	Regulates sleep cycles
Pancreas	Insulin	Protein	Reduces blood glucose levels
Pancreas	Glucagon	Protein	Increases blood glucose levels
Testes	Testosterone	Steroid	Stimulates development of sex characteristics including a deeper voice, increased muscle mass, development of body hair, and sperm production
Ovaries	Estrogens and progesterone	Steroid	Stimulates development of sex characteristics including the development of adipose and breast tissue and prepares the body for childbirth

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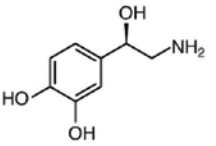
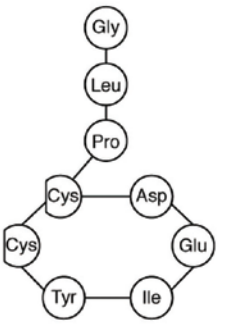
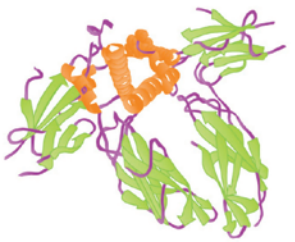
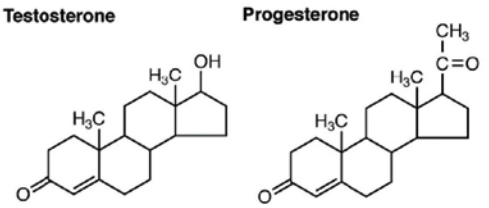
Hormone Class	Components	Example(s)
Amine Hormone	Amino acids with modified groups (e.g. norepinephrine's carboxyl group is replaced with a benzene ring)	**Norepinephrine** 
Peptide Hormone	Short chains of linked amino acids	**Oxytocin** 
Protein Hormone	Long chains of linked amino acids	**Human Growth Hormone** 
Steroid Hormones	Derived from the lipid cholesterol	**Testosterone** **Progesterone** 

Figure 16.2 **Amine, Peptide, Protein, and Steroid Hormone Structure.**

Steroid Hormones

The primary hormones derived from lipids are steroids. Steroid hormones are derived from the lipid cholesterol. For example, the reproductive hormones testosterone and estrogen—which are produced by the gonads (testes and ovaries)—are steroid hormones. The adrenal glands produce the steroid hormone aldosterone, which is involved in osmoregulation, and cortisol, which plays a role in metabolism.

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Like cholesterol, steroid hormones are not soluble in water (they are hydrophobic). Because blood is water based, lipid-derived hormones must travel to their target cell bound to a transport protein. This more complex structure extends the half-life of steroid hormones much longer than that of hormones derived from amino acids. A hormone's half-life is the time required for half the concentration of the hormone to be degraded. For example, the lipid-derived hormone cortisol has a half-life of approximately 60 to 90 minutes. In contrast, the amino acid–derived hormone epinephrine has a half-life of approximately 1 minute.

Pathways of Hormone Action

The message a hormone sends is received by a **hormone receptor**, a protein located either inside the cell or within the cell membrane. The receptor will process the message by initiating other signalling events or cellular mechanisms that result in the target cell's response. Hormone receptors recognize molecules with specific shapes and side groups and respond only to those hormones that are recognized. The same type of receptor may be located on cells in different body tissues and trigger somewhat different responses. Thus, the response triggered by a hormone depends not only on the hormone but also on the target cell.

Once the target cell receives the hormone signal, it can respond in a variety of ways. The response may include the stimulation of protein synthesis, activation or deactivation of enzymes, alteration in the permeability of the cell membrane, altered rates of mitosis and cell growth, and stimulation of the secretion of products. Moreover, a single hormone may be capable of inducing different responses in a given cell.

Pathways Involving Intracellular Hormone Receptors

Intracellular hormone receptors are located inside the cell. Hormones that bind to this type of receptor must be able to cross the cell membrane. Steroid hormones are derived from cholesterol and therefore can readily diffuse through the lipid bilayer of the cell membrane to reach the intracellular receptor (Figure 16.3). Thyroid hormones cross the cell membrane by a specific carrier-mediated mechanism that is energy and Na^+ dependent.

The location of steroid and thyroid hormone binding differs slightly: A steroid hormone may bind to its receptor within the cytosol or within the nucleus. In either case, this binding generates a hormone-receptor complex that moves toward the chromatin in the cell nucleus and binds to a particular segment of the cell's DNA. In contrast, thyroid hormones bind to receptors already bound to DNA. For both steroid and thyroid hormones, binding of the

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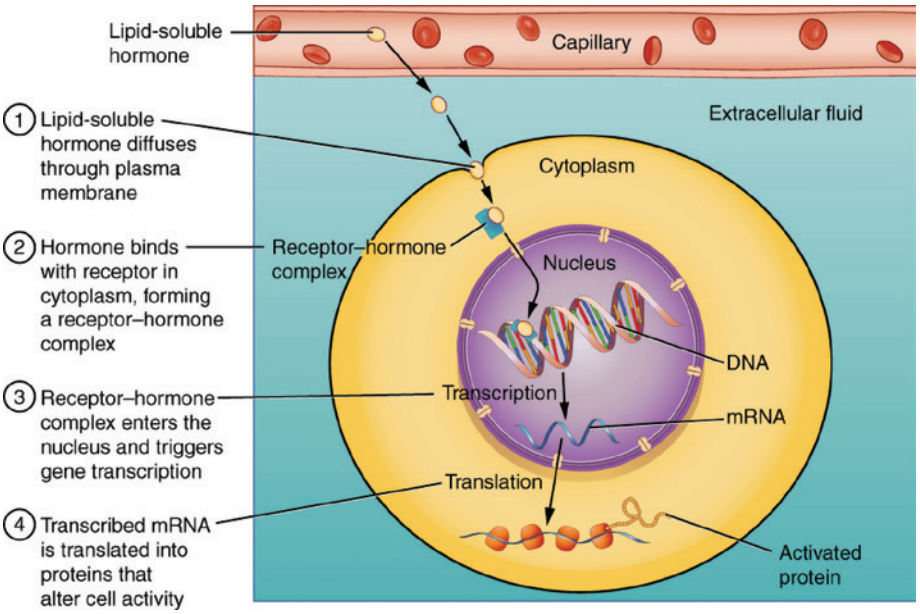


Figure 16.3 Binding of Lipid-Soluble Hormones. A steroid hormone directly initiates the production of proteins within a target cell. Steroid hormones easily diffuse through the cell membrane. The hormone binds to its receptor in the cytosol, forming a receptor-hormone complex. The receptor-hormone complex then enters the nucleus and binds to the target gene on the DNA. Transcription of the gene creates a messenger RNA that is translated into the desired protein within the cytoplasm.

hormone-receptor complex with DNA triggers transcription of a target gene to mRNA, which moves to the cytosol and directs protein synthesis by ribosomes.

Pathways Involving Cell Membrane Hormone Receptors

Hydrophilic, or water-soluble, hormones are unable to diffuse through the lipid bilayer of the cell membrane and must therefore pass on their message to a receptor located at the surface of the cell. Except for thyroid hormones, which are lipid soluble, all amino acid–derived hormones bind to cell membrane receptors that are located, at least in part, on the extracellular surface of the cell membrane. Therefore, they do not directly affect the transcription of target genes but instead initiate a signalling cascade that is carried out by a molecule called a **second messenger**. In this case, the hormone is called a **first messenger**.

The second messenger used by most hormones is **cyclic adenosine monophosphate** (**cAMP**). In the cAMP second messenger system, a water-soluble hormone binds to its receptor in the cell membrane (Step 1 in Figure 16.4). This receptor is associated with an intracellular component called a **G protein**, and binding of the hormone activates the G-protein component (Step 2). The activated G protein in turn activates an enzyme called **adenylyl cyclase**, also

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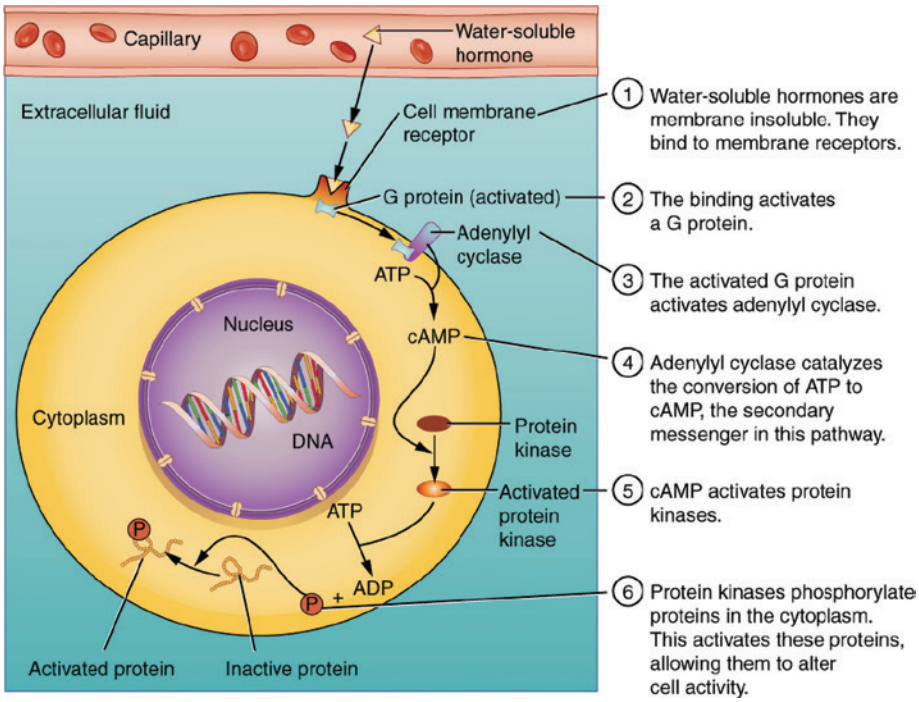


Figure 16.4 Binding of Water-Soluble Hormones. Water-soluble hormones cannot diffuse through the cell membrane. These hormones must bind to a surface cell-membrane receptor. The receptor then initiates a cell-signalling pathway within the cell involving G proteins, adenylyl cyclase, the secondary messenger cyclic AMP (cAMP), and protein kinases. In the final step, these protein kinases phosphorylate proteins in the cytoplasm. This activates proteins in the cell that carry out the changes specified by the hormone.

known as adenylate cyclase (Step 3), which converts adenosine triphosphate (ATP) to cAMP (Step 4). As the second messenger, cAMP activates a type of enzyme called a **protein kinase** that is present in the cytosol (Step 5).

Activated protein kinases initiate a phosphorylation cascade, in which multiple protein kinases phosphorylate (add a phosphate group to) numerous and various cellular proteins, including other enzymes (Step 6).

Factors Affecting Target Cell Response

You will recall that target cells must have receptors specific to a given hormone if that hormone is to trigger a response. But several other factors influence the target cell response. For example, the presence of a significant level of a hormone circulating in the bloodstream can cause its target cells to decrease their number of receptors for that hormone. This process is called **downregulation**, and it allows cells to become less reactive to the excessive hormone levels. When the level of a hormone is chronically reduced, target cells engage in **upregulation** to increase their number of receptors. This process allows cells

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to be more sensitive to the hormone that is present. Cells can also alter the sensitivity of the receptors themselves to various hormones.

Two or more hormones can interact to affect the response of cells in a variety of ways. The three most common types of interaction are as follows:

- The permissive effect, in which the presence of one hormone enables another hormone to act. For example, thyroid hormones have complex permissive relationships with certain reproductive hormones. A dietary deficiency of iodine, a component of thyroid hormones, can therefore affect reproductive system development and functioning.
- The synergistic effect, in which two hormones with similar effects produce an amplified response. In some cases, two hormones are required for an adequate response. For example, two different reproductive hormones—FSH from the pituitary gland and estrogens from the ovaries—are required for the maturation of female ova (egg cells).
- The antagonistic effect, in which two hormones have opposing effects. A familiar example is the effect of two pancreatic hormones, insulin and glucagon. Insulin increases the liver's storage of glucose as glycogen, decreasing blood glucose, whereas glucagon stimulates the breakdown of glycogen stores, increasing blood glucose.

Regulation of Hormone Secretion

To prevent abnormal hormone levels and a potential disease state, hormone levels must be tightly controlled. The body maintains this control by balancing hormone production and degradation. Feedback loops govern the initiation and maintenance of most hormone secretion in response to various stimuli.

Role of Feedback Loops

The contribution of feedback loops to homeostasis will only be briefly reviewed here. Positive feedback loops are characterized by the release of additional hormones in response to an original hormone release. The release of oxytocin during childbirth is a positive feedback loop. The initial release of oxytocin begins to signal the uterine muscles to contract, which pushes the fetus toward the cervix, causing it to stretch. This, in turn, signals the pituitary gland to release more oxytocin, causing labour contractions to intensify. The release of oxytocin decreases after the birth of the child.

The more common method of hormone regulation is the negative-feedback loop. Negative feedback is characterized by the inhibition of further secretion

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of a hormone in response to adequate levels of that hormone. This allows blood levels of the hormone to be regulated within a narrow range. An example of a negative-feedback loop is the release of glucocorticoid hormones from the adrenal glands as directed by the hypothalamus and pituitary gland. As glucocorticoid concentrations in the blood rise, the hypothalamus and pituitary gland reduce their signalling to the adrenal glands to prevent additional glucocorticoid secretion (Figure 16.5).

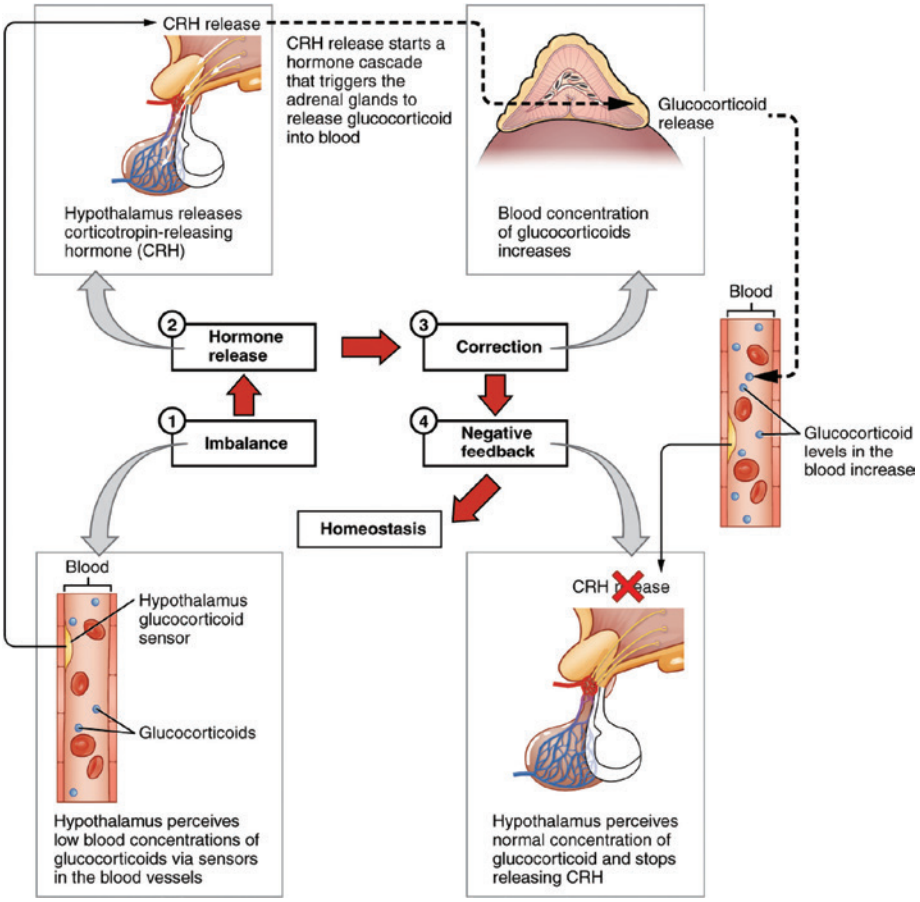


Figure 16.5 Negative-Feedback Loop. The release of adrenal glucocorticoids is stimulated by the release of hormones from the hypothalamus and pituitary gland. This signalling is inhibited when glucocorticoid levels become elevated by causing negative signals to the pituitary gland and hypothalamus.

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Role of Endocrine Gland Stimuli

Reflexes triggered by both chemical and neural stimuli control endocrine activity. These reflexes may be simple, involving only one hormone response, or they may be more complex and involve many hormones, as is the case with the hypothalamic control of various anterior pituitary–controlled hormones.

Humoral stimuli are changes in blood levels of nonhormone chemicals, such as nutrients or ions, that cause the release or inhibition of a hormone to, in turn, maintain homeostasis. For example, osmoreceptors in the hypothalamus detect changes in blood osmolarity (the concentration of solutes in the blood plasma). If blood osmolarity is too high, meaning that the blood is not dilute enough, osmoreceptors signal the hypothalamus to release ADH. The hormone causes the kidneys to reabsorb more water and reduce the volume of urine produced. This reabsorption causes a reduction of the osmolarity of the blood, diluting the blood to the appropriate level. The regulation of blood glucose is another example. High blood glucose levels cause the release of insulin from the pancreas, which increases glucose uptake by cells and liver storage of glucose as glycogen.

An endocrine gland may also secrete a hormone in response to the presence of another hormone produced by a different endocrine gland. Such hormonal stimuli often involve the hypothalamus, which produces releasing and inhibiting hormones that control the secretion of a variety of pituitary hormones.

In addition to these chemical signals, hormones can also be released in response to neural stimuli. A common example of neural stimuli is the activation of the fight-or-flight response by the sympathetic nervous system. When an individual perceives danger, sympathetic neurons signal the adrenal glands to secrete norepinephrine and epinephrine. The two hormones dilate blood vessels, increase the heart and respiratory rate, and suppress the digestive and immune systems. These responses boost the body's transport of oxygen to the brain and muscles, thereby improving the body's ability to fight or flee.

16.3 The Pituitary Gland and Hypothalamus

Learning Objectives

By the end of this section, you will be able to:

- Explain the interrelationships of the anatomy and functions of the hypothalamus and the posterior and anterior lobes of the pituitary gland

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- Identify the two hormones released from the posterior pituitary, their target cells, and their principal actions
- Identify the six hormones produced by the anterior lobe of the pituitary gland, their target cells, their principal actions, and their regulation by the hypothalamus

The hypothalamus-pituitary complex can be thought of as the "command centre" of the endocrine system. This complex secretes several hormones that directly produce responses in target tissues as well as hormones that regulate the synthesis and secretion of hormones of other glands. In addition, the hypothalamus-pituitary complex coordinates the messages of the endocrine and nervous systems. In many cases, a stimulus received by the nervous system must pass through the hypothalamus-pituitary complex to be translated into hormones that can initiate a response.

The **hypothalamus** is a structure of the diencephalon of the brain located anterior and inferior to the thalamus (Figure 16.6). It has both neural and endocrine functions, producing and secreting many hormones. In addition, the hypothalamus is anatomically and functionally related to the **pituitary gland** (or hypophysis), a bean-sized organ suspended from it by a stem called the **infundibulum** (or pituitary stalk). The pituitary gland is cradled within the sella

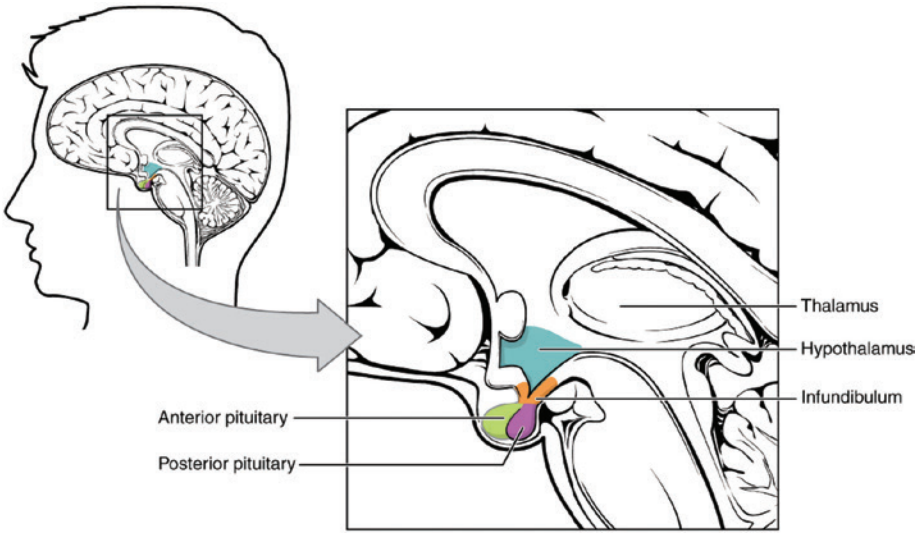


Figure 16.6 Hypothalamus-Pituitary Complex. The hypothalamus region lies inferior and anterior to the thalamus. It connects to the pituitary gland by the stalk-like infundibulum. The pituitary gland consists of an anterior and posterior lobe, with each lobe secreting different hormones in response to signals from the hypothalamus.

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turcica of the sphenoid bone of the skull. It consists of two lobes that arise from distinct parts of embryonic tissue: The **posterior pituitary** (**neurohypophysis**) is neural tissue, whereas the **anterior pituitary** (**adenohypophysis**) is glandular tissue that develops from the primitive digestive tract. The hormones secreted by the posterior and anterior pituitary and the intermediate zone between the lobes are summarized in Table 16.3.

Table 16.3 Pituitary Hormones

Pituitary lobe	Associated hormones	Chemical class	Effect
Anterior	Growth hormone (GH)	Protein	Promotes growth of body tissues
Anterior	Prolactin (PRL)	Peptide	Promotes milk production from mammary glands
Anterior	Thyroid-stimulating hormone (TSH)	Glycoprotein	Stimulates thyroid hormone release from thyroid
Anterior	Adrenocorticotropic hormone (ACTH)	Peptide	Stimulates hormone release by adrenal cortex
Anterior	Follicle-stimulating hormone (FSH)	Glycoprotein	Stimulates gamete production in gonads
Anterior	Luteinizing hormone (LH)	Glycoprotein	Stimulates androgen production by gonads
Posterior	Antidiuretic hormone (ADH)	Peptide	Stimulates water reabsorption by kidneys
Posterior	Oxytocin	Peptide	Stimulates uterine contractions during childbirth
Intermediate zone	Melanocyte-stimulating hormone	Peptide	Stimulates melanin formation in melanocytes

Posterior Pituitary

The **posterior pituitary** (**neurohypophysis**) is actually an extension of the neurons of the paraventricular and supraoptic nuclei of the hypothalamus. The cell bodies of these regions rest in the hypothalamus, but their axons descend as the hypothalamic-hypophyseal tract within the infundibulum and end in axon terminals that compose the posterior pituitary (Figure 16.7).

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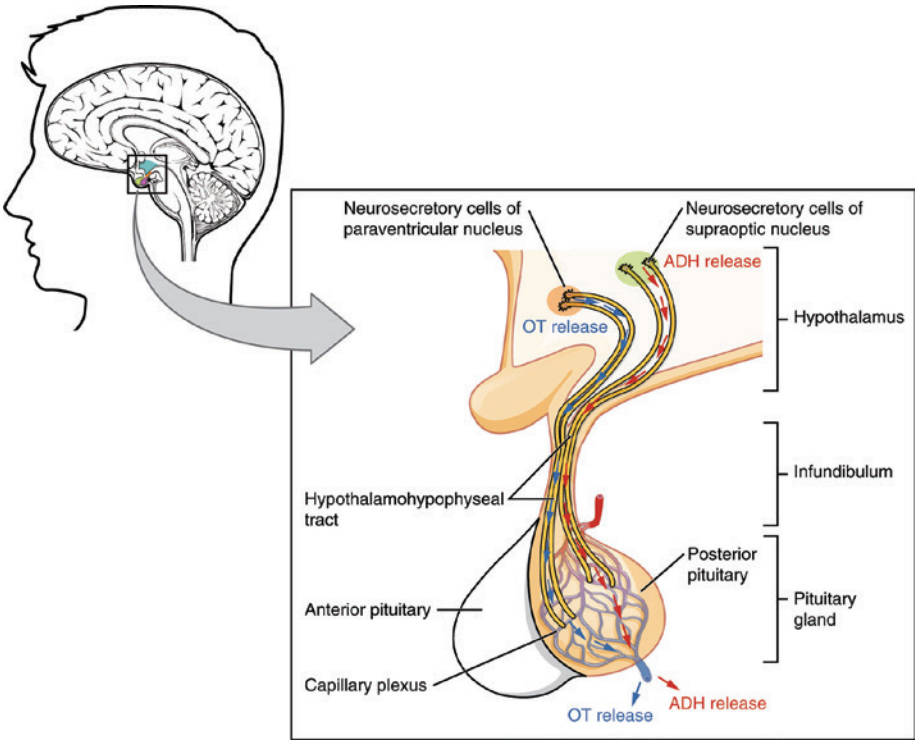


Figure 16.7 Posterior Pituitary. Neurosecretory cells in the hypothalamus release oxytocin (OT) or ADH into the posterior lobe of the pituitary gland. These hormones are stored or released into the blood via the capillary plexus.

The posterior pituitary gland does not produce hormones but rather stores and secretes hormones produced by the hypothalamus. The paraventricular nuclei produce the hormone oxytocin, whereas the supraoptic nuclei produce ADH. These hormones travel along the axons into storage sites in the axon terminals of the posterior pituitary. In response to signals from the same hypothalamic neurons, the hormones are released from the axon terminals into the bloodstream.

Oxytocin

When fetal development is complete, the peptide-derived hormone **oxytocin** (**OT**) stimulates uterine contractions and dilation of the cervix. Throughout most of pregnancy, oxytocin hormone receptors are not expressed at high levels in the uterus. Toward the end of pregnancy, the synthesis of oxytocin receptors in the uterus increases, and the smooth muscle cells of the uterus become more sensitive to its effects. Oxytocin is continually released throughout childbirth through a positive feedback mechanism. As noted in section 16.2 Hormones, oxytocin prompts uterine contractions that push the fetal head toward the

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cervix. In response, cervical stretching stimulates additional oxytocin to be synthesized by the hypothalamus and released from the pituitary. This increases the intensity and effectiveness of uterine contractions and prompts additional dilation of the cervix. The feedback loop continues until birth.

Although the high blood levels of oxytocin begin to decrease immediately following birth, oxytocin continues to play a role in female and newborn health. First, oxytocin is necessary for the milk ejection reflex (commonly referred to as "letdown") in breastfeeding people. As the newborn begins suckling, sensory receptors in the nipples transmit signals to the hypothalamus. In response, oxytocin is secreted and released into the bloodstream. Within seconds, cells in the milk ducts contract, ejecting milk into the infant's mouth. Secondly, in all people, oxytocin is thought to contribute to parent-newborn bonding, known as attachment. Oxytocin is also thought to be involved in feelings of love and closeness, as well as in the sexual response.

Antidiuretic Hormone (ADH)

The solute concentration of the blood, or blood osmolarity, may change in response to the consumption of certain foods and fluids, as well as in response to disease, injury, medications, or other factors. Blood osmolarity is constantly monitored by **osmoreceptors**—specialized cells within the hypothalamus that are particularly sensitive to the concentration of sodium ions and other solutes.

In response to high blood osmolarity, which can occur during dehydration or following a very salty meal, the osmoreceptors signal the posterior pituitary to release **antidiuretic hormone** (**ADH**). The target cells of ADH are located in the tubular cells of the kidneys. The effect of ADH is to increase epithelial permeability to water, allowing increased water reabsorption. The more water reabsorbed from the filtrate, the greater the amount of water that is returned to the blood and the less that is excreted in the urine. A greater concentration of water results in a reduced concentration of solutes. ADH is also known as vasopressin because in very high concentrations, it causes constriction of blood vessels, which increases blood pressure by increasing peripheral resistance. The release of ADH is controlled by a negative-feedback loop. As blood osmolarity decreases, the hypothalamic osmoreceptors sense the change and prompt a corresponding decrease in the secretion of ADH. As a result, less water is reabsorbed from the urine filtrate.

Interestingly, chemicals and drugs can affect the secretion of ADH. For example, alcohol consumption inhibits the release of ADH, resulting in increased urine production that can eventually lead to dehydration and a hangover. A disease called diabetes insipidus is characterized by chronic underproduction of ADH that causes chronic dehydration. Because little ADH is produced and

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secreted, not enough water is reabsorbed by the kidneys. Although patients feel thirsty and increase their fluid consumption, this doesn't effectively decrease the solute concentration in their blood because ADH levels are not high enough to trigger water reabsorption in the kidneys. Electrolyte imbalances can occur in severe cases of diabetes insipidus.

Anterior Pituitary

The **anterior pituitary** (**adenohypophysis**) originates from the digestive tract in the embryo and migrates toward the brain during fetal development. There are three regions: The pars distalis is the most anterior, the pars intermedia is adjacent to the posterior pituitary, and the pars tuberalis is a slender "tube" that wraps the infundibulum.

Recall that the posterior pituitary does not synthesize hormones but merely stores them. In contrast, the anterior pituitary does manufacture hormones. However, the secretion of hormones from the anterior pituitary is regulated by two classes of hormones. These hormones—secreted by the hypothalamus—are the **releasing hormones** that stimulate the secretion of hormones from the anterior pituitary and the **inhibiting hormones** that inhibit secretion.

Hypothalamic hormones are secreted by neurons but enter the anterior pituitary through blood vessels (Figure 16.8). Within the infundibulum is a bridge of capillaries that connects the hypothalamus to the anterior pituitary.

This network, called the **hypophyseal portal system**, allows hypothalamic hormones to be transported to the anterior pituitary without first entering the systemic circulation. The system originates from the superior hypophyseal artery, which branches off the carotid arteries and transports blood to the hypothalamus. The branches of the superior hypophyseal artery form the hypophyseal portal system (see Figure 16.8). Hypothalamic releasing and inhibiting hormones travel through a primary capillary plexus to the portal veins, which carry them into the anterior pituitary. Hormones produced by the anterior pituitary (in response to releasing hormones) enter a secondary capillary plexus and, from there, drain into the circulation.

The anterior pituitary produces six major hormones. These are the growth hormone (GH), thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin. Of the hormones of the anterior pituitary, TSH, ACTH, FSH, and LH are collectively referred to as tropic hormones (*trope-* = "turning") because they turn on the function of other endocrine glands.

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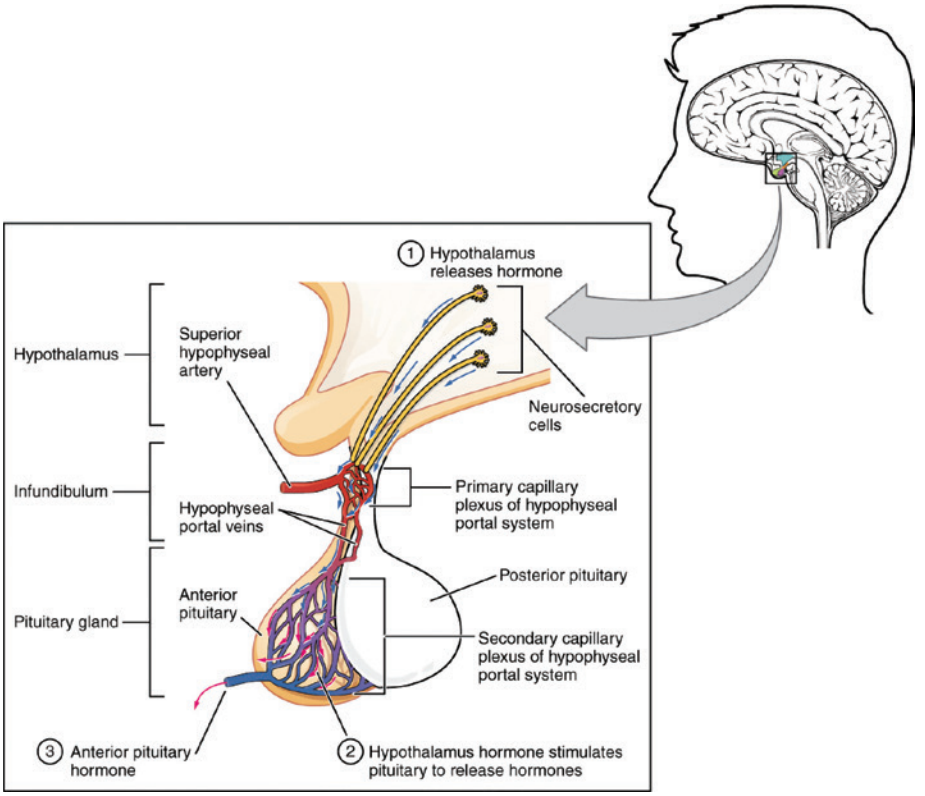


Figure 16.8 Anterior Pituitary. The anterior pituitary manufactures seven hormones. The hypothalamus produces separate hormones that stimulate or inhibit hormone production in the anterior pituitary. Hormones from the hypothalamus reach the anterior pituitary via the hypophyseal portal system.

Growth Hormone

The endocrine system regulates the growth of the human body, protein synthesis, and cellular replication. A major hormone involved in this process is **growth hormone** (**GH**), also called somatotropin—a protein hormone produced and secreted by the anterior pituitary gland. Its primary function is anabolic; it promotes protein synthesis and tissue building through direct and indirect mechanisms (Figure 16.9). GH levels are controlled by the release of GHRH and GHIH (also known as somatostatin) from the hypothalamus.

A glucose-sparing effect occurs when GH stimulates lipolysis, or the breakdown of adipose tissue, releasing fatty acids into the blood. As a result, many tissues switch from glucose to fatty acids as their main energy source, which means that less glucose is taken up from the bloodstream.

GH also initiates the diabetogenic effect, in which GH stimulates the liver to break down glycogen to glucose, which is then deposited into the blood. The

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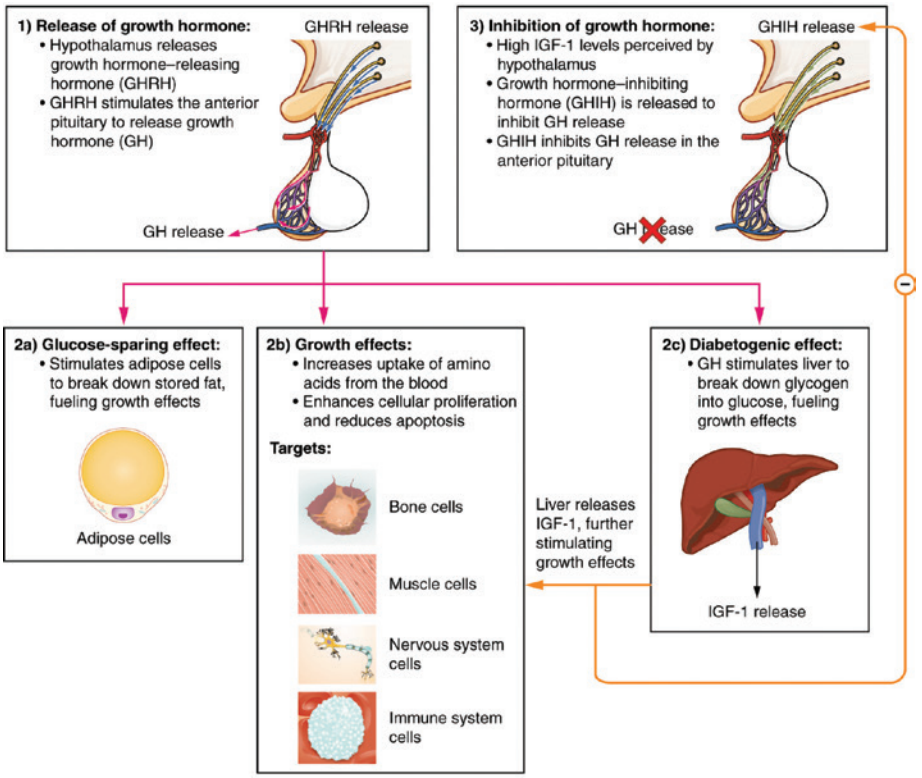


Figure 16.9 Hormonal Regulation of Growth. Growth hormone (GH) directly accelerates the rate of protein synthesis in skeletal muscle and bones. Insulin-like growth factor 1 (IGF-1) is activated by growth hormone and indirectly supports the formation of new proteins in muscle cells and bone.

name *diabetogenic* is derived from the similarity in elevated blood glucose levels observed between individuals with untreated diabetes mellitus and individuals experiencing GH excess. Blood glucose levels rise as the result of a combination of glucose-sparing and diabetogenic effects.

GH indirectly mediates growth and protein synthesis by triggering the liver and other tissues to produce a group of proteins called **insulin-like growth factors** (**IGFs**). These proteins enhance cellular proliferation and inhibit apoptosis, or programmed cell death. IGFs stimulate cells to increase their uptake of amino acids from the blood for protein synthesis. Skeletal muscle and cartilage cells are particularly sensitive to stimulation from IGFs.

Dysfunction of the endocrine system's control of growth can result in several disorders. For example, **gigantism** is a disorder in children that is caused by the secretion of abnormally large amounts of GH, resulting in excessive growth. A similar condition in adults is **acromegaly**, a disorder that results in the thickening of bones in the face, hands, and feet in response to excessive

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levels of GH in individuals who have stopped growing. Abnormally low levels of GH in children can cause growth impairment—a disorder called **pituitary dwarfism** (also known as growth hormone deficiency).

Thyroid-Stimulating Hormone

The activity of the thyroid gland is regulated by **thyroid-stimulating hormone** (**TSH**), also called thyrotropin. TSH is released from the anterior pituitary in response to thyrotropin-releasing hormone (TRH) from the hypothalamus. As discussed shortly, it triggers the secretion of thyroid hormones by the thyroid gland. In a classic negative-feedback loop, elevated levels of thyroid hormones in the bloodstream then trigger a drop in production of TRH and, subsequently, TSH.

Adrenocorticotropic Hormone

The **adrenocorticotropic hormone** (**ACTH**), also called corticotropin, stimulates the adrenal cortex (the more superficial "bark" of the adrenal glands) to secrete corticosteroid hormones such as cortisol. ACTH comes from a precursor molecule that produces several biologically active molecules when cleaved, including ACTH, melanocyte-stimulating hormone, and the brain opioid peptides known as endorphins.

The release of ACTH is regulated by the corticotropin-releasing hormone (CRH) from the hypothalamus in response to normal physiologic rhythms. A variety of stressors can also influence its release, and the role of ACTH in the stress response is discussed later in this chapter.

Follicle-Stimulating Hormone and Luteinizing Hormone

The endocrine glands secrete a variety of hormones that control the development and regulation of the reproductive system (these glands include the anterior pituitary, the adrenal cortex, and the gonads—the testes and the ovaries). Much of the development of the reproductive system occurs during puberty and is marked by the development of sex-specific characteristics in adolescents. Puberty is initiated by gonadotropin-releasing hormone (GnRH), a hormone produced and secreted by the hypothalamus. GnRH stimulates the anterior pituitary to secrete **gonadotropins**—hormones that regulate the function of the gonads. The levels of GnRH are regulated through a negative-feedback loop; high levels of reproductive hormones inhibit the release of GnRH. Throughout life, gonadotropins regulate reproductive function and, in the case of females, the onset and cessation of reproductive capacity.

The gonadotropins include two glycoprotein hormones: **Follicle-stimulating hormone** (**FSH**) stimulates the production and maturation of sex cells, or

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gametes, including ova and sperm. FSH also promotes follicular growth; these follicles then release estrogens in ovaries. **Luteinizing hormone** (**LH**) triggers ovulation as well as the production of estrogens and progesterone by the ovaries. LH stimulates production of testosterone by the testes.

Prolactin

As its name implies, **prolactin** (**PRL**) promotes lactation (milk production). During pregnancy, it contributes to development of the mammary glands, and after birth, it stimulates the mammary glands to produce breast milk. However, the effects of prolactin depend heavily on the permissive effects of estrogens, progesterone, and other hormones. And as noted earlier, the letdown of milk occurs in response to stimulation from oxytocin.

In nonpregnant females, prolactin secretion is inhibited by prolactin-inhibiting hormone (PIH), which is actually the neurotransmitter dopamine, and is released from neurons in the hypothalamus. Only during pregnancy do prolactin levels rise in response to prolactin-releasing hormone (PRH) from the hypothalamus.

Intermediate Pituitary: Melanocyte-Stimulating Hormone

The cells in the zone between the pituitary lobes secrete a hormone known as melanocyte-stimulating hormone (MSH). Local production of MSH in the skin is responsible for melanin production in response to UV light exposure. The role of MSH made by the pituitary is more complicated. For instance, people with lighter skin generally have the same amount of MSH as people with darker skin. Nevertheless, this hormone is capable of darkening the skin by inducing melanin production in the skin's melanocytes. People also show increased MSH production during pregnancy; in combination with estrogens, it can lead to darker skin pigmentation, especially the skin of the areolas and labia minora. Figure 16.10 is a summary of the pituitary hormones and their principal effects.

Interactive Link 16.2

Visit this link (http://oer.aupress.ca/oer-202505/16.2) to watch an animation showing the role of the hypothalamus and the pituitary gland. Which hormone is released by the pituitary to stimulate the thyroid gland?

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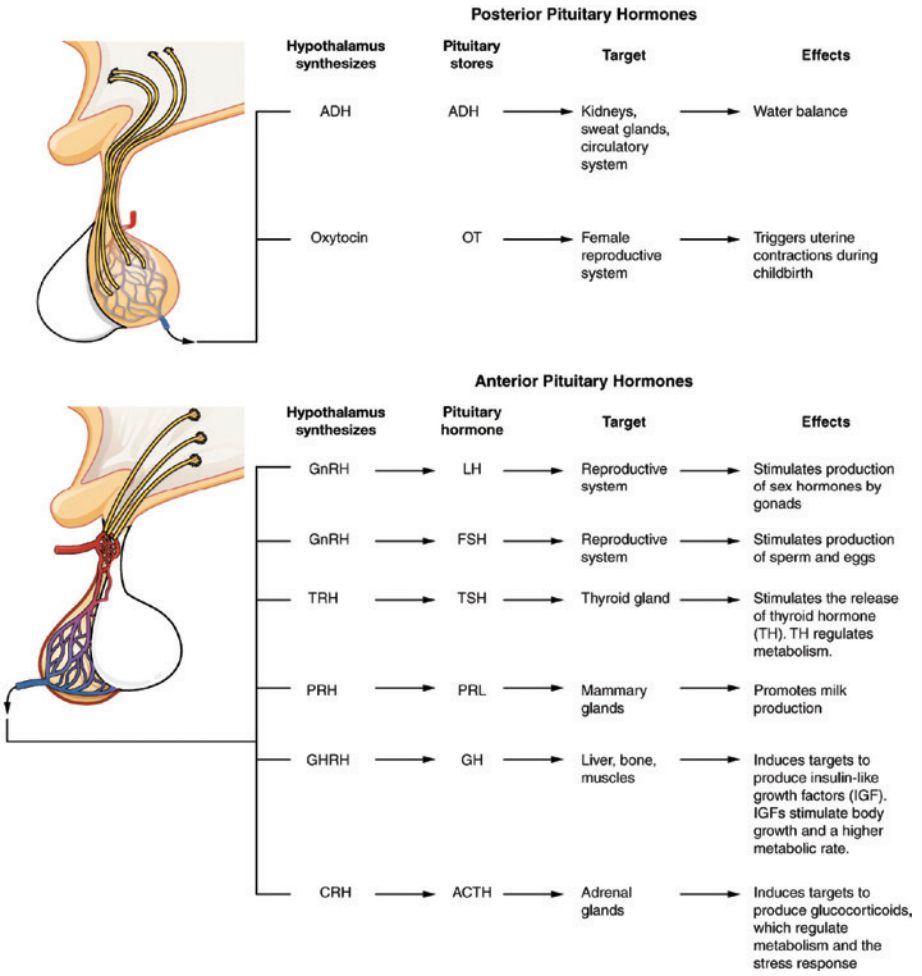


Figure 16.10 Major Pituitary Hormones. Major pituitary hormones and their target organs.

16.4 The Thyroid Gland

Learning Objectives

By the end of this section, you will be able to:

- Describe the location and anatomy of the thyroid gland
- Discuss the synthesis of triiodothyronine and thyroxine
- Explain the role of thyroid hormones in the regulation of basal metabolism
- Identify the hormone produced by the parafollicular cells of the thyroid

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A butterfly-shaped organ, the **thyroid gland** is located anterior to the trachea, just inferior to the larynx (Figure 16.11).

The medial region, called the isthmus, is flanked by wing-shaped left and right lobes. Each of the thyroid lobes is embedded with parathyroid glands, primarily on their posterior surfaces. The tissue of the thyroid gland is composed mostly of thyroid follicles. The follicles are made up of a central cavity filled with a sticky fluid called **colloid**. Surrounded by a wall of epithelial follicle cells, the colloid is the centre of thyroid hormone production, and that production is dependent on the hormones' essential and unique component: iodine.

Synthesis and Release of Thyroid Hormones (TH)

Hormones are produced in the colloid when atoms of the mineral iodine attach to a glycoprotein, called thyroglobulin, that is secreted into the colloid by the follicle cells. The following steps outline the hormones' assembly:

1. Binding of TSH to its receptors in the follicle cells of the thyroid gland causes the cells to actively transport iodide ions (I^-) across their cell membrane, from the bloodstream into the cytosol. As a result, the concentration of iodide ions "trapped" in the follicular cells is many times higher than the concentration in the bloodstream.
2. Iodide ions then move to the lumen of the follicle cells that border the colloid. There, the ions undergo oxidation (their negatively charged electrons are removed). The oxidation of two iodide ions ($2\ I^-$) results in iodine (I_2), which passes through the follicle cell membrane into the colloid.
3. In the colloid, peroxidase enzymes link the iodine to the tyrosine amino acids in thyroglobulin to produce two intermediaries: a tyrosine attached to one iodine and a tyrosine attached to two iodines. When one of each of these intermediaries is linked by covalent bonds, the resulting compound is **triiodothyronine** (T_3), a thyroid hormone with three iodines. Much more commonly, two copies of the second intermediary bond together to form tetraiodothyronine, also known as **thyroxine** (T4), a thyroid hormone that contains four iodine atoms.

These hormones remain in the colloid centre of the thyroid follicles until TSH stimulates endocytosis of colloid back into the follicle cells. There, lysosomal enzymes break apart the thyroglobulin colloid, releasing free T_3 and T_4, which diffuse across the follicle cell membrane and enter the bloodstream.

In the bloodstream, less than 1 percent of the circulating T_3 and T_4 remains unbound. This free T_3 and T_4 can cross the lipid bilayer of cell membranes

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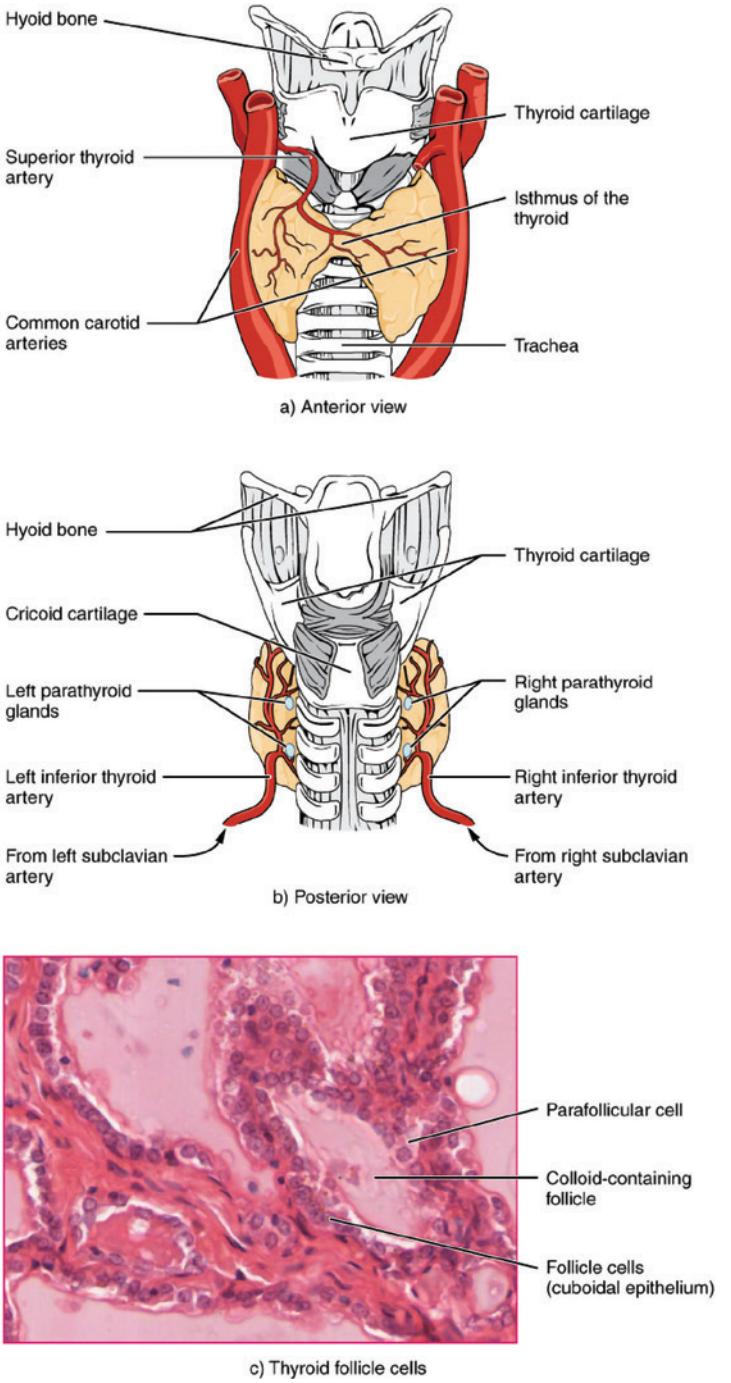


Figure 16.11 Thyroid Gland. The thyroid gland is located in the neck, where it wraps around the trachea. (a) Anterior view of the thyroid gland. (b) Posterior view of the thyroid gland. (c) The glandular tissue is composed primarily of thyroid follicles. The larger parafollicular cells often appear within the matrix of follicle cells. LM × 1332. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

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and be taken up by cells. The remaining 99 percent of circulating T_3 and T_4 is bound to specialized transport proteins called thyroxine-binding globulins (TBGs), to albumin, or to other plasma proteins. This "packaging" prevents their free diffusion into body cells. When blood levels of T_3 and T_4 begin to decline, bound T_3 and T_4 are released from these plasma proteins and readily cross the membrane of target cells. T_3 is more potent than T_4, and many cells convert T_4 to T_3 through the removal of an iodine atom.

Regulation of Thyroid Hormones Synthesis

The release of T_3 and T_4 from the thyroid gland is regulated by thyroid-stimulating hormone (TSH). As shown in Figure 16.12, low blood levels of T_3 and T_4 stimulate the release of thyrotropin-releasing hormone (TRH) from the hypothalamus, which triggers secretion of TSH from the anterior pituitary. In

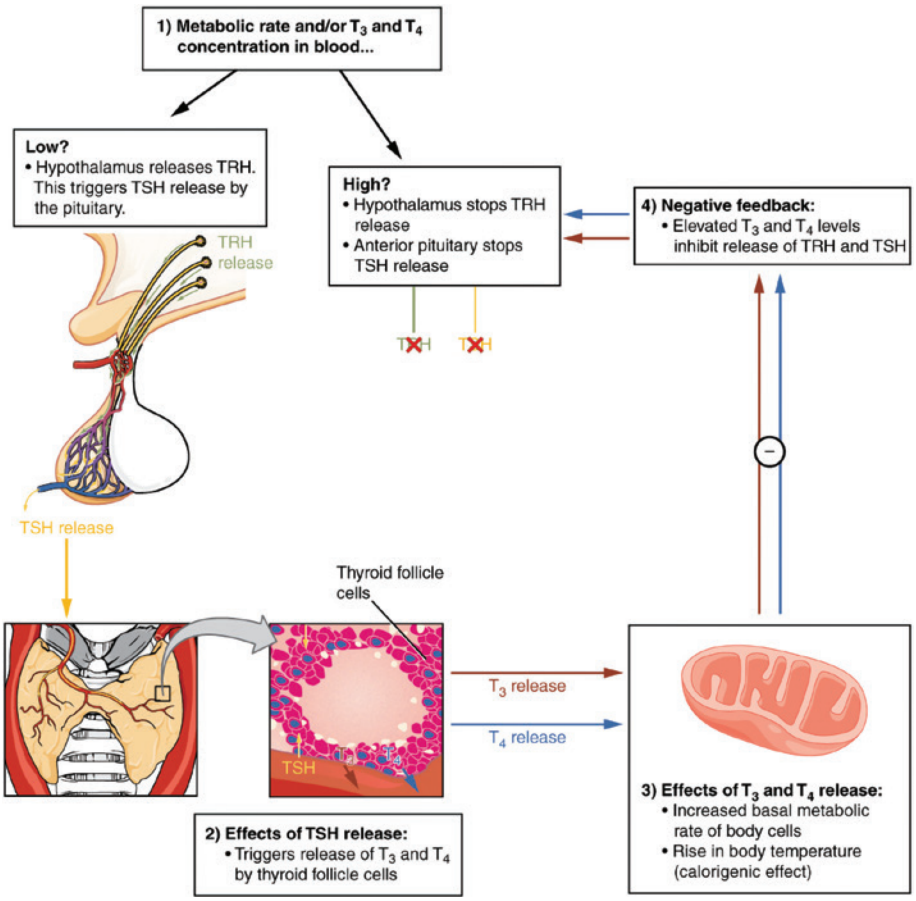


Figure 16.12 Classic Negative-Feedback Loop. A classic negative-feedback loop controls the regulation of thyroid hormone levels.

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turn, TSH stimulates the thyroid gland to secrete T_3 and T_4. The levels of TRH, TSH, T_3, and T_4 are regulated by a negative-feedback system in which increasing levels of T_3 and T_4 decrease the production and secretion of TSH.

Functions of Thyroid Hormones

The thyroid hormones, T_3 and T_4, are often referred to as metabolic hormones because their levels influence the body's basal metabolic rate, the amount of energy used by the body at rest. When T_3 and T_4 bind to intracellular receptors located on the mitochondria, they cause an increase in nutrient breakdown and the use of oxygen to produce ATP. In addition, T_3 and T_4 initiate the transcription of genes involved in glucose oxidation. Although these mechanisms prompt cells to produce more ATP, the process is inefficient, and an abnormally increased level of heat is released as a by-product of these reactions. This so-called calorigenic effect raises body temperature.

Adequate levels of thyroid hormones are also required for protein synthesis and for fetal and childhood tissue development and growth. They are especially critical for normal development of the nervous system both in utero and in early childhood, and they continue to support neurological function in adults. As noted earlier, these thyroid hormones have a complex interrelationship with reproductive hormones, and deficiencies can influence libido, fertility, and other aspects of reproductive function. Finally, thyroid hormones increase the body's sensitivity to catecholamines (epinephrine and norepinephrine) from the adrenal medulla by upregulation of receptors in the blood vessels. When levels of T_3 and T_4 hormones are excessive, this effect accelerates the heart rate, strengthens the heartbeat, and increases blood pressure. Because thyroid hormones regulate metabolism, heat production, protein synthesis, and many other body functions, thyroid disorders can have severe and widespread consequences.

Calcitonin

The thyroid gland also secretes a hormone called **calcitonin** that is produced by the parafollicular cells (also called C cells) that stud the tissue between distinct follicles. Calcitonin is released in response to a rise in blood calcium levels. It appears to have a function in decreasing blood calcium concentrations by

- inhibiting the activity of osteoclasts, bone cells that release calcium into the circulation by degrading the bone matrix;
- increasing osteoblastic activity;
- decreasing calcium absorption in the intestines;
- increasing calcium loss in the urine.

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However, these functions are usually not significant in maintaining calcium homeostasis, so the importance of calcitonin is not entirely understood. Pharmaceutical preparations of calcitonin are sometimes prescribed to reduce osteoclast activity in people with osteoporosis and to reduce the degradation of cartilage in people with osteoarthritis. The hormones secreted by the thyroid are summarized in Table 16.4.

Table 16.4 Thyroid Hormones

Associated hormones	Chemical class	Effect
Thyroxine (T_4), triiodothyronine (T_3)	Amine	Stimulates basal metabolic rate
Calcitonin	Peptide	Reduces blood Ca^{2+} levels

Of course, calcium is critical for many other biological processes. It is a second messenger in many signalling pathways and is essential for muscle contraction, nerve impulse transmission, and blood clotting. Given these roles, it is not surprising that blood calcium levels are tightly regulated by the endocrine system. The organs involved in the regulation are the parathyroid glands.

16.5 The Parathyroid Glands

Learning Objectives

By the end of this section, you will be able to:

- Describe the location and structure of the parathyroid glands
- Describe the hormonal control of blood calcium levels
- Discuss the physiological response of parathyroid dysfunction

The **parathyroid glands** are tiny, round structures usually found embedded in the posterior surface of the thyroid gland (Figure 16.13). A thick connective tissue capsule separates the glands from the thyroid tissue. Most people have four parathyroid glands, but occasionally there are more in tissues of the neck or chest. The function of one type of parathyroid cells, the oxyphil cells, is not clear. The primary functional cells of the parathyroid glands are the chief cells. These epithelial cells produce and secrete **parathyroid hormone** (**PTH**), the major hormone involved in the regulation of blood calcium levels.

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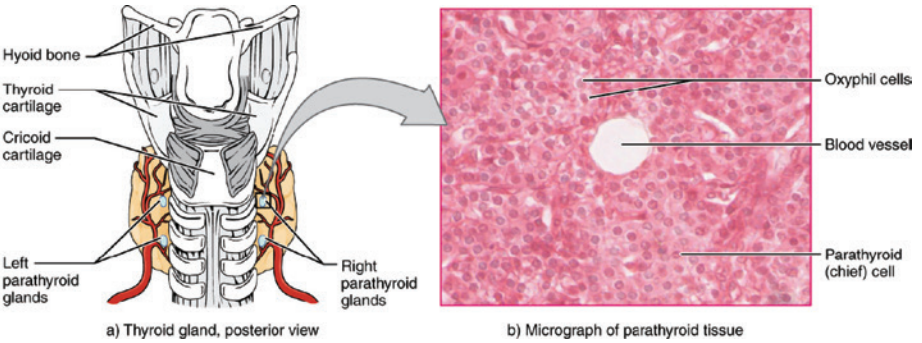


Figure 16.13 Parathyroid Glands. The small parathyroid glands are embedded in the posterior surface of the thyroid gland. LM × 760. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Interactive Link 16.3

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/16.3) to explore the tissue sample in greater detail.

The parathyroid glands produce and secrete PTH, a peptide hormone, in response to low blood calcium levels (Figure 16.14). PTH secretion causes the release of calcium from the bones by stimulating osteoclasts, which secrete enzymes that degrade bone and release calcium into the interstitial fluid. PTH also inhibits osteoblasts, the cells involved in bone deposition, thereby sparing blood calcium. PTH causes increased reabsorption of calcium (and magnesium) in the kidney tubules from the urine filtrate. In addition, PTH initiates the production of the steroid hormone calcitriol (also known as 1,25-dihydroxyvitamin D), which is the active form of vitamin D_3, in the kidneys. Calcitriol then stimulates increased absorption of dietary calcium by the intestines. A negative-feedback loop regulates the levels of PTH, with rising blood calcium levels inhibiting further release of PTH.

Abnormally high activity of the parathyroid gland can cause **hyperparathyroidism**, a disorder caused by an overproduction of PTH that results in excessive calcium reabsorption from bone. Hyperparathyroidism can significantly decrease bone density, leading to spontaneous fractures or deformities. As blood calcium levels rise, cell membrane permeability to sodium is decreased, and the responsiveness of the nervous system is reduced. At the same time, calcium deposits may collect in the body's tissues and organs, impairing their functioning.

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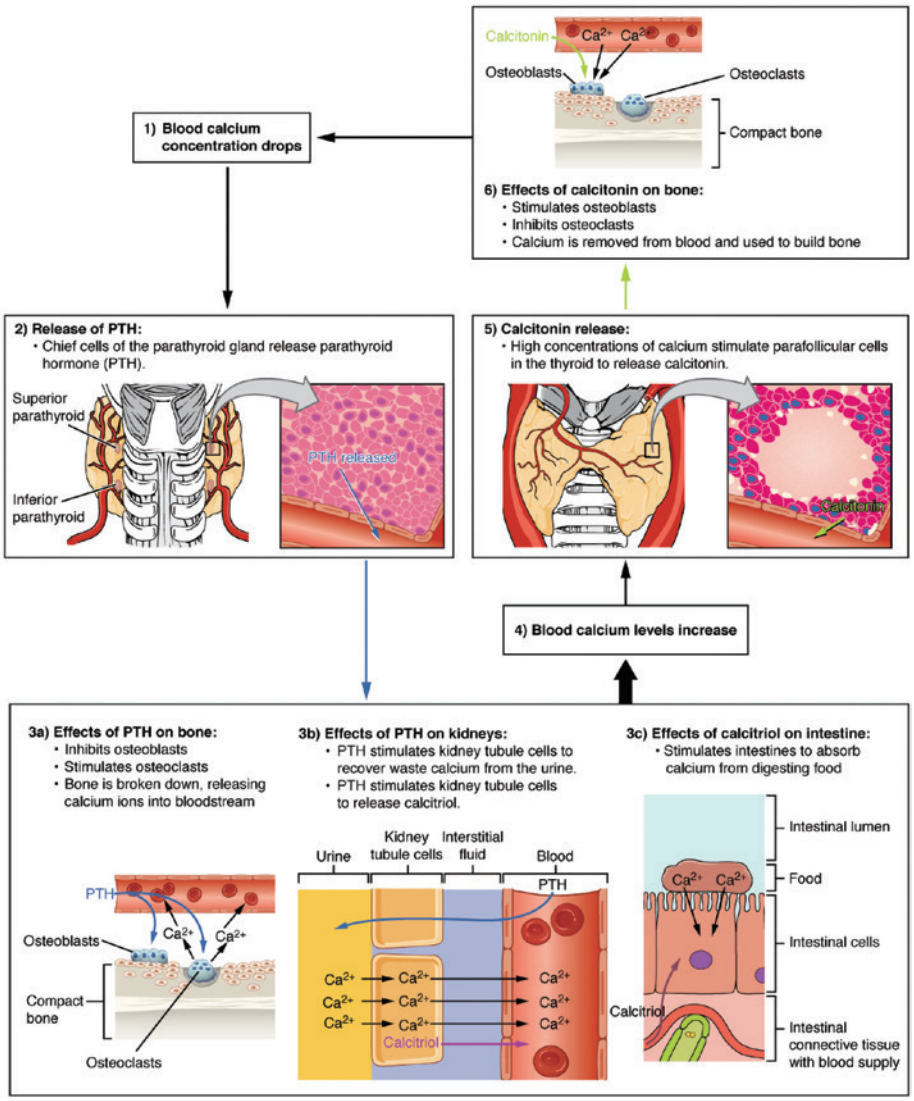


Figure 16.14 Parathyroid Hormone in Maintaining Blood Calcium Homeostasis. Parathyroid hormone increases blood calcium levels when they drop too low. Conversely, calcitonin, which is released from the thyroid gland, decreases blood calcium levels when they become too high. These two mechanisms constantly maintain blood calcium concentration at homeostasis.

In contrast, abnormally low blood calcium levels may be caused by parathyroid hormone deficiency, called **hypoparathyroidism**, which may develop following injury or surgery involving the thyroid gland. Low blood calcium increases membrane permeability to sodium, resulting in muscle twitching, cramping, spasms, or convulsions. Severe deficits can paralyze muscles, including those involved in breathing, and can be fatal.

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When blood calcium levels are high, calcitonin is produced and secreted by the parafollicular cells of the thyroid gland. As discussed earlier, calcitonin inhibits the activity of osteoclasts, reduces the absorption of dietary calcium in the intestine, and signals the kidneys to reabsorb less calcium, resulting in larger amounts of calcium excreted in the urine.

16.6 The Adrenal Glands

Learning Objectives

By the end of this section, you will be able to:

- Describe the location and structure of the adrenal glands
- Identify the hormones produced by the adrenal cortex and adrenal medulla, and summarize their target cells and effects

The **adrenal glands** are wedges of glandular and neuroendocrine tissue adhering to the top of the kidneys by a fibrous capsule (Figure 16.15). The adrenal glands have a rich blood supply and experience one of the highest rates of blood flow in the body. They are served by several arteries branching off the aorta, including the suprarenal and renal arteries. Blood flows to each adrenal gland at the adrenal cortex and then drains into the adrenal medulla.

Adrenal hormones are released into the circulation via the left and right suprarenal veins.

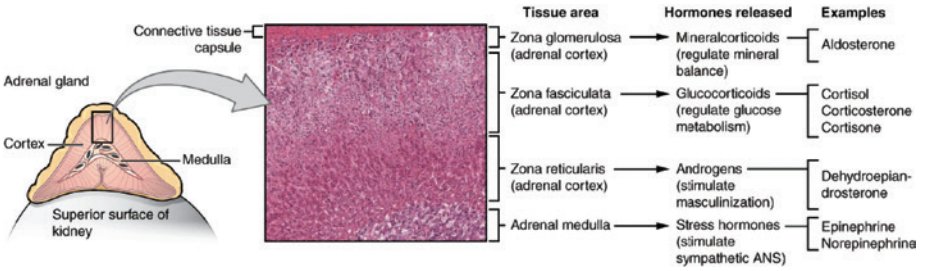


Figure 16.15 Adrenal Glands. Both adrenal glands sit atop the kidneys and are composed of an outer cortex and an inner medulla, all surrounded by a connective tissue capsule. The cortex can be subdivided into additional zones, all of which produce different types of hormones. LM × 204. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

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Interactive Link 16.4

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/16.4) to explore the tissue sample in greater detail.

The adrenal gland consists of an outer cortex of glandular tissue and an inner medulla of nervous tissue. The cortex itself is divided into three zones: the **zona glomerulosa**, the **zona fasciculata**, and the **zona reticularis**. Each region secretes its own set of hormones.

The **adrenal cortex**, as a component of the hypothalamic-pituitary-adrenal (HPA) axis, secretes steroid hormones important for the regulation of the long-term stress response, blood pressure and blood volume, nutrient uptake and storage, fluid and electrolyte balance, and inflammation. The HPA axis involves the stimulation of the release of adrenocorticotropic hormone (ACTH) from the pituitary by the hypothalamus. ACTH then stimulates the adrenal cortex to produce the hormone cortisol. This pathway will be discussed in more detail below.

The **adrenal medulla** is neuroendocrine tissue composed of postganglionic sympathetic nervous system (SNS) neurons. It is really an extension of the autonomic nervous system, which regulates homeostasis in the body. The sympathomedullary (SAM) pathway involves the stimulation of the medulla by impulses from the hypothalamus via neurons from the thoracic spinal cord. The medulla is stimulated to secrete the amine hormones epinephrine and norepinephrine.

One of the major functions of the adrenal gland is to respond to stress. Stress can be either physical or psychological or both. Physical stresses include exposing the body to injury, walking outside in cold and wet conditions without a coat on, or malnutrition. Psychological stresses include the perception of a physical threat, a fight with a loved one, or just a bad day at school.

The body responds in different ways to short-term stress and long-term stress following a pattern known as the **general adaptation syndrome** (**GAS**). Stage one of GAS is called the **alarm reaction**. This is short-term stress, the fight-or-flight response, mediated by the hormones epinephrine and norepinephrine from the adrenal medulla via the SAM pathway. Their function is to prepare the body for extreme physical exertion. Once this stress is relieved, the body quickly returns to normal. The section on the adrenal medulla covers this response in more detail.

If the stress is not soon relieved, the body adapts to the stress in the second stage, called the **stage of resistance**. If a person is starving, for example, the

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body may send signals to the gastrointestinal tract to maximize the absorption of nutrients from food.

If the stress continues for a longer term, however, the body responds with symptoms quite different from the fight-or-flight response. During the **stage of exhaustion**, individuals may begin to suffer depression, the suppression of their immune response, severe fatigue, or even a fatal heart attack. These symptoms are mediated by the hormones of the adrenal cortex, especially cortisol, released as a result of signals from the HPA axis.

Adrenal hormones also have several non-stress-related functions, including the increase of blood sodium and glucose levels, which will be described in detail below.

Adrenal Cortex

The adrenal cortex consists of multiple layers of lipid-storing cells that occur in three structurally distinct regions. Each of these regions produces different hormones.

Interactive Link 16.5

Visit this link (http://oer.aupress.ca/oer-202505/16.5) to view an animation describing the location and function of the adrenal glands. Which hormone produced by the adrenal glands is responsible for the mobilization of energy stores?

Hormones of the Zona Glomerulosa

The most superficial region of the adrenal cortex is the zona glomerulosa, which produces a group of hormones collectively referred to as **mineralocorticoids** because of their effect on body minerals, especially sodium and potassium. These hormones are essential for fluid and electrolyte balance.

Aldosterone is the major mineralocorticoid. It is important in the regulation of the concentration of sodium and potassium ions in urine, sweat, and saliva. For example, it is released in response to elevated blood K^+, low blood Na^+, low blood pressure, or low blood volume. In response, aldosterone increases the excretion of K^+ and the retention of Na^+, which, in turn, increases blood volume and blood pressure. Its secretion is prompted when CRH from the hypothalamus triggers ACTH release from the anterior pituitary.

Aldosterone is also a key component of the **renin-angiotensin-aldosterone system** (**RAAS**), in which specialized cells of the kidneys secrete the enzyme renin in response to low blood volume or low blood pressure. Renin then

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catalyzes the conversion of the blood protein angiotensinogen, produced by the liver, to the hormone angiotensin I. Angiotensin I is converted in the lungs to angiotensin II by **angiotensin-converting enzyme** (ACE). Angiotensin II has three major functions:

1. Initiating vasoconstriction of the arterioles, decreasing blood flow
2. Stimulating kidney tubules to reabsorb NaCl and water, increasing blood volume
3. Signalling the adrenal cortex to secrete aldosterone, the effects of which further contribute to fluid retention, restoring blood pressure and blood volume

For individuals with hypertension, or high blood pressure, drugs are available that block the production of angiotensin II. These drugs, known as ACE inhibitors, block the ACE enzyme from converting angiotensin I to angiotensin II, thus mitigating the latter's ability to increase blood pressure.

Hormones of the Zona Fasciculata

The intermediate region of the adrenal cortex is the zona fasciculata, named as such because the cells form small fascicles (bundles) separated by tiny blood vessels. The cells of the zona fasciculata produce hormones called **glucocorticoids** because of their role in glucose metabolism. The most important of these is **cortisol**, some of which the liver converts to cortisone. A glucocorticoid produced in much smaller amounts is corticosterone. In response to long-term stressors, the hypothalamus secretes CRH, which, in turn, triggers the release of ACTH by the anterior pituitary. ACTH triggers the release of the glucocorticoids. Their overall effect is to inhibit tissue building while stimulating the breakdown of stored nutrients to maintain adequate fuel supplies. In conditions of long-term stress, for example, cortisol promotes the catabolism of glycogen to glucose, the catabolism of stored triglycerides into fatty acids and glycerol, and the catabolism of muscle proteins into amino acids. These raw materials can then be used to synthesize additional glucose and ketones for use as body fuels. The hippocampus, which is part of the temporal lobe of the cerebral cortices and important in memory formation, is highly sensitive to stress levels because of its many glucocorticoid receptors.

Hormones of the Zona Reticularis

The deepest region of the adrenal cortex is the zona reticularis, which produces small amounts of a class of steroid sex hormones called androgens. During puberty and most of adulthood, androgens are produced in the gonads. The

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androgens produced in the zona reticularis supplement the gonadal androgens. They are produced in response to ACTH from the anterior pituitary and are converted in the tissues to testosterone or estrogens. In adult females, they may contribute to the sex drive, but their function in adult males is not well understood. In postmenopausal people, as the functions of the ovaries decline, the main source of estrogens becomes the androgens produced by the zona reticularis.

Adrenal Medulla

As noted earlier, the adrenal cortex releases glucocorticoids in response to long-term stress such as severe illness. In contrast, the adrenal medulla releases its hormones in response to acute, short-term stress mediated by the sympathetic nervous system (SNS).

The medullary tissue is composed of unique postganglionic SNS neurons called **chromaffin** cells, which are large and irregularly shaped, and produce the neurotransmitters **epinephrine** (also called adrenaline) and **norepinephrine** (or noradrenaline). Epinephrine is produced in greater quantities—approximately a 4 to 1 ratio with norepinephrine—and is the more powerful hormone. Because the chromaffin cells release epinephrine and norepinephrine into the systemic circulation, where they travel widely and exert effects on distant cells, they are considered hormones. Derived from the amino acid tyrosine, they are chemically classified as catecholamines.

The secretion of medullary epinephrine and norepinephrine is controlled by a neural pathway that originates from the hypothalamus in response to danger or stress (the SAM pathway). Both epinephrine and norepinephrine signal the liver and skeletal muscle cells to convert glycogen into glucose, resulting in increased blood glucose levels.

These hormones increase the heart rate, pulse, and blood pressure to prepare the body to fight the perceived threat or flee from it. In addition, the pathway dilates the airways, raising blood oxygen levels. It also prompts vasodilation, further increasing the oxygenation of important organs such as the lungs, brain, and heart and skeletal muscle. At the same time, it triggers vasoconstriction to blood vessels serving less essential organs such as the gastrointestinal tract, kidneys, and skin and downregulates some components of the immune system. Other effects include a dry mouth, loss of appetite, pupil dilation, and a loss of peripheral vision. The major hormones of the adrenal glands are summarized in Table 16.5.

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Table 16.5 Hormones of the Adrenal Glands

Adrenal gland	Associated hormones	Chemical class	Effect
Adrenal cortex	Aldosterone	Steroid	Increases blood Na^+ levels
Adrenal cortex	Cortisol, corticosterone, cortisone	Steroid	Increases blood glucose levels
Adrenal medulla	Epinephrine, norepinephrine	Amine	Stimulates fight-or-flight response

Disorders Involving the Adrenal Glands

Several disorders are caused by the dysregulation of the hormones produced by the adrenal glands. For example, Cushing's disease is a disorder characterized by high blood glucose levels and the accumulation of lipid deposits on the face and neck. It is caused by hypersecretion of cortisol. The most common source of Cushing's disease is a pituitary tumor that secretes cortisol or ACTH in abnormally high amounts. Other common signs of Cushing's disease include the development of a moon-shaped face, a buffalo hump on the back of the neck, rapid weight gain, and hair loss. Chronically elevated glucose levels are also associated with an elevated risk of developing type 2 diabetes. In addition to hyperglycemia, chronically elevated glucocorticoids compromise immunity, resistance to infection, and memory and can result in rapid weight gain and hair loss.

In contrast, the hyposecretion of corticosteroids can result in Addison's disease, a rare disorder that causes low blood glucose levels and low blood sodium levels. The signs and symptoms of Addison's disease are vague and are typical of other disorders as well, making diagnosis difficult. They may include general weakness, abdominal pain, weight loss, nausea, vomiting, sweating, and cravings for salty food.

16.7 The Pineal Gland

Learning Objectives

By the end of this section, you will be able to:

- Describe the location and structure of the pineal gland
- Discuss the function of melatonin

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Recall that the hypothalamus, part of the diencephalon of the brain, sits inferior and somewhat anterior to the thalamus. Inferior but somewhat posterior to the thalamus is the **pineal gland** (Figure 16.1), a tiny endocrine gland whose functions are not entirely clear. The **pinealocyte** cells that make up the pineal gland are known to produce and secrete the amine hormone **melatonin**, which is derived from serotonin.

The secretion of melatonin varies according to the level of light received from the environment. When photons of light stimulate the retinas of the eyes, a nerve impulse is sent to a region of the hypothalamus called the suprachiasmatic nucleus (SCN), which is important in regulating biological rhythms. From the SCN, the nerve signal is carried to the spinal cord and eventually to the pineal gland, where the production of melatonin is inhibited. As a result, blood levels of melatonin fall, promoting wakefulness. In contrast, as light levels decline—such as during the evening—melatonin production increases, boosting blood levels and causing drowsiness.

Interactive Link 16.6

Visit this link (http://oer.aupress.ca/oer-202505/16.6) to view an animation describing the function of the hormone melatonin. What should you avoid doing in the middle of your sleep cycle that would lower melatonin?

The secretion of melatonin may influence the body's circadian rhythms, the dark-light fluctuations that affect not only sleepiness and wakefulness but also appetite and body temperature. Interestingly, children have higher melatonin levels than adults, which may prevent the release of gonadotropins from the anterior pituitary, thereby inhibiting the onset of puberty. Finally, an antioxidant role of melatonin is the subject of current research. Jet lag occurs when a person travels across several time zones and feels sleepy during the day or wakeful at night. Travelling across multiple time zones significantly disturbs the light-dark cycle regulated by melatonin. It can take up to several days for melatonin synthesis to adjust to the light-dark patterns in the new environment, resulting in jet lag. Some air travellers take melatonin supplements to induce sleep.

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16.8 Gonadal and Placental Hormones

Learning Objectives

By the end of this section, you will be able to:

- Identify the most important hormones produced by the testes and ovaries
- Name the hormones produced by the placenta and state their functions

This section briefly discusses the hormonal role of the gonads—the testes and ovaries—which produce the sex cells (sperm and ova) and secrete the gonadal hormones. The roles of the gonadotropins released from the anterior pituitary (FSH and LH) were discussed earlier.

The primary hormone produced by the testes is **testosterone**, a steroid hormone important in the development of the testicular reproductive system, the maturation of sperm cells, and the development of secondary sex characteristics such as a deepened voice, body hair, and increased muscle mass. Interestingly, testosterone is also produced in the ovaries, but at a much reduced level. In addition, the testes produce the peptide hormone **inhibin**, which inhibits the secretion of FSH from the anterior pituitary gland. FSH stimulates spermatogenesis.

The primary hormones produced by the ovaries are **estrogens**, which include estradiol, estriol, and estrone. Estrogens play an important role in a larger number of physiological processes, including the development of the ovarian reproductive system, regulation of the menstrual cycle, the development of secondary sex characteristics such as increased adipose tissue and the development of breast tissue, and the maintenance of pregnancy. Another significant ovarian hormone is **progesterone**, which contributes to regulation of the menstrual cycle and is important in preparing the body for pregnancy as well as maintaining pregnancy. In addition, the granulosa cells of the ovarian follicles produce inhibin, which inhibits the secretion of FSH. During the initial stages of pregnancy, an organ called the placenta develops within the uterus. The placenta supplies oxygen and nutrients to the fetus, excretes waste products, and produces and secretes estrogens and progesterone. The placenta produces human chorionic gonadotropin (hCG) as well. The hCG hormone promotes progesterone synthesis and reduces the mother's immune function to protect the fetus from immune rejection. It also secretes human placental lactogen (hPL), which plays a role in preparing the breasts for lactation, and relaxin, which is thought to

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help soften and widen the pubic symphysis in preparation for childbirth. The hormones controlling reproduction are summarized in Table 16.6.

Table 16.6 Reproductive Hormones

Gonad	Associated hormones	Chemical class	Effect
Testes	Testosterone	Steroid	Stimulates development of secondary sex characteristics and sperm production
Testes	Inhibin	Protein	Inhibits FSH release from pituitary
Ovaries	Estrogens and progesterone	Steroid	Stimulates development of secondary sex characteristics and prepares the body for childbirth
Placenta	Human chorionic gonadotropin	Protein	Promotes progesterone synthesis during pregnancy and inhibits immune response against fetus

16.9 The Endocrine Pancreas

Learning Objectives

By the end of this section, you will be able to:

- Describe the location and structure of the pancreas and the morphology and function of the pancreatic islets
- Compare and contrast the functions of insulin and glucagon

The **pancreas** is a long, slender organ, most of which is located posterior to the bottom half of the stomach (Figure 16.16). Although it is primarily an exocrine gland, secreting a variety of digestive enzymes, the pancreas has an endocrine function. Its **pancreatic islets**—clusters of cells formerly known as the islets of Langerhans—secrete the hormones glucagon, insulin, somatostatin, and pancreatic polypeptide (PP).

Interactive Link 16.7

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/16.7) to explore the tissue sample in greater detail.

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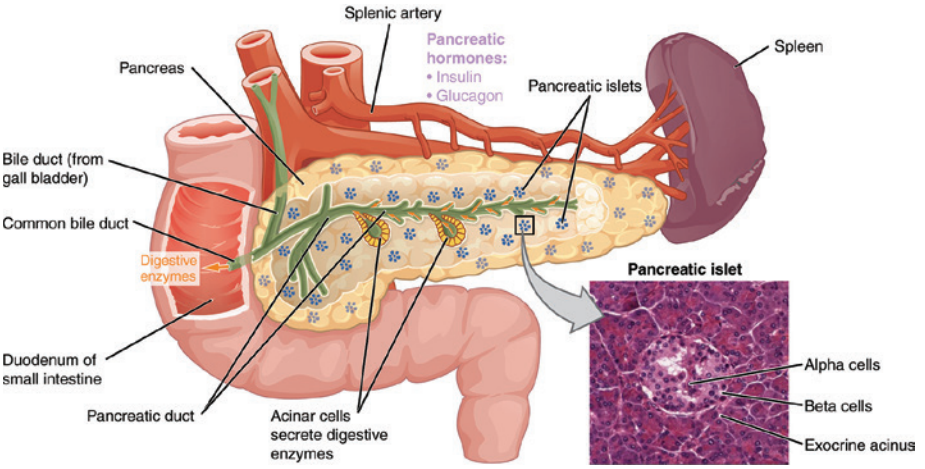


Figure 16.16 Pancreas. The pancreatic exocrine function involves the acinar cells secreting digestive enzymes that are transported into the small intestine by the pancreatic duct. Its endocrine function involves the secretion of insulin (produced by beta cells) and glucagon (produced by alpha cells) within the pancreatic islets. These two hormones regulate the rate of glucose metabolism in the body. The micrograph reveals pancreatic islets. LM × 760. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Cells and Secretions of the Pancreatic Islets

The pancreatic islets each contain four varieties of cells:

- The **alpha cell** produces the hormone **glucagon** and makes up approximately 20 percent of each islet. Glucagon plays an important role in blood glucose regulation; low blood glucose levels stimulate its release.
- The **beta cell** produces the hormone **insulin** and makes up approximately 75 percent of each islet. Elevated blood glucose levels stimulate the release of insulin.
- The **delta cell** accounts for 4 percent of the islet cells and secretes the peptide hormone somatostatin. Recall that somatostatin is also released by the hypothalamus (as GHIH), and the stomach and intestines also secrete it. An inhibiting hormone, pancreatic somatostatin inhibits the release of both glucagon and insulin.
- The **PP cell** accounts for about 1 percent of islet cells and secretes the pancreatic polypeptide hormone. It is thought to play a role in appetite as well as in the regulation of pancreatic exocrine and endocrine secretions. Pancreatic polypeptide released following a meal may reduce further food consumption; however, it is also released in response to fasting.

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Regulation of Blood Glucose Levels by Insulin and Glucagon

Glucose is required for cellular respiration and is the preferred fuel for all body cells. The body derives glucose from the breakdown of the carbohydrate-containing foods and drinks we consume. Glucose not immediately taken up by cells for fuel can be stored by the liver and muscles as glycogen or converted to triglycerides and stored in the adipose tissue. Hormones regulate both the storage and the utilization of glucose as required. Receptors located in the pancreas sense blood glucose levels, and subsequently, the pancreatic cells secrete glucagon or insulin to maintain normal levels.

Glucagon

Receptors in the pancreas can sense the decline in blood glucose levels, such as during periods of fasting or during prolonged labour or exercise (Figure 16.16).

In response, the alpha cells of the pancreas secrete the hormone **glucagon**, which has several effects:

- It stimulates the liver to convert its stores of glycogen back into glucose. This response is known as glycogenolysis. The glucose is then released into the circulation for use by body cells.
- It stimulates the liver to take up amino acids from the blood and convert them into glucose. This response is known as gluconeogenesis.
- It stimulates lipolysis, the breakdown of stored triglycerides into free fatty acids and glycerol. Some of the free glycerol released into the bloodstream travels to the liver, which converts it into glucose. This is also a form of gluconeogenesis.

Taken together, these actions increase blood glucose levels. The activity of glucagon is regulated through a negative-feedback mechanism; rising blood glucose levels inhibit further glucagon production and secretion.

Insulin

The primary function of **insulin** is to facilitate the uptake of glucose into body cells. Red blood cells, as well as cells of the brain, liver, kidneys, and the lining of the small intestine, do not have insulin receptors on their cell membranes and do not require insulin for glucose uptake. Although all other body cells do require insulin if they are to take glucose from the bloodstream, skeletal muscle cells and adipose cells are the primary targets of insulin. The presence of food in the intestine triggers the release of gastrointestinal tract hormones such as glucose-dependent insulinotropic peptide (previously known as gastric inhibitory peptide). This is, in turn, the initial trigger for insulin production and

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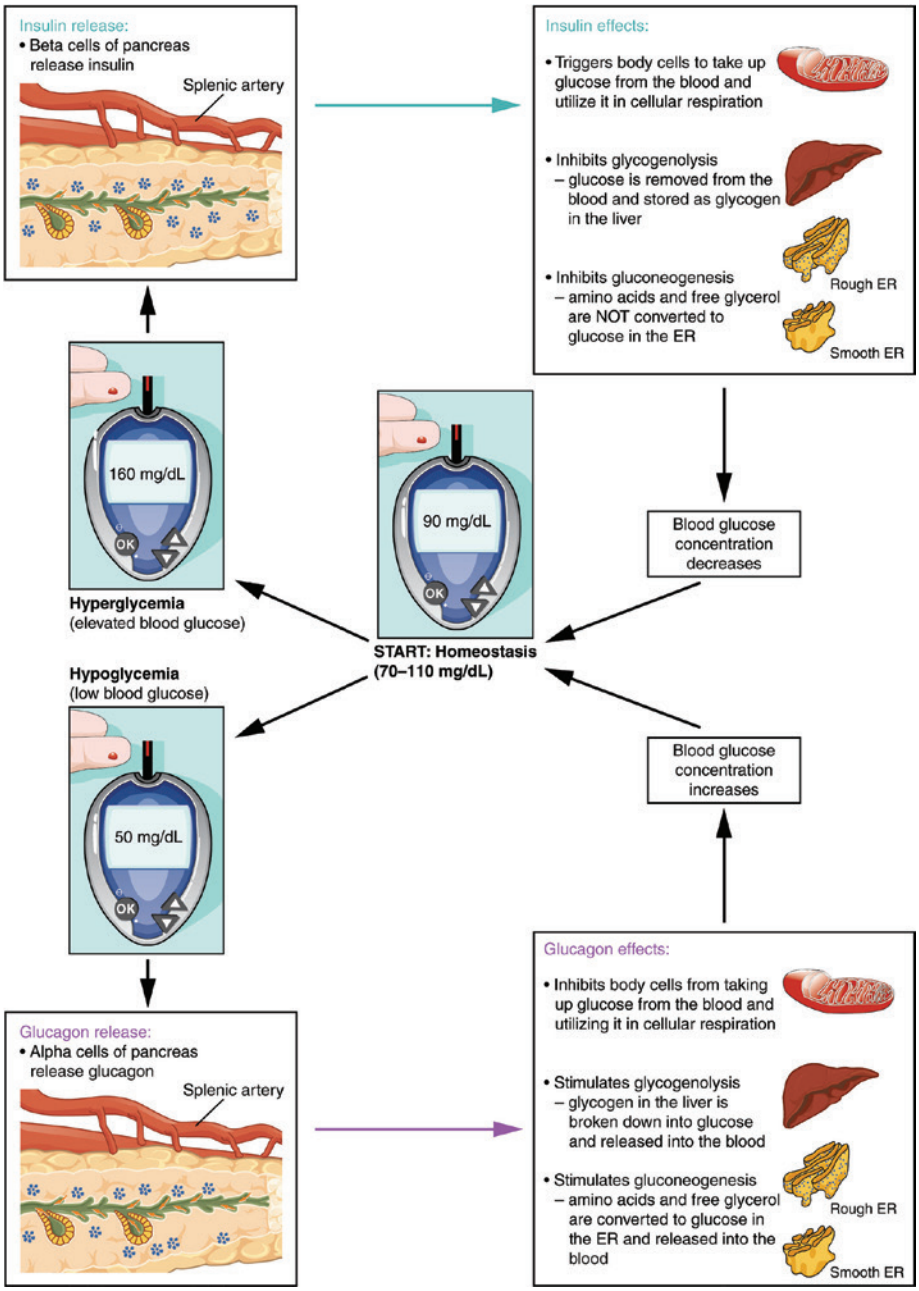


Figure 16.17 Homeostatic Regulation of Blood Glucose Levels. Blood glucose concentration is tightly maintained between 70 mg/dL and 110 mg/dL. If blood glucose concentration rises above this range, insulin is released, which stimulates body cells to remove glucose from the blood. If blood glucose concentration drops below this range, glucagon is released, which stimulates body cells to release glucose into the blood.

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secretion by the beta cells of the pancreas. Once nutrient absorption occurs, the resulting surge in blood glucose levels further stimulates insulin secretion.

Precisely how insulin facilitates glucose uptake is not entirely clear. However, insulin appears to activate a tyrosine kinase receptor, triggering the phosphorylation of many substrates within the cell. These multiple biochemical reactions converge to support the movement of intracellular vesicles containing facilitative glucose transporters to the cell membrane. In the absence of insulin, these transport proteins are normally recycled slowly between the cell membrane and cell interior. Insulin triggers the rapid movement of a pool of glucose transporter vesicles to the cell membrane, where they fuse and expose the glucose transporters to the extracellular fluid. The transporters then move glucose by facilitated diffusion into the cell interior.

Interactive Link 16.8

Visit this link (http://oer.aupress.ca/oer-202505/16.8) to view an animation describing the location and function of the pancreas. What goes wrong in the function of insulin in type 2 diabetes?

Insulin also reduces blood glucose levels by stimulating glycolysis, the metabolism of glucose for generation of ATP. Moreover, it stimulates the liver to convert excess glucose into glycogen for storage, and it inhibits enzymes involved in glycogenolysis and gluconeogenesis. Finally, insulin promotes triglyceride and protein synthesis. The secretion of insulin is regulated through a negative-feedback mechanism. As blood glucose levels decrease, further insulin release is inhibited. The pancreatic hormones are summarized in Table 16.7.

Table 16.7 Hormones of the Pancreas

Associated hormones	Chemical class	Effect
Insulin (beta cells)	Protein	Reduces blood glucose levels
Glucagon (alpha cells)	Protein	Increases blood glucose levels
Somatostatin (delta cells)	Protein	Inhibits insulin and glucagon release
Pancreatic polypeptide (PP cells)	Protein	Plays a role in appetite

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Interactive Link 16.9

Visit this link (http://oer.aupress.ca/oer-202505/16.9) to view an animation describing the role of insulin and the pancreas in diabetes.

16.10 Organs with Secondary Endocrine Functions

Learning Objectives

By the end of this section, you will be able to:

- Identify the organs with a secondary endocrine function, the hormone they produce, and its effects

In your study of anatomy and physiology, you have already encountered a few of the many organs of the body that have secondary endocrine functions. Here, you will learn about the hormone-producing activities of the heart, gastrointestinal tract, kidneys, skeleton, adipose tissue, skin, and thymus.

Heart

When the body experiences an increase in blood volume or pressure, the cells of the heart's atrial wall stretch. In response, specialized cells in the wall of the atria produce and secrete the peptide hormone **atrial natriuretic peptide** (**ANP**). ANP signals the kidneys to reduce sodium reabsorption, thereby decreasing the amount of water reabsorbed from the urine filtrate and reducing blood volume. Other actions of ANP include the inhibition of renin secretion, thus inhibition of the renin-angiotensin-aldosterone system (RAAS) and vasodilation. Therefore, ANP aids in decreasing blood pressure, blood volume, and blood sodium levels.

Gastrointestinal Tract

The endocrine cells of the GI tract are located in the mucosa of the stomach and small intestine. Some of these hormones are secreted in response to eating a meal and aid in digestion. An example of a hormone secreted by the stomach cells is gastrin, a peptide hormone secreted in response to stomach distention that stimulates the release of hydrochloric acid. Secretin is a peptide hormone secreted by the small intestine as acidic chyme (partially digested food and fluid) moves from the stomach. It stimulates the release of bicarbonate from the pancreas, which buffers the acidic chyme, and inhibits the further secretion of hydrochloric acid by the stomach. Cholecystokinin (CCK) is another

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peptide hormone released from the small intestine. It promotes the secretion of pancreatic enzymes and the release of bile from the gallbladder, both of which facilitate digestion. Other hormones produced by the intestinal cells aid in glucose metabolism, such as by stimulating the pancreatic beta cells to secrete insulin, reducing glucagon secretion from the alpha cells, or enhancing cellular sensitivity to insulin.

Kidneys

The kidneys participate in several complex endocrine pathways and produce certain hormones. A decline in blood flow to the kidneys stimulates them to release the enzyme renin, triggering the renin-angiotensin-aldosterone system (RAAS) and stimulating the reabsorption of sodium and water. The reabsorption increases blood flow and blood pressure. The kidneys also play a role in regulating blood calcium levels through the production of calcitriol from vitamin D_3, which is released in response to the secretion of parathyroid hormone (PTH). In addition, the kidneys produce the hormone **erythropoietin** (**EPO**) in response to low oxygen levels. EPO stimulates the production of red blood cells (erythrocytes) in the bone marrow, thereby increasing oxygen delivery to tissues. You may have heard of EPO as a performance-enhancing drug (in a synthetic form).

Skeleton

Although bone has long been recognized as a target for hormones, only recently have researchers recognized that the skeleton itself produces at least two hormones. Fibroblast growth factor 23 (FGF23) is produced by bone cells in response to increased blood levels of vitamin D_3 or phosphate. It triggers the kidneys to inhibit the formation of calcitriol from vitamin D_3 and to increase phosphorus excretion. Osteocalcin, produced by osteoblasts, stimulates the pancreatic beta cells to increase insulin production. It also acts on peripheral tissues to increase their sensitivity to insulin and their utilization of glucose.

Adipose Tissue

Adipose tissue produces and secretes several hormones involved in lipid metabolism and storage. One important example is **leptin**, a protein manufactured by adipose cells that circulates in amounts directly proportional to levels of body fat. Leptin is released in response to food consumption and acts by binding to brain neurons involved in energy intake and expenditure. Binding of leptin produces a feeling of satiety after a meal, thereby reducing appetite. It also appears that the binding of leptin to brain receptors triggers the sympathetic

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nervous system to regulate bone metabolism, increasing deposition of cortical bone. Adiponectin—another hormone synthesized by adipose cells—appears to reduce cellular insulin resistance and to protect blood vessels from inflammation and atherosclerosis. Its levels are lower in people who are obese and rise following weight loss.

Skin

The skin functions as an endocrine organ in the production of the inactive form of vitamin D_3, cholecalciferol. When cholesterol present in the epidermis is exposed to ultraviolet radiation, it is converted to cholecalciferol, which then enters the blood. In the liver, cholecalciferol is converted to an intermediate that travels to the kidneys and is further converted to calcitriol, the active form of vitamin D_3. Vitamin D is important in a variety of physiological processes, including intestinal calcium absorption and immune system function. In some studies, low levels of vitamin D have been associated with increased risks of cancer, severe asthma, and multiple sclerosis. See Table 16.8.

Thymus

The **thymus** is an organ of the immune system that is larger and more active during infancy and early childhood and begins to atrophy as we age. Its endocrine function is the production of a group of hormones called **thymosins** that contribute to the development and differentiation of T lymphocytes, which are immune cells. Although the role of thymosins is not yet well understood, it is clear that they contribute to the immune response. Thymosins have been found in tissues other than the thymus and have a wide variety of functions, so the thymosins cannot be strictly categorized as thymic hormones.

Liver

The liver is responsible for secreting at least four important hormones or hormone precursors: insulin-like growth factor (somatomedin), angiotensinogen, thrombopoietin, and hepcidin. Insulin-like growth factor-1 is the immediate stimulus for growth in the body, especially of the bones. Angiotensinogen is the precursor to angiotensin, mentioned earlier, which increases blood pressure. Thrombopoietin stimulates the production of the blood's platelets.

Hepcidins block the release of iron from cells in the body, helping regulate iron homeostasis in our body fluids.

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Table 16.8 Organs with Secondary Endocrine Functions and Their Major Hormones

Organ	Major hormones	Effects
Heart	Atrial natriuretic peptide (ANP)	Reduces blood volume, blood pressure, and Na^+ concentration
Gastrointestinal tract	Gastrin, secretin, and cholecystokinin	Aids digestion of food and buffering of stomach acids
Gastrointestinal tract	Glucose-dependent insulinotropic peptide (GIP) and glucagon-like peptide 1 (GLP-1)	Stimulates beta cells of the pancreas to release insulin
Kidneys	Renin	Stimulates release of aldosterone
Kidneys	Calcitriol	Aids in the absorption of Ca^{2+}
Kidneys	Erythropoietin	Triggers the formation of red blood cells in the bone marrow
Skeleton	FGF23	Inhibits production of calcitriol and increases phosphate excretion
Skeleton	Osteocalcin	Increases insulin production
Adipose tissue	Leptin	Promotes satiety signals in the brain
Adipose tissue	Adiponectin	Reduces insulin resistance
Skin	Cholecalciferol	Modified to form vitamin D
Thymus (and other organs)	Thymosins	Among other things, aids in the development of T lymphocytes of the immune system
Liver	Insulin-like growth factor-1	Stimulates bodily growth
Liver	Angiotensinogen	Raises blood pressure
Liver	Thrombopoietin	Causes increase in platelets
Liver	Hepcidin	Blocks release of iron into body fluids

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Key Terms

acromegaly: Disorder in adults caused when abnormally high levels of GH trigger growth of bones in the face, hands, and feet.

adenylyl cyclase: Membrane-bound enzyme that converts ATP to cyclic AMP, creating cAMP, as a result of G-protein activation.

adrenal cortex: Outer region of the adrenal glands consisting of multiple layers of epithelial cells and capillary networks that produces mineralocorticoids and glucocorticoids.

adrenal glands: Endocrine glands located at the top of each kidney that are important for the regulation of the stress response, blood pressure and blood volume, water homeostasis, and electrolyte levels.

adrenal medulla: Inner layer of the adrenal glands that plays an important role in the stress response by producing epinephrine and norepinephrine.

adrenocorticotropic hormone (ACTH): Anterior pituitary hormone that stimulates the adrenal cortex to secrete corticosteroid hormones (also called corticotropin).

alarm reaction: The short-term stress, or fight-or-flight, response of stage one of the general adaptation syndrome mediated by the hormones epinephrine and norepinephrine.

aldosterone: Hormone produced and secreted by the adrenal cortex that stimulates sodium and fluid retention and increases blood volume and blood pressure.

alpha cell: Pancreatic islet cell type that produces the hormone glucagon.

angiotensin-converting enzyme: The enzyme that converts angiotensin I to angiotensin II.

anterior pituitary (adenohypophysis): Produces two classes of regulatory hormones: releasing hormones, which stimulate the secretion of specific hormones from the anterior pituitary, and inhibiting hormones, which suppress their secretion.

antidiuretic hormone (ADH): Hypothalamic hormone that is stored by the posterior pituitary and signals the kidneys to reabsorb water.

atrial natriuretic peptide (ANP): Peptide hormone produced by the walls of the atria in response to high blood pressure, blood volume, or blood sodium that reduces the reabsorption of sodium and water in the kidneys and promotes vasodilation.

autocrine: Chemical signal that elicits a response in the same cell that secreted it.

beta cell: Pancreatic islet cell type that produces the hormone insulin.

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calcitonin: Peptide hormone produced and secreted by the parafollicular cells (C cells) of the thyroid gland that functions to decrease blood calcium levels.

chromaffin: Neuroendocrine cells of the adrenal medulla.

colloid: Viscous fluid in the central cavity of thyroid follicles, containing the glycoprotein thyroglobulin.

cortisol: Glucocorticoid important in gluconeogenesis, the catabolism of glycogen, and downregulation of the immune system.

cyclic adenosine monophosphate (cAMP): Second messenger that, in response to adenylyl cyclase activation, triggers a phosphorylation cascade.

delta cell: Minor cell type in the pancreas that secretes the hormone somatostatin.

downregulation: Decrease in the number of hormone receptors, typically in response to chronically excessive levels of a hormone.

endocrine gland: Tissue or organ that secretes hormones into the blood and lymph without ducts such that they may be transported to organs distant from the site of secretion.

endocrine system: Cells, tissues, and organs that secrete hormones as a primary or secondary function and play an integral role in normal bodily processes.

epinephrine: Primary and most potent catecholamine hormone secreted by the adrenal medulla in response to short-term stress; also called adrenaline.

erythropoietin (EPO): Protein hormone secreted in response to low oxygen levels that triggers the bone marrow to produce red blood cells.

estrogens: Class of predominantly female sex hormones important for the development and growth of the female reproductive tract, secondary sex characteristics, the female reproductive cycle, and the maintenance of pregnancy.

exocrine system: Cells, tissues, and organs that secrete substances directly to target tissues via glandular ducts.

first messenger: Hormone that binds to a cell membrane hormone receptor and triggers activation of a second messenger system.

follicle-stimulating hormone (FSH): Anterior pituitary hormone that stimulates the production and maturation of sex cells.

general adaptation syndrome (GAS): The human body's three-stage response pattern to short- and long-term stress.

G protein: Protein associated with a cell membrane hormone receptor that initiates the next step in a second messenger system upon activation by hormone-receptor binding.

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gigantism: Disorder in children caused when abnormally high levels of GH prompt excessive growth.

glucagon: Pancreatic hormone that stimulates the catabolism of glycogen to glucose, thereby increasing blood glucose levels.

glucocorticoids: Hormones produced by the zona fasciculata of the adrenal cortex that influence glucose metabolism.

gonadotropins: Hormones that regulate the function of the gonads.

growth hormone (GH): Anterior pituitary hormone that promotes tissue building and influences nutrient metabolism (also called somatotropin).

hormone: Secretion of an endocrine organ that travels via the bloodstream or lymphatics to induce a response in target cells or tissues in another part of the body.

hormone receptor: Protein within a cell or on the cell membrane that binds a hormone, initiating the target cell response.

hyperparathyroidism: Disorder caused by overproduction of PTH that results in abnormally elevated blood calcium.

hypoparathyroidism: Disorder caused by underproduction of PTH that results in abnormally low blood calcium.

hypophyseal portal system: Network of blood vessels that enables hypothalamic hormones to travel into the anterior lobe of the pituitary without entering the systemic circulation.

hypothalamus: Region of the diencephalon inferior to the thalamus that functions in neural and endocrine signalling.

infundibulum: Stalk containing vasculature and neural tissue that connects the pituitary gland to the hypothalamus (also called the pituitary stalk).

inhibin: Hormone secreted by the male and female gonads that inhibits FSH production by the anterior pituitary.

inhibiting hormones: Hormones that inhibit secretion from the anterior pituitary.

insulin: Pancreatic hormone that enhances the cellular uptake and utilization of glucose, thereby decreasing blood glucose levels.

insulin-like growth factors (IGF): Protein that enhances cellular proliferation, inhibits apoptosis, and stimulates the cellular uptake of amino acids for protein synthesis.

leptin: Protein hormone secreted by adipose tissues in response to food consumption that promotes satiety.

luteinizing hormone (LH): Anterior pituitary hormone that triggers ovulation and the production of ovarian hormones and the production of testosterone.

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melatonin: Amino acid–derived hormone that is secreted in response to low light and causes drowsiness.

mineralocorticoids: Hormones produced by the zona glomerulosa cells of the adrenal cortex that influence fluid and electrolyte balance.

norepinephrine: Secondary catecholamine hormone secreted by the adrenal medulla in response to short-term stress; also called noradrenaline.

osmoreceptor: Hypothalamic sensory receptor that is stimulated by changes in solute concentration (osmotic pressure) in the blood.

oxytocin (OT): Hypothalamic hormone stored in the posterior pituitary gland and important in stimulating uterine contractions in labour, milk ejection during breastfeeding, and feelings of attachment (produced by males and females).

pancreas: Organ with both exocrine and endocrine functions located posterior to the stomach that is important for digestion and the regulation of blood glucose.

pancreatic islets: Specialized clusters of pancreatic cells that have endocrine functions; also called islets of Langerhans.

paracrine: Chemical signal that elicits a response in neighbouring cells; also called paracrine factor.

parathyroid glands: Small, round glands embedded in the posterior thyroid gland that produce parathyroid hormone.

parathyroid hormone (PTH): Peptide hormone produced and secreted by the parathyroid glands in response to low blood calcium levels.

pineal gland: Endocrine gland that secretes melatonin, which is important in regulating the sleep-wake cycle.

pinealocyte: Cell of the pineal gland that produces and secretes the hormone melatonin.

pituitary dwarfism: Disorder in children caused when abnormally low levels of GH result in growth retardation.

pituitary gland: Bean-sized organ suspended from the hypothalamus that produces, stores, and secretes hormones in response to hypothalamic stimulation (also called hypophysis).

posterior pituitary (neurohypophysis): Extension of the neurons of the paraventricular and supraoptic nuclei of the hypothalamus.

PP cell: Minor cell type in the pancreas that secretes the hormone pancreatic polypeptide.

progesterone: Predominantly female sex hormone important in regulating the female reproductive cycle and the maintenance of pregnancy.

prolactin (PRL): Anterior pituitary hormone that promotes development of the mammary glands and the production of breast milk.

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protein kinase: Enzyme that initiates a phosphorylation cascade upon activation.

releasing hormones: Hormones that stimulate the secretion of hormones from the anterior pituitary.

renin-angiotensin-aldosterone system (RAAS): Hormone system that has specialized cells of the kidneys secrete the enzyme renin in response to low blood volume or low blood pressure.

second messenger: Molecule that initiates a signalling cascade in response to hormone binding on a cell membrane receptor and activation of a G protein.

stage of exhaustion: Stage three of the general adaptation syndrome; the body's long-term response to stress mediated by the hormones of the adrenal cortex.

stage of resistance: Stage two of the general adaptation syndrome; the body's continued response to stress after stage one diminishes.

testosterone: Steroid hormone secreted by the testes and important in the maturation of sperm cells, growth and development of the reproductive system, and development of secondary sex characteristics.

thymosins: Hormones produced and secreted by the thymus that play an important role in the development and differentiation of T cells.

thymus: Organ involved in the development and maturation of T cells; particularly active during infancy and childhood.

thyroid gland: Large endocrine gland responsible for the synthesis of thyroid hormones.

thyroid-stimulating hormone (TSH): Anterior pituitary hormone that triggers secretion of thyroid hormones by the thyroid gland (also called thyrotropin).

thyroxine (also tetraiodothyronine, T4): Amino acid–derived thyroid hormone that is more abundant but less potent than T_3 and often converted to T_3 by target cells.

triiodothyronine (also T3): Amino acid–derived thyroid hormone that is less abundant but more potent than T_4.

upregulation: Increase in the number of hormone receptors, typically in response to chronically reduced levels of a hormone.

zona fasciculata: Intermediate region of the adrenal cortex that produces hormones called glucocorticoids.

zona glomerulosa: Most superficial region of the adrenal cortex; produces the hormones collectively referred to as mineralocorticoids.

zona reticularis: Deepest region of the adrenal cortex; produces the steroid sex hormones called androgens.

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Chapter Review

16.1 An Overview of the Endocrine System

The endocrine system consists of cells, tissues, and organs that secrete hormones critical to homeostasis. The body coordinates its functions through two major types of communication: neural and endocrine. Neural communication includes both electrical and chemical signalling between neurons and target cells. Endocrine communication involves chemical signalling via the release of hormones into the extracellular fluid. From there, hormones diffuse into the bloodstream and may travel to distant body regions, where they elicit a response in target cells. Endocrine glands are ductless glands that secrete hormones. Many organs of the body with other primary functions—such as the heart, stomach, and kidneys—also have hormone-secreting cells.

16.2 Hormones

Hormones are derived from amino acids or lipids. Amine hormones originate from the amino acids tryptophan or tyrosine. Larger amino acid hormones include peptides and protein hormones. Steroid hormones are derived from cholesterol.

Steroid hormones and thyroid hormone are lipid soluble. All other amino acid–derived hormones are water soluble. Hydrophobic hormones are able to diffuse through the membrane and interact with an intracellular receptor. In contrast, hydrophilic hormones must interact with cell membrane receptors. These are typically associated with a G protein, which becomes activated when the hormone binds to the receptor. This initiates a signalling cascade that involves a second messenger, such as cyclic adenosine monophosphate (cAMP). Second messenger systems greatly amplify the hormone signal, creating a broader, more efficient, and faster response.

Hormones are released upon stimulation of either chemical or neural origin. Regulation of hormone release is primarily achieved through negative feedback. Various stimuli may cause the release of hormones, but there are three major types. Humoral stimuli are changes in ion or nutrient levels in the blood. Hormonal stimuli are changes in hormone levels that initiate or inhibit the secretion of another hormone. Finally, a neural stimulus occurs when a nerve impulse prompts the secretion or inhibition of a hormone.

16.3 The Pituitary Gland and Hypothalamus

The hypothalamus-pituitary complex is located in the diencephalon of the brain. The hypothalamus and the pituitary gland are connected by a structure called the infundibulum, which contains vasculature and nerve axons. The pituitary

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gland is divided into two distinct structures with different embryonic origins. The posterior lobe houses the axon terminals of hypothalamic neurons. It stores and releases into the bloodstream two hypothalamic hormones: oxytocin and antidiuretic hormone (ADH). The anterior lobe is connected to the hypothalamus by vasculature in the infundibulum and produces and secretes six hormones. Their secretion is regulated, however, by releasing and inhibiting hormones from the hypothalamus. The six anterior pituitary hormones are growth hormone (GH), thyroid-stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin (PRL).

16.4 The Thyroid Gland

The thyroid gland is a butterfly-shaped organ located in the neck anterior to the trachea. Its hormones regulate basal metabolism, oxygen use, nutrient metabolism, the production of ATP, and calcium homeostasis. They also contribute to protein synthesis and the normal growth and development of body tissues, including maturation of the nervous system, and they increase the body's sensitivity to catecholamines. The thyroid hormones triiodothyronine (T_3) and thyroxine (T_4) are produced and secreted by the thyroid gland in response to thyroid-stimulating hormone (TSH) from the anterior pituitary. Synthesis of the amino acid–derived T_3 and T_4 hormones requires iodine.

16.5 The Parathyroid Glands

Calcium is required for a variety of important physiologic processes, including neuromuscular functioning; thus, blood calcium levels are closely regulated. The parathyroid glands are small structures located on the posterior thyroid gland that produce parathyroid hormone (PTH), which regulates blood calcium levels. Low blood calcium levels cause the production and secretion of PTH. In contrast, elevated blood calcium levels inhibit secretion of PTH and trigger secretion of the thyroid hormone calcitonin.

Underproduction of PTH can result in hypoparathyroidism. In contrast, overproduction of PTH can result in hyperparathyroidism.

16.6 The Adrenal Glands

The adrenal glands, located superior to each kidney, consist of two regions: the adrenal cortex and adrenal medulla. The adrenal cortex—the outer layer of the gland—produces mineralocorticoids, glucocorticoids, and androgens. The adrenal medulla at the core of the gland produces epinephrine and norepinephrine.

The adrenal glands mediate a short-term stress response and a long-term stress response. A perceived threat results in the secretion of epinephrine and

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norepinephrine from the adrenal medulla, which mediate the fight-or-flight response. The long-term stress response is mediated by the secretion of CRH from the hypothalamus, which triggers ACTH, which, in turn, stimulates the secretion of corticosteroids from the adrenal cortex. The mineralocorticoids, chiefly aldosterone, cause sodium and fluid retention, which increases blood volume and blood pressure.

16.7 The Pineal Gland

The pineal gland is an endocrine structure of the diencephalon of the brain and is located inferior and posterior to the thalamus. It is made up of pinealocytes. These cells produce and secrete the hormone melatonin in response to low light levels. High blood levels of melatonin induce drowsiness. Jet lag, caused by travelling across several time zones, occurs because melatonin synthesis takes several days to readjust to the light-dark patterns in the new environment.

16.8 Gonadal and Placental Hormones

The reproductive system is regulated by follicle-stimulating hormone (FSH) and luteinizing hormone (LH) produced by the anterior lobe of the pituitary gland in response to gonadotropin-releasing hormone (GnRH) from the hypothalamus. FSH stimulates sperm maturation, which is inhibited by the hormone inhibin. The steroid hormone testosterone, a type of androgen, is released in response to LH and is responsible for the maturation and maintenance of the testicular reproductive system as well as the development of secondary sex characteristics. FSH also promotes egg maturation, and LH signals the secretion of the sex hormones, the estrogens and progesterone. Both of these hormones are important in the development and maintenance of the ovarian reproductive system as well as in maintaining pregnancy. The placenta develops during early pregnancy and secretes several hormones important for maintaining the pregnancy.

16.9 The Endocrine Pancreas

The pancreas has both exocrine and endocrine functions. The pancreatic islet cell types include alpha cells, which produce glucagon; beta cells, which produce insulin; delta cells, which produce somatostatin; and PP cells, which produce pancreatic polypeptide. Insulin and glucagon are involved in the regulation of glucose metabolism. Insulin is produced by the beta cells in response to high blood glucose levels. It enhances glucose uptake and utilization by target cells as well as the storage of excess glucose for later use. Dysfunction of the production of insulin or target cell resistance to the effects of insulin causes diabetes mellitus, a disorder characterized by high blood glucose levels. The

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hormone glucagon is produced and secreted by the alpha cells of the pancreas in response to low blood glucose levels. Glucagon stimulates mechanisms that increase blood glucose levels, such as the catabolism of glycogen into glucose.

16.10 Organs with Secondary Endocrine Functions

Some organs have a secondary endocrine function. For example, the walls of the atria of the heart produce the hormone atrial natriuretic peptide (ANP); the gastrointestinal tract produces the hormones gastrin, secretin, and cholecystokinin, which aid in digestion; and the kidneys produce erythropoietin (EPO), which stimulates the formation of red blood cells. Even bone, adipose tissue, and the skin have secondary endocrine functions.

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PART 4

Fluids and Transport

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17

The Cardiovascular System: Blood

Chapter Objectives

After studying this chapter, you will be able to:

- Identify the primary functions of blood, its fluid and cellular components, and its physical characteristics
- Identify the most important proteins and other solutes present in blood plasma
- Describe the formation of the formed element components of blood
- Discuss the structure and function of red blood cells and hemoglobin
- Classify and characterize white blood cells
- Describe the structure of platelets and explain the process of hemostasis
- Explain the significance of AB and Rh blood groups in blood transfusions

Single-celled organisms do not need blood. They obtain nutrients directly from and excrete wastes directly into their environment. The human organism cannot do that. Our large, complex bodies need blood to deliver nutrients to and remove wastes from our trillions of cells. The heart pumps blood throughout the body in a network of blood vessels. Together, these three components—blood, heart, and vessels—make up the cardiovascular system. This chapter focuses on the medium of transport: blood.

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17.1 An Overview of Blood

Learning Objectives

By the end of this section, you will be able to:

- Identify the primary functions of blood in transportation, defence, and maintenance of homeostasis
- Name the fluid component of blood and the three major types of formed elements, and identify their relative proportions in a blood sample
- Discuss the unique physical characteristics of blood
- Identify the composition of blood plasma, including its most important solutes and plasma proteins

Recall that **blood** is a connective tissue. Like all connective tissues, it is made up of cellular elements and an extracellular matrix. The cellular elements—referred to as the **formed elements**—include **red blood cells** (**RBCs**), **white blood cells** (**WBCs**), and cell fragments called **platelets**. The extracellular matrix, called **plasma**, makes blood unique among connective tissues because it is fluid. This fluid, which is mostly water, perpetually suspends the formed elements and enables them to circulate throughout the body within the cardiovascular system.

Functions of Blood

The primary function of blood is to deliver oxygen and nutrients to and remove wastes from body cells, but that is only the beginning of the story. The specific functions of blood also include defence, distribution of heat, and maintenance of homeostasis.

Transportation

Nutrients from the foods you eat are absorbed in the digestive tract. Most of these travel in the bloodstream directly to the liver, where they are processed and released back into the bloodstream for delivery to body cells. Oxygen from the air you breathe diffuses into the blood, which moves from the lungs to the heart, which then pumps it out to the rest of the body. Moreover, endocrine glands scattered throughout the body release their products, called hormones, into the bloodstream, which carries them to distant target cells. Blood also picks up cellular wastes and by-products and transports them to various organs for removal. For instance, blood moves carbon dioxide to the lungs for exhalation

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from the body, and various waste products are transported to the kidneys and liver for excretion from the body in the form of urine or bile.

Defence

Many types of WBCs protect the body from external threats, such as disease-causing bacteria that have entered the bloodstream through a wound. Other WBCs seek out and destroy internal threats, such as cells with mutated DNA that could multiply to become cancerous or body cells infected with viruses.

When damage to the vessels results in bleeding, blood platelets and certain proteins dissolved in the plasma, the fluid portion of the blood, interact to block the ruptured areas of the blood vessels involved. This protects the body from further blood loss.

Maintenance of Homeostasis

Recall that body temperature is regulated via a classic negative-feedback loop. If you were exercising on a warm day, your rising core body temperature would trigger several homeostatic mechanisms, including increased transport of blood from your core to your body periphery, which is typically cooler. As blood passes through the vessels of the skin, heat would be dissipated to the environment, and the blood returning to your body core would be cooler. In contrast, on a cold day, blood is diverted away from the skin to maintain a warmer body core. In extreme cases, this may result in frostbite.

Blood also helps maintain the chemical balance of the body. Proteins and other compounds in blood act as buffers, which thereby help regulate the pH of body tissues. Blood also helps regulate the water content of body cells.

Composition of Blood

You have probably had blood drawn from a superficial vein in your arm, which was then sent to a lab for analysis. Some of the most common blood tests—for instance, those measuring lipid or glucose levels in plasma—determine which substances are present within blood and in what quantities. Other blood tests check for the composition of the blood itself, including the quantities and types of formed elements.

One such test, called a **hematocrit**, measures the percentage of RBCs, clinically known as erythrocytes, in a blood sample. It is performed by spinning the blood sample in a specialized centrifuge, a process that causes the heavier elements suspended within the blood sample to separate from the lightweight, liquid plasma (Figure 17.1). Because the heaviest elements in blood are the erythrocytes, these settle at the very bottom of the hematocrit tube. Located above the erythrocytes is a pale, thin layer composed of the remaining formed

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elements of blood. These are the WBCs, clinically known as leukocytes, and the platelets, cell fragments also called thrombocytes. This layer is referred to as the **buffy coat** because of its colour; it normally constitutes less than 1 percent of a blood sample.

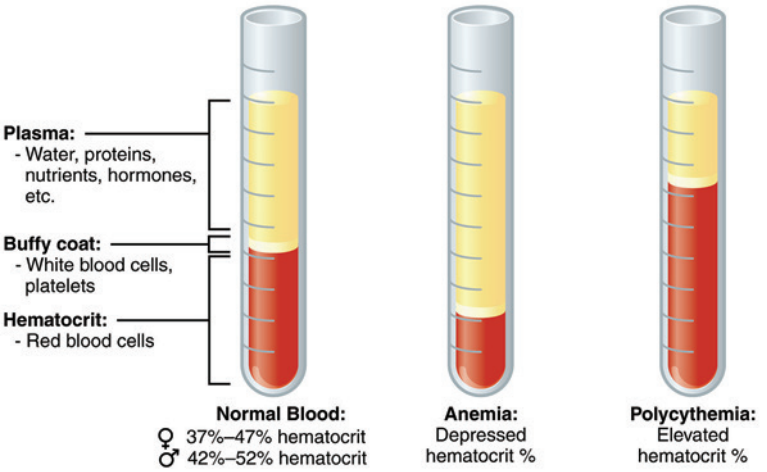


Figure 17.1 Composition of Blood. The cellular elements of blood include a vast number of erythrocytes and comparatively fewer leukocytes and platelets. Plasma is the fluid in which the formed elements are suspended. A sample of blood spun in a centrifuge reveals that plasma is the lightest component. It floats at the top of the tube, separated from the heaviest elements, the erythrocytes, by a buffy coat of leukocytes and platelets. Hematocrit is the percentage of the total sample that is composed of erythrocytes. Depressed and elevated hematocrit levels are shown for comparison.

Above the buffy coat is the blood plasma, normally a pale, straw-coloured fluid, which constitutes the remainder of the sample.

The volume of erythrocytes after centrifugation is also commonly referred to as **packed cell volume** (**PCV**). In normal blood, about 45 percent of a sample is erythrocytes. The hematocrit of any one sample can vary significantly, from about 36 to 50 percent, according to gender and other factors. Normal hematocrit values for females range from 37 to 47, with a mean value of 41; for males, hematocrit ranges from 42 to 52, with a mean of 47. The percentage of other formed elements, the WBCs and platelets, is extremely small, so it is not normally considered with the hematocrit. So the mean plasma percentage is the percentage of blood that is not erythrocytes: For females, it is approximately 59 (or 100 minus 41), and for males, it is approximately 53 (or 100 minus 47).

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Characteristics of Blood

When you think about blood, the first characteristic that probably comes to mind is its colour. Blood that has just taken up oxygen in the lungs is bright red, and blood that has released oxygen in the tissues is a duskier red. This is because hemoglobin is a pigment that changes colour depending on the degree of oxygen saturation.

Blood is viscous and somewhat sticky to the touch. It has a viscosity approximately five times greater than water. Viscosity is a measure of a fluid's thickness or resistance to flow and is influenced by the presence of the plasma proteins and formed elements within the blood. The viscosity of blood has a dramatic impact on blood pressure and flow. Consider the difference in flow between water and honey. The more viscous honey would demonstrate a greater resistance to flow than the less viscous water. The same principle applies to blood.

The normal temperature of blood is slightly higher-than-normal body temperature—about 38°C, compared to 37°C for an internal body temperature reading, although daily variations of 0.5°C are normal. Although the surface of blood vessels is relatively smooth, as blood flows through them, it experiences some friction and resistance, especially as vessels age and lose their elasticity, thereby producing heat. This accounts for its slightly higher temperature.

The pH of blood averages about 7.4; however, it can range from 7.35 to 7.45 in a healthy person. Blood is therefore somewhat more basic (alkaline) on a chemical scale than pure water, which has a pH of 7.0. Blood contains numerous buffers that actually help regulate pH.

Blood constitutes approximately 8 percent of adult body weight. Adult males typically average about 5 to 6 L of blood. Females average 4–5 L.

Blood Plasma

Like other fluids in the body, plasma is composed primarily of water: In fact, it is about 92 percent water. Dissolved or suspended within this water is a mixture of substances, most of which are proteins. There are literally hundreds of substances dissolved or suspended in the plasma, although many of them are found only in very small quantities.

Interactive Link 17.1

Visit this site (http://oer.aupress.ca/oer-202505/17.1) for a list of normal levels established for many of the substances found in a sample of blood. Serum, one of the specimen types included, refers to a sample of plasma after clotting factors have been removed. What types of measurements are given for levels of glucose in the blood?

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Plasma Proteins

About 7 percent of the volume of plasma—nearly all that is not water—is made of proteins. These include several plasma proteins (proteins that are unique to the plasma), plus a much smaller number of regulatory proteins, including enzymes and some hormones. The major components of plasma are summarized in Table 17.1.

The three major groups of plasma proteins are as follows:

- **Albumin** is the most abundant of the plasma proteins. Manufactured by the liver, albumin molecules serve as binding proteins—transport vehicles for fatty acids and steroid hormones. Recall that lipids are hydrophobic; however, their binding to albumin enables their transport in the watery plasma. Albumin is also the most significant contributor to the osmotic pressure of blood; that is, its presence holds water inside the blood vessels and draws water from the tissues, across blood vessel walls, and into the bloodstream. This, in turn, helps maintain both blood volume and blood pressure. Albumin normally accounts for approximately 54 percent of the total plasma protein content, with clinical levels ranging from 3.5–5.0 g/dL of blood.
- The second most common plasma protein is the **globulins**. A heterogeneous group, there are three main subgroups known as alpha, beta, and gamma globulins. The alpha and beta globulins transport iron, lipids, and the fat-soluble vitamins A, D, E, and K to the cells; like albumin, they also contribute to osmotic pressure. The gamma globulins are proteins involved in immunity and are better known as **antibodies** or **immunoglobulins**. Although other plasma proteins are produced by the liver, immunoglobulins are produced by specialized leukocytes known as plasma cells. Globulins make up approximately 38 percent of the total plasma protein volume, in clinical levels of 1.0–1.5 g/dL blood.
- **Fibrinogen** is the third of the three major groups of plasma proteins. Like albumin and the alpha and beta globulins, fibrinogen is produced by the liver. It is essential for blood clotting, a process described later in this chapter. Fibrinogen accounts for about 7 percent of the total plasma protein volume, in clinical levels of 0.2–0.45 g/dL blood.

Other Plasma Solutes

In addition to proteins, plasma contains a wide variety of other substances. These include various electrolytes, such as sodium, potassium, and calcium ions; dissolved gases, such as oxygen, carbon dioxide, and nitrogen; various organic nutrients, such as vitamins, lipids, glucose, and amino acids; and metabolic wastes. All of these nonprotein solutes combined contribute approximately 1 percent to the total volume of plasma.

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Table 17.1 Major Blood Components

Component and % of blood	Subcomponent and % of component	Type and % (where appropriate)	Site of production	Major function(s)
Plasma 46–63 percent	Water 92 percent	Fluid	Absorbed by intestinal tract or produced by metabolism	Transport medium
	Plasma proteins 7 percent	Albumin 54–60 percent	Liver	Maintain osmotic concentration, transport lipid molecules
		Globulins 35–38 percent	Alpha globulins—liver Beta globulins—liver	Transport, maintain osmotic concentration
			Gamma globulins (immunoglobulins) —plasma cells	Immune responses
		Fibrinogen 4–7 percent	Liver	Blood clotting in hemostasis
	Regulatory proteins <1 percent	Hormones and enzymes	Various sources	Regulate various body functions
	Other solutes 1 percent	Nutrients, gases, and wastes	Absorbed by intestinal tract, exchanged in respiratory system, or produced by cells	Numerous and varied
Formed elements 37–54 percent	Erythrocytes 99 percent	Erythrocytes	Red bone marrow	Transport gases, primarily oxygen and some carbon dioxide
	Leukocytes <1 percent	Granular leukocytes: neutrophils, eosinophils, basophils	Red bone marrow	Nonspecific immunity
		Agranular leukocytes: lymphocytes, monocytes	Lymphocytes: bone marrow and lymphatic tissue	Lymphocytes: specific immunity
			Monocytes: red bone marrow	Monocytes: nonspecific immunity
	Platelets <1 percent	Platelets	Megakaryocytes: red bone marrow	Hemostasis

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17.2 Production of the Formed Elements

Learning Objectives

By the end of this section, you will be able to:

- Trace the generation of the formed elements of blood from bone marrow stem cells
- Discuss the role of hemopoietic growth factors in promoting the production of the formed elements

The lifespan of the formed elements is very brief. Although one type of leukocyte called memory cells can survive for years, most erythrocytes, leukocytes, and platelets normally live only a few hours to a few weeks. Thus, the body must form new blood cells and platelets quickly and continuously. When you donate a unit of blood during a blood drive (approximately 475 mL), your body typically replaces the donated plasma within 24 hours, but it takes about 4 to 6 weeks to replace the blood cells. This restricts the frequency with which donors can contribute their blood. The process by which this replacement occurs is called **hemopoiesis**, or hematopoiesis.

Sites of Hemopoiesis

Prior to birth, hemopoiesis occurs in a number of tissues, beginning with the yolk sac of the developing embryo and continuing in the fetal liver, spleen, lymphatic tissue, and eventually the red bone marrow. Following birth, most hemopoiesis occurs in the **red marrow**, a connective tissue within the spaces of spongy (cancellous) bone tissue. In children, hemopoiesis can occur in the medullary cavity of long bones; in adults, the process is largely restricted to the cranial and pelvic bones, the vertebrae, the sternum, and the proximal epiphyses of the femur and humerus.

Throughout adulthood, the liver and spleen maintain their ability to generate the formed elements. This process is referred to as extramedullary hemopoiesis (meaning hemopoiesis outside the medullary cavity of adult bones).

When a disease such as bone cancer destroys the bone marrow, causing hemopoiesis to fail, extramedullary hemopoiesis may be initiated.

Differentiation of Formed Elements from Stem Cells

All formed elements arise from stem cells of the red bone marrow. Recall that stem cells undergo mitosis plus cytokinesis (cellular division) to give rise to

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new daughter cells: One of these remains a stem cell, and the other differentiates into one of any number of diverse cell types. Stem cells may be viewed as occupying a hierarchal system, with some loss of the ability to diversify at each step. The **totipotent stem cell** is the zygote, or fertilized egg. The totipotent (multipotent) stem cell gives rise to all cells of the human body. The next level is the **pluripotent stem cell**, which gives rise to multiple types of cells of the body and some of the supporting fetal membranes.

Beneath this level, the mesenchymal cell is a stem cell that develops only into types of connective tissue, including fibrous connective tissue, bone, cartilage, and blood, but not epithelium, muscle, and nervous tissue. One step lower on the hierarchy of stem cells is the **hematopoietic stem cell**, or **hemocytoblast**. All of the formed elements of blood originate from this specific type of cell.

Hemopoiesis begins when the hematopoietic stem cell is exposed to appropriate chemical stimuli collectively called **hemopoietic growth factors**, which prompt it to divide and differentiate. One daughter cell remains a hematopoietic stem cell, allowing hemopoiesis to continue. The other daughter cell becomes either of two types of more specialized stem cells (Figure 17.2):

- **Lymphoid stem cells** give rise to a class of leukocytes known as lymphocytes, which include the various T cells, B cells, and natural killer (NK) cells, all of which function in immunity. However, hemopoiesis of lymphocytes progresses somewhat differently from the process for the other formed elements. In brief, lymphoid stem cells quickly migrate from the bone marrow to lymphatic tissues, including the lymph nodes, spleen, and thymus, where their production and differentiation continues. B cells are so named because they mature in the bone marrow, while T cells mature in the thymus.
- **Myeloid stem cells** give rise to all the other formed elements, including the erythrocytes; megakaryocytes that produce platelets; and a myeloblast lineage that gives rise to monocytes and three forms of granular leukocytes: neutrophils, eosinophils, and basophils.

Lymphoid and myeloid stem cells do not immediately divide and differentiate into mature formed elements. As you can see in Figure 17.2, there are several intermediate stages of precursor cells (literally, forerunner cells), many of which can be recognized by their names, which have the suffix *-blast*. For instance, megakaryoblasts are the precursors of megakaryocytes, and proerythroblasts become reticulocytes, which eject their nucleus and most other organelles before maturing into erythrocytes.

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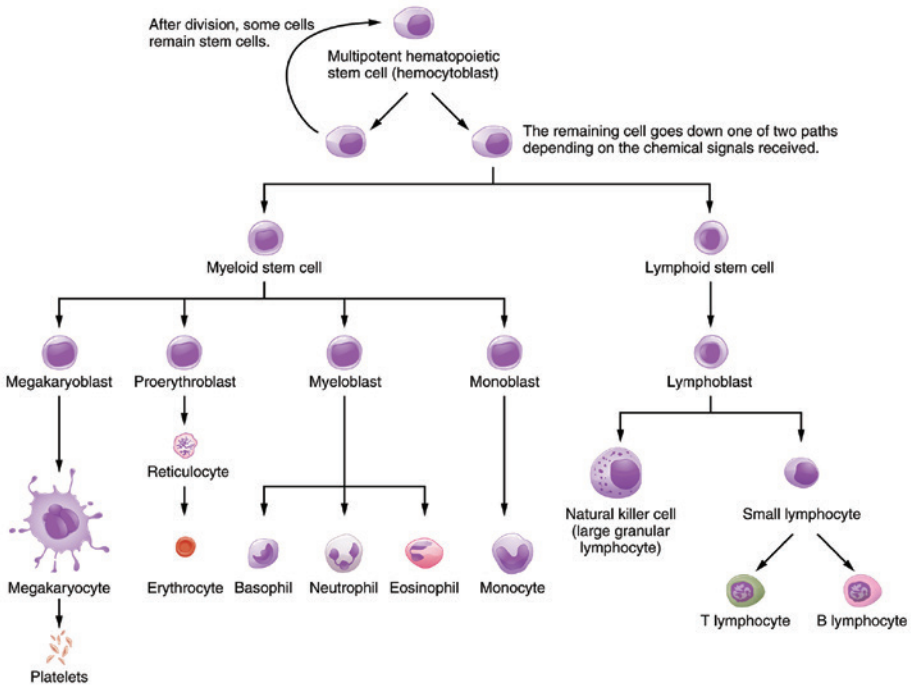


Figure 17.2 Hematopoietic System of Bone Marrow. Hemopoiesis is the proliferation and differentiation of the formed elements of blood.

Hemopoietic Growth Factors

Development from stem cells to precursor cells to mature cells is again initiated by hemopoietic growth factors. These include the following:

- **Erythropoietin** (**EPO**) is a glycoprotein hormone secreted by the interstitial fibroblast cells of the kidneys in response to low oxygen levels. It prompts the production of erythrocytes. Some athletes use synthetic EPO as a performance-enhancing drug (called blood doping) to increase RBC counts and subsequently increase oxygen delivery to tissues throughout the body.
- **Thrombopoietin**, another glycoprotein hormone, is produced by the liver and kidneys. It triggers the development of megakaryocytes into platelets.
- **Cytokines** are glycoproteins secreted by a wide variety of cells, including red bone marrow, leukocytes, macrophages, fibroblasts, and endothelial cells. They act locally as autocrine or paracrine factors, stimulating the proliferation of progenitor cells and helping stimulate both nonspecific and specific resistance to disease. There are two major subtypes of cytokines known as colony-stimulating factors and interleukins.

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- **Colony-stimulating factors** (**CSFs**) are glycoproteins that act locally, as autocrine or paracrine factors. Some trigger the differentiation of myeloblasts into granular leukocytes—namely, neutrophils, eosinophils, and basophils. These are referred to as granulocyte CSFs. A different CSF induces the production of monocytes, called monocyte CSFs. Both granulocytes and monocytes are stimulated by GM-CSF; granulocytes, monocytes, platelets, and erythrocytes are stimulated by multi-CSF. Synthetic forms of these hormones are often administered to patients with various forms of cancer who are receiving chemotherapy to revive their WBC counts.
- **Interleukins** are another class of cytokine signalling molecules important in hemopoiesis. They were initially thought to be secreted uniquely by leukocytes and to communicate only with other leukocytes and were named accordingly but are now known to be produced by a variety of cells including bone marrow and endothelium. Researchers now suspect that interleukins may play other roles in body functioning, including differentiation and maturation of cells, producing immunity and inflammation. To date, more than a dozen interleukins have been identified, with others likely to follow. They are generally numbered IL-1, IL-2, IL-3, and so on.

Interactive Link 17.2

Watch this video (http://oer.aupress.ca/oer-202505/17.2) to see doctors discuss the dangers of blood doping in sports. What are some potential side effects of blood doping?

17.3 Erythrocytes

Learning Objectives

By the end of this section, you will be able to:

- Describe the anatomy of erythrocytes
- Discuss the various steps in the life cycle of an erythrocyte
- Explain the composition and function of hemoglobin

The **erythrocyte**, commonly known as a red blood cell (or RBC), is by far the most common formed element: A single drop of blood contains millions of

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erythrocytes and just thousands of leukocytes. Specifically, males have about 5.4 million erythrocytes per microlitre (μL) of blood, and females have approximately 4.8 million per μL. In fact, erythrocytes are estimated to make up about 25 percent of the total cells in the body. As you can imagine, they are quite small cells, with a mean diameter of only about 7–8 μm (Table 17.2). The primary functions of erythrocytes are to pick up inhaled oxygen from the lungs and transport it to the body's tissues and to pick up some (about 24 percent) carbon dioxide waste at the tissues and transport it to the lungs for exhalation.

Erythrocytes remain within the vascular network. Although leukocytes typically leave the blood vessels to perform their defensive functions, movement of erythrocytes from the blood vessels is abnormal.

Table 17.2 Summary of Formed Elements in Blood

Formed element	Major subtypes	Numbers per μL (mean and range)	Appearance in a standard blood smear	Summary of functions	Comments
Erythrocytes (red blood cells)		5.2 million (4.4–6.0 million)	Flattened biconcave disk; no nucleus; pale-red colour	Transport oxygen and some carbon dioxide between tissues and lungs	Lifespan of approximately 120 days
Leukocytes (white blood cells)		7000 (5000–10,000)	Obvious dark-staining nucleus	All function in body defences	Exit capillaries and move into tissues; usual lifespan of a few hours or days
	Granulocytes (neutrophils, eosinophils, basophils)	4360 (1800–9950)	Abundant granules in cytoplasm; nucleus normally lobed	Nonspecific (innate) resistance to disease	Classified according to membrane-bound granules in cytoplasm
	Neutrophils	4150 (1800–7300)	Nuclear lobes increase with age; pale-lilac granules	Phagocytic; effective against bacteria; release cytotoxic chemicals	Most common leukocyte; lifespan of minutes to days

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Table 17.2 Summary of Formed Elements in Blood (*continued*)

Formed element	Major subtypes	Numbers per µL (mean and range)	Appearance in a standard blood smear	Summary of functions	Comments
	Eosinophils	165 (0–700)	Nucleus generally two-lobed; bright-red-orange granules	Phagocytic; attack antigen-antibody complexes; release antihistamines	Lifespan of minutes to days
	Basophils	44 (0–150)	Nucleus generally two-lobed but obscured by dense, dark-purple granules	Promote inflammation	Least common leukocyte; lifespan unknown
	Agranulocytes (lymphocytes and monocytes)	2640 (1700–4950)	Lack abundant granules; simple/indented nucleus	Body defences	Group includes two major cell types from different lineages
	Lymphocytes	2185 (1500–4000)	Spherical cell; large nucleus; stains purple; seen in NK, B, and T cells	Specific (adaptive) immunity; T cells attack; B cells release antibodies	Originate in bone marrow; secondary production in lymphatic tissue; lifespan of many years
	Monocytes	455 (200–950)	Largest leukocyte; indented or horseshoe-shaped nucleus	Phagocytic; engulf pathogens; act as antigen-presenting cells	Produced in red bone marrow; become macrophages
Platelets		350,000 (150,000–500,000)	Cellular fragments with granules; purple stain	Hemostasis; release growth factors for healing	From megakaryocytes in red bone marrow

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Shape and Structure of Erythrocytes

As an erythrocyte matures in the red bone marrow, it extrudes its nucleus and most of its other organelles. During the first day or two that it is in the circulation, an immature erythrocyte, known as a **reticulocyte**, will still typically contain remnants of organelles. Reticulocytes should comprise approximately 1 to 2 percent of the erythrocyte count and provide a rough estimate of the rate of RBC production, with abnormally low or high rates indicating deviations in the production of these cells. These remnants, primarily of networks (reticulum) of ribosomes, are quickly shed, however, and mature, circulating erythrocytes have few internal cellular structural components. Lacking mitochondria, for example, they rely on anaerobic respiration. This means that they do not utilize any of the oxygen they are transporting, so they can deliver it all to the tissues. They also lack endoplasmic reticula and do not synthesize proteins. Erythrocytes do, however, contain some structural proteins that help the blood cells maintain their unique structure and enable them to change their shape to squeeze through capillaries. This includes the protein spectrin, a cytoskeletal protein element.

Erythrocytes are biconcave disks; that is, they are plump at their periphery and very thin in the centre (Figure 17.3). Since they lack most organelles, there is more interior space for the presence of the hemoglobin molecules that, as you will see shortly, transport gases. The biconcave shape also provides a greater surface area across which gas exchange can occur relative to its volume; a sphere of a similar diameter would have a lower ratio of surface area to volume. In the capillaries, the oxygen carried by the erythrocytes can diffuse into the plasma and then through the capillary walls to reach the cells, whereas some of the carbon dioxide produced by the cells as a waste product diffuses into the capillaries to be picked up by the erythrocytes. Capillary beds are extremely narrow, slowing the passage of the erythrocytes and providing an extended opportunity for gas exchange to occur. However, the space within capillaries can be so minute that, despite their own small size, erythrocytes may have to fold in on themselves if they are to make their way through. Fortunately, their structural proteins like spectrin are flexible, allowing them to bend over themselves to a surprising degree, then spring back again when they enter a wider vessel. In wider vessels, erythrocytes may stack up much like a roll of coins, forming a rouleaux.

Hemoglobin

Hemoglobin is a large molecule made up of proteins and iron. It consists of four folded chains of a protein called **globin**, designated alpha 1 and 2 and beta 1 and 2 (Figure 17.4a). Each of these globin molecules is bound to a red pigment molecule called **heme**, which contains an ion of iron (Fe^{2+}; Figure 17.4b).

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Figure 17.3 Shape of Red Blood Cells. Erythrocytes are biconcave discs with very shallow centres. This shape optimizes the ratio of surface area to volume, facilitating gas exchange. It also enables them to fold up as they move through narrow blood vessels.

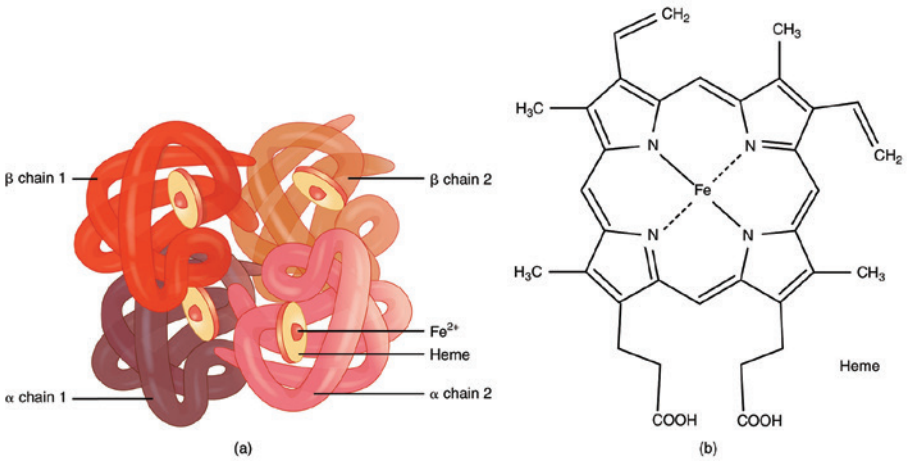


Figure 17.4 Hemoglobin. (a) A molecule of hemoglobin contains four globin proteins, each of which is bound to one molecule of the iron-containing pigment heme. (b) A single erythrocyte can contain 300 million hemoglobin molecules and thus more than 1 billion oxygen molecules.

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Each iron ion in the heme can bind to one oxygen molecule; therefore, each hemoglobin molecule can transport four oxygen molecules. An individual erythrocyte may contain about 300 million hemoglobin molecules and therefore can bind to and transport up to 1.2 billion oxygen molecules (see Figure 17.4b).

In the lungs, hemoglobin picks up oxygen, which binds to the iron ions, forming **oxyhemoglobin**. The bright-red, oxygenated hemoglobin travels to the body tissues, where it releases some of the oxygen molecules, becoming darker-red **deoxyhemoglobin**, sometimes referred to as reduced hemoglobin. Oxygen release depends on the need for oxygen in the surrounding tissues, so hemoglobin rarely, if ever, leaves all of its oxygen behind. In the capillaries, carbon dioxide enters the bloodstream. About 76 percent dissolves in the plasma, some of it remaining as dissolved CO_2 and the remainder forming bicarbonate ion. About 23 to 24 percent of it binds to the amino acids in hemoglobin, forming a molecule known as **carbaminohemoglobin**. From the capillaries, the hemoglobin carries carbon dioxide back to the lungs, where it releases it in exchange for oxygen.

Changes in the levels of RBCs can have significant effects on the body's ability to effectively deliver oxygen to the tissues. Ineffective hematopoiesis results in insufficient numbers of RBCs and results in one of several forms of anemia. An overproduction of RBCs produces a condition called polycythemia. The primary drawback with polycythemia is not a failure to directly deliver enough oxygen to the tissues but rather the increased viscosity of the blood, which makes it more difficult for the heart to circulate the blood.

In patients with insufficient hemoglobin, the tissues may not receive sufficient oxygen, resulting in another form of anemia. In determining oxygenation of tissues, the value of greatest interest in health care is the percent saturation—that is, the percentage of hemoglobin sites occupied by oxygen in a patient's blood. Clinically this value is commonly referred to simply as "percent sat."

The kidneys filter about 180 L of blood in an average adult each day, or about 20 percent of the total resting volume, and thus serve as ideal sites for receptors that determine oxygen saturation. In response to hypoxemia, less oxygen will exit the vessels supplying the kidney, resulting in hypoxia (low oxygen concentration) in the tissue fluid of the kidney, where oxygen concentration is actually monitored. Interstitial fibroblasts within the kidney secrete EPO, thereby increasing erythrocyte production and restoring oxygen levels. In a classic negative-feedback loop, as oxygen saturation rises, EPO secretion falls, and vice versa, thereby maintaining homeostasis.

Populations dwelling at high elevations, with inherently lower levels of oxygen in the atmosphere, naturally maintain a hematocrit higher than people

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living at sea level. Consequently, people travelling to high elevations may experience symptoms of hypoxemia, such as fatigue, headache, and shortness of breath, for a few days after their arrival. In response to the hypoxemia, the kidneys secrete EPO to step up the production of erythrocytes until homeostasis is achieved once again. To avoid the symptoms of hypoxemia, or altitude sickness, mountain climbers typically rest for several days to a week or more at a series of camps situated at increasing elevations to allow EPO levels and, consequently, erythrocyte counts to rise. When climbing the tallest peaks, such as Mt. Everest and K2 in the Himalayas, many mountain climbers rely on bottled oxygen as they near the summit.

Life Cycle of Erythrocytes

Production of erythrocytes in the marrow occurs at the staggering rate of more than 2 million cells per second. For this production to occur, a number of raw materials must be present in adequate amounts. These include the same nutrients that are essential to the production and maintenance of any cell, such as glucose, lipids, and amino acids. However, erythrocyte production also requires several trace elements:

- *Iron.* We have said that each heme group in a hemoglobin molecule contains an ion of the trace mineral iron. On average, less than 20 percent of the iron we consume is absorbed. Heme iron, from animal foods such as meat, poultry, and fish, is absorbed more efficiently than nonheme iron from plant foods. Upon absorption, iron becomes part of the body's total iron pool. The bone marrow, liver, and spleen can store iron in the protein compounds **ferritin** and **hemosiderin**. Ferroportin transports the iron across the intestinal cell plasma membranes and from its storage sites into tissue fluid, where it enters the blood. When EPO stimulates the production of erythrocytes, iron is released from storage, bound to transferrin, and carried to the red marrow, where it attaches to erythrocyte precursors.
- *Copper.* A trace mineral, copper is a component of two plasma proteins, hephaestin and ceruloplasmin. Without these, hemoglobin could not be adequately produced. Located in intestinal villi, hephaestin enables iron to be absorbed by intestinal cells. Ceruloplasmin transports copper. Both enable the oxidation of iron from Fe^{2+} to Fe^{3+}, a form in which it can be bound to its transport protein, **transferrin**, for transport to body cells. In a state of copper deficiency, the transport of iron for heme synthesis decreases, and iron can accumulate in tissues, where it can eventually lead to organ damage.

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- *Zinc.* The trace mineral zinc functions as a coenzyme that facilitates the synthesis of the heme portion of hemoglobin.
- *B vitamins.* The B vitamins folate and vitamin B_{12} function as coenzymes that facilitate DNA synthesis. Thus, both are critical for the synthesis of new cells, including erythrocytes.

Erythrocytes live an average of 120 days in the circulation, after which the worn-out cells are removed by a type of myeloid phagocytic cell called a **macrophage**, located primarily within the bone marrow, liver, and spleen. The components of the degraded erythrocytes' hemoglobin are further processed as follows:

- Globin, the protein portion of hemoglobin, is broken down into amino acids, which can be sent back to the bone marrow to be used in the production of new erythrocytes. Hemoglobin that is not phagocytized is broken down in the circulation, releasing alpha and beta chains that are removed from circulation by the kidneys.
- The iron contained in the heme portion of hemoglobin may be stored in the liver or spleen, primarily in the form of ferritin or hemosiderin, or carried through the bloodstream by transferrin to the red bone marrow for recycling into new erythrocytes.
- The noniron portion of heme is degraded into the waste product **biliverdin**, a green pigment, and then into another waste product, **bilirubin**, a yellow pigment. Bilirubin binds to albumin and travels in the blood to the liver, which uses it in the manufacture of bile, a compound released into the intestines to help emulsify dietary fats. In the large intestine, bacteria break the bilirubin apart from the bile and convert it to urobilinogen and then into stercobilin. It is then eliminated from the body in the feces. Broad-spectrum antibiotics typically eliminate these bacteria as well and may alter the colour of feces. The kidneys also remove any circulating bilirubin and other related metabolic by-products such as urobilins and secrete them into the urine.

The breakdown pigments formed from the destruction of hemoglobin can be seen in a variety of situations. At the site of an injury, biliverdin from damaged RBCs produces some of the dramatic colours associated with a **bruise**. With a failing liver, bilirubin cannot be removed effectively from circulation and causes the body to assume a yellowish tinge associated with **jaundice**. Stercobilins within the feces produce the typical brown colour associated with this waste. And the yellow of urine is associated with the urobilins.

The erythrocyte life cycle is summarized in Figure 17.5.

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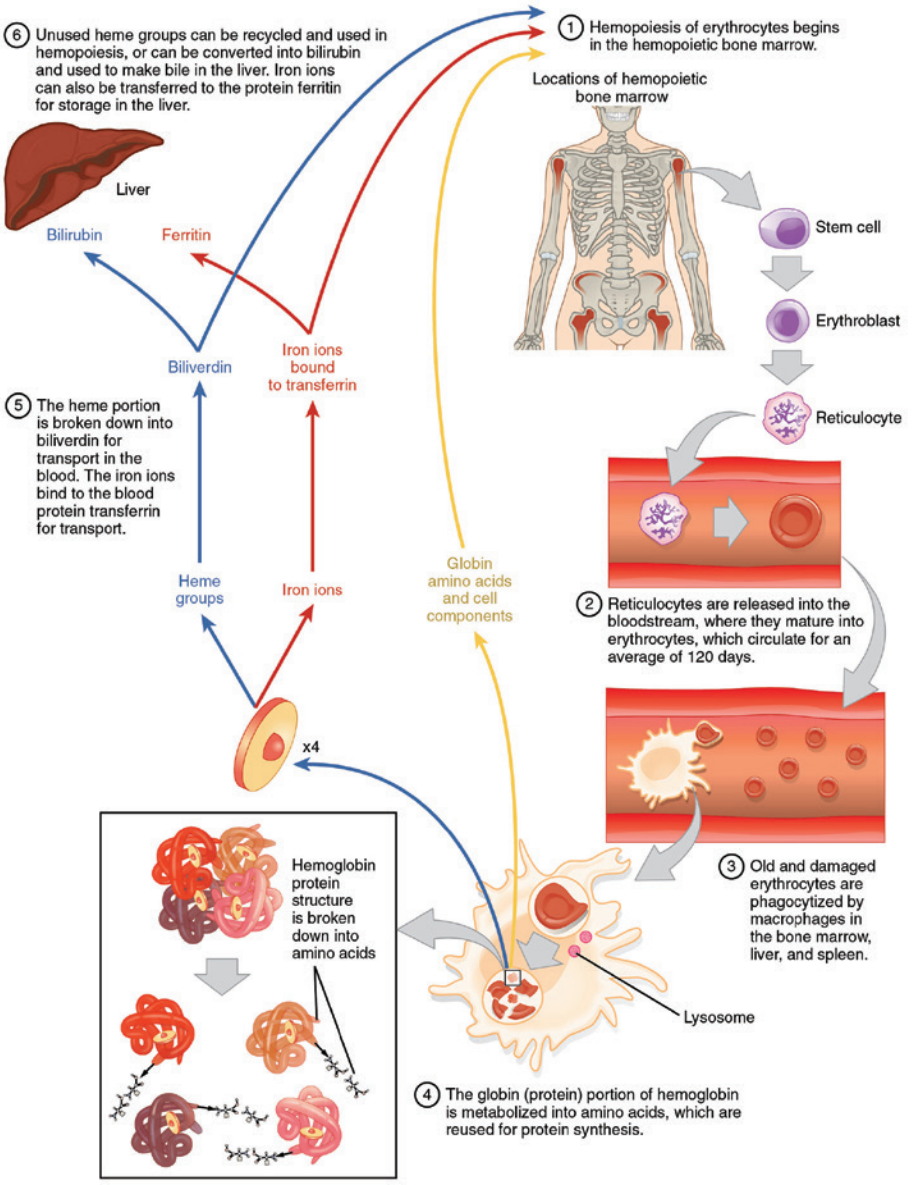


Figure 17.5 Erythrocyte Life Cycle. Erythrocytes are produced in the bone marrow and sent into the circulation. At the end of their life cycle, they are destroyed by macrophages, and their components are recycled.

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17.4 Leukocytes and Platelets

Learning Objectives

By the end of this section, you will be able to:

- Describe the general characteristics of leukocytes
- Classify leukocytes according to their lineage, their main structural features, and their primary functions
- Discuss the most common malignancies involving leukocytes
- Identify the lineage, basic structure, and function of platelets

The **leukocyte**, commonly known as a white blood cell (or WBC), is a major component of the body's defences against disease. Leukocytes protect the body against invading microorganisms and body cells with mutated DNA, and they clean up debris. Platelets are essential for the repair of blood vessels when damage to them has occurred; they also provide growth factors for healing and repair. See Table 17.2 for a summary of leukocytes and platelets.

Characteristics of Leukocytes

Although leukocytes and erythrocytes both originate from hematopoietic stem cells in the bone marrow, they are very different from each other in many significant ways. For instance, leukocytes are far less numerous than erythrocytes: Typically there are only 5,000 to 10,000 per μL. They are also larger than erythrocytes and are the only formed elements that are complete cells, possessing a nucleus and organelles. And although there is just one type of erythrocyte, there are many types of leukocytes. Most of these types have a much shorter lifespan than that of erythrocytes, some as short as a few hours or even a few minutes in the case of acute infection.

One of the most distinctive characteristics of leukocytes is their movement. Whereas erythrocytes spend their days circulating within the blood vessels, leukocytes routinely leave the bloodstream to perform their defensive functions in the body's tissues. For leukocytes, the vascular network is simply a highway they travel and soon exit to reach their true destination. When they arrive, they are often given distinct names, such as macrophage or microglia, depending on their function. As shown in Figure 17.6, they leave the capillaries—the smallest blood vessels—or other small vessels through a process known as **emigration** or **diapedesis** in which they squeeze through adjacent cells in a blood vessel wall.

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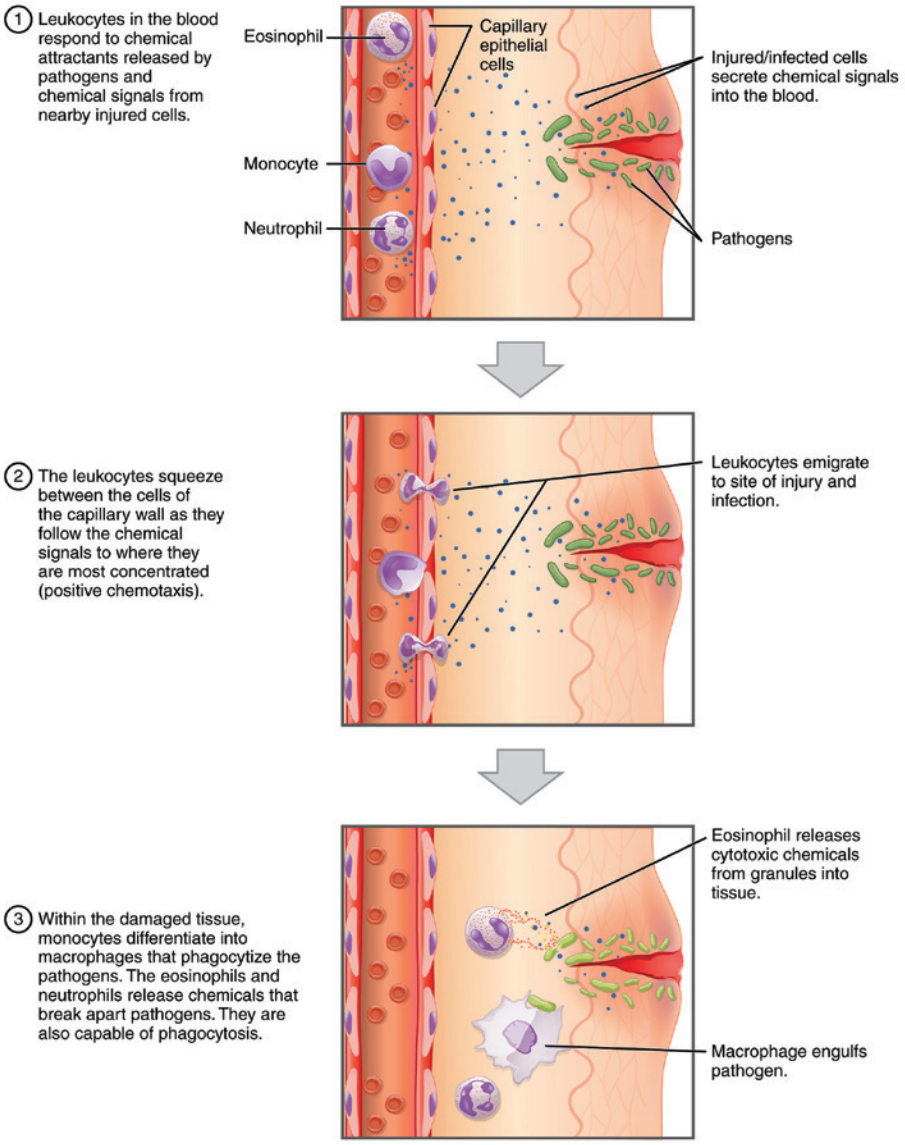


Figure 17.6 Emigration. Leukocytes exit the blood vessel and then move through the connective tissue of the dermis toward the site of a wound. Some leukocytes, such as the eosinophil and neutrophil, are characterized as granular leukocytes. They release chemicals from their granules that destroy pathogens; they are also capable of phagocytosis. The monocyte, an agranular leukocyte, differentiates into a macrophage that then phagocytizes the pathogens.

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Once they have exited the capillaries, some leukocytes will take up fixed positions in lymphatic tissue, bone marrow, the spleen, the thymus, or other organs. Others will move about through the tissue spaces very much like amoebas, continuously extending their plasma membranes, sometimes wandering freely, and sometimes moving toward the direction in which they are drawn by chemical signals. This attracting of leukocytes occurs because of **positive chemotaxis** (literally "movement in response to chemicals"), a phenomenon in which injured or infected cells and nearby leukocytes emit the equivalent of a chemical "911" call, attracting more leukocytes to the site. In clinical medicine, the differential counts of the types and percentages of leukocytes present are often key indicators in making a diagnosis and selecting a treatment.

Classification of Leukocytes

When scientists first began to observe stained blood slides, it quickly became evident that leukocytes could be divided into two groups according to whether their cytoplasm contained highly visible granules:

- **Granular leukocytes** contain abundant granules within the cytoplasm. They include neutrophils, eosinophils, and basophils (you can view their lineage from myeloid stem cells in Figure 17.2).
- While granules are not totally lacking in **agranular leukocytes**, they are far fewer and less obvious. Agranular leukocytes include monocytes, which mature into macrophages that are phagocytic, and lymphocytes, which arise from the lymphoid stem cell line.

Granular Leukocytes

We will consider the granular leukocytes in order from most common to least common. All of these are produced in the red bone marrow and have a short lifespan of hours to days. They typically have a lobed nucleus and are classified according to which type of stain best highlights their granules (Figure 17.7).

The most common of all the leukocytes, **neutrophils** will normally comprise 50–70 percent of total leukocyte count. They are 10–12 μm in diameter, significantly larger than erythrocytes. They are called neutrophils because their granules show up most clearly with stains that are chemically neutral (neither acidic nor basic). The granules are numerous but quite fine and normally appear light lilac in colour. The nucleus has a distinct lobed appearance and may have two to five lobes, the number increasing with the age of the cell. Older neutrophils have increasing numbers of lobes and are often referred to as **polymorphonuclear** (a nucleus with many forms) **neutrophils**, or simply "polys." Younger and immature neutrophils begin to develop lobes and are known as "bands."

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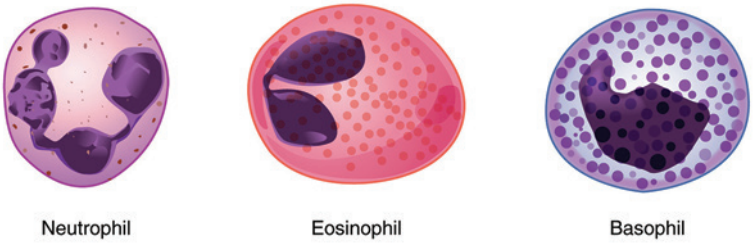


Figure 17.7 Granular Leukocytes. A neutrophil has small granules that stain light lilac and a nucleus with two to five lobes. An eosinophil's granules are slightly larger and stain reddish-orange, and its nucleus has two to three lobes. A basophil has large granules that stain dark blue to purple and a two-lobed nucleus.

Neutrophils are rapid responders to the site of infection and are efficient phagocytes with a preference for bacteria. Their granules include **lysozyme**, an enzyme capable of lysing, or breaking down, bacterial cell walls; oxidants such as hydrogen peroxide; and **defensins**, proteins that bind to and puncture bacterial and fungal plasma membranes so that the cell contents leak out. Abnormally high counts of neutrophils indicate infection and/or inflammation, particularly triggered by bacteria, but are also found in burn patients and others experiencing unusual stress. A burn injury increases the proliferation of neutrophils in order to fight off infection that can result from the destruction of the barrier of the skin. Low counts may be caused by drug toxicity and other disorders and may increase an individual's susceptibility to infection.

Eosinophils typically represent 2–4 percent of total leukocyte count. They are also 10–12 μm in diameter. The granules of eosinophils stain best with an acidic stain known as eosin. The nucleus of the eosinophil will typically have two to three lobes, and if stained properly, the granules will have a distinct red to orange colour.

The granules of eosinophils include antihistamine molecules, which counteract the activities of histamines, inflammatory chemicals produced by basophils and mast cells. Some eosinophil granules contain molecules toxic to parasitic worms, which can enter the body through the integument, or when an individual consumes raw or undercooked fish or meat. Eosinophils are also capable of phagocytosis and are particularly effective when antibodies bind to the target and form an antigen-antibody complex. High counts of eosinophils are typical of patients experiencing allergies, parasitic worm infestations, and some autoimmune diseases. Low counts may be due to drug toxicity and stress.

Basophils are the least common leukocytes, typically comprising less than 1 percent of the total leukocyte count. They are slightly smaller than neutrophils and eosinophils at 8–10 μm in diameter. The granules of basophils stain

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best with basic (alkaline) stains. Basophils contain large granules that pick up a dark-blue stain and are so common they may make it difficult to see the two-lobed nucleus.

In general, basophils intensify the inflammatory response. They share this trait with mast cells. In the past, mast cells were considered to be basophils that left the circulation. However, this appears not to be the case, as the two cell types develop from different lineages.

The granules of basophils release histamines, which contribute to inflammation, and heparin, which opposes blood clotting. High counts of basophils are associated with allergies, parasitic infections, and hypothyroidism. Low counts are associated with pregnancy, stress, and hyperthyroidism.

Agranular Leukocytes

Agranular leukocytes contain smaller, less-visible granules in their cytoplasm than do granular leukocytes. The nucleus is simple in shape, sometimes with an indentation but without distinct lobes. There are two major types of agranulocytes: lymphocytes and monocytes (see Figure 17.2).

Lymphocytes are the only formed element of blood that arises from lymphoid stem cells. Although they form initially in the bone marrow, much of their subsequent development and reproduction occurs in the lymphatic tissues. Lymphocytes are the second most common type of leukocyte, accounting for about 20–30 percent of all leukocytes, and are essential for the immune response. The size range of lymphocytes is quite extensive, with some authorities recognizing two size classes and others three. Typically, the large cells are 10–14 μm and have a smaller nucleus-to-cytoplasm ratio and more granules. The smaller cells are typically 6–9 μm with a larger volume of nucleus to cytoplasm, creating a "halo" effect. A few cells may fall outside these ranges, at 14–17 μm. This finding has led to the three size range classification.

The three major groups of lymphocytes include natural killer cells, B cells, and T cells. **Natural killer** (**NK**) **cells** are capable of recognizing cells that do not express "self" proteins on their plasma membrane or that contain foreign or abnormal markers. These "nonself" cells include cancer cells, cells infected with a virus, and other cells with atypical surface proteins. Thus, they provide generalized, nonspecific immunity. The larger lymphocytes are typically NK cells.

B cells and T cells, also called **B lymphocytes** and **T lymphocytes**, play prominent roles in defending the body against specific pathogens (disease-causing microorganisms) and are involved in specific immunity. One form of B cells, the **plasma cell**, produces the antibodies or immunoglobulins that bind to specific foreign or abnormal components of plasma membranes. This is also referred to as humoral (body fluid) immunity. T cells provide cellular-level immunity

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by physically attacking foreign or diseased cells. A **memory cell** is a variety of both B and T cells that forms after exposure to a pathogen and mounts rapid responses upon subsequent exposures. Unlike other leukocytes, memory cells live for many years. B cells undergo a maturation process in the bone marrow, whereas T cells undergo maturation in the thymus. This site of the maturation process gives rise to the name B and T cells. The functions of lymphocytes are complex and will be covered in detail in the chapter covering the lymphatic system and immunity. Smaller lymphocytes are either B or T cells, although they cannot be differentiated in a normal blood smear.

Abnormally high lymphocyte counts are characteristic of viral infections as well as some types of cancer. Abnormally low lymphocyte counts are characteristic of prolonged (chronic) illness or immunosuppression, including that caused by HIV infection and drug therapies that often involve steroids.

Monocytes originate from myeloid stem cells. They normally represent 2–8 percent of the total leukocyte count. They are typically easily recognized by their large size of 12–20 μm and indented or horseshoe-shaped nuclei. Macrophages are monocytes that have left the circulation and phagocytize debris, foreign pathogens, worn-out erythrocytes, and many other dead, worn out, or damaged cells. Macrophages also release antimicrobial defensins and chemotactic chemicals that attract other leukocytes to the site of an infection. Some macrophages occupy fixed locations, whereas others wander through the tissue fluid.

Abnormally high counts of monocytes are associated with viral or fungal infections, tuberculosis, and some forms of leukemia and other chronic diseases. Abnormally low counts are typically caused by suppression of the bone marrow.

Life Cycle of Leukocytes

Most leukocytes have a relatively short lifespan, typically measured in hours or days. Production of all leukocytes begins in the bone marrow under the influence of CSFs and interleukins. Secondary production and maturation of lymphocytes occurs in specific regions of lymphatic tissue known as germinal centres. Lymphocytes are fully capable of mitosis and may produce clones of cells with identical properties. This capacity enables an individual to maintain immunity throughout life to many threats that have been encountered in the past.

Disorders of Leukocytes

Leukopenia is a condition in which too few leukocytes are produced. If this condition is pronounced, the individual may be unable to ward off disease. Excessive leukocyte proliferation is known as **leukocytosis**. Although leukocyte counts are high, the cells themselves are often nonfunctional, leaving the individual at increased risk for disease.

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Leukemia is a cancer involving an abundance of leukocytes. It may involve only one specific type of leukocyte from either the myeloid line (myelocytic leukemia) or the lymphoid line (lymphocytic leukemia). In chronic leukemia, mature leukocytes accumulate and fail to die. In acute leukemia, there is an overproduction of young, immature leukocytes. In both conditions the cells do not function properly.

Lymphoma is a form of cancer in which masses of malignant T and/or B lymphocytes collect in lymph nodes, the spleen, the liver, and other tissues. As in leukemia, the malignant leukocytes do not function properly, and the patient is vulnerable to infection. Some forms of lymphoma tend to progress slowly and respond well to treatment. Others tend to progress quickly and require aggressive treatment, without which they are rapidly fatal.

Platelets

You may occasionally see platelets referred to as **thrombocytes**, but because this name suggests they are a type of cell, it is not accurate. A platelet is not a cell but rather a fragment of the cytoplasm of a cell called a **megakaryocyte** that is surrounded by a plasma membrane. Megakaryocytes are descended from myeloid stem cells (see Figure 17.1) and are large, typically 50–100 μm in diameter, and contain an enlarged, lobed nucleus. As noted earlier, thrombopoietin, a glycoprotein secreted by the kidneys and liver, stimulates the proliferation of megakaryoblasts, which mature into megakaryocytes. These remain within bone marrow tissue (Figure 17.8) and ultimately form platelet-precursor extensions that extend through the walls of bone marrow capillaries to release into the circulation thousands of cytoplasmic fragments, each enclosed by a bit of plasma membrane. These enclosed fragments are platelets. Each megakaryocyte releases 2000–3000 platelets during its lifespan. Following platelet release, megakaryocyte remnants, which are little more than a cell nucleus, are consumed by macrophages.

Platelets are relatively small, 2–4 μm in diameter, but numerous, with typically 150,000–160,000 per μL of blood. After entering the circulation, approximately one-third migrate to the spleen for storage for later release in response to any rupture in a blood vessel. They then become activated to perform their primary function, which is to limit blood loss. Platelets remain only about 10 days, then are phagocytized by macrophages.

Platelets are critical to **hemostasis**, the stoppage of blood flow following damage to a vessel. They also secrete a variety of growth factors essential for growth and repair of tissue, particularly connective tissue. Infusions of concentrated platelets are now being used in some therapies to stimulate healing.

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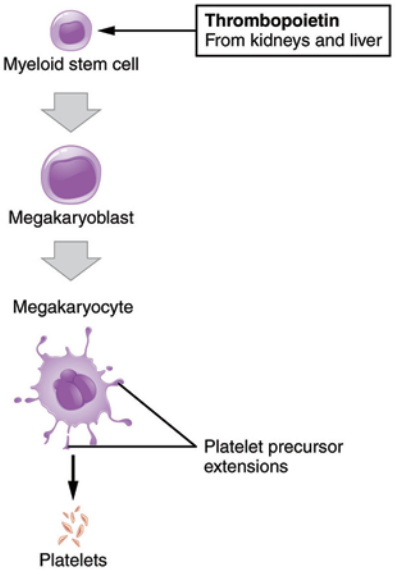


Figure 17.8 Platelets. Platelets are derived from cells called megakaryocytes.

Disorders of Platelets

Thrombocytosis is a condition in which there are too many platelets. This may trigger formation of unwanted blood clots (thrombosis), a potentially fatal disorder. If there is an insufficient number of platelets, called **thrombocytopenia**, blood may not clot properly, and excessive bleeding may result.

Interactive Link 17.3

View University of Michigan WebScopes (http://oer.aupress.ca/oer-202505/17.3), and explore the blood slides in greater detail. The WebScope feature (Figure 17.9) allows you to move the slides as you would with a mechanical stage. You can increase and decrease the magnification. There is a chance to review each of the leukocytes individually after you have attempted to identify them from the first two blood smears. In addition, there are a few multiple-choice questions.

Are you able to recognize and identify the various formed elements? You will need to do this in a systematic manner, scanning along the image. The standard method is to use a grid, but this is not possible with this resource. Try constructing a simple table with each leukocyte type and then making a mark for each cell type you identify.

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Attempt to classify at least 50 and perhaps as many as 100 different cells. Based on the percentage of cells that you count, do the numbers represent a normal blood smear, or does something appear to be abnormal?

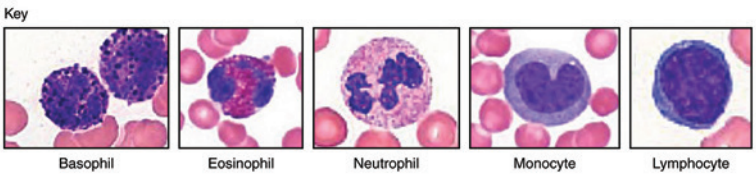


Figure 17.9 Leukocytes. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)

17.5 Hemostasis

Learning Objectives

By the end of this section, you will be able to:

- Describe the three mechanisms involved in hemostasis
- Explain how the extrinsic and intrinsic coagulation pathways lead to the common pathway and the coagulation factors involved in each

Platelets are key players in **hemostasis**, the process by which the body seals a ruptured blood vessel and prevents further loss of blood. Although rupture of larger vessels usually requires medical intervention, hemostasis is quite effective in dealing with small, simple wounds. There are three steps to the process: vascular spasm, the formation of a platelet plug, and coagulation (blood clotting). Failure of any of these steps will result in **hemorrhage**—excessive bleeding.

Vascular Spasm

When a vessel is severed or punctured, or when the wall of a vessel is damaged, vascular spasm occurs. In **vascular spasm**, the smooth muscle in the walls of the vessel contracts dramatically. This smooth muscle has both circular layers; larger vessels also have longitudinal layers. The circular layers tend to constrict the flow of blood, whereas the longitudinal layers, when present, draw the vessel back into the surrounding tissue, often making it more difficult for a surgeon to locate, clamp, and tie off a severed vessel. The vascular spasm

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response is believed to be triggered by several chemicals called endothelins that are released by vessel-lining cells and by pain receptors in response to vessel injury. This phenomenon typically lasts for up to 30 minutes, although it can last for hours.

Formation of the Platelet Plug

In the second step, platelets, which normally float free in the plasma, encounter the area of vessel rupture with the exposed underlying connective tissue and collagenous fibres. The platelets begin to clump together, become spiked and sticky, and bind to the exposed collagen and endothelial lining. This process is assisted by a glycoprotein in the blood plasma called von Willebrand factor, which helps stabilize the growing **platelet plug**. As platelets collect, they simultaneously release chemicals from their granules into the plasma that further contribute to hemostasis. Among the substances released by the platelets are

- adenosine diphosphate (ADP), which helps additional platelets to adhere to the injury site, reinforcing and expanding the platelet plug;
- serotonin, which maintains vasoconstriction; and
- prostaglandins and phospholipids, which also maintain vasoconstriction and help activate further clotting chemicals, as discussed next.

A platelet plug can temporarily seal a small opening in a blood vessel. Plug formation, in essence, buys the body time while more sophisticated and durable repairs are being made. In a similar manner, even modern naval warships still carry an assortment of wooden plugs to temporarily repair small breaches in their hulls until permanent repairs can be made.

Coagulation

Those more sophisticated and more durable repairs are collectively called **coagulation**, the formation of a blood clot. The process is sometimes characterized as a cascade, because one event prompts the next as in a multilevel waterfall. The result is the production of a gelatinous but robust clot made up of a mesh of **fibrin**—an insoluble filamentous protein derived from fibrinogen, the plasma protein introduced earlier—in which platelets and blood cells are trapped. Figure 17.10 summarizes the three steps of hemostasis.

Clotting Factors Involved in Coagulation

In the coagulation cascade, chemicals called **clotting factors** (or coagulation factors) prompt reactions that activate still more coagulation factors. The process is complex but is initiated along two basic pathways:

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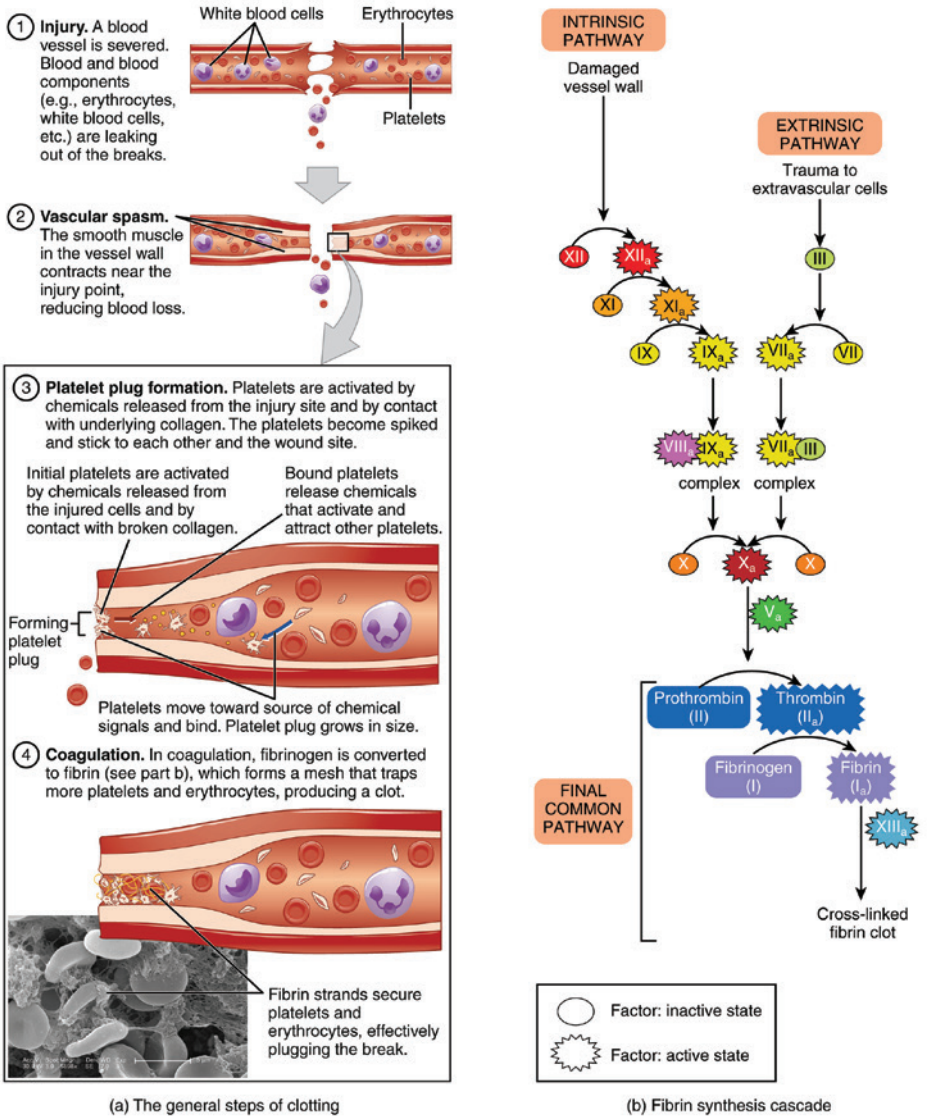


Figure 17.10 Hemostasis. (a) An injury to a blood vessel initiates the process of hemostasis. Blood clotting involves three steps. First, vascular spasm constricts the flow of blood. Next, a platelet plug forms to temporarily seal small openings in the vessel. Coagulation then enables the repair of the vessel wall once the leakage of blood has stopped. (b) The synthesis of fibrin in blood clots involves either an intrinsic pathway or an extrinsic pathway, both of which lead to a common pathway. (credit a: Kevin MacKenzie)

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- the extrinsic pathway, which normally is triggered by trauma
- the intrinsic pathway, which begins in the bloodstream and is triggered by internal damage to the wall of the vessel

Both of these merge into a third pathway, referred to as the common pathway (see Figure 17.10b). All three pathways are dependent on the 12 known clotting factors, including Ca^{2+} and vitamin K. Clotting factors are secreted primarily by the liver and the platelets. The liver requires the fat-soluble vitamin K to produce many of them. Vitamin K (along with biotin and folate) is somewhat unusual among vitamins in that it is not only consumed in the diet but also synthesized by bacteria residing in the large intestine. The calcium ion, considered factor IV, is derived from the diet and from the breakdown of bone. Some recent evidence indicates that activation of various clotting factors occurs on specific receptor sites on the surfaces of platelets.

The 12 clotting factors are numbered I through XIII according to the order of their discovery. Factor VI was once believed to be a distinct clotting factor but is now thought to be identical to factor V. Rather than renumber the other factors, factor VI was allowed to remain as a placeholder and also a reminder that knowledge changes over time.

Extrinsic Pathway

The quicker responding and more direct **extrinsic pathway** (also known as the **tissue factor** pathway) begins when damage occurs to the surrounding tissues, such as in a traumatic injury. Upon contact with blood plasma, the damaged extravascular cells, which are extrinsic to the bloodstream, release factor III (thromboplastin).

Sequentially, Ca^{2+} and then factor VII (proconvertin), which is activated by factor III, are added, forming an enzyme complex. This enzyme complex leads to activation of factor X (Stuart-Prower factor), which activates the common pathway discussed in the Common Pathway section The events in the extrinsic pathway are completed in a matter of seconds.

Intrinsic Pathway

The **intrinsic pathway** (also known as the contact activation pathway) is longer and more complex. In this case, the factors involved are intrinsic to (present within) the bloodstream. The pathway can be prompted by damage to the tissues, resulting from internal factors such as arterial disease; however, it is most often initiated when factor XII (Hageman factor) comes into contact with foreign materials, such as when a blood sample is put into a glass test tube. Within the body, factor XII is typically activated when it encounters negatively charged

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molecules, such as inorganic polymers and phosphate produced earlier in the series of intrinsic pathway reactions. Factor XII sets off a series of reactions that in turn activates factor XI (antihemolytic factor C or plasma thromboplastin antecedent), then factor IX (antihemolytic factor B or plasma thromboplasmin). In the meantime, chemicals released by the platelets increase the rate of these activation reactions. Finally, factor VIII (antihemolytic factor A) from the platelets and endothelial cells combines with factor IX (antihemolytic factor B or plasma thromboplasmin) to form an enzyme complex that activates factor X (Stuart-Prower factor or thrombokinase), leading to the common pathway. The events in the intrinsic pathway are completed in a few minutes.

Common Pathway

Both the intrinsic and extrinsic pathways lead to the **common pathway**, in which fibrin is produced to seal off the vessel. Once factor X has been activated by either the intrinsic or extrinsic pathway, the enzyme prothrombinase converts factor II, the inactive enzyme prothrombin, into the active enzyme **thrombin**. (Note that if the enzyme thrombin were not normally in an inactive form, clots would form spontaneously, a condition not consistent with life.) Then thrombin converts factor I, the soluble fibrinogen, into the insoluble fibrin protein strands. Factor XIII then stabilizes the fibrin clot.

Fibrinolysis

The stabilized clot is acted upon by contractile proteins within the platelets. As these proteins contract, they pull on the fibrin threads, bringing the edges of the clot more tightly together, somewhat as we do when tightening loose shoelaces (see Figure 17.10a). This process also wrings out of the clot a small amount of fluid called **serum**, which is blood plasma without its clotting factors.

To restore normal blood flow as the vessel heals, the clot must eventually be removed. **Fibrinolysis** is the gradual degradation of the clot. Again, there is a fairly complicated series of reactions that involves factor XII and protein-catabolizing enzymes. During this process, the inactive protein plasminogen is converted into the active **plasmin**, which gradually breaks down the fibrin of the clot. Additionally, bradykinin, a vasodilator, is released, reversing the effects of the serotonin and prostaglandins from the platelets. This allows the smooth muscle in the walls of the vessels to relax and helps restore the circulation.

Plasma Anticoagulants

An **anticoagulant** is any substance that opposes coagulation. Several circulating plasma anticoagulants play a role in limiting the coagulation process to the region of injury and restoring a normal, clot-free condition of blood. As

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noted earlier, basophils release **heparin**, a short-acting anticoagulant that also opposes prothrombin. Heparin is also found on the surfaces of cells lining the blood vessels. A pharmaceutical form of heparin is often administered therapeutically, for example, in surgical patients at risk for blood clots.

Interactive Link 17.4

View these animations (http://oer.aupress.ca/oer-202505/17.4) to explore the intrinsic, extrinsic, and common pathways that are involved in the process of coagulation. The coagulation cascade restores hemostasis by activating coagulation factors in the presence of an injury. How does the endothelium of the blood vessel walls prevent the blood from coagulating as it flows through the blood vessels?

17.6 Blood Typing

Learning Objectives

By the end of this section, you will be able to:

- Describe the two basic physiological consequences of transfusion of incompatible blood
- Compare and contrast ABO and Rh blood groups
- Identify which blood groups may be safely transfused into patients with different ABO types
- Discuss the pathophysiology of hemolytic disease of the newborn

Blood transfusions in humans were risky procedures until the discovery of the major human blood groups by Karl Landsteiner, an Austrian biologist and physician, in 1900. Until that point, physicians did not understand that death sometimes followed blood transfusions when the type of donor blood infused into the patient was incompatible with the patient's own blood. Blood groups are determined by the presence or absence of specific marker molecules on the plasma membranes of erythrocytes. With this discovery, it became possible for the first time to match patient-donor blood types and prevent transfusion reactions and deaths.

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Antigens, Antibodies, and Transfusion Reactions

Antigens are substances that the body does not recognize as belonging to the "self" and that therefore trigger a defensive response from the leukocytes of the immune system. Here, we will focus on the role of immunity in blood transfusion reactions. With RBCs in particular, you may see the antigens referred to as isoantigens or agglutinogens (surface antigens) and the antibodies referred to as isoantibodies or agglutinins. In this chapter, we will use the more common terms *antigens* and *antibodies*.

Antigens are generally large proteins but may include other classes of organic molecules, including carbohydrates, lipids, and nucleic acids. Following an infusion of incompatible blood, erythrocytes with foreign antigens appear in the bloodstream and trigger an immune response. Proteins called **antibodies** (**immunoglobulins**), which are produced by certain B lymphocytes called **plasma cells**, attach to the antigens on the plasma membranes of the infused erythrocytes and cause them to adhere to one another.

- Because the arms of the Y-shaped antibodies attach randomly to more than one nonself erythrocyte surface, they form clumps of erythrocytes. This process is called **agglutination**.
- The clumps of erythrocytes block small blood vessels throughout the body, depriving tissues of oxygen and nutrients.
- As the erythrocyte clumps are degraded, in a process called **hemolysis**, their hemoglobin is released into the bloodstream. This hemoglobin travels to the kidneys, which are responsible for filtration of the blood. However, the load of hemoglobin released can easily overwhelm the kidneys' capacity to clear it, and the patient can quickly develop kidney failure.

More than 50 antigens have been identified on erythrocyte membranes, but the most significant in terms of their potential harm to patients are classified in two groups: the ABO blood group and the Rh blood group.

The ABO Blood Group

Although the **ABO blood group** name consists of three letters, ABO blood typing designates the presence or absence of just two antigens, A and B. Both are glycoproteins. People whose erythrocytes have A antigens on their erythrocyte membrane surfaces are designated blood type A, and those whose erythrocytes have B antigens are blood type B. People can also have both A and B antigens on their erythrocytes, in which case they are blood type AB. People with neither

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A nor B antigens are designated blood type O. ABO blood types are genetically determined.

The body must be exposed to a foreign antigen before an antibody can be produced. ABO blood group antigens are found in foods and microbes throughout nature. Thus, the human immune system is exposed to A and B antigens at an early age, and antibodies are formed naturally. Individuals with type A blood—without any prior exposure to incompatible blood—have naturally formed antibodies to the B antigen circulating in their blood plasma. These antibodies, referred to as anti-B antibodies, will cause agglutination and hemolysis if they ever encounter erythrocytes with B antigens. Similarly, an individual with type B blood has naturally formed anti-A antibodies.

Individuals with type AB blood, which has both antigens, do not have naturally formed antibodies to either of these. People with type O blood lack antigens A and B on their erythrocytes, but both anti-A and anti-B antibodies circulate in their blood plasma.

Rh Blood Groups

The **Rh blood group** is classified according to the presence or absence of a second erythrocyte antigen identified as Rh. (It was first discovered in a type of primate known as a rhesus macaque, which is often used in research, because its blood is similar to that of humans.) Although dozens of Rh antigens have been identified, only one, designated D, is clinically important. Those who have the Rh D antigen present on their erythrocytes—about 85 percent of Americans—are described as Rh positive (Rh^+), and those who lack it are Rh negative (Rh^-). Note that the Rh group is distinct from the ABO group, so any individual, no matter their ABO blood type, may have or lack this Rh antigen. When identifying a patient's blood type, the Rh group is designated by adding the word *positive* or *negative* to the ABO type.

For example, A positive (A^+) means ABO group A blood with the Rh antigen present, and AB negative (AB^-) means ABO group AB blood without the Rh antigen.

In contrast to the ABO group antibodies, which are preformed, antibodies to the Rh antigen are produced only in Rh^- individuals after exposure to the antigen. This process, called sensitization, occurs following a transfusion with Rh-incompatible blood or, more commonly, with the birth of an Rh^+ baby to an Rh^- person. Problems are rare in a first pregnancy, since the baby's Rh^+ cells rarely cross the placenta (the organ of gas and nutrient exchange between the fetus and the pregnant person). However, during or immediately after birth, the Rh^- parent can be exposed to the baby's Rh^+ cells (Figure 17.11).

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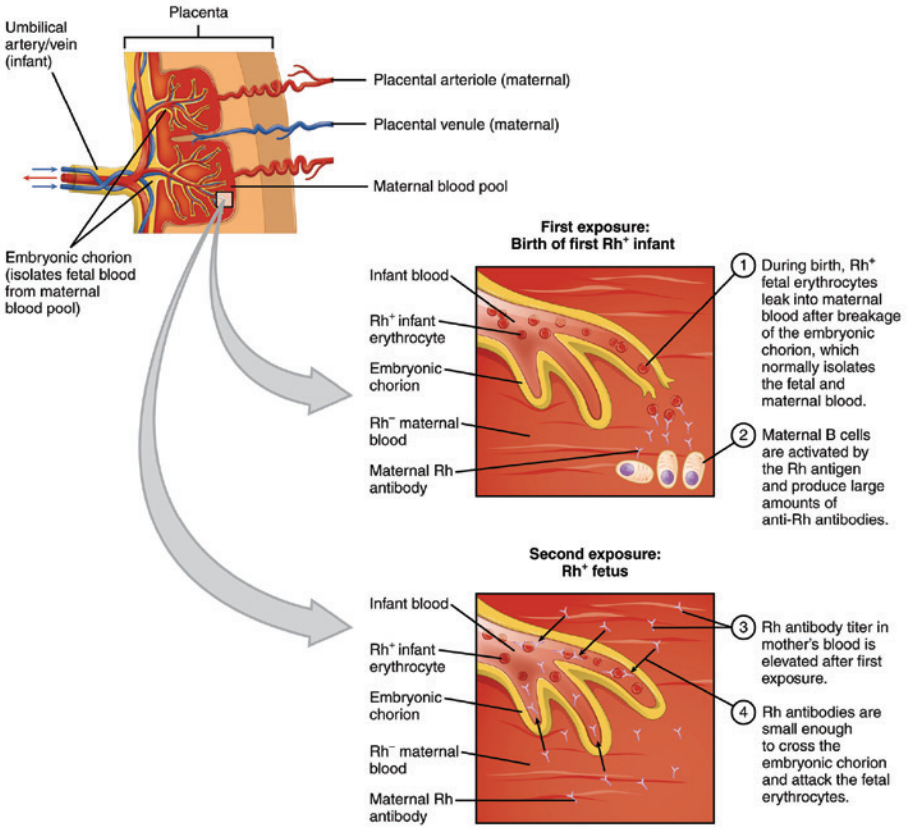


Figure 17.11 Erythroblastosis Fetalis. The first exposure of an Rh^- person to Rh^+ erythrocytes during pregnancy induces sensitization. Anti-Rh antibodies begin to circulate in the pregnant person's bloodstream. A second exposure occurs with a subsequent pregnancy with an Rh^+ fetus in the uterus. During that subsequent pregnancy, the pregnant person's anti-Rh antibodies may cross the placenta and enter the fetal bloodstream, causing agglutination and hemolysis of fetal erythrocytes.

Determining ABO Blood Types

Clinicians are able to determine a patient's blood type quickly and easily using commercially prepared antibodies. An unknown blood sample is allocated into separate wells. Into one well a small amount of anti-A antibody is added, and to another a small amount of anti-B antibody. If the antigen is present, the antibodies will cause visible agglutination of the cells (Figure 17.12). The blood should also be tested for Rh antibodies.

ABO Transfusion Protocols

To avoid transfusion reactions, it is best to transfuse only matching blood types; that is, a type B^+ recipient should ideally receive blood only from a type B^+ donor and so on. That said, in emergency situations, when acute hemorrhage

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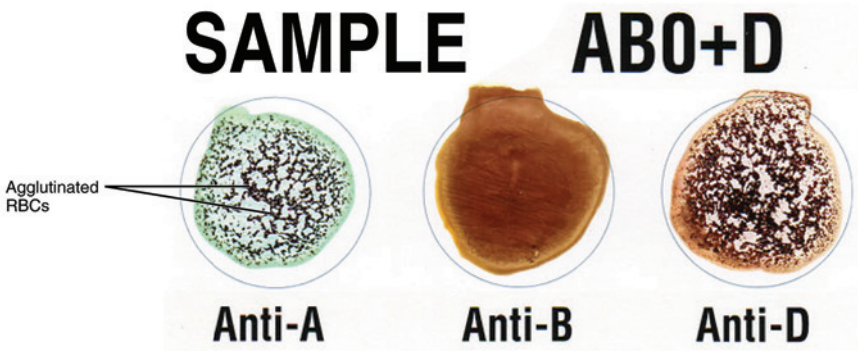


Figure 17.12 Cross Matching Blood Types. This sample of a commercially produced "bedside" card enables quick typing of both a recipient's and a donor's blood before transfusion. The card contains three reaction sites or wells. One is coated with an anti-A antibody, one with an anti-B antibody, and one with an anti-D antibody (tests for the presence of Rh factor D). Mixing a drop of blood and saline into each well enables the blood to interact with a preparation of type-specific antibodies, also called antiseras. Agglutination of RBCs in a given site indicates a positive identification of the blood antigens, in this case A and Rh antigens for blood type A^+. For the purpose of transfusion, the donor's and recipient's blood types must match.

threatens the patient's life, there may not be time for cross matching to identify blood type. In these cases, blood from a **universal donor**—an individual with type O^- blood—may be transfused. Recall that type O erythrocytes do not display A or B antigens. Thus, anti-A or anti-B antibodies that might be circulating in the patient's blood plasma will not encounter any erythrocyte surface antigens on the donated blood and therefore will not be provoked into a response. One problem with this designation of universal donor is if the O^- individual had prior exposure to Rh antigen, Rh antibodies may be present in the donated blood. Also, introducing type O blood into an individual with type A, B, or AB blood will nevertheless introduce antibodies against both A and B antigens, as these are always circulating in the type O blood plasma. This may cause problems for the recipient, but because the volume of blood transfused is much lower than the volume of the patient's own blood, the adverse effects of the relatively few infused plasma antibodies are typically limited. Rh factor also plays a role. If Rh^- individuals receiving blood have had prior exposure to Rh antigen, antibodies for this antigen may be present in the blood and trigger agglutination to some degree. Although it is always preferable to cross match a patient's blood before transfusing, in a true life-threatening emergency situation, this is not always possible, and these procedures may be implemented.

A patient with blood type AB^+ is known as the **universal recipient**. This patient can theoretically receive any type of blood because the patient's own blood—having both A and B antigens on the erythrocyte surface—does not produce anti-A or anti-B antibodies. In addition, an Rh^+ patient can receive both

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Rh^+ and Rh^- blood. However, keep in mind that the donor's blood will contain circulating antibodies, again with possible negative implications. Table 17.3 summarizes the blood types and compatibilities.

Table 17.3 ABO Blood Group

	A	B	AB	O
Red blood cell type	A	B	AB	O
Antibodies in plasma	Anti-B	Anti-A	None	Anti-A and anti-B
Antigens in red blood cells	A antigen	B antigen	A and B antigens	None
Compatible blood types (emergency)	A, O	B, O	A, B, AB, O (AB^+ is the universal recipient)	O (O is the universal donor)

This chart summarizes the characteristics of the blood types in the ABO blood group. See the text for more on the concept of a universal donor or recipient.

Key Terms

ABO blood group: Blood-type classification based on the presence or absence of A and B glycoproteins on the erythrocyte membrane surface.

agglutination: Clustering of cells into masses linked by antibodies.

agranular leukocytes: Leukocytes with few granules in their cytoplasm; specifically, monocytes, lymphocytes, and NK cells.

albumin: Most abundant plasma protein, accounting for most of the osmotic pressure of plasma.

antibodies (also immunoglobulins or gamma globulins): Antigen-specific proteins produced by specialized B lymphocytes that protect the body by binding to foreign objects such as bacteria and viruses.

anticoagulant: Substance such as heparin that opposes coagulation.

antigens: Substances that the body does not recognize as belonging to the "self" and that therefore trigger a defensive response from the leukocytes of the immune system.

basophils: Granulocytes that stain with a basic (alkaline) stain and store histamine and heparin.

bilirubin: Yellowish bile pigment produced when iron is removed from heme and is further broken down into waste products.

biliverdin: Green bile pigment produced when the noniron portion of heme is degraded into a waste product; converted to bilirubin in the liver.

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blood: Liquid connective tissue composed of formed elements—erythrocytes, leukocytes, and platelets—and a fluid extracellular matrix called plasma; component of the cardiovascular system.

B lymphocytes (also B cells): Lymphocytes that defend the body against specific pathogens and thereby provide specific immunity.

bruise: Localized bleeding under the skin due to damaged blood vessels.

buffy coat: Thin, pale layer of leukocytes and platelets that separates the erythrocytes from the plasma in a sample of centrifuged blood.

carbaminohemoglobin: Compound of carbon dioxide and hemoglobin and one of the ways in which carbon dioxide is carried in the blood.

clotting factors: Group of 12 identified substances active in coagulation.

coagulation: Formation of a blood clot; part of the process of hemostasis.

colony-stimulating factors (CSFs): Glycoproteins that trigger the proliferation and differentiation of myeloblasts into granular leukocytes (basophils, neutrophils, and eosinophils).

common pathway: Final coagulation pathway activated by either the intrinsic or the extrinsic pathway and ending in the formation of a blood clot.

cytokines: Class of proteins that act as autocrine or paracrine signalling molecules; in the cardiovascular system, they stimulate the proliferation of progenitor cells and help stimulate both nonspecific and specific resistance to disease.

defensins: Antimicrobial proteins released from neutrophils and macrophages that create openings in the plasma membranes to kill cells.

deoxyhemoglobin: Molecule of hemoglobin without an oxygen molecule bound to it.

diapedesis (also emigration): Process by which leukocytes squeeze through adjacent cells in a blood vessel wall to enter tissues.

emigration (also diapedesis): Process by which leukocytes squeeze through adjacent cells in a blood vessel wall to enter tissues.

eosinophils: Granulocytes that stain with eosin; they release antihistamines and are especially active against parasitic worms.

erythrocyte (also red blood cell): Mature myeloid blood cell that is composed mostly of hemoglobin and functions primarily in the transportation of oxygen and carbon dioxide.

erythropoietin (EPO): Glycoprotein that triggers the bone marrow to produce RBCs; secreted by the kidney in response to low oxygen levels.

extrinsic pathway: Initial coagulation pathway that begins with tissue damage and results in the activation of the common pathway.

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ferritin: Protein-containing storage form of iron found in the bone marrow, liver, and spleen.

fibrin: Insoluble, filamentous protein that forms the structure of a blood clot.

fibrinogen: Plasma protein produced in the liver and involved in blood clotting.

fibrinolysis: Gradual degradation of a blood clot.

formed elements: Cellular components of blood (erythrocytes, leukocytes, and platelets).

globin: Heme-containing globular protein that is a constituent of hemoglobin.

globulins: Heterogeneous group of plasma proteins that includes transport proteins, clotting factors, immune proteins, and others.

granular leukocytes: Leukocytes with abundant granules in their cytoplasm; specifically, neutrophils, eosinophils, and basophils.

hematocrit (also packed cell volume): Volume percentage of erythrocytes in a sample of centrifuged blood.

hematopoietic stem cell: Type of pluripotent stem cell that gives rise to the formed elements of blood (hemocytoblast).

heme: Red, iron-containing pigment to which oxygen binds in hemoglobin.

hemocytoblast: Hematopoietic stem cell that gives rise to the formed elements of blood.

hemoglobin: Oxygen-carrying compound in erythrocytes.

hemolysis: Destruction (lysis) of erythrocytes and the release of their hemoglobin into circulation.

hemopoiesis: Production of the formed elements of blood.

hemopoietic growth factors: Chemical signals including erythropoietin, thrombopoietin, colony-stimulating factors, and interleukins that regulate the differentiation and proliferation of particular blood progenitor cells.

hemorrhage: Excessive bleeding.

hemosiderin: Protein-containing storage form of iron found in the bone marrow, liver, and spleen.

hemostasis: Physiological process by which bleeding ceases.

heparin: Short-acting anticoagulant stored in mast cells and released when tissues are injured; opposes prothrombin.

immunoglobulins (also antibodies or gamma globulins): Antigen-specific proteins produced by specialized B lymphocytes that protect the body by binding to foreign objects such as bacteria and viruses.

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interleukins: Signalling molecules that may function in hemopoiesis, inflammation, and specific immune responses.

intrinsic pathway: Initial coagulation pathway that begins with vascular damage or contact with foreign substances and results in the activation of the common pathway.

jaundice: Yellowing of the skin or whites of the eyes due to excess bilirubin in the blood.

leukemia: Cancer involving leukocytes.

leukocyte (also white blood cell): Colourless, nucleated blood cell, the chief function of which is to protect the body from disease.

leukocytosis: Excessive leukocyte proliferation.

leukopenia: Below-normal production of leukocytes.

lymphocytes: Agranular leukocytes of the lymphoid stem cell line, many of which function in specific immunity.

lymphoid stem cells: Type of hematopoietic stem cells that gives rise to lymphocytes, including various T cells, B cells, and NK cells, all of which function in immunity.

lymphoma: Form of cancer in which masses of malignant T and/or B lymphocytes collect in lymph nodes, the spleen, the liver, and other tissues.

lysozyme: Digestive enzyme with bactericidal properties.

macrophage: Phagocytic cell of the myeloid lineage; a matured monocyte.

megakaryocyte: Bone marrow cell that produces platelets.

memory cell: Type of B or T lymphocyte that forms after exposure to a pathogen.

monocytes: Agranular leukocytes of the myeloid stem cell line that circulate in the bloodstream; tissue monocytes are macrophages.

myeloid stem cells: Type of hematopoietic stem cell that gives rise to some formed elements, including erythrocytes, megakaryocytes that produce platelets, and a myeloblast lineage that gives rise to monocytes and three forms of granular leukocytes (neutrophils, eosinophils, and basophils).

natural killer (NK) cells: Cytotoxic lymphocytes capable of recognizing cells that do not express "self" proteins on their plasma membrane or that contain foreign or abnormal markers; provide generalized, nonspecific immunity.

neutrophils: Granulocytes that stain with a neutral dye and are the most numerous of the leukocytes; especially active against bacteria.

oxyhemoglobin: Molecule of hemoglobin to which oxygen is bound.

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packed cell volume (PCV; also hematocrit): Volume percentage of erythrocytes present in a sample of centrifuged blood.

plasma: In blood, the liquid extracellular matrix composed mostly of water that circulates the formed elements and dissolved materials throughout the cardiovascular system.

plasma cell: One form of B cells that produces the antibodies or immunoglobulins.

plasmin: Blood protein active in fibrinolysis.

platelet plug: Accumulation and adhesion of platelets at the site of blood vessel injury.

platelets (also thrombocytes): One of the formed elements of blood that consists of cell fragments broken off from megakaryocytes.

pluripotent stem cell: Stem cell that derives from totipotent stem cells and is capable of differentiating into many, but not all, cell types.

polymorphonuclear neutrophil: White blood cells with a lobed nucleus.

positive chemotaxis: Process in which a cell is attracted to move in the direction of chemical stimuli.

red blood cells (RBCs; also erythrocytes): One of the formed elements of blood that transports oxygen.

red marrow: Connective tissue within the spaces of spongy (cancellous) bone tissue; site of hematopoiesis.

reticulocyte: Immature erythrocyte that may still contain fragments of organelles.

Rh blood group: Blood-type classification based on the presence or absence of the antigen Rh on the erythrocyte membrane surface.

serum: Blood plasma that does not contain clotting factors.

thrombin: Enzyme essential for the final steps in formation of a fibrin clot.

thrombocytes: Platelets, one of the formed elements of blood that consists of cell fragments broken off from megakaryocytes.

thrombocytopenia: Condition in which there are too few platelets, resulting in abnormal bleeding (hemophilia).

thrombocytosis: Condition in which there are too many platelets, resulting in abnormal clotting (thrombosis).

thrombopoietin: Hormone secreted by the liver and kidneys that prompts the development of megakaryocytes into thrombocytes (platelets).

tissue factor: Protein thromboplastin, which initiates the extrinsic pathway when released in response to tissue damage.

T lymphocytes (also T cells): Lymphocytes that provide cellular-level immunity by physically attacking foreign or diseased cells.

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totipotent stem cell: Embryonic stem cell that is capable of differentiating into any and all cells of the body, enabling the full development of an organism.

transferrin: Plasma protein that binds reversibly to iron and distributes it throughout the body.

universal donor: Individual with type O^- blood.

universal recipient: Individual with type AB^+ blood.

vascular spasm: Initial step in hemostasis, in which the smooth muscle in the walls of the ruptured or damaged blood vessel contracts.

white blood cells (WBCs; also leukocytes): One of the formed elements of blood that provides defence against disease agents and foreign materials.

Chapter Review

17.1 An Overview of Blood

Blood is a fluid connective tissue critical to the transportation of nutrients, gases, and wastes throughout the body; to defend the body against infection and other threats; and to the homeostatic regulation of pH, temperature, and other internal conditions. Blood is composed of formed elements—erythrocytes, leukocytes, and cell fragments called platelets—and a fluid extracellular matrix called plasma. More than 90 percent of plasma is water. The remainder is mostly plasma proteins—mainly albumin, globulins, and fibrinogen—and other dissolved solutes such as glucose, lipids, electrolytes, and dissolved gases. Because of the formed elements and the plasma proteins and other solutes, blood is sticky and more viscous than water. It is also slightly alkaline, and its temperature is slightly higher-than-normal body temperature.

17.2 Production of the Formed Elements

Through the process of hemopoiesis, the formed elements of blood are continually produced, replacing the relatively short-lived erythrocytes, leukocytes, and platelets. Hemopoiesis begins in the red bone marrow, with hematopoietic stem cells that differentiate into myeloid and lymphoid lineages. Myeloid stem cells give rise to most of the formed elements. Lymphoid stem cells give rise only to the various lymphocytes designated as B and T cells and NK cells. Hemopoietic growth factors, including erythropoietin, thrombopoietin, colony-stimulating factors, and interleukins, promote the proliferation and differentiation of formed elements.

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17.3 Erythrocytes

The most abundant formed elements in blood, erythrocytes are red, biconcave disks packed with an oxygen-carrying compound called hemoglobin. The hemoglobin molecule contains four globin proteins bound to a pigment molecule called heme, which contains an ion of iron. In the bloodstream, iron picks up oxygen in the lungs and drops it off in the tissues; the amino acids in hemoglobin then transport carbon dioxide from the tissues back to the lungs.

Erythrocytes live only 120 days on average and thus must be continually replaced. Worn-out erythrocytes are phagocytized by macrophages, and their hemoglobin is broken down. The breakdown products are recycled or removed as wastes: Globin is broken down into amino acids for synthesis of new proteins, iron is stored in the liver or spleen or used by the bone marrow for production of new erythrocytes, and the remnants of heme are converted into bilirubin or other waste products that are taken up by the liver and excreted in the bile or removed by the kidneys. Anemia is a deficiency of RBCs or hemoglobin, whereas polycythemia is an excess of RBCs.

17.4 Leukocytes and Platelets

Leukocytes function in body defences. They squeeze out of the walls of blood vessels through emigration or diapedesis, then may move through tissue fluid or become attached to various organs, where they fight against pathogenic organisms, diseased cells, or other threats to health. Granular leukocytes, which include neutrophils, eosinophils, and basophils, originate with myeloid stem cells, as do the agranular monocytes.

The other agranular leukocytes—NK cells, B cells, and T cells—arise from the lymphoid stem cell line. The most abundant leukocytes are the neutrophils, which are first responders to infections, especially with bacteria. About 20–30 percent of all leukocytes are lymphocytes, which are critical to the body's defence against specific threats. Leukemia and lymphoma are malignancies involving leukocytes. Platelets are fragments of cells known as megakaryocytes that dwell within the bone marrow. While many platelets are stored in the spleen, others enter the circulation and are essential for hemostasis; they also produce several growth factors important for repair and healing.

17.5 Hemostasis

Hemostasis is the physiological process by which bleeding ceases. Hemostasis involves three basic steps: vascular spasm, the formation of a platelet plug, and coagulation, in which clotting factors promote the formation of a fibrin clot. Fibrinolysis is the process in which a clot is degraded in a healing vessel.

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Anticoagulants are substances that oppose coagulation. They are important in limiting the extent and duration of clotting. Inadequate clotting can result from too few platelets or inadequate production of clotting factors, for instance, in the genetic disorder hemophilia. Excessive clotting, called thrombosis, can be caused by an excessive number of platelets. A thrombus is a collection of fibrin, platelets, and erythrocytes that has accumulated along the lining of a blood vessel, whereas an embolus is a thrombus that has broken free from the vessel wall and is circulating in the bloodstream.

17.6 Blood Typing

Antigens are nonself molecules, usually large proteins, which provoke an immune response. In transfusion reactions, antibodies attach to antigens on the surfaces of erythrocytes and cause agglutination and hemolysis. ABO blood group antigens are designated A and B. People with type A blood have A antigens on their erythrocytes, whereas those with type B blood have B antigens. Those with AB blood have both A and B antigens, and those with type O blood have neither A nor B antigens. The blood plasma contains preformed antibodies against the antigens not present on a person's erythrocytes.

A second group of blood antigens is the Rh group, the most important of which is Rh D. People with Rh^- blood do not have this antigen on their erythrocytes, whereas those who are Rh^+ do. About 85 percent of Americans are Rh^+. When a person who is Rh^- becomes pregnant with an Rh^+ fetus, their body may begin to produce anti-Rh antibodies. If the person subsequently becomes pregnant with a second Rh^+ fetus, the fetus will be at risk for an antigen-antibody reaction, including agglutination and hemolysis. This is known as hemolytic disease of the newborn. Cross matching to determine blood type is necessary before transfusing blood, unless the patient is experiencing a hemorrhage that is an immediate threat to life, in which case type O^- blood may be transfused.

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18

The Cardiovascular System: The Heart

Chapter Objectives

After studying this chapter, you will be able to:

- Identify and describe the interior and exterior parts of the human heart
- Describe the path of blood through the cardiac circuits
- Describe the size, shape, and location of the heart
- Compare cardiac muscle to skeletal and smooth muscle
- Explain the cardiac conduction system
- Describe the process and purpose of an electrocardiogram
- Explain the cardiac cycle
- Calculate cardiac output
- Describe the effects of exercise on cardiac output and heart rate
- Name the centres of the brain that control heart rate and describe their function
- Identify other factors affecting heart rate

In this chapter, you will explore the remarkable pump that propels the blood into the vessels. There is no single better word to describe the function of the heart other than *pump*, since its contraction develops the pressure that ejects blood into the major vessels: the aorta and pulmonary trunk. From these vessels, the blood is distributed to the remainder of the body. Although the connotation of the term *pump* suggests a mechanical device made of steel and plastic, the anatomical structure is a living, sophisticated muscle. As you read this chapter, try to keep these twin concepts in mind: pump and muscle.

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18.1 Heart Anatomy

Learning Objectives

By the end of this section, you will be able to:

- Describe the location and position of the heart within the body cavity
- Describe the internal and external anatomy of the heart
- Identify the tissue layers of the heart
- Relate the structure of the heart to its function as a pump
- Compare systemic circulation to pulmonary circulation
- Identify the veins and arteries of the coronary circulation system
- Trace the pathway of oxygenated and deoxygenated blood through the chambers of the heart

The vital importance of the heart is obvious. If one assumes an average rate of 75 contractions per minute, a human heart would contract approximately 108,000 times in 1 day, more than 39 million times in 1 year, and nearly 3 billion times during a 75-year lifespan. Each of the major pumping chambers of the heart ejects approximately 70 mL of blood per contraction in a resting adult. This would be equal to 5.25 L of fluid per minute and approximately 14,000 L per day. Over 1 year, that would equal 10,000,000 L of blood sent through roughly 100,000 km of vessels. In order to understand how that happens, it is necessary to understand the anatomy and physiology of the heart.

Location of the Heart

The human heart is located within the thoracic cavity, medially between the lungs in the space known as the mediastinum. Figure 18.1 shows the position of the heart within the thoracic cavity. Within the mediastinum, the heart is separated from the other mediastinal structures by a tough membrane known as the **pericardium** (**pericardial sac**) and sits in its own space called the **pericardial cavity**.

The inferior tip of the heart, the apex, lies just to the left of the sternum between the junction of the fourth and fifth ribs near their articulation with the costal cartilages. The right side of the heart is deflected anteriorly, and the left side is deflected posteriorly. It is important to remember the position and orientation of the heart when placing a stethoscope on the chest of a patient and listening for heart sounds and also when looking at images taken from a midsagittal perspective. The slight deviation of the apex to the left is reflected in a depression in the medial surface of the inferior lobe of the left lung called

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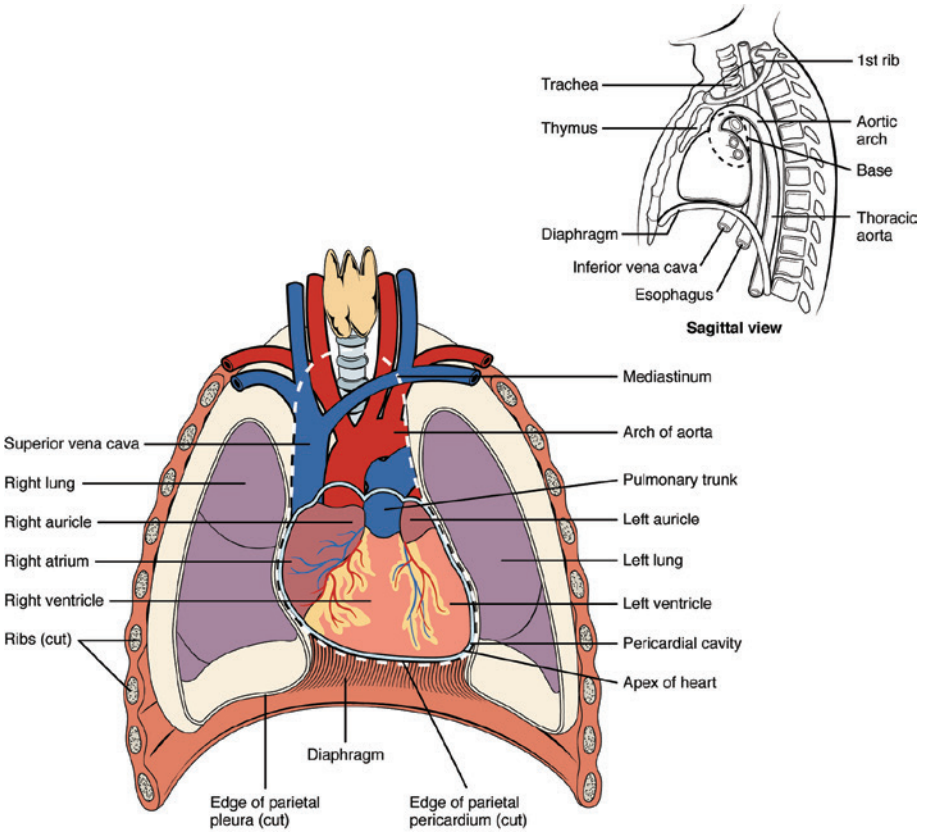


Figure 18.1 Position of the Heart in the Thorax. The heart is located within the thoracic cavity, medially between the lungs in the mediastinum. It is about the size of a fist, is broad at the top, and tapers toward the base.

the **cardiac notch**. The dorsal surface of the heart lies near the bodies of the vertebrae, and its anterior surface sits deep to the sternum and costal cartilages. The great veins (the superior and inferior venae cavae) and the great arteries (the aorta and pulmonary trunk) are attached to the superior surface of the heart called the base. The base of the heart is located at the level of the third costal cartilage, as seen in Figure 18.1.

Interactive Link 18.1

Visit the Canadian Heart Association website (http://oer.aupress.ca/oer-202505/18.1) to help locate a course near your home in Canada. There are also many other national and regional heart associations that offer the same service depending on the location.

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Shape and Size of the Heart

The shape of the heart is similar to a pine cone, rather broad at the superior surface and tapering to the apex (see Figure 18.1). A typical heart is approximately the size of your fist: 12 cm (5 in) in length, 8 cm (3.5 in) wide, and 6 cm (2.5 in) in thickness. Given the size difference between most members of the sexes, the weight of a female heart is approximately 250–300 g, and the weight of a male heart is approximately 300–350 g. The heart of a well-trained athlete, especially one specializing in aerobic sports, can be considerably larger than this. Cardiac muscle responds to exercise in a manner similar to that of skeletal muscle.

That is, exercise results in the addition of protein myofilaments that increase the size of the individual cells without increasing their numbers, a concept called hypertrophy. Hearts of athletes can pump blood more effectively at lower rates than those of nonathletes. Enlarged hearts are not always a result of exercise; they can result from pathologies, such as **hypertrophic cardiomyopathy**. The cause of an abnormally enlarged heart muscle is unknown, but the condition is often undiagnosed and can cause sudden death in apparently otherwise healthy young people.

Chambers and Circulation Through the Heart

The human heart consists of four chambers: The left side and the right side each have one **atrium** and one **ventricle**. Each of the upper chambers, the right atrium (plural = atria) and the left atrium, acts as a receiving chamber and contracts to push blood into the lower chambers, the right ventricle and the left ventricle. The ventricles serve as the primary pumping chambers of the heart, propelling blood to the lungs or to the rest of the body.

There are two distinct but linked circuits in the human circulation called the pulmonary and systemic circuits. Although both circuits transport blood and everything it carries, we can initially view the circuits from the point of view of gases. The **pulmonary circuit** transports blood to and from the lungs, where it picks up oxygen and delivers carbon dioxide for exhalation. The **systemic circuit** transports oxygenated blood to virtually all of the tissues of the body and returns relatively deoxygenated blood and carbon dioxide to the heart to be sent back to the pulmonary circulation.

The right ventricle pumps deoxygenated blood into the **pulmonary trunk**, which leads toward the lungs and bifurcates into the left and right **pulmonary arteries**. These vessels in turn branch many times before reaching the **pulmonary capillaries**, where gas exchange occurs: Carbon dioxide exits the blood, and oxygen enters. The pulmonary trunk arteries and their branches are the only arteries in the postnatal body that carry relatively deoxygenated blood. Highly

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oxygenated blood returning from the pulmonary capillaries in the lungs passes through a series of vessels that join together to form the **pulmonary veins**—the only postnatal veins in the body that carry highly oxygenated blood. The pulmonary veins conduct blood into the left atrium, which pumps the blood into the left ventricle, which in turn pumps oxygenated blood into the aorta and on to the many branches of the systemic circuit. Eventually, these vessels will lead to the systemic capillaries, where exchange with the tissue fluid and cells of the body occurs. In this case, oxygen and nutrients exit the systemic capillaries to be used by the cells in their metabolic processes, and carbon dioxide and waste products will enter the blood.

The blood exiting the systemic capillaries is lower in oxygen concentration than when it entered. The capillaries will ultimately unite to form venules, joining to form ever-larger veins, eventually flowing into the two major systemic veins, the **superior vena cava** and the **inferior vena cava**, which return blood to the right atrium. The blood in the superior and inferior venae cavae flows into the right atrium, which pumps blood into the right ventricle. This process of blood circulation continues as long as the individual remains alive. Understanding the flow of blood through the pulmonary and systemic circuits is critical to all health professions (Figure 18.2).

Membranes, Surface Features, and Layers

Our exploration of more in-depth heart structures begins by examining the membrane that surrounds the heart, the prominent surface features of the heart, and the layers that form the wall of the heart. Each of these components plays its own unique role in terms of function.

Membranes

The membrane that directly surrounds the heart and defines the pericardial cavity is called the **pericardium** or pericardial sac. It also surrounds the "roots" of the major vessels, or the areas of closest proximity to the heart. The pericardium, which literally translates as "around the heart," consists of two distinct sublayers: the sturdy outer fibrous pericardium and the inner serous pericardium. The **fibrous pericardium** is made of tough, dense connective tissue that protects the heart and maintains its position in the thorax. The more delicate **serous pericardium** consists of two layers: the **parietal pericardium**, which is fused to the fibrous pericardium, and an inner **visceral pericardium**, or **epicardium**, which is fused to the heart and is part of the heart wall. The **pericardial cavity**, filled with lubricating serous fluid, lies between the epicardium and the pericardium.

In most organs within the body, visceral serous membranes such as the epicardium are microscopic. However, in the case of the heart, it is not a microscopic

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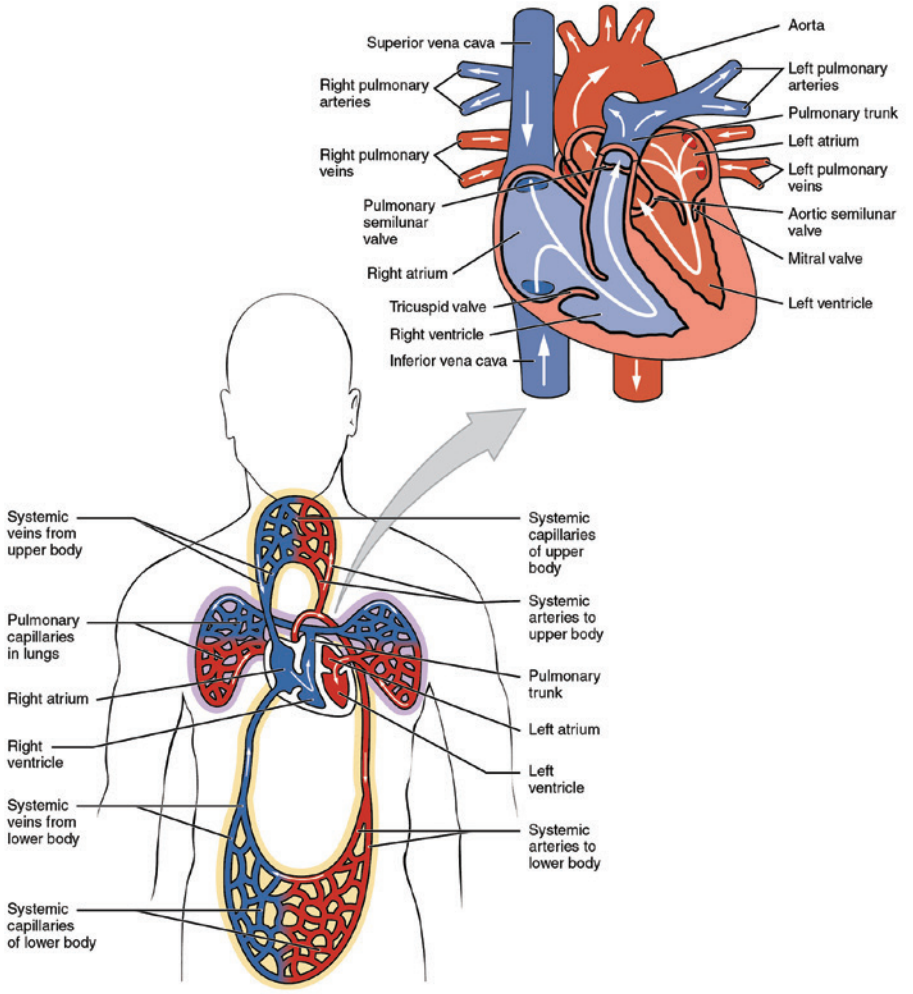


Figure 18.2 Dual System of the Human Blood Circulation. Blood flows from the right atrium to the right ventricle, where it is pumped into the pulmonary circuit. The blood in the pulmonary artery branches is low in oxygen but relatively high in carbon dioxide. Gas exchange occurs in the pulmonary capillaries (oxygen into the blood, carbon dioxide out), and blood high in oxygen and low in carbon dioxide is returned to the left atrium. From here, blood enters the left ventricle, which pumps it into the systemic circuit. Following exchange in the systemic capillaries (oxygen and nutrients out of the capillaries and carbon dioxide and waste in), blood returns to the right atrium, and the cycle is repeated.

layer but rather a macroscopic layer, consisting of a simple squamous epithelium, reinforced with loose, irregular, or areolar connective tissue that attaches to the pericardium. This mesothelium secretes the lubricating serous fluid that fills the pericardial cavity and reduces friction as the heart contracts. Figure 18.3 illustrates the pericardial membrane and the layers of the heart.

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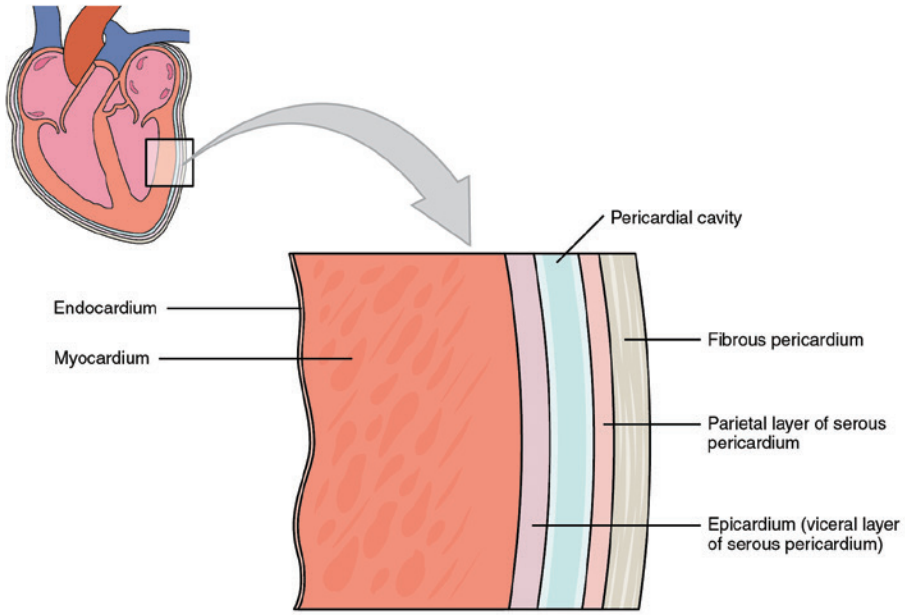


Figure 18.3 Pericardial Membranes and Layers of the Heart Wall. The pericardial membrane that surrounds the heart consists of three layers and the pericardial cavity. The heart wall also consists of three layers. The pericardial membrane and the heart wall share the epicardium.

Surface Features of the Heart

Inside the pericardium, the surface features of the heart are visible, including the four chambers. There is a superficial leaf-like extension of the atria near the superior surface of the heart, one on each side, called an **auricle**—a name that means "ear-like"—because its shape resembles the external ear of a human (Figure 18.4). Auricles are relatively thin-walled structures that can fill with blood and empty into the atria or upper chambers of the heart. You may also hear them referred to as atrial appendages. Also prominent is a series of fat-filled grooves, each of which is known as a **sulcus** (plural = sulci), along the superior surfaces of the heart. Major coronary blood vessels are located in these sulci. The deep **coronary sulcus** is located between the atria and ventricles. Located between the left and right ventricles are two additional sulci that are not as deep as the coronary sulcus. The **anterior interventricular sulcus** is visible on the anterior surface of the heart, whereas the **posterior interventricular sulcus** is visible on the posterior surface of the heart. Figure 18.4 illustrates anterior and posterior views of the surface of the heart.

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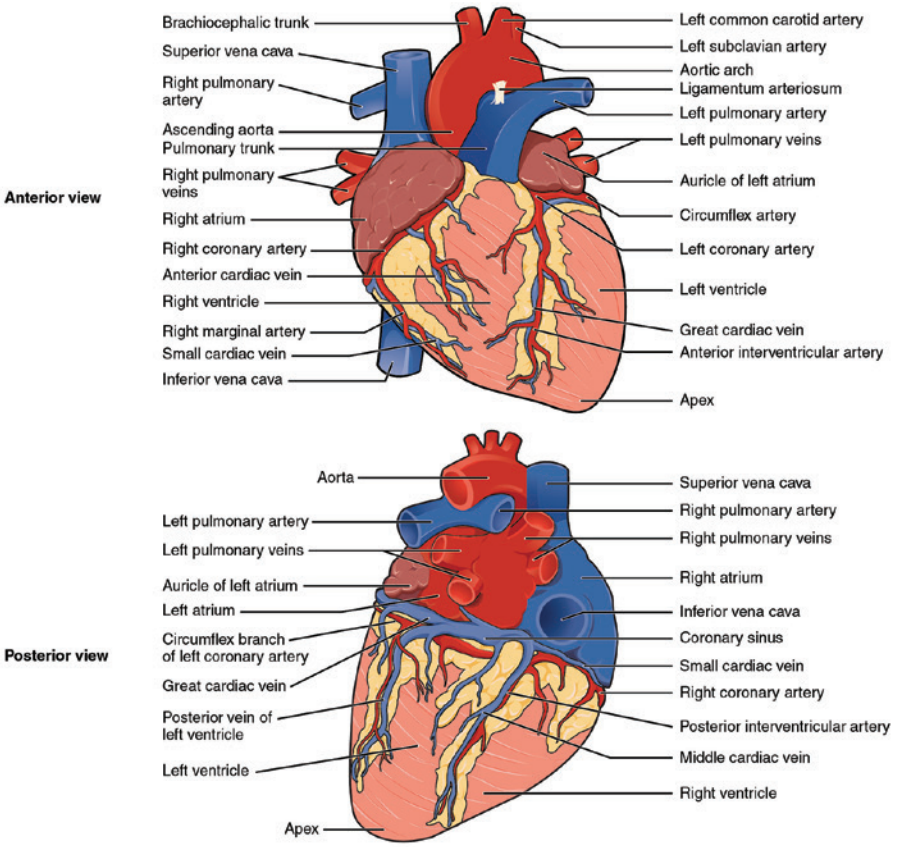


Figure 18.4 External Anatomy of the Heart. Inside the pericardium, the surface features of the heart are visible.

Layers

The wall of the heart is composed of three layers of unequal thickness. From superficial to deep, these are the epicardium, the myocardium, and the endocardium (see Figure 18.3). The outermost layer of the wall of the heart is also the innermost layer of the pericardium, the epicardium, or the visceral pericardium discussed earlier.

The middle and thickest layer is the **myocardium**, made largely of cardiac muscle cells. It is built upon a framework of collagenous fibres, plus the blood vessels that supply the myocardium and the nerve fibres that help regulate the heart. It is the contraction of the myocardium that pumps blood through the heart and into the major arteries. The muscle pattern is elegant and complex, as the muscle cells swirl and spiral around the chambers of the heart. They form a figure eight pattern around the atria and around the bases of the great vessels. Deeper ventricular muscles also form a figure eight around the two ventricles

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and proceed toward the apex. More superficial layers of ventricular muscle wrap around both ventricles. This complex swirling pattern allows the heart to pump blood more effectively than a simple linear pattern would. Figure 18.5 illustrates the arrangement of muscle cells.

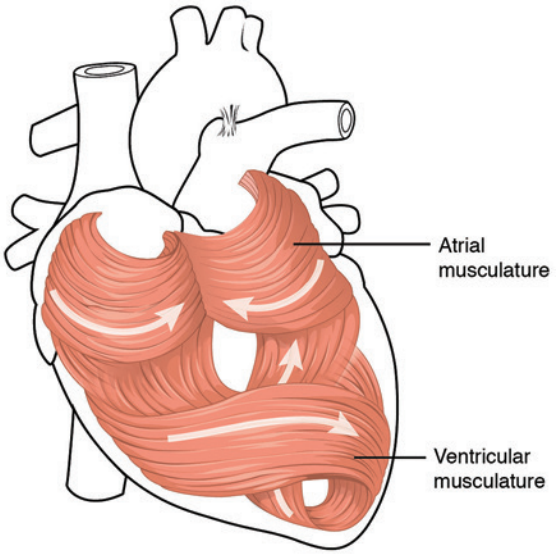


Figure 18.5 Heart Musculature. The swirling pattern of cardiac muscle tissue contributes significantly to the heart's ability to pump blood effectively.

Although the ventricles on the right and left sides pump the same amount of blood per contraction, the muscle of the left ventricle is much thicker and better developed than that of the right ventricle. In order to overcome the high resistance required to pump blood into the long systemic circuit, the left ventricle must generate a great amount of pressure. The right ventricle does not need to generate as much pressure, since the pulmonary circuit is shorter and provides less resistance. Figure 18.6 illustrates the differences in muscular thickness needed for each of the ventricles.

The innermost layer of the heart wall, the **endocardium**, is joined to the myocardium with a thin layer of connective tissue. The endocardium lines the chambers where the blood circulates and covers the heart valves. It is made of simple squamous epithelium called **endothelium**, which is continuous with the endothelial lining of the blood vessels (see Figure 18.3).

Once regarded as a simple lining layer, recent evidence indicates that the endothelium of the endocardium and the coronary capillaries may play active roles in regulating the contraction of the muscle within the myocardium. The endothelium may also regulate the growth patterns of the cardiac muscle

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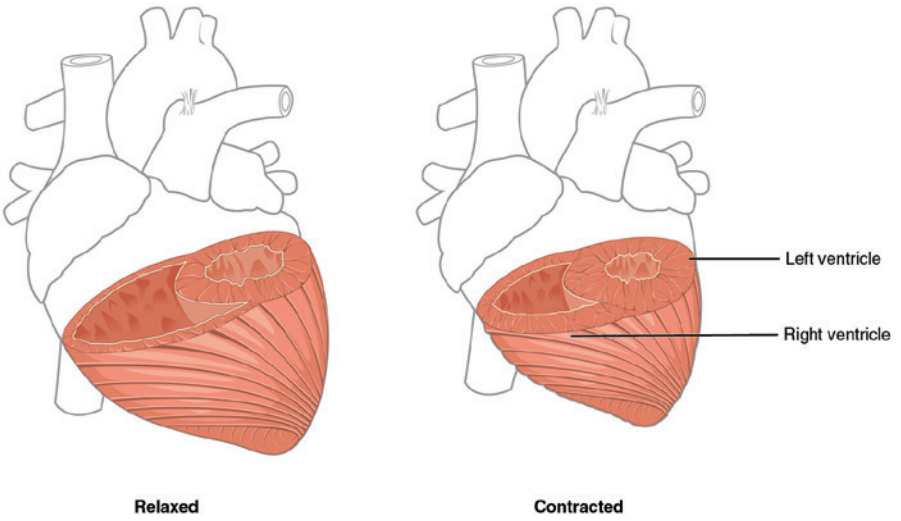


Figure 18.6 Differences in Ventricular Muscle Thickness. The myocardium in the left ventricle is significantly thicker than that of the right ventricle. Both ventricles pump the same amount of blood, but the left ventricle must generate much greater pressure to overcome greater resistance in the systemic circuit. The ventricles are shown in both relaxed and contracting states. Note the differences in the relative size of the lumens, the region inside each ventricle where the blood is contained.

cells throughout life, and the endothelins secreted create an environment in the surrounding tissue fluids that regulates ionic concentrations and states of contractility. Endothelins are potent vasoconstrictors and, in a normal individual, establish a homeostatic balance with other vasoconstrictors and vasodilators.

Internal Structure of the Heart

Recall that the heart's contraction cycle follows a dual pattern of circulation—the pulmonary and systemic circuits—because of the pairs of chambers that pump blood into the circulation. In order to develop a more precise understanding of cardiac function, it is first necessary to explore the internal anatomical structures in more detail.

Septa of the Heart

A **septum** (plural = septa) refers to a wall or partition that divides the heart into chambers. The septa are physical extensions of the myocardium lined with endocardium. Located between the two atria is the **interatrial septum**. Normally in an adult heart, the interatrial septum bears an oval-shaped depression known as the **fossa ovalis**, a remnant of an opening in the fetal

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heart known as the **foramen ovale**. The foramen ovale allowed blood in the fetal heart to pass directly from the right atrium to the left atrium, allowing some blood to bypass the pulmonary circuit.

Between the two ventricles is a second septum known as the **interventricular septum**. Unlike the interatrial septum, the interventricular septum is normally intact after its formation during fetal development. It is substantially thicker than the interatrial septum, since the ventricles generate far greater pressure when they contract.

The septum between the atria and ventricles is known as the **atrioventricular septum**. It is marked by the presence of four openings that allow blood to move from the atria into the ventricles and from the ventricles into the pulmonary trunk and aorta. Located in each of these openings between the atria and ventricles is a **valve**, a specialized structure that ensures one-way flow of blood. The valves between the atria and ventricles are known generically as **atrioventricular valves** (**or AV valves**). The valves at the openings that lead to the pulmonary trunk and aorta are known generically as **semilunar valves**. The interventricular septum is visible in Figure 18.7.

In Figure 18.7, the atrioventricular septum has been removed to better show the bicuspid and tricuspid valves; the interatrial septum is not visible, since its

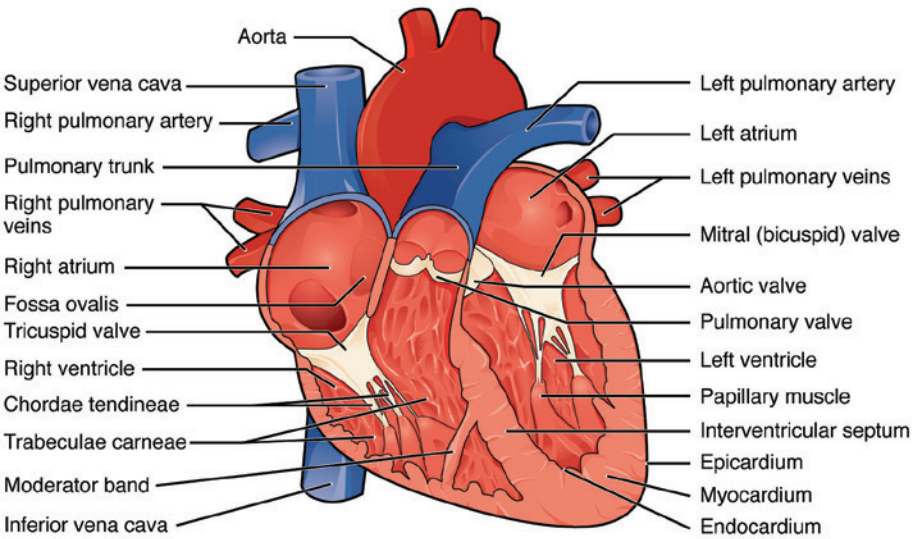


Figure 18.7 Internal Structures of the Heart. This anterior view of the heart shows the four chambers, the major vessels and their early branches, as well as the valves. The presence of the pulmonary trunk and aorta covers the interatrial septum, and the atrioventricular septum is cut away to show the atrioventricular valves.

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location is covered by the aorta and pulmonary trunk. Since these openings and valves structurally weaken the atrioventricular septum, the remaining tissue is heavily reinforced with dense connective tissue called the **cardiac skeleton**, or skeleton of the heart. It includes four rings that surround the openings between the atria and ventricles and the openings to the pulmonary trunk and aorta and serve as the point of attachment for the heart valves. The cardiac skeleton also provides an important boundary in the heart's electrical conduction system.

Right Atrium

The right atrium serves as the receiving chamber for blood returning to the heart from the systemic circulation. The two major systemic veins, the superior and inferior venae cavae, and the large coronary vein called the **coronary sinus** that drains the heart myocardium empty into the right atrium. The superior vena cava drains blood from regions superior to the diaphragm: the head, neck, upper limbs, and thoracic region. It empties into the superior and posterior portions of the right atrium. The inferior vena cava drains blood from areas inferior to the diaphragm: the lower limbs and abdominopelvic region of the body. It, too, empties into the posterior portion of the atria, but inferior to the opening of the superior vena cava. Immediately superior and slightly medial to the opening of the inferior vena cava on the posterior surface of the atrium is the opening of the coronary sinus. This thin-walled vessel drains most of the coronary veins that return systemic blood from the heart. The majority of the internal heart structures discussed in this and subsequent sections are illustrated in Figure 18.7.

While the bulk of the internal surface of the right atrium is smooth, the depression of the fossa ovalis is medial, and the anterior surface demonstrates prominent ridges of muscle called the **pectinate muscles**. The right auricle also has pectinate muscles. The left atrium does not have pectinate muscles except in the auricle.

The atria receive venous blood on a nearly continuous basis, preventing venous flow from stopping while the ventricles are contracting. While most ventricular filling occurs while the atria are relaxed, they do demonstrate a contractile phase and actively pump blood into the ventricles just prior to ventricular contraction. The opening between the atrium and ventricle is guarded by the tricuspid valve.

Right Ventricle

The right ventricle receives blood from the right atrium through the tricuspid valve. Each flap of the valve is attached to strong strands of connective tissue, the **chordae tendineae**, literally "tendinous cords," or sometimes more poetically

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referred to as "heart strings." There are several chordae tendineae associated with each of the flaps. They are composed of approximately 80 percent collagenous fibres with the remainder consisting of elastic fibres and endothelium. They connect each of the flaps to a **papillary muscle** that extends from the inferior ventricular surface. There are three papillary muscles in the right ventricle, called the anterior, posterior, and septal muscles, which correspond to the three sections of the valves.

When the myocardium of the ventricle contracts, pressure within the ventricular chamber rises. Blood, like any fluid, flows from higher-pressure to lower-pressure areas—in this case, toward the pulmonary trunk and the atrium. To prevent any potential backflow, the papillary muscles also contract, generating tension on the chordae tendineae.

This prevents the flaps of the valves from being forced into the atria and regurgitation of the blood back into the atria during ventricular contraction. Figure 18.8 shows papillary muscles and chordae tendineae attached to the tricuspid valve.

The walls of the ventricle are lined with **trabeculae carneae**, ridges of cardiac muscle covered by endocardium. In addition to these muscular ridges, a band of cardiac muscle, also covered by endocardium, known as the moderator band (see Figure 18.7) reinforces the thin walls of the right ventricle and plays a crucial role in cardiac conduction. It arises from the inferior portion of

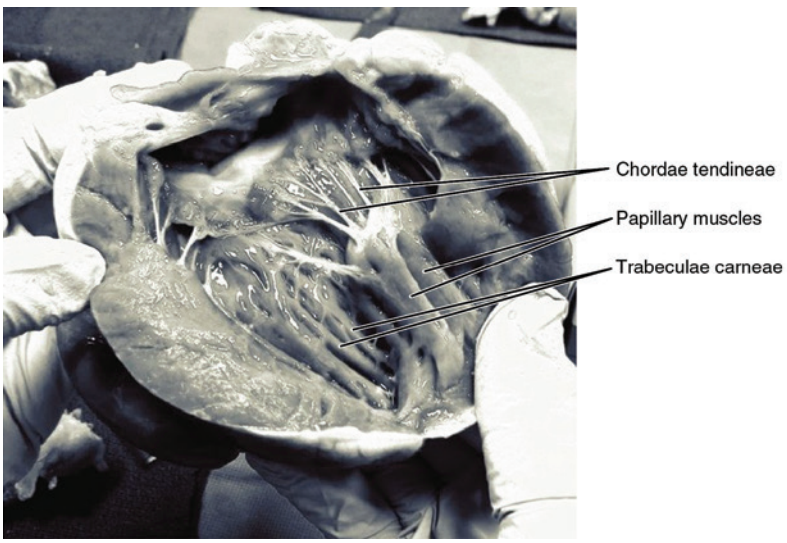


Figure 18.8 Chordae Tendineae and Papillary Muscles. In this frontal section, you can see papillary muscles attached to the tricuspid valve on the right as well as the mitral valve on the left via chordae tendineae. (credit: modification of work by "PV KS"/flickr.com)

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the interventricular septum and crosses the interior space of the right ventricle to connect with the inferior papillary muscle.

When the right ventricle contracts, it ejects blood into the pulmonary trunk, which branches into the left and right pulmonary arteries that carry it to each lung. The superior surface of the right ventricle begins to taper as it approaches the pulmonary trunk. At the base of the pulmonary trunk is the pulmonary semilunar valve that prevents backflow from the pulmonary trunk.

Left Atrium

After the exchange of gases in the pulmonary capillaries, blood returns to the left atrium high in oxygen via one of the four pulmonary veins. While the left atrium does not contain pectinate muscles, it does have an auricle that includes these pectinate ridges. Blood flows nearly continuously from the pulmonary veins back into the atrium, which acts as the receiving chamber, and from here through an opening into the left ventricle. Most blood flows passively into the heart while both the atria and the ventricles are relaxed, but toward the end of the ventricular relaxation period, the left atrium will contract, pumping blood into the ventricle. This atrial contraction accounts for approximately 20 percent of ventricular filling. The opening between the left atrium and ventricle is guarded by the mitral valve.

Left Ventricle

Recall that although both sides of the heart will pump the same amount of blood, the muscular layer is much thicker in the left ventricle compared to the right (see Figure 18.6). Like the right ventricle, the left also has trabeculae carneae, but there is no moderator band. The mitral valve is connected to papillary muscles via chordae tendineae. There are two papillary muscles on the left—the anterior and posterior—as opposed to three on the right.

The left ventricle is the major pumping chamber for the systemic circuit; it ejects blood into the aorta through the aortic semilunar valve.

Heart Valve Structure and Function

A transverse section through the heart slightly above the level of the atrioventricular septum reveals all four heart valves along the same plane (Figure 18.9). The valves ensure unidirectional blood flow through the heart. Between the right atrium and the right ventricle is the **right atrioventricular valve**, or **tricuspid valve**. It typically consists of three flaps, or leaflets, made of endocardium reinforced with additional connective tissue. The flaps are connected by chordae tendineae to the papillary muscles, which control the opening and closing of the valves.

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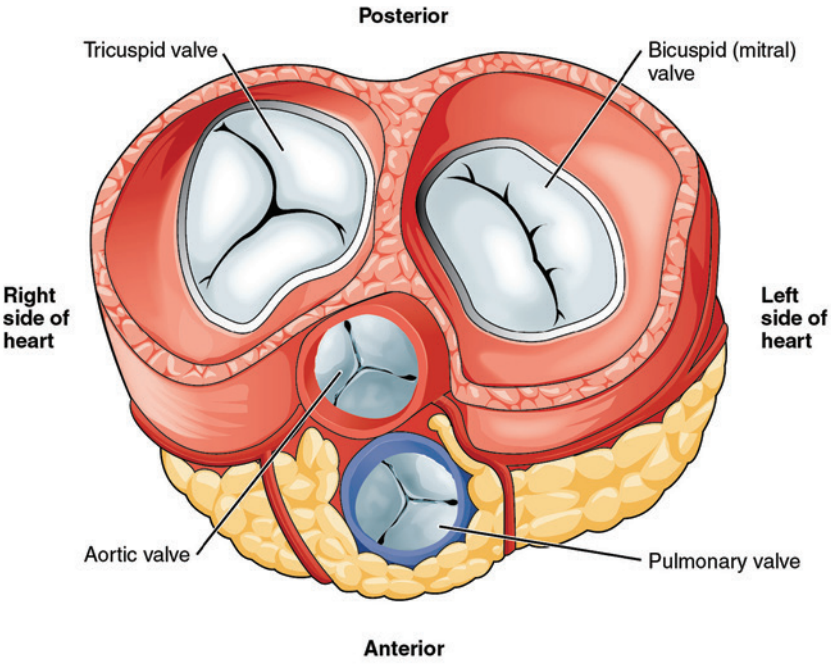


Figure 18.9 Heart Valves. With the atria and major vessels removed, all four valves are clearly visible, although it is difficult to distinguish the three separate cusps of the tricuspid valve.

Emerging from the right ventricle at the base of the pulmonary trunk is the pulmonary semilunar valve, or the **pulmonary valve**; it is also known as the pulmonic valve or the right semilunar valve. The pulmonary valve comprises three small flaps of endothelium reinforced with connective tissue. When the ventricle relaxes, the pressure differential causes blood to flow back into the ventricle from the pulmonary trunk. This flow of blood fills the pocket-like flaps of the pulmonary valve, causing the valve to close and produce an audible sound. Unlike the atrioventricular valves, there are no papillary muscles or chordae tendineae associated with the pulmonary valve.

Located at the opening between the left atrium and left ventricle is the **mitral valve**, also called the **bicuspid valve** or the **left atrioventricular valve**. Structurally, this valve consists of two cusps, compared to the three cusps of the tricuspid valve. In a clinical setting, the valve is referred to as the mitral valve rather than the bicuspid valve. The two cusps of the mitral valve are attached by chordae tendineae to two papillary muscles that project from the wall of the ventricle.

At the base of the aorta is the aortic semilunar valve, or the **aortic valve**, which prevents backflow from the aorta. It normally is composed of three flaps. When the ventricle relaxes and blood attempts to flow back into the ventricle

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from the aorta, blood will fill the cusps of the valve, causing it to close and produce an audible sound.

In Figure 18.10a, the two atrioventricular valves are open, and the two semilunar valves are closed. This occurs when both atria and ventricles are relaxed and when the atria contract to pump blood into the ventricles. Figure 18.10b shows a frontal view. Although only the left side of the heart is illustrated, the process is virtually identical on the right.

Figure 18.11a shows the atrioventricular valves closed while the two semilunar valves are open. This occurs when the ventricles contract to eject blood into the pulmonary trunk and aorta. Closure of the two atrioventricular valves prevents blood from being forced back into the atria. This stage can be seen from a frontal view in Figure 18.11b.

When the ventricles begin to contract, pressure within the ventricles rises and blood flows toward the area of lowest pressure, which is initially in the atria. This backflow causes the cusps of the tricuspid and mitral (bicuspid) valves to close. These valves are tied down to the papillary muscles by chordae tendineae. During the relaxation phase of the cardiac cycle, the papillary muscles are also relaxed, and the tension on the chordae tendineae is slight (see Figure 18.10b). However, as the myocardium of the ventricle contracts, so do the papillary muscles. This creates tension on the chordae tendineae (see Figure 18.11b), helping hold the cusps of the atrioventricular valves in place and preventing them from being blown back into the atria.

The aortic and pulmonary semilunar valves lack the chordae tendineae and papillary muscles associated with the atrioventricular valves. Instead, they consist of pocket-like folds of endocardium reinforced with additional connective tissue. When the ventricles relax and the change in pressure forces the blood toward the ventricles, the blood presses against these cusps and seals the openings.

Interactive Link 18.2

Visit this site (http://oer.aupress.ca/oer-202505/18.2) to observe an echocardiogram of actual heart valves opening and closing. Although much of the heart has been “removed” from this gif loop so the chordae tendineae are not visible, why is their presence more critical for the atrioventricular valves (tricuspid and mitral) than the semilunar (aortic and pulmonary) valves?

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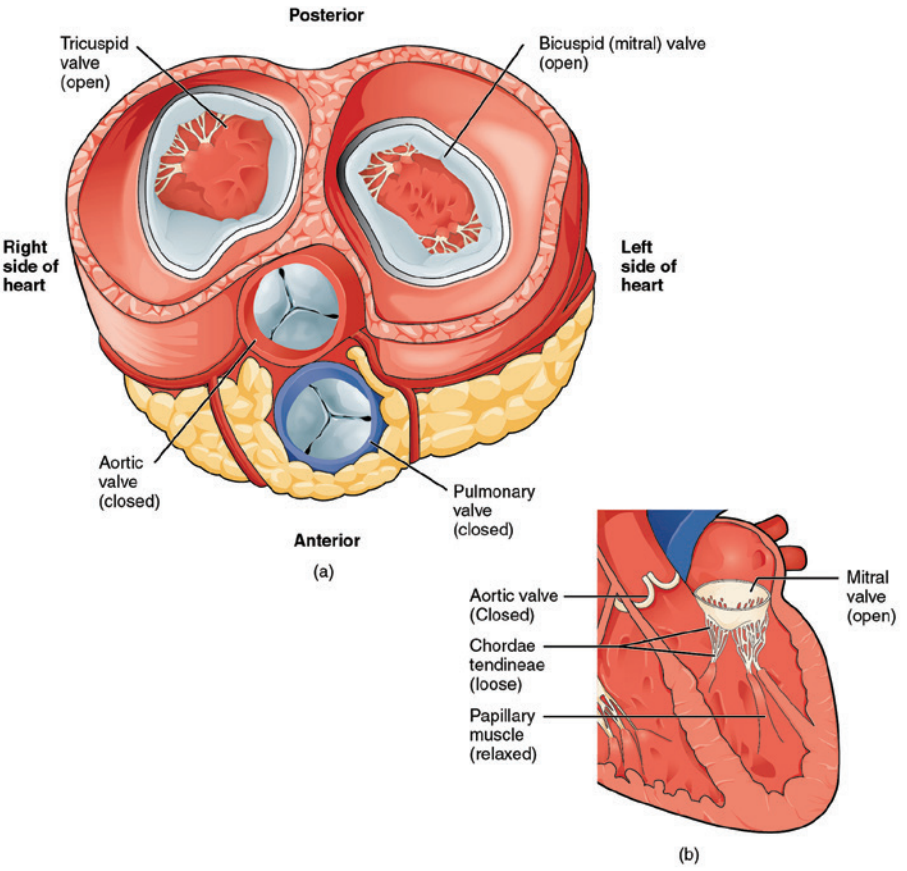


Figure 18.10 Blood Flow from the Left Atrium to the Left Ventricle. (a) A transverse section through the heart illustrates the four heart valves. The two atrioventricular valves are open; the two semilunar valves are closed. The atria and vessels have been removed. (b) A frontal section through the heart illustrates blood flow through the mitral valve. When the mitral valve is open, it allows blood to move from the left atrium to the left ventricle. The aortic semilunar valve is closed to prevent backflow of blood from the aorta to the left ventricle.

Interactive Link 18.3

Visit this site (http://oer.aupress.ca/oer-202505/18.3) for a free download, including excellent animations and audio of heart sounds.

Coronary Circulation

You will recall that the heart is a remarkable pump composed largely of cardiac muscle cells that are incredibly active throughout life. Like all other cells, a **cardiomyocyte** requires a reliable supply of oxygen and nutrients and a way

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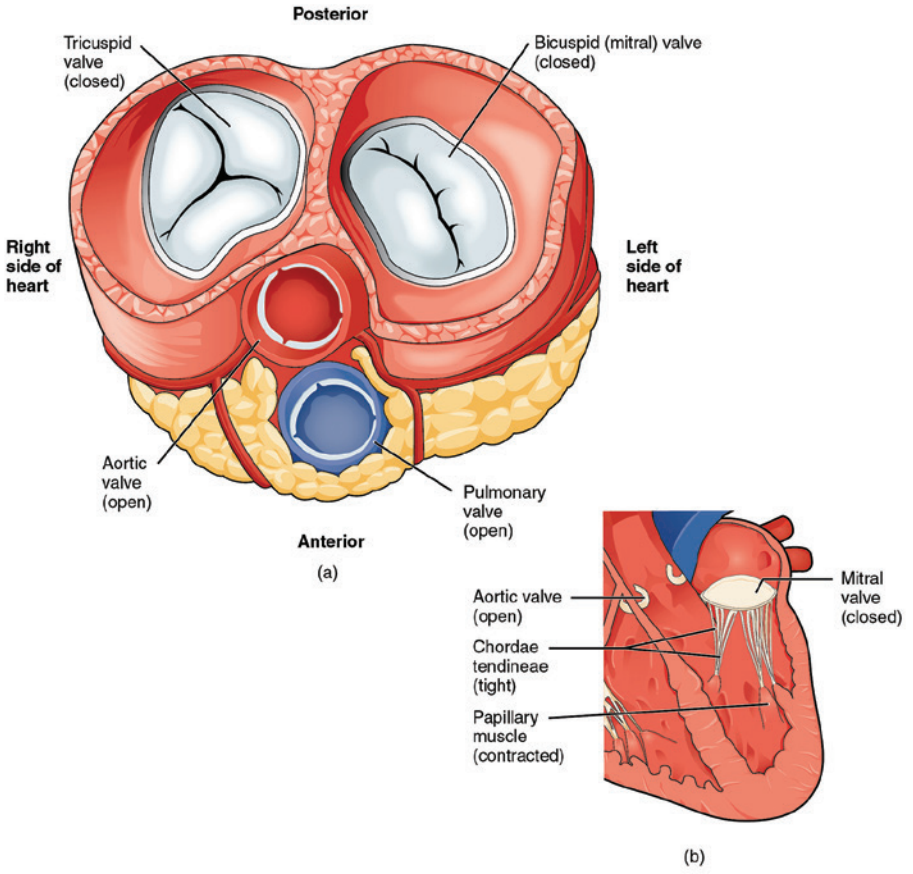


Figure 18.11 Blood Flow from the Left Ventricle into the Great Vessels. (a) A transverse section through the heart illustrates the four heart valves during ventricular contraction. The two atrioventricular valves are closed, but the two semilunar valves are open. The atria and vessels have been removed. (b) A frontal view shows the closed mitral (bicuspid) valve that prevents backflow of blood into the left atrium. The aortic semilunar valve is open to allow blood to be ejected into the aorta.

to remove wastes, so it needs a dedicated, complex, and extensive coronary circulation. And because of the critical and nearly ceaseless activity of the heart throughout life, this need for a blood supply is even greater than for a typical cell. However, coronary circulation is not continuous; rather, it cycles, reaching a peak when the heart muscle is relaxed and nearly ceasing while it is contracting.

Coronary Arteries

Coronary arteries supply blood to the myocardium and other components of the heart. The first portion of the aorta after it arises from the left ventricle gives rise to the coronary arteries. There are three dilations in the wall of the aorta just superior to the aortic semilunar valve. Two of these, the left posterior aortic

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sinus and anterior aortic sinus, give rise to the left and right coronary arteries, respectively. The third sinus, the right posterior aortic sinus, typically does not give rise to a vessel. Coronary vessel branches that remain on the surface of the artery and follow the sulci are called **epicardial coronary arteries**.

The left coronary artery distributes blood to the left side of the heart, the left atrium and ventricle, and the interventricular septum. The **circumflex artery** arises from the left coronary artery and follows the coronary sulcus to the left. Eventually, it will fuse with the small branches of the right coronary artery. The larger **anterior interventricular artery**, also known as the left anterior descending (LAD) artery, is the second major branch arising from the left coronary artery. It follows the anterior interventricular sulcus around the pulmonary trunk. Along the way it gives rise to numerous smaller branches that interconnect with the branches of the posterior interventricular artery, forming anastomoses. An **anastomosis** is an area where vessels unite to form interconnections that normally allow blood to circulate to a region even if there may be partial blockage in another branch. The anastomoses in the heart are very small. Therefore, this ability is somewhat restricted in the heart, so a coronary artery blockage often results in death of the cells (myocardial infarction) supplied by the particular vessel.

The right coronary artery proceeds along the coronary sulcus and distributes blood to the right atrium, portions of both ventricles, and the heart conduction system. Normally, one or more marginal arteries arise from the right coronary artery inferior to the right atrium. The **marginal arteries** supply blood to the superficial portions of the right ventricle. On the posterior surface of the heart, the right coronary artery gives rise to the **posterior interventricular artery**, also known as the posterior descending artery. It runs along the posterior portion of the interventricular sulcus toward the apex of the heart, giving rise to branches that supply the interventricular septum and portions of both ventricles. Figure 18.12 presents views of the coronary circulation from both the anterior and posterior views.

Coronary Veins

Coronary veins drain the heart and generally parallel the large surface arteries (see Figure 18.12). The **great cardiac vein** can be seen initially on the surface of the heart following the interventricular sulcus, but it eventually flows along the coronary sulcus into the coronary sinus on the posterior surface. The great cardiac vein initially parallels the anterior interventricular artery and drains the areas supplied by this vessel. It receives several major branches, including the posterior cardiac vein, the middle cardiac vein, and the small cardiac vein. The **posterior cardiac vein** parallels and drains the areas supplied

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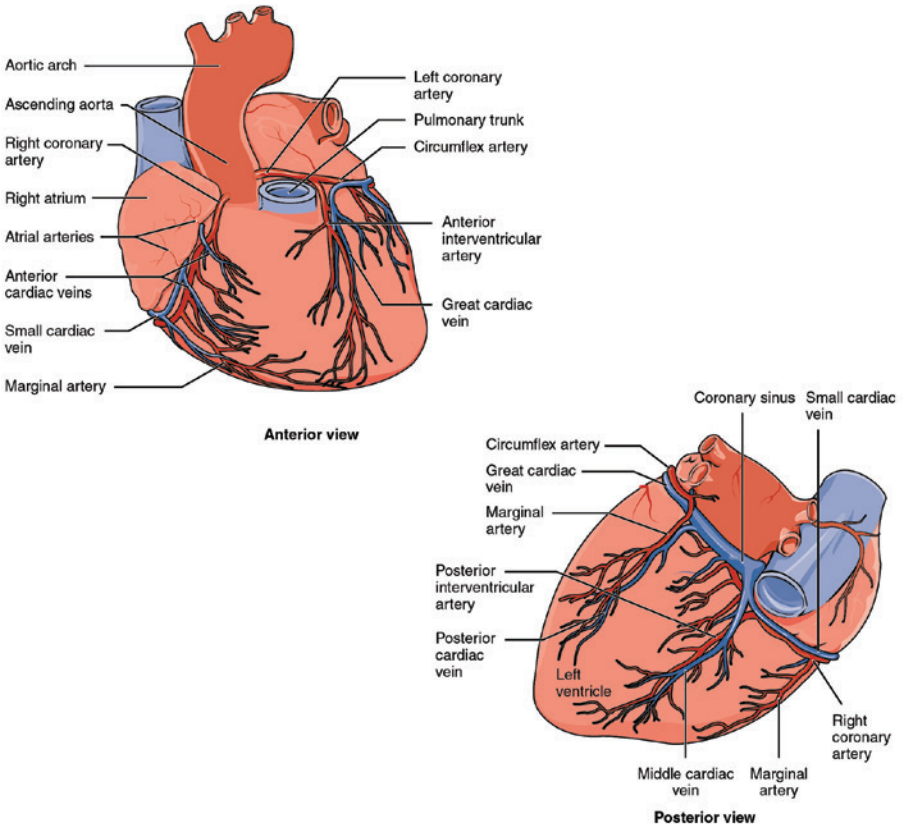


Figure 18.12 Coronary Circulation. The anterior and posterior views of the heart show the prominent coronary surface vessels.

by the marginal artery branch of the circumflex artery. The **middle cardiac vein** parallels and drains the areas supplied by the posterior interventricular artery. The **small cardiac vein** parallels the right coronary artery and drains the blood from the posterior surfaces of the right atrium and ventricle. The coronary sinus is a large, thin-walled vein on the posterior surface of the heart lying within the atrioventricular sulcus and emptying directly into the right atrium. The **anterior cardiac veins** parallel the small cardiac arteries and drain the anterior surface of the right ventricle. Unlike these other cardiac veins, they bypass the coronary sinus and drain directly into the right atrium.

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18.2 Cardiac Muscle and Electrical Activity

Learning Objectives

By the end of this section, you will be able to:

- Describe the structure of cardiac muscle
- Identify and describe the components of the conducting system that distribute electrical impulses through the heart
- Compare the effect of ion movement on the membrane potential of cardiac conductive and contractile cells
- Relate characteristics of an electrocardiogram to events in the cardiac cycle

Recall that cardiac muscle shares a few characteristics with both skeletal muscle and smooth muscle, but it has some unique properties of its own. Not the least of these exceptional properties is its ability to initiate an electrical potential at a fixed rate that spreads rapidly from cell to cell to trigger the contractile mechanism. This property is known as **autorhythmicity**. Neither smooth nor skeletal muscle can do this. Even though cardiac muscle has autorhythmicity, heart rate is modulated by the endocrine and nervous systems.

There are two major types of cardiac muscle cells: myocardial contractile cells and myocardial conducting cells. The **myocardial contractile cells** constitute the bulk (99 percent) of the cells in the atria and ventricles. Contractile cells conduct impulses and are responsible for contractions that pump blood through the body. The **myocardial conducting cells** (1 percent of the cells) form the conduction system of the heart. Except for Purkinje cells, they are generally much smaller than the contractile cells and have few of the myofibrils or filaments needed for contraction. Their function is similar in many respects to neurons, although they are specialized muscle cells. Myocardial conduction cells initiate and propagate the action potential (the electrical impulse) that travels throughout the heart and triggers the contractions that propel the blood.

Structure of Cardiac Muscle

Compared to the giant cylinders of skeletal muscle, cardiac muscle cells, or cardiomyocytes, are considerably shorter with much smaller diameters. Cardiac muscle also demonstrates striations, the alternating pattern of dark A bands and light I bands attributed to the precise arrangement of the myofilaments and fibrils that are organized in sarcomeres along the length of the cell

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(Figure 18.13a). These contractile elements are virtually identical to skeletal muscle. T (transverse) tubules penetrate from the surface plasma membrane, the sarcolemma, to the interior of the cell, allowing the electrical impulse to reach the interior. The T tubules are only found at the Z discs, whereas in skeletal muscle, they are found at the junction of the A and I bands. Therefore, there are one-half as many T tubules in cardiac muscle as in skeletal muscle. In addition, the sarcoplasmic reticulum stores few calcium ions, so most of the calcium ions must come from outside the cells. The result is a slower onset of contraction. Mitochondria are plentiful, providing energy for the contractions of the heart. Typically, cardiomyocytes have a single, central nucleus, but two or more nuclei may be found in some cells.

Cardiac muscle cells branch freely. A junction between two adjoining cells is marked by a critical structure called an **intercalated disc**, which helps support the synchronized contraction of the muscle (Figure 18.13b). The sarcolemmas from adjacent cells bind together at the intercalated discs. They consist of desmosomes, specialized linking proteoglycans, tight junctions, and large numbers of gap junctions that allow the passage of ions between the cells and help synchronize the contraction (Figure 18.13c). Intercellular connective tissue also helps bind the cells together. The importance of strongly binding these cells together is necessitated by the forces exerted by contraction.

Cardiac muscle undergoes aerobic respiration patterns, primarily metabolizing lipids and carbohydrates. Myoglobin, lipids, and glycogen are all stored within the cytoplasm. Cardiac muscle cells undergo twitch-type contractions with long refractory periods followed by brief relaxation periods. The relaxation is essential so the heart can fill with blood for the next cycle. The refractory period is very long to prevent the possibility of tetany, a condition in which muscle remains involuntarily contracted. In the heart, tetany is not compatible with life, since it would prevent the heart from pumping blood.

Conduction System of the Heart

If embryonic heart cells are separated into a Petri dish and kept alive, each is capable of generating its own electrical impulse followed by contraction. When two independently beating embryonic cardiac muscle cells are placed together, the cell with the higher inherent rate sets the pace, and the impulse spreads from the faster to the slower cell to trigger a contraction. As more cells are joined together, the fastest cell continues to assume control of the rate. A fully developed adult heart maintains the capability of generating its own electrical impulse, triggered by the fastest cells, as part of the cardiac conduction system. The components of the cardiac conduction system include

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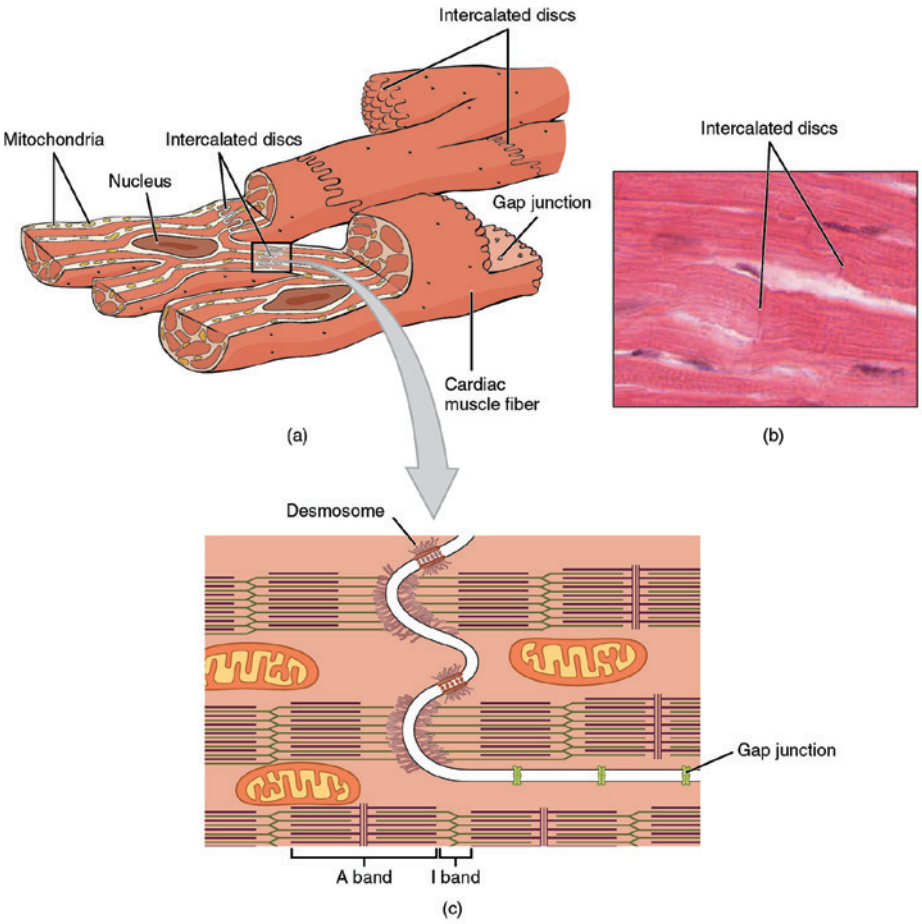


Figure 18.13 Cardiac Muscle. (a) Cardiac muscle cells have myofibrils composed of myofilaments arranged in sarcomeres, T tubules to transmit the impulse from the sarcolemma to the interior of the cell, numerous mitochondria for energy, and intercalated discs that are found at the junction of different cardiac muscle cells. (b) A photomicrograph of cardiac muscle cells shows the nuclei and intercalated discs. (c) An intercalated disc connects cardiac muscle cells and consists of desmosomes and gap junctions. LM × 1600. (Micrograph provided by the Regents of the University of Michigan Medical School © 2012)

the sinoatrial node, the atrioventricular node, the atrioventricular bundle, the atrioventricular bundle branches, and the Purkinje cells (Figure 18.14).

Sinoatrial (SA) Node

Normal cardiac rhythm is established by the **sinoatrial (SA) node**, a specialized clump of myocardial conducting cells located in the superior and posterior walls of the right atrium in close proximity to the orifice of the superior vena cava. The SA node has the highest inherent rate of depolarization and is known

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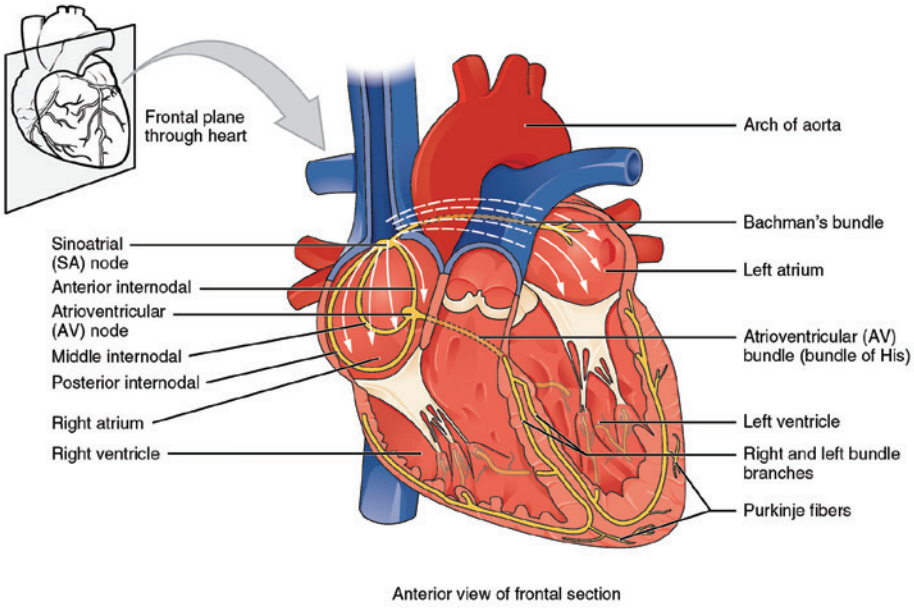


Figure 18.14 Conduction System of the Heart. Specialized conducting components of the heart include the sinoatrial node, the internodal pathways, the atrioventricular node, the atrioventricular bundle, the right and left bundle branches, and the Purkinje fibres.

as the **pacemaker** of the heart. It initiates the **sinus rhythm**, or the normal electrical pattern followed by contraction of the heart.

This impulse spreads from its initiation in the SA node throughout the atria through specialized **internodal pathways** to the atrial myocardial contractile cells and the atrioventricular node. The internodal pathways consist of three bands (anterior, middle, and posterior) that lead directly from the SA node to the next node in the conduction system, the atrioventricular node (see Figure 18.14). The impulse takes approximately 50 ms to travel between these two nodes. The relative importance of this pathway has been debated, since the impulse would reach the atrioventricular node simply following the cell-by-cell pathway through the contractile cells of the myocardium in the atria. Regardless of the pathway, as the impulse reaches the atrioventricular septum, the connective tissue of the cardiac skeleton prevents the impulse from spreading into the myocardial cells in the ventricles except at the atrioventricular node.

The electrical event, the wave of depolarization, is the trigger for muscular contraction. The wave of depolarization begins in the right atrium, and the impulse spreads across the superior portions of both atria and then down through the contractile cells. The contractile cells then begin contraction from the superior to the inferior portions of the atria, efficiently pumping blood into the ventricles.

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Atrioventricular (AV) Node

The **atrioventricular** (**AV**) **node** is a second clump of specialized myocardial conductive cells located in the inferior portion of the right atrium within the atrioventricular septum. The septum prevents the impulse from spreading directly to the ventricles without passing through the AV node. There is a critical pause before the AV node depolarizes and transmits the impulse to the atrioventricular bundle. This delay in transmission is partially attributable to the small diameter of the cells of the node, which slows the impulse. Also, conduction between nodal cells is less efficient than between conducting cells. These factors mean that it takes the impulse approximately 100 ms to pass through the node. This pause is critical to heart function, as it allows the atrial cardiomyocytes to complete their contraction that pumps blood into the ventricles before the impulse is transmitted to the cells of the ventricle itself. With extreme stimulation by the SA node, the AV node can transmit impulses maximally at 220 per minute. This establishes the typical maximum heart rate in a healthy young individual. Damaged hearts or those stimulated by drugs can contract at higher rates, but at these rates, the heart can no longer effectively pump blood.

Atrioventricular Bundle (Bundle of His), Bundle Branches, and Purkinje Fibres

Arising from the AV node, the **atrioventricular bundle**, or **bundle of His**, proceeds through the interventricular septum before dividing into two **atrioventricular bundle branches**, commonly called the left and right bundle branches. The left bundle branch has two fascicles. The left bundle branch supplies the left ventricle, and the right bundle branch the right ventricle. Since the left ventricle is much larger than the right, the left bundle branch is also considerably larger than the right. Portions of the right bundle branch are found in the moderator band and supply the right papillary muscles. Because of this connection, each papillary muscle receives the impulse at approximately the same time, so they begin to contract simultaneously just prior to the remainder of the myocardial contractile cells of the ventricles. This is believed to allow tension to develop on the chordae tendineae prior to right ventricular contraction. There is no corresponding moderator band on the left. Both bundle branches descend and reach the apex of the heart, where they connect with the Purkinje fibres. This passage takes approximately 25 ms.

The **Purkinje fibres** are additional myocardial conductive fibres that spread the impulse to the myocardial contractile cells in the ventricles. They extend throughout the myocardium from the apex of the heart toward the atrioventricular septum and the base of the heart. The Purkinje fibres have a

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fast inherent conduction rate, and the electrical impulse reaches all of the ventricular muscle cells in about 75 ms. Since the electrical stimulus begins at the apex, the contraction also begins at the apex and travels toward the base of the heart, similar to squeezing a tube of toothpaste from the bottom. This allows the blood to be pumped out of the ventricles and into the aorta and pulmonary trunk. The total time elapsed from the initiation of the impulse in the SA node until depolarization of the ventricles is approximately 225 ms.

Membrane Potentials and Ion Movement in Cardiac Conductive Cells

Action potentials are considerably different between cardiac conductive cells and cardiac contractive cells. While Na^+ and K^+ play essential roles, Ca^{2+} is also critical for both types of cells. Unlike skeletal muscles and neurons, cardiac conductive cells do not have a stable resting potential. Conductive cells contain a series of sodium ion channels that allow a normal and slow influx of sodium ions that causes the membrane potential to rise slowly from an initial value of −60 mV up to about −40 mV. The resulting movement of sodium ions creates **spontaneous depolarization** (or **prepotential depolarization**). At this point, calcium ion channels open and Ca^{2+} enters the cell, further depolarizing it at a more rapid rate until it reaches a value of approximately +15 mV. At this point, the calcium ion channels close and K^+ channels open, allowing an outflux of K^+ and resulting in repolarization. When the membrane potential reaches approximately −60 mV, the K^+ channels close and Na^+ channels open, and the prepotential phase begins again. This phenomenon explains the autorhythmicity properties of cardiac muscle (Figure 18.15).

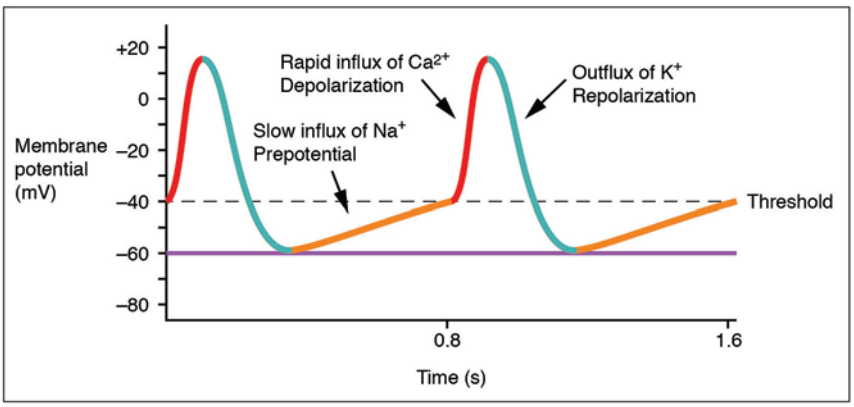


Figure 18.15 Action Potential at the SA Node. The prepotential is due to a slow influx of sodium ions until the threshold is reached followed by a rapid depolarization and repolarization. The prepotential accounts for the membrane reaching threshold and initiates the spontaneous depolarization and contraction of the cell. Note the lack of a resting potential.

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Membrane Potentials and Ion Movement in Cardiac Contractile Cells

There is a distinctly different electrical pattern involving the contractile cells. In this case, there is a rapid depolarization, followed by a **plateau phase** and then repolarization. This phenomenon accounts for the long refractory periods required for the cardiac muscle cells to pump blood effectively before they are capable of firing for a second time. These cardiac myocytes normally do not initiate their own electrical potential but rather wait for an impulse to reach them.

Contractile cells demonstrate a much more stable resting phase than conductive cells at approximately −80 mV for cells in the atria and −90 mV for cells in the ventricles. Despite this initial difference, the other components of their action potentials are virtually identical. In both cases, when stimulated by an action potential, voltage-gated channels rapidly open, beginning the positive feedback mechanism of depolarization. This rapid influx of positively charged ions raises the membrane potential to approximately +30 mV, at which point the sodium channels close. The rapid depolarization period typically lasts 3–5 ms. Depolarization is followed by the plateau phase, in which membrane potential declines relatively slowly. This is due in large part to the opening of the slow Ca^{2+} channels, allowing Ca^{2+} to enter the cell while few K^+ channels are open, allowing K^+ to exit the cell. The relatively long plateau phase lasts approximately 175 ms. Once the membrane potential reaches approximately zero, the Ca^{2+} channels close and K^+ channels open, allowing K^+ to exit the cell. The repolarization lasts approximately 75 ms. At this point, membrane potential drops until it reaches resting levels once more, and the cycle repeats. The entire event lasts between 250 and 300 ms (Figure 18.16).

The absolute refractory period for cardiac contractile muscle lasts approximately 200 ms, and the relative refractory period lasts approximately 50 ms, for a total of 250 ms. This extended period is critical, since the heart muscle must contract to pump blood effectively, and the contraction must follow the electrical events. Without extended refractory periods, premature contractions would occur in the heart and would not be compatible with life.

Calcium Ions

Calcium ions play two critical roles in the physiology of cardiac muscle. Their influx through slow calcium channels accounts for the prolonged plateau phase and absolute refractory period that enable cardiac muscle to function properly. Calcium ions also combine with the regulatory protein troponin in the troponin-tropomyosin complex; this complex removes the inhibition that prevents the heads of the myosin molecules from forming cross-bridges with the active sites on actin that provide the power stroke of contraction. This

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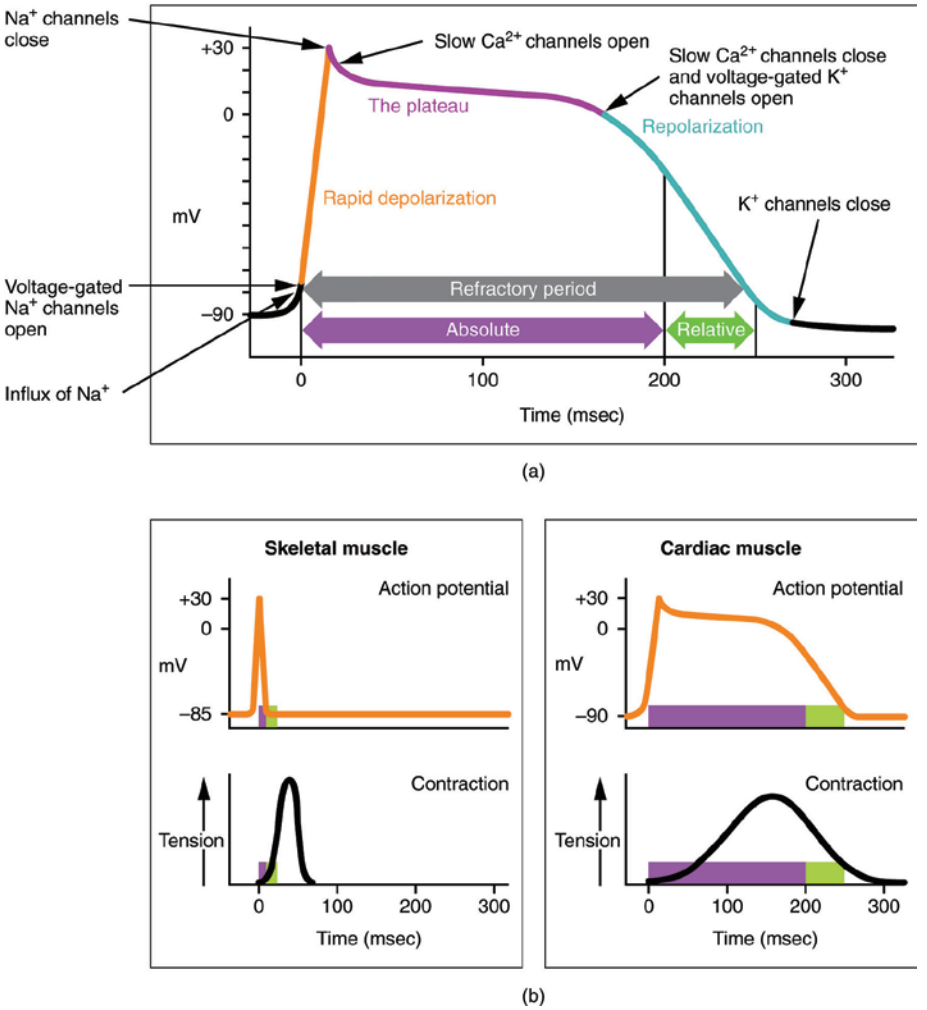


Figure 18.16 Action Potential in Cardiac Contractile Cells. (a) Note the long plateau phase due to the influx of calcium ions. The extended refractory period allows the cell to fully contract before another electrical event can occur. (b) The action potential for heart muscle is compared to that of skeletal muscle.

mechanism is virtually identical to that of skeletal muscle. Approximately 20 percent of the calcium required for contraction is supplied by the influx of Ca^{2+} during the plateau phase. The remaining Ca^{2+} for contraction is released from storage in the sarcoplasmic reticulum.

Comparative Rates of Conduction System Firing

The pattern of prepotential or spontaneous depolarization followed by the rapid depolarization and repolarization just described is seen in the SA node and a few other conductive cells in the heart. Since the SA node is the pacemaker, it

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reaches threshold faster than any other component of the conduction system. It will initiate the impulses spreading to the other conducting cells. The SA node, without nervous or endocrine control, would initiate a heart impulse approximately 80–100 times per minute. Although each component of the conduction system is capable of generating its own impulse, the rate progressively slows as you proceed from the SA node to the Purkinje fibres. Without the SA node, the AV node would generate a heart rate of 40–60 beats per minute. If the AV node were blocked, the atrioventricular bundle would fire at a rate of approximately 30–40 impulses per minute. The bundle branches would have an inherent rate of 20–30 impulses per minute, and the Purkinje fibres would fire at 15–20 impulses per minute. While a few exceptionally trained aerobic athletes demonstrate resting heart rates in the range of 30–40 beats per minute, for most individuals, rates lower than 50 beats per minute would indicate a condition called bradycardia.

Depending on the specific individual, as rates fall much below this level, the heart would be unable to maintain adequate flow of blood to vital tissues, initially resulting in a decrease of function across the systems, unconsciousness, and ultimately death.

Electrocardiogram

By careful placement of surface electrodes on the body, it is possible to record the complex, compound electrical signal of the heart. This tracing of the electrical signal is the **electrocardiogram** (**ECG**). Careful analysis of the ECG reveals a detailed picture of both normal and abnormal heart function and is an indispensable clinical diagnostic tool.

A normal ECG tracing is presented in Figure 18.17. Each component, segment, and interval is labelled and corresponds to important electrical events, demonstrating the relationship between these events and contraction in the heart.

There are five prominent points on the ECG: the P wave, the QRS complex, and the T wave. The small **P wave** represents the depolarization of the atria. The atria begin contracting approximately 25 ms after the start of the P wave. The large **QRS complex** represents the depolarization of the ventricles, which requires a much stronger electrical signal because of the larger size of the ventricular cardiac muscle. The ventricles begin to contract as the QRS reaches the peak of the R wave. Lastly, the **T wave** represents the repolarization of the ventricles. The repolarization of the atria occurs during the QRS complex, which masks it on an ECG.

The major segments and intervals of an ECG tracing are indicated in Figure 18.17. Segments are defined as the regions between two waves. Intervals

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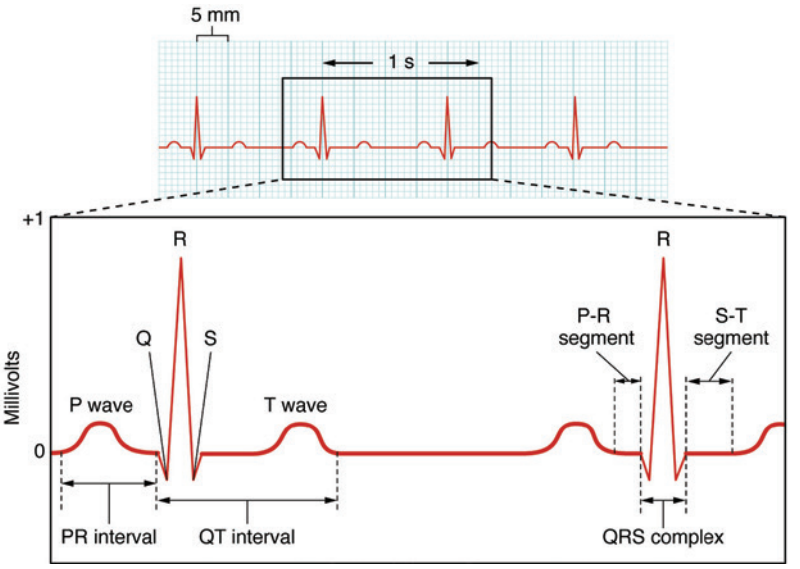


Figure 18.17 Electrocardiogram. A normal tracing shows the P wave, QRS complex, and T wave. Also indicated are the PR, QT, QRS, and ST intervals, plus the P-R and S-T segments.

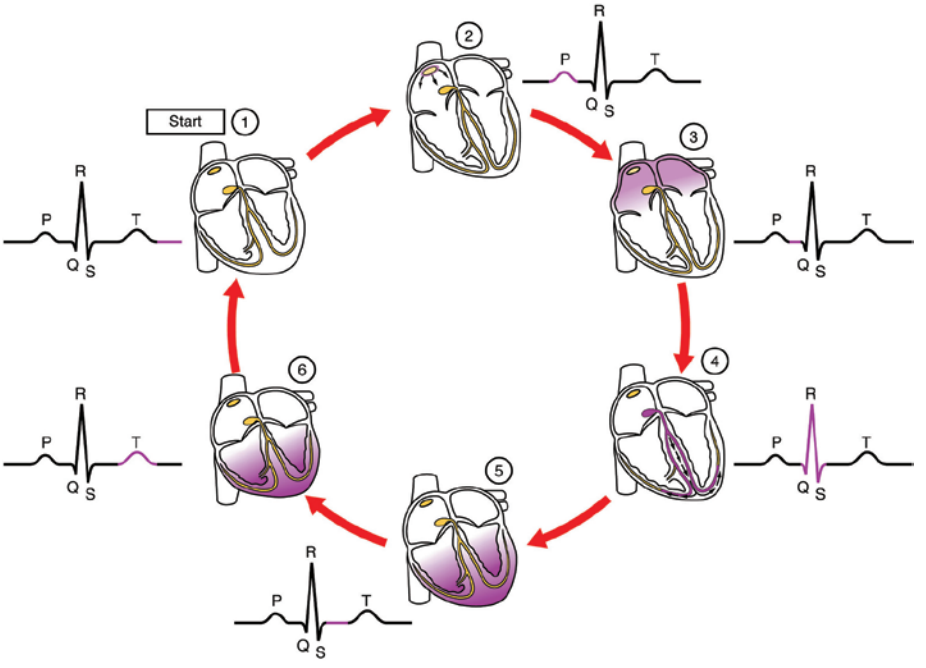


Figure 18.18 ECG Tracing Correlated to the Cardiac Cycle. This diagram correlates an ECG tracing with the electrical and mechanical events of a heart contraction. Each segment of an ECG tracing corresponds to one event in the cardiac cycle (see 18.3 Cardiac Cycle).

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include one segment plus one or more waves. For example, the PR segment begins at the end of the P wave and ends at the beginning of the QRS complex. The PR interval starts at the beginning of the P wave and ends with the beginning of the QRS complex. The PR interval is more clinically relevant, as it measures the duration from the beginning of atrial depolarization (the P wave) to the initiation of the QRS complex. Since the Q wave may be difficult to view in some tracings, the measurement is often extended to the R that is more easily visible. Should there be a delay in passage of the impulse from the SA node to the AV node, it would be visible in the PR interval. Figure 18.18 correlates events of heart contraction to the corresponding segments and intervals of an ECG.

Interactive Link 18.4

Visit this site (http://oer.aupress.ca/oer-202505/18.4) for a more detailed analysis of ECGs.

Interactive Link 18.5

Visit this site (http://oer.aupress.ca/oer-202505/18.5) for a more complete library of abnormal ECGs.

Cardiac Muscle Metabolism

Normally, cardiac muscle metabolism is entirely aerobic. Oxygen from the lungs is brought to the heart and every other organ attached to the hemoglobin molecules within the erythrocytes. Heart cells also store appreciable amounts of oxygen in myoglobin. Normally, these two mechanisms, circulating oxygen and oxygen attached to myoglobin, can supply sufficient oxygen to the heart, even during peak performance.

Fatty acids and glucose from the circulation are broken down within the mitochondria to release energy in the form of ATP. Both fatty acid droplets and glycogen are stored within the sarcoplasm and provide additional nutrient supply.

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18.3 Cardiac Cycle

Learning Objectives

By the end of this section, you will be able to:

- Describe the relationship between blood pressure and blood flow
- Summarize the events of the cardiac cycle
- Compare atrial and ventricular systole and diastole
- Relate heart sounds detected by auscultation to action of the heart's valves

The period of time that begins with contraction of the atria and ends with ventricular relaxation is known as the **cardiac cycle** (Figure 18.19). The period of contraction that the heart undergoes while it pumps blood into circulation is called **systole**. The period of relaxation that occurs as the chambers fill with blood is called **diastole**. Both the atria and ventricles undergo systole and diastole, and it is essential that these components be carefully regulated and coordinated to ensure blood is pumped efficiently to the body.

Pressures and Flow

Fluids, whether gases or liquids, are materials that flow according to pressure gradients—that is, they move from regions that are higher in pressure to regions that are lower in pressure. Accordingly, when the heart chambers are relaxed (diastole), blood will flow into the atria from the veins, which are higher in pressure. As blood flows into the atria, the pressure will rise, so the blood will initially move passively from the atria into the ventricles. When the action potential triggers the muscles in the atria to contract (atrial systole), the pressure within the atria rises further, pumping blood into the ventricles. During ventricular systole, pressure rises in the ventricles, pumping blood into the pulmonary trunk from the right ventricle and into the aorta from the left ventricle. Again, as you consider this flow and relate it to the conduction pathway, the elegance of the system should become apparent.

Phases of the Cardiac Cycle

At the beginning of the cardiac cycle, both the atria and the ventricles are relaxed (diastole). Blood is flowing into the right atrium from the superior and inferior venae cavae and the coronary sinus. Blood flows into the left atrium from the four pulmonary veins. The two atrioventricular valves, the tricuspid and mitral valves, are both open, so blood flows unimpeded from the atria and

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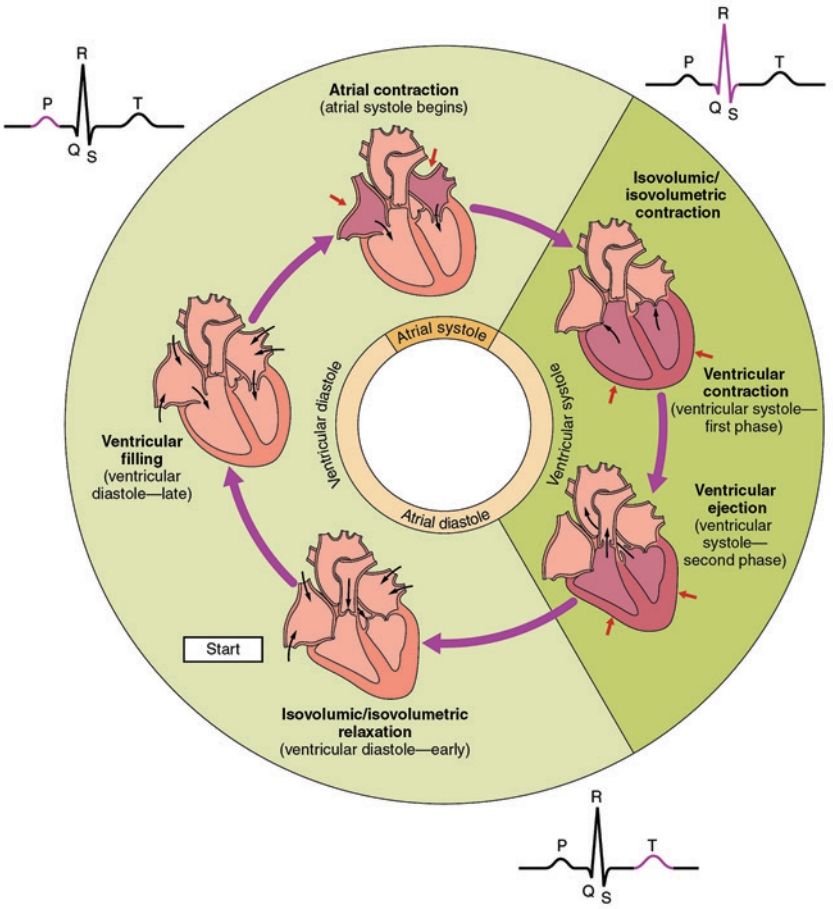


Figure 18.19 Overview of the Cardiac Cycle. The cardiac cycle begins with atrial systole and progresses to ventricular systole, atrial diastole, and ventricular diastole, when the cycle begins again. Correlations to the ECG are highlighted.

into the ventricles. Approximately 70–80 percent of ventricular filling occurs by this method. The two semilunar valves, the pulmonary and aortic valves, are closed, preventing backflow of blood into the right and left ventricles from the pulmonary trunk on the right and the aorta on the left.

Atrial Systole and Diastole

Contraction of the atria follows depolarization, represented by the P wave of the ECG. As the atrial muscles contract from the superior portion of the atria toward the atrioventricular septum, pressure rises within the atria, and blood is pumped into the ventricles through the open atrioventricular (tricuspid and mitral or bicuspid) valves. At the start of atrial systole, the ventricles are normally filled with approximately 70–80 percent of their capacity due to inflow during diastole. Atrial contraction, also referred to as the "atrial kick,"

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contributes the remaining 20–30 percent of filling (see Figure 18.19). Atrial systole lasts approximately 100 ms and ends prior to ventricular systole, as the atrial muscle returns to diastole.

Ventricular Systole

Ventricular systole (see Figure 18.19) follows the depolarization of the ventricles and is represented by the QRS complex in the ECG. It may be conveniently divided into two phases lasting a total of 270 ms. At the end of atrial systole and just prior to ventricular contraction, the ventricles contain approximately 130 mL of blood in a resting adult in a standing position. This volume is known as the **end diastolic volume** (**EDV**) or **preload**.

Initially, as the muscles in the ventricle contract, the pressure of the blood within the chamber rises, but it is not yet high enough to open the semilunar (pulmonary and aortic) valves and be ejected from the heart. However, blood pressure quickly rises above that of the atria that are now relaxed and in diastole. This increase in pressure causes blood to flow back toward the atria, closing the tricuspid and mitral valves. Since blood is not being ejected from the ventricles at this early stage, the volume of blood within the chamber remains constant. Consequently, this initial phase of ventricular systole is known as **isovolumic contraction**, also called isovolumetric contraction (see Figure 18.19).

In the second phase of ventricular systole, the **ventricular ejection phase**, the contraction of the ventricular muscle has raised the pressure within the ventricle to the point that it is greater than the pressures in the pulmonary trunk and the aorta. Blood is pumped from the heart, pushing open the pulmonary and aortic semilunar valves. Pressure generated by the left ventricle will be appreciably greater than the pressure generated by the right ventricle, since the existing pressure in the aorta will be so much higher. Nevertheless, both ventricles pump the same amount of blood. This quantity is referred to as stroke volume. Stroke volume will normally be in the range of 70–80 mL. Since ventricular systole began with an EDV of approximately 130 mL of blood, this means that there is still 50–60 mL of blood remaining in the ventricle following contraction. This volume of blood is known as the **end systolic volume** (**ESV**).

Ventricular Diastole

Ventricular relaxation, or diastole, follows repolarization of the ventricles and is represented by the T wave of the ECG. It too is divided into two distinct phases and lasts approximately 430 ms.

During the early phase of ventricular diastole, as the ventricular muscle relaxes, pressure on the remaining blood within the ventricle begins to fall. When pressure within the ventricles drops below pressure in both the

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pulmonary trunk and the aorta, blood flows back toward the heart, producing the dicrotic notch (small dip) seen in blood pressure tracings. The semilunar valves close to prevent backflow into the heart. Since the atrioventricular valves remain closed at this point, there is no change in the volume of blood in the ventricle, so the early phase of ventricular diastole is called the **isovolumic ventricular relaxation phase**, also called the isovolumetric ventricular relaxation phase (see Figure 18.19).

In the second phase of ventricular diastole, called late ventricular diastole, as the ventricular muscle relaxes, pressure on the blood within the ventricles drops even further. Eventually, it drops below the pressure in the atria. When this occurs, blood flows from the atria into the ventricles, pushing open the tricuspid and mitral valves. As pressure drops within the ventricles, blood flows from the major veins into the relaxed atria and from there into the ventricles. Both chambers are in diastole, the atrioventricular valves are open, and the semilunar valves remain closed (see Figure 18.19). The cardiac cycle is complete.

Figure 18.20 illustrates the relationship between the cardiac cycle and the ECG.

Heart Sounds

One of the simplest yet most effective diagnostic techniques applied to assess the state of a patient's heart is auscultation using a stethoscope.

In a normal, healthy heart, there are only two audible **heart sounds**: S_1 and S_2. S_1 is the sound created by the closing of the atrioventricular valves during

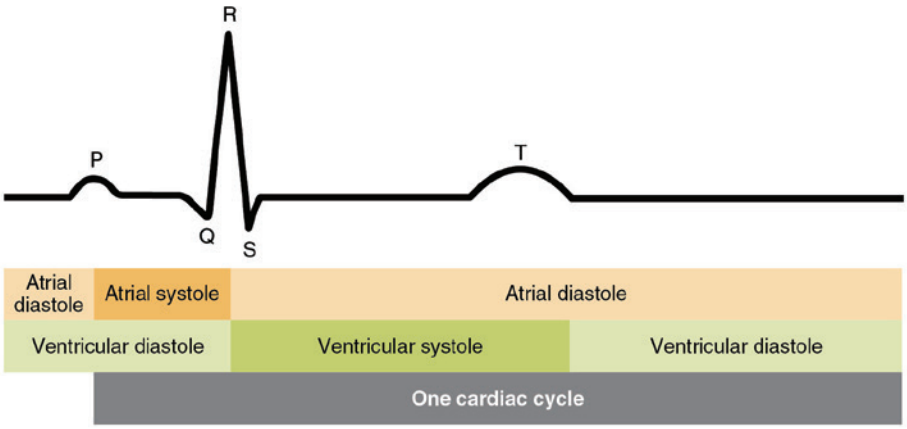


Figure 18.20 Relationship Between the Cardiac Cycle and ECG. Initially, both the atria and ventricles are relaxed (diastole). The P wave represents depolarization of the atria and is followed by atrial contraction (systole). Atrial systole extends until the QRS complex, at which point, the atria relax. The QRS complex represents depolarization of the ventricles and is followed by ventricular contraction. The T wave represents the repolarization of the ventricles and marks the beginning of ventricular relaxation.

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ventricular contraction and is normally described as a "lub," or first heart sound. The second heart sound, S_2, is the sound of the closing of the semilunar valves during ventricular diastole and is described as a "dub" (Figure 18.21). In both cases, as the valves close, the openings within the atrioventricular septum guarded by the valves will become reduced, and blood flow through the opening will become more turbulent until the valves are fully closed.

The term **murmur** is used to describe an unusual sound coming from the heart that is caused by the turbulent flow of blood. Murmurs are graded on a scale of 1 to 6, with 1 being the most common, the most difficult sound to detect, and the least serious. The most severe is a 6. Phonocardiograms or auscultograms can be used to record both normal and abnormal sounds using specialized electronic stethoscopes.

During auscultation, it is common practice for the clinician to ask the patient to breathe deeply. This procedure not only allows for listening to airflow, but it may also amplify heart murmurs. Inhalation increases blood flow into the right side of the heart and may increase the amplitude of right-sided heart murmurs. Expiration partially restricts blood flow into the left side of the heart and may amplify left-sided heart murmurs. Figure 18.22 indicates proper placement of the bell of the stethoscope to facilitate auscultation.

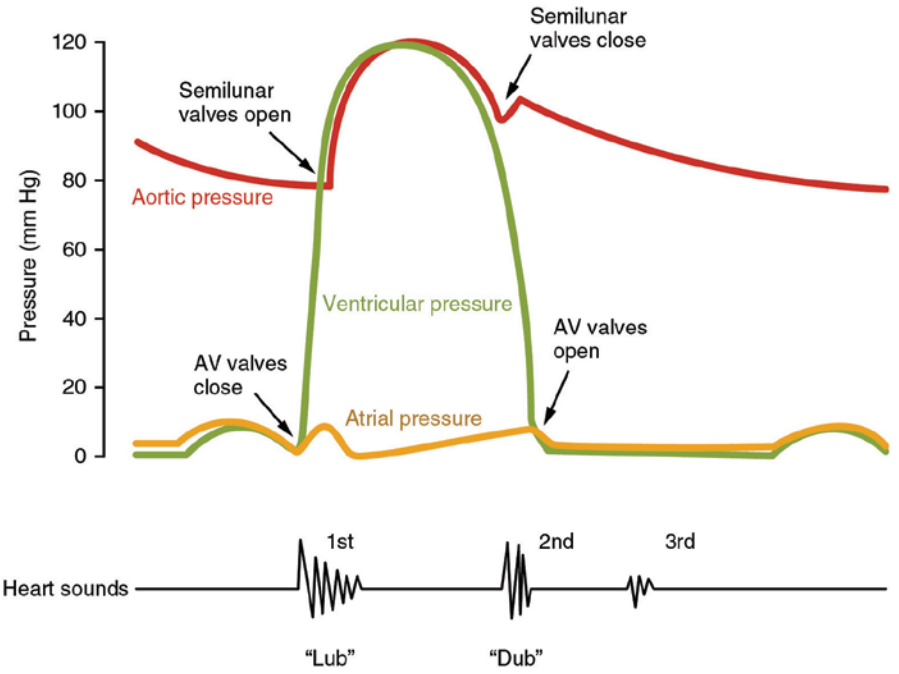


Figure 18.21 Heart Sounds and the Cardiac Cycle. In this illustration, the x-axis reflects time with a recording of the heart sounds. The y-axis represents pressure.

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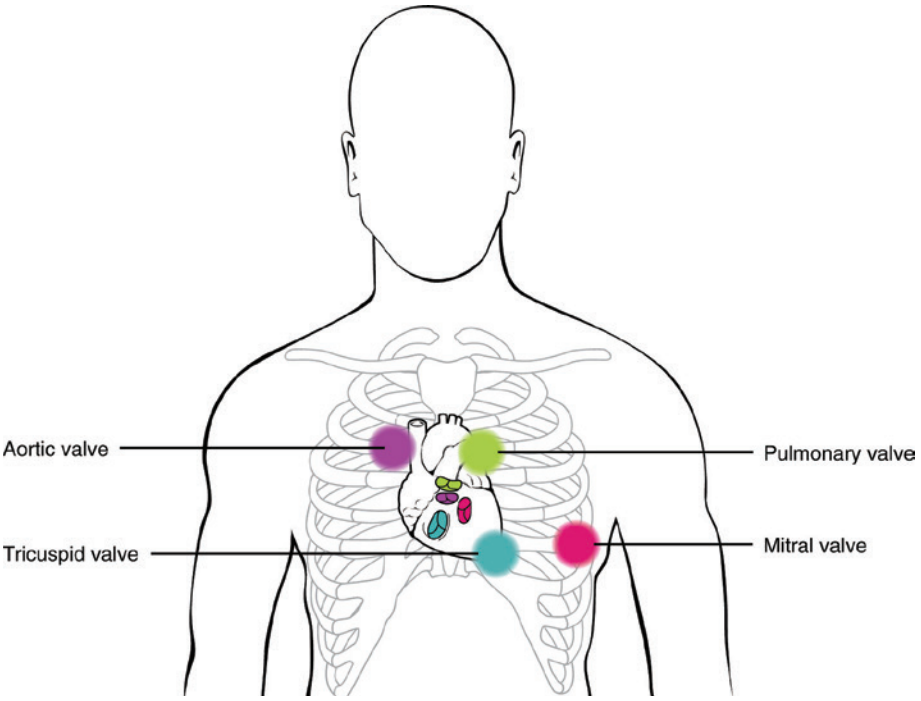


Figure 18.22 Stethoscope Placement for Auscultation. Proper placement of the bell of the stethoscope facilitates auscultation. At each of the four locations on the chest, a different valve can be heard.

18.4 Cardiac Physiology

Learning Objectives

By the end of this section, you will be able to:

- Relate heart rate to cardiac output
- Describe the effect of exercise on heart rate
- Identify cardiovascular centres and cardiac reflexes that regulate heart function
- Describe factors affecting heart rate
- Distinguish between positive and negative factors that affect heart contractility
- Summarize factors affecting stroke volume and cardiac output
- Describe the cardiac response to variations in blood flow and pressure

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The autorhythmicity inherent in cardiac cells keeps the heart beating at a regular pace; however, the heart is regulated by and responds to outside influences as well. Neural and endocrine controls are vital to the regulation of cardiac function. In addition, the heart is sensitive to several environmental factors, including electrolytes.

Resting Cardiac Output

Cardiac output (**CO**) is a measurement of the amount of blood pumped by each ventricle in 1 minute. To calculate this value, multiply **stroke volume** (**SV**), the amount of blood pumped by each ventricle each time that it contracts, by **heart rate** (**HR**), in contractions per minute (or beats per minute, bpm). It can be represented mathematically by the following equation:

$$CO = HR \times SV.$$

SV is normally measured using an echocardiogram to record EDV and ESV and calculating the difference: SV = EDV − ESV. SV can also be measured using a specialized catheter, but this is an invasive procedure and far more dangerous to the patient. A mean SV for a resting 70 kg individual would be approximately 70 mL. There are several important variables, including size of the heart, physical and mental condition of the individual, sex, contractility, duration of contraction, preload or EDV, and afterload or resistance. Normal range for SV would be 55–100 mL. An average resting HR would be approximately 75 bpm but could range from 60 to 100 in some individuals.

Using these numbers, the mean CO is 5.25 L/min, with a range of 4.0–8.0 L/min. Remember, however, that these numbers refer to CO from each ventricle separately, not the total for the heart. Factors influencing CO are summarized in Figure 18.23.

SVs are also used to calculate **ejection fraction**, which is the portion of the blood that is pumped or ejected from the heart with each contraction. To calculate ejection fraction, SV is divided by EDV. Despite the name, the ejection fraction is normally expressed as a percentage. Ejection fractions range from approximately 55–70 percent, with a mean of 58 percent.

Exercise and Maximum Cardiac Output

In healthy young individuals, HR may increase to 150 bpm during exercise. SV can also increase from 70 to approximately 130 mL due to increased strength of contraction. This would increase CO to approximately 19.5 L/min, 4–5 times

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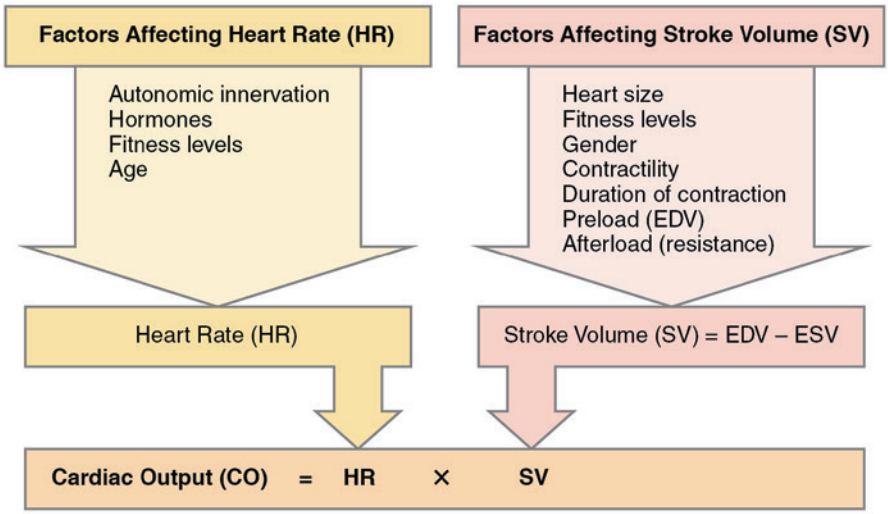


Figure 18.23 Major Factors Influencing Cardiac Output. Cardiac output is influenced by heart rate and stroke volume, both of which are also variable.

the resting rate. Top cardiovascular athletes can achieve even higher levels. At their peak performance, they may increase resting CO by 7–8 times.

Since the heart is a muscle, exercising it increases its efficiency. The difference between maximum and resting CO is known as the **cardiac reserve**. It measures the residual capacity of the heart to pump blood.

Heart Rates

HRs vary considerably, not only with exercise and fitness levels, but also with age. Newborn resting HRs may be 120 bpm. HR gradually decreases until young adulthood and then gradually increases again with age.

Maximum HRs are normally in the range of 200–220 bpm, although there are some extreme cases in which they may reach higher levels. As one ages, the ability to generate maximum rates decreases. This may be estimated by taking the maximal value of 220 bpm and subtracting the individual's age. So a 40-year-old individual would be expected to hit a maximum rate of approximately 180, and a 60-year-old person would achieve a HR of 160.

Correlation Between Heart Rates and Cardiac Output

Initially, physiological conditions that cause HR to increase also trigger an increase in SV. During exercise, the rate of blood returning to the heart increases. However, as the HR rises, there is less time spent in diastole and consequently less time for the ventricles to fill with blood. Even though there

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is less filling time, SV will initially remain high. However, as HR continues to increase, SV gradually decreases due to decreased filling time. CO will initially stabilize as the increasing HR compensates for the decreasing SV, but at very high rates, CO will eventually decrease as increasing rates are no longer able to compensate for the decreasing SV. Consider this phenomenon in a healthy young individual. Initially, as HR increases from resting to approximately 120 bpm, CO will rise. As HR increases from 120 to 160 bpm, CO remains stable, since the increase in rate is offset by decreasing ventricular filling time and, consequently, SV. As HR continues to rise above 160 bpm, CO actually decreases as SV falls faster than HR increases. So although aerobic exercises are critical to maintain the health of the heart, individuals are cautioned to monitor their HR to ensure they stay within the **target heart rate** range of between 120 and 160 bpm so that CO is maintained. The target HR is loosely defined as the range in which both the heart and the lungs receive the maximum benefit from the aerobic workout and is dependent on age.

Cardiovascular Centres

Nervous control over HR is centralized within the two paired cardiovascular centres of the medulla oblongata (Figure 18.24). The cardioaccelerator regions stimulate activity via sympathetic stimulation of the cardioaccelerator nerves, and the cardioinhibitory centres decrease heart activity via parasympathetic stimulation as one component of the vagus nerve, cranial nerve X. During rest, both centres provide slight stimulation to the heart, contributing to **autonomic tone**. This is a similar concept to tone in skeletal muscles. Normally, vagal stimulation predominates, as left unregulated, the SA node would initiate a sinus rhythm of approximately 100 bpm.

Both sympathetic and parasympathetic stimulations flow through a paired complex network of nerve fibres known as the **cardiac plexus** near the base of the heart. The cardioaccelerator centre also sends additional fibres, forming the cardiac nerves via sympathetic ganglia (the cervical ganglia plus superior thoracic ganglia T1–T4) to both the SA and the AV nodes, plus additional fibres to the atria and ventricles. The ventricles are more richly innervated by sympathetic fibres than parasympathetic fibres. Sympathetic stimulation causes the release of the neurotransmitter norepinephrine (NE) at the neuromuscular junction of the cardiac nerves. NE shortens the repolarization period, thus speeding the rate of depolarization and contraction, which results in an increase in HR. It opens chemical- or ligand-gated sodium and calcium ion channels, allowing an influx of positively charged ions.

NE binds to the beta-1 receptor. Some cardiac medications (for example, beta blockers) work by blocking these receptors, thereby slowing HR, and are

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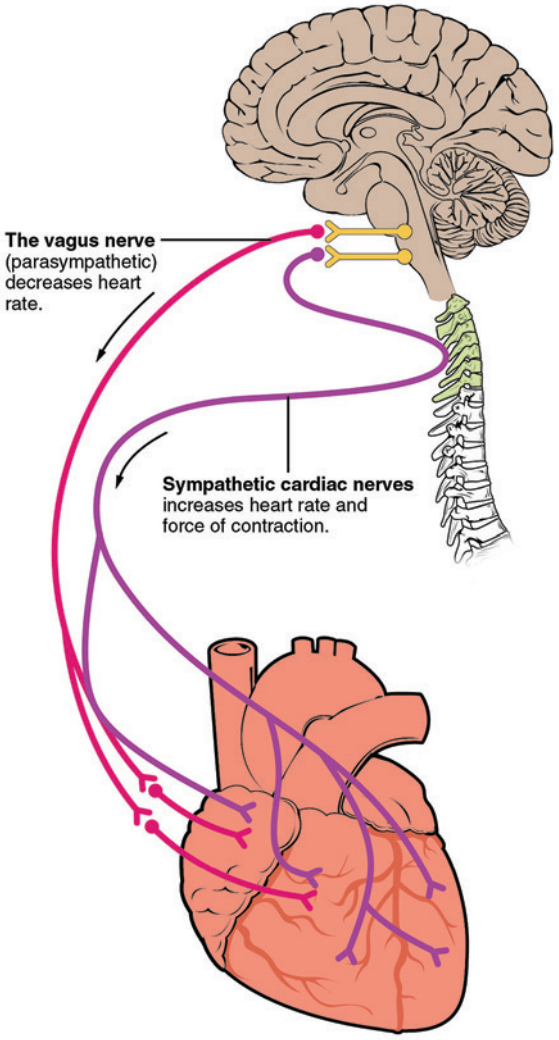


Figure 18.24 Autonomic Innervation of the Heart. Cardioaccelerator and cardioinhibitory areas are components of the paired cardiac centres located in the medulla oblongata of the brain. They innervate the heart via sympathetic cardiac nerves that increase cardiac activity and vagus (parasympathetic) nerves that slow cardiac activity.

one possible treatment for hypertension. Overprescription of these drugs may lead to bradycardia and even stoppage of the heart.

Parasympathetic stimulation originates from the cardioinhibitory region with impulses travelling via the vagus nerve (cranial nerve X). The vagus nerve sends branches to both the SA and AV nodes and to portions of both the atria and the ventricles. Parasympathetic stimulation releases the neurotransmitter acetylcholine (ACh) at the neuromuscular junction. ACh slows HR by opening chemical- or ligand-gated potassium ion channels to slow the rate of

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spontaneous depolarization, which extends repolarization and increases the time before the next spontaneous depolarization occurs. Without any nervous stimulation, the SA node would establish a sinus rhythm of approximately 100 bpm. Since resting rates are considerably less than this, it becomes evident that parasympathetic stimulation normally slows HR. This is similar to an individual driving a car with one foot on the brake pedal. To speed up, one need merely remove one's foot from the brake and let the engine increase speed. In the case of the heart, decreasing parasympathetic stimulation decreases the release of ACh, which allows HR to increase up to approximately 100 bpm. Any increases beyond this rate would require sympathetic stimulation. Figure 18.25 illustrates the effects of parasympathetic and sympathetic stimulation on the normal sinus rhythm.

Input to the Cardiovascular Centre

The cardiovascular centre receives input from a series of visceral receptors with impulses travelling through visceral sensory fibres within the vagus and sympathetic nerves via the cardiac plexus. Among these receptors are various proprioreceptors, baroreceptors, and chemoreceptors, plus stimuli from the limbic system. Collectively, these inputs normally enable the cardiovascular centres to regulate heart function precisely, a process known as **cardiac reflexes**. Increased physical activity results in increased rates of firing by various proprioreceptors located in muscles, joint capsules, and tendons. Any such increase in physical activity would logically warrant increased blood flow. The cardiac centres monitor these increased rates of firing and suppress parasympathetic stimulation and increase sympathetic stimulation as needed in order to increase blood flow.

Similarly, baroreceptors are stretch receptors located in the aortic sinus, carotid bodies, venae cavae, and other locations, including pulmonary vessels and the right side of the heart itself. Rates of firing from the baroreceptors represent blood pressure, the level of physical activity, and the relative distribution of blood. The cardiac centres monitor baroreceptor firing to maintain cardiac homeostasis, a mechanism called the **baroreceptor reflex**. With increased pressure and stretch, the rate of baroreceptor firing increases, and the cardiac centres decrease sympathetic stimulation and increase parasympathetic stimulation. As pressure and stretch decrease, the rate of baroreceptor firing decreases, and the cardiac centres increase sympathetic stimulation and decrease parasympathetic stimulation.

There is a similar reflex, called the **atrial reflex** or **Bainbridge reflex**, associated with varying rates of blood flow to the atria. Increased venous return stretches the walls of the atria where specialized baroreceptors are located.

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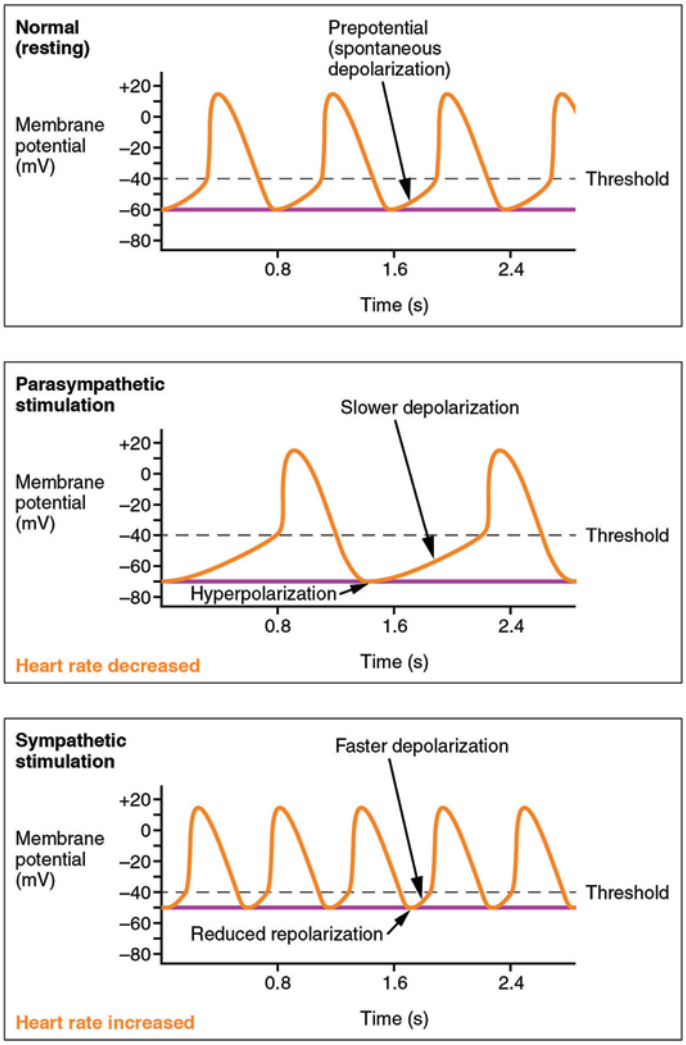


Figure 18.25 Effects of Parasympathetic and Sympathetic Stimulation on Normal Sinus Rhythm. The wave of depolarization in a normal sinus rhythm shows a stable resting HR. Following parasympathetic stimulation, HR slows. Following sympathetic stimulation, HR increases.

However, as the atrial baroreceptors increase their rate of firing and as they stretch due to the increased blood pressure, the cardiac centre responds by increasing sympathetic stimulation and inhibiting parasympathetic stimulation to increase HR. The opposite is also true.

Increased metabolic by-products associated with increased activity, such as carbon dioxide, hydrogen ions, and lactic acid, plus falling oxygen levels, are detected by a suite of chemoreceptors innervated by the glossopharyngeal and vagus nerves. These chemoreceptors provide feedback to the cardiovascular

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centres about the need for increased or decreased blood flow based on the relative levels of these substances.

The limbic system can also significantly impact HR related to emotional state. During periods of stress, it is not unusual to identify higher-than-normal HRs, often accompanied by a surge in the stress hormone cortisol.

Individuals experiencing extreme anxiety may manifest panic attacks with symptoms that resemble those of heart attacks. These events are typically transient and treatable. Meditation techniques have been developed to ease anxiety and have been shown to lower HR effectively. Doing simple deep and slow breathing exercises with one's eyes closed can also significantly reduce this anxiety and HR.

Other Factors Influencing Heart Rate

Using a combination of autorhythmicity and innervation, the cardiovascular centre is able to provide relatively precise control over HR. However, there are a number of other factors that have an impact on HR as well, including epinephrine, NE, and thyroid hormones; levels of various ions, including calcium, potassium, and sodium; body temperature; hypoxia; and pH balance (Table 18.1 and Table 18.2). After reading this section, the importance of maintaining homeostasis should become even more apparent.

Stroke Volume

Many of the same factors that regulate HR also impact cardiac function by altering SV. While a number of variables are involved, SV is ultimately dependent on the difference between EDV and ESV. The three primary factors to consider are preload, or the stretch on the ventricles prior to contraction; the contractility, or the force or strength of the contraction itself; and afterload, the force the ventricles must generate to pump blood against the resistance in the vessels. These factors are summarized in Table 18.1 and Table 18.2.

Preload

Preload is directly proportional to EDV. Therefore, the greater the EDV is, the greater the preload is. One of the primary factors to consider is **filling time**, or the duration of ventricular diastole during which filling occurs. The more rapidly the heart contracts, the shorter the filling time becomes and the lower the EDV and preload are. This effect can be partially overcome by increasing the second variable, contractility, and raising SV, but over time, the heart is unable to compensate for decreased filling time, and preload also decreases.

With increasing ventricular filling, EDV increases and, as a result, preload increases, stretching the cardiac muscle to a greater degree. At rest, there is

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Table 18.1 Major Factors Increasing Heart Rate and Force of Contraction

Factor	Effect
Cardioaccelerator nerves	Release of norepinephrine by cardioaccelerator nerves
Proprioreceptors	Increase in firing rates of proprioreceptors (e.g., during exercise)
Chemoreceptors	Chemoreceptors sense decreased levels of O_2 or increased levels of H^+, CO_2, and lactic acid
Baroreceptors	Decrease in firing rates of baroreceptors (indicating falling blood volume/pressure)
Limbic system	Anticipation of physical exercise or strong emotions by the limbic system
Catecholamines	Decrease in epinephrine and norepinephrine release by the adrenal glands
Thyroid hormones	Increase in T_3 and T_4 in the blood (released by thyroid)
Calcium	Decrease in calcium ions in the blood
Potassium	Decrease in potassium ions in the blood
Sodium	Decrease in sodium ions in the blood
Body temperature	Increase in body temperature
Nicotine and caffeine	Presence of nicotine, caffeine, or other stimulants

Table 18.2 Factors Decreasing Heart Rate and Force of Contraction

Factor	Effect
Cardioinhibitor nerves (vagus)	Release of acetylcholine by cardioinhibitor nerves
Proprioreceptors	Decrease in firing rates of proprioreceptors (e.g., during rest)
Chemoreceptors	Chemoreceptors sense increased levels of O_2 or decreased levels of H^+, CO_2, and lactic acid
Baroreceptors	Increase in firing rates of baroreceptors (indicating rising blood volume/pressure)
Limbic system	Anticipation of relaxation by the limbic system
Catecholamines	Decrease in epinephrine and norepinephrine release by the adrenal glands
Thyroid hormones	Decrease of T_3 and T_4 in the blood (released by thyroid)
Calcium	Decrease in calcium ions in the blood
Potassium	Increase in potassium ions in the blood
Sodium	Increase in sodium ions in the blood
Body temperature	Decrease in body temperature
Opiates and tranquilizers	Presence of opiates (heroin), tranquilizers, or other depressants

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little stretch of the ventricular muscle, and the sarcomeres remain short. With increased ventricular filling, the ventricular muscle is increasingly stretched, and the sarcomere length increases. As the sarcomeres reach their optimal lengths, they will contract more powerfully, because more of the myosin heads can bind to the actin on the thin filaments, forming cross-bridges and increasing the strength of contraction and SV. If this process were to continue and the sarcomeres stretched beyond their optimal lengths, the force of contraction would decrease. However, due to the physical constraints of the location of the heart, this excessive stretch is not a concern.

The relationship between ventricular stretch and contraction has been stated in the well-known **Frank-Starling mechanism**, or simply Starling's law of the heart. This principle states that, within physiological limits, the force of heart contraction is directly proportional to the initial length of the muscle fibre. This means that the greater the stretch of the ventricular muscle (within limits), the more powerful the contraction is, which in turn increases SV. Therefore, by increasing preload, you increase the second variable, contractility.

Any sympathetic stimulation to the venous system will increase venous return to the heart, which contributes to ventricular filling, and EDV and preload. While much of the ventricular filling occurs while both atria and ventricles are in diastole, the contraction of the atria, the atrial kick, plays a crucial role by providing the last 20–30 percent of ventricular filling.

Contractility

It is virtually impossible to consider preload or ESV without including an early mention of the concept of contractility. Indeed, the two parameters are intimately linked. Contractility refers to the force of the contraction of the heart muscle, which controls SV, and is the primary parameter for impacting ESV. The more forceful the contraction is, the greater the SV and smaller the ESV are. Less forceful contractions result in smaller SVs and larger ESVs. Factors that increase contractility are described as **positive inotropic factors**, and those that decrease contractility are described as **negative inotropic factors**.

Not surprisingly, sympathetic stimulation is a positive inotrope, whereas parasympathetic stimulation is a negative inotrope. Sympathetic stimulation triggers the release of NE at the neuromuscular junction from the cardiac nerves and also stimulates the adrenal cortex to secrete epinephrine and NE. In addition to their stimulatory effects on HR, they also bind to both alpha and beta receptors on the cardiac muscle cell membrane to increase metabolic rate and the force of contraction. This combination of actions has the net effect of increasing SV and leaving a smaller residual ESV in the ventricles. In

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comparison, parasympathetic stimulation releases ACh at the neuromuscular junction from the vagus nerve. The membrane hyperpolarizes and inhibits contraction to decrease the strength of contraction and SV and to raise ESV. Since parasympathetic fibres are more widespread in the atria than in the ventricles, the primary site of action is in the upper chambers. Parasympathetic stimulation in the atria decreases the atrial kick and reduces EDV, which decreases ventricular stretch and preload, thereby further limiting the force of ventricular contraction. Stronger parasympathetic stimulation also directly decreases the force of contraction of the ventricles.

Several synthetic drugs, including dopamine and isoproterenol, have been developed that mimic the effects of epinephrine and NE by stimulating the influx of calcium ions from the extracellular fluid. Higher concentrations of intracellular calcium ions increase the strength of contraction. Excess calcium (hypercalcemia) also acts as a positive inotropic agent. The drug digitalis lowers HR and increases the strength of the contraction, acting as a positive inotropic agent by blocking the sequestering of calcium ions into the sarcoplasmic reticulum. This leads to higher intracellular calcium levels and greater strength of contraction. In addition to the catecholamines from the adrenal medulla, other hormones also demonstrate positive inotropic effects. These include thyroid hormones and glucagon from the pancreas.

Negative inotropic agents include hypoxia, acidosis, hyperkalemia, and a variety of synthetic drugs. These include numerous beta blockers and calcium channel blockers. Early beta blocker drugs include propranolol and pronethalol and are credited with revolutionizing treatment of cardiac patients experiencing angina pectoris. There is also a large class of dihydropyridine, phenylalkylamine, and benzothiazepine calcium channel blockers that may be administered, decreasing the strength of contraction and SV.

Afterload

Afterload refers to the tension the ventricles must develop to pump blood effectively against the resistance in the vascular system. Any condition that increases resistance requires a greater afterload to force open the semilunar valves and pump the blood. Damage to the valves, such as stenosis, which makes them harder to open, will also increase afterload. Any decrease in resistance decreases the afterload. Table 18.3 summarizes the major factors influencing SV, Figure 18.26 summarizes the major factors influencing CO, and Table 18.4 and Table 18.5 summarize cardiac responses to increased and decreased blood flow and pressure in order to restore homeostasis.

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Table 18.3 Major Factors Influencing Stroke Volume

Condition	Preload	Contractility	Afterload
Raised due to:	• Fast filling time • Increased venous return	• Sympathetic stimulation • Epinephrine and norepinephrine • High intracellular calcium ions • High blood calcium level • Thyroid hormones • Glucagon	• Increased vascular resistance • Semilunar valve damage
Effects:	**Increases end diastolic volume** **Increases stroke volume**	**Decreases end systolic volume** **Increases stroke volume**	**Increases end systolic volume** **Decreases stroke volume**
Lowered due to:	• Decreased thyroid hormones • Decreased calcium ions • High or low potassium ions • High or low sodium • Low body temperature • Hypoxia • Abnormal pH balance • Drugs (i.e., calcium channel blockers)	• Parasympathetic stimulation • Acetylcholine • Hypoxia • Hyperkalemia	• Decreased vascular resistance
Effects:	**Decreases end diastolic volume** **Decreases stroke volume**	**Increases end systolic volume** **Decreases stroke volume**	**Decreases end systolic volume** **Increases stroke volume**

Multiple factors impact preload, afterload, and contractility and are the major considerations influencing SV.

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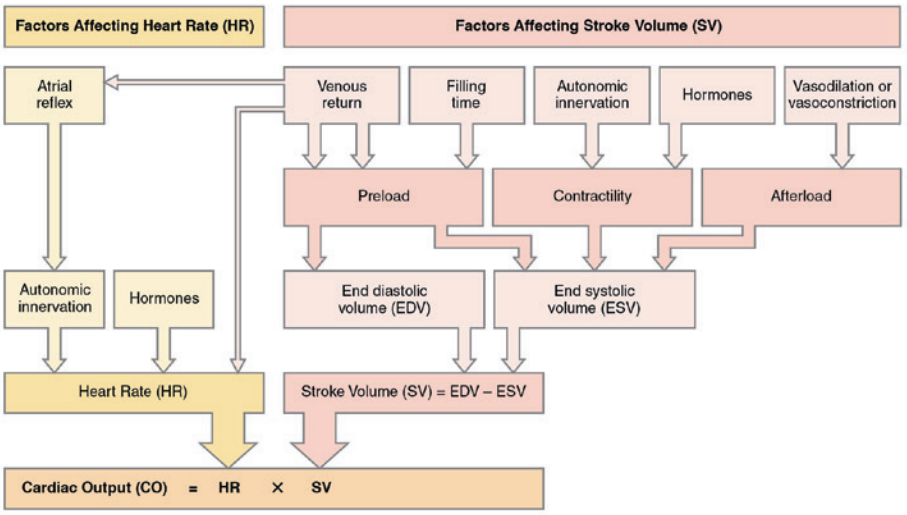


Figure 18.26 Summary of Major Factors Influencing Cardiac Output. The primary factors influencing HR include autonomic innervation plus endocrine control. Not shown are environmental factors, such as electrolytes, metabolic products, and temperature. The primary factors controlling SV include preload, contractility, and afterload. Other factors such as electrolytes may be classified as either positive or negative inotropic agents.

Table 18.4 Cardiac Response to Decreasing Blood Flow and Pressure Due to Decreasing Cardiac Output

	Baroreceptors (aorta, carotid arteries, venae cavae, and atria)	**Chemoreceptors (both central nervous system and in proximity to baroreceptors)**
Sensitive to	Decreased stretch	Decreased O_2 and increasing CO_2, H^+, and lactic acid
Target	Suppressed parasympathetic stimulation	Increased sympathetic stimulation
Response of heart	Increased heart rate and increased stroke volume	Increased heart rate and increased stroke volume
Overall effect	Increased blood flow and pressure due to increased cardiac output; homeostasis restored	Increased blood flow and pressure due to increased cardiac output; homeostasis restored

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Table 18.5 Cardiac Response to Increasing Blood Flow and Pressure Due to Increasing Cardiac Output

	Baroreceptors (aorta, carotid arteries, venae cavae, and atria)	Chemoreceptors (both central nervous system and in proximity to baroreceptors)
Sensitive to	Increased stretch	Increased O_2 and decreasing CO_2, H^+, and lactic acid
Target	Increased parasympathetic stimulation	Sympathetic stimulation suppressed
Response of heart	Decreased heart rate and decreased stroke volume	Decreased heart rate and decreased stroke volume
Overall effect	Decreased blood flow and pressure due to decreased cardiac output; homeostasis restored	Decreased blood flow and pressure due to decreased cardiac output; homeostasis restored

Key Terms

afterload: Force the ventricles must develop to effectively pump blood against the resistance in the vessels.

anastomosis (plural = anastomoses): Area where vessels unite to allow blood to circulate even if there may be partial blockage in another branch.

anterior cardiac veins: Vessels that parallel the small cardiac arteries and drain the anterior surface of the right ventricle, bypass the coronary sinus, and drain directly into the right atrium.

anterior interventricular artery (also left anterior descending artery or LAD): Major branch of the left coronary artery that follows the anterior interventricular sulcus.

anterior interventricular sulcus: Sulcus located between the left and right ventricles on the anterior surface of the heart.

aortic valve (also aortic semilunar valve): Valve located at the base of the aorta.

atrial reflex (also called Bainbridge reflex): Autonomic reflex that responds to stretch receptors in the atria that send impulses to the cardioaccelerator area to increase HR when venous flow into the atria increases.

atrioventricular (AV) node: Clump of myocardial cells located in the inferior portion of the right atrium within the atrioventricular septum;

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receives the impulse from the SA node, pauses, and then transmits it into specialized conducting cells within the interventricular septum.

atrioventricular bundle (also bundle of His): Group of specialized myocardial conductile cells that transmit the impulse from the AV node through the interventricular septum; form the left and right atrioventricular bundle branches.

atrioventricular bundle branches (also left or right bundle branches): Specialized myocardial conductile cells that arise from the bifurcation of the atrioventricular bundle and pass through the interventricular septum; lead to the Purkinje fibres and also to the right papillary muscle via the moderator band.

atrioventricular septum: Cardiac septum located between the atria and ventricles; atrioventricular valves are located here.

atrioventricular valves (AV valves): One-way valves located between the atria and ventricles; the valve on the right is called the tricuspid valve, and the one on the left is the mitral or bicuspid valve.

atrium (plural = atria): Upper or receiving chamber of the heart that pumps blood into the lower chambers just prior to their contraction; the right atrium receives blood from the systemic circuit that flows into the right ventricle; the left atrium receives blood from the pulmonary circuit that flows into the left ventricle.

auricle: Extension of an atrium visible on the superior surface of the heart.

autonomic tone: Contractile state during resting cardiac activity produced by mild sympathetic and parasympathetic stimulation.

autorhythmicity: Ability of cardiac muscle to initiate its own electrical impulse that triggers the mechanical contraction that pumps blood at a fixed pace without nervous or endocrine control.

Bainbridge reflex (also called atrial reflex): Autonomic reflex that responds to stretch receptors in the atria that send impulses to the cardioaccelerator area to increase HR when venous flow into the atria increases.

baroreceptor reflex: Autonomic reflex in which the cardiac centres monitor signals from the baroreceptor stretch receptors and regulate heart function based on blood flow.

bicuspid valve (also mitral valve or left atrioventricular valve): Valve located between the left atrium and ventricle; consists of two flaps of tissue.

bundle of His (also atrioventricular bundle): Group of specialized myocardial conductile cells that transmit the impulse from the AV node through the interventricular septum; form the left and right atrioventricular bundle branches.

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cardiac cycle: Period of time between the onset of atrial contraction (atrial systole) and ventricular relaxation (ventricular diastole).

cardiac notch: Depression in the medial surface of the inferior lobe of the left lung where the apex of the heart is located.

cardiac output (CO): Amount of blood pumped by each ventricle in 1 minute; equals HR multiplied by SV.

cardiac plexus: Paired complex network of nerve fibres near the base of the heart that receive sympathetic and parasympathetic stimulations to regulate HR.

cardiac reflexes: Series of autonomic reflexes that enable the cardiovascular centres to regulate heart function based on sensory information from a variety of visceral sensors.

cardiac reserve: Difference between maximum and resting CO.

cardiac skeleton (also skeleton of the heart): Reinforced connective tissue located within the atrioventricular septum; includes four rings that surround the openings between the atria and ventricles and the openings to the pulmonary trunk and aorta; the point of attachment for the heart valves.

cardiomyocyte: Muscle cell of the heart.

chordae tendineae: String-like extensions of tough connective tissue that extend from the flaps of the atrioventricular valves to the papillary muscles.

circumflex artery: Branch of the left coronary artery that follows the coronary sulcus.

coronary arteries: Branches of the ascending aorta that supply blood to the heart; the left coronary artery feeds the left side of the heart, the left atrium and ventricle, and the interventricular septum; the right coronary artery feeds the right atrium, portions of both ventricles, and the heart conduction system.

coronary sinus: Large, thin-walled vein on the posterior surface of the heart that lies within the atrioventricular sulcus and drains the heart myocardium directly into the right atrium.

coronary sulcus: Sulcus that marks the boundary between the atria and ventricles.

coronary veins: Vessels that drain the heart and generally parallel the large surface arteries.

diastole: Period of time when the heart muscle is relaxed and the chambers fill with blood.

ejection fraction: Portion of the blood that is pumped or ejected from the heart with each contraction; mathematically represented by SV divided by EDV.

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electrocardiogram (ECG): Surface recording of the electrical activity of the heart that can be used for diagnosis of irregular heart function; also abbreviated as EKG.

end diastolic volume (EDV; also preload): The amount of blood in the ventricles at the end of atrial systole just prior to ventricular contraction.

endocardium: Innermost layer of the heart lining the heart chambers and heart valves; composed of endothelium reinforced with a thin layer of connective tissue that binds to the myocardium.

endothelium: Layer of smooth, simple squamous epithelium that lines the endocardium and blood vessels.

end systolic volume (ESV): Amount of blood remaining in each ventricle following systole.

epicardial coronary arteries: Surface arteries of the heart that generally follow the sulci.

epicardium: Innermost layer of the serous pericardium and the outermost layer of the heart wall.

fibrous pericardium: Sturdy outer layer made of tough, dense connective tissue that protects the heart and maintains its position in the thorax.

filling time: Duration of ventricular diastole during which filling occurs.

foramen ovale: Opening in the fetal heart that allows blood to flow directly from the right atrium to the left atrium, bypassing the fetal pulmonary circuit.

fossa ovalis: Oval-shaped depression in the interatrial septum that marks the former location of the foramen ovale.

Frank-Starling mechanism: Relationship between ventricular stretch and contraction in which the force of heart contraction is directly proportional to the initial length of the muscle fibre.

great cardiac vein: Vessel that follows the interventricular sulcus on the anterior surface of the heart and flows along the coronary sulcus into the coronary sinus on the posterior surface; parallels the anterior interventricular artery and drains the areas supplied by this vessel.

heart rate (HR): Number of times the heart contracts (beats) per minute.

heart sounds: Sounds heard via auscultation with a stethoscope of the closing of the atrioventricular valves (“lub”) and semilunar valves (“dub”).

hypertrophic cardiomyopathy: Pathological enlargement of the heart, generally for no known reason.

inferior vena cava: Large systemic vein that returns blood to the heart from the inferior portion of the body.

interatrial septum: Cardiac septum located between the two atria; contains the fossa ovalis after birth.

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intercalated disc: Physical junction between adjacent cardiac muscle cells; consisting of desmosomes, specialized linking proteoglycans, and gap junctions that allow passage of ions between the two cells.

internodal pathways: Specialized conductile cells within the atria that transmit the impulse from the SA node throughout the myocardial cells of the atrium and to the AV node.

interventricular septum: Cardiac septum located between the two ventricles.

isovolumic contraction (also isovolumetric contraction): Initial phase of ventricular contraction in which tension and pressure in the ventricle increase but no blood is pumped or ejected from the heart.

isovolumic ventricular relaxation phase: Initial phase of the ventricular diastole when pressure in the ventricles drops below pressure in the two major arteries, the pulmonary trunk and the aorta, and blood attempts to flow back into the ventricles, producing the dicrotic notch of the ECG and closing the two semilunar valves.

left atrioventricular valve (also mitral valve or bicuspid valve): Valve located between the left atrium and ventricle; consists of two flaps of tissue.

marginal arteries: Branches of the right coronary artery that supply blood to the superficial portions of the right ventricle.

middle cardiac vein: Vessel that parallels and drains the areas supplied by the posterior interventricular artery; drains into the great cardiac vein.

mitral valve (also left atrioventricular valve or bicuspid valve): Valve located between the left atrium and ventricle; consists of two flaps of tissue.

murmur: Unusual heart sound detected by auscultation; typically related to septal or valve defects.

myocardial conducting cells: Specialized cells that transmit electrical impulses throughout the heart and trigger contraction by the myocardial contractile cells.

myocardial contractile cells: Bulk of the cardiac muscle cells in the atria and ventricles that conduct impulses and contract to propel blood.

myocardium: Thickest layer of the heart composed of cardiac muscle cells built on a framework of primarily collagenous fibres and blood vessels that supply it and the nervous fibres that help regulate it.

negative inotropic factors: Factors that negatively impact or lower heart contractility.

pacemaker: Cluster of specialized myocardial cells known as the SA node that initiates the sinus rhythm.

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papillary muscle: Extension of the myocardium in the ventricles to which the chordae tendineae attach.

parietal pericardium: Layer of serous pericardium that is fused to the fibrous pericardium.

pectinate muscles: Muscular ridges seen on the anterior surface of the right atrium.

pericardial cavity: Cavity surrounding the heart filled with a lubricating serous fluid that reduces friction as the heart contracts.

pericardium (also pericardial sac): Membrane that separates the heart from other mediastinal structures; consists of two distinct, fused sublayers: the fibrous pericardium and the parietal pericardium.

plateau phase: Long refractory periods required for the cardiac muscle cells to pump blood effectively before they are capable of firing for a second time.

positive inotropic factors: Factors that positively impact or increase heart contractility.

posterior cardiac vein: Vessel that parallels and drains the areas supplied by the marginal artery branch of the circumflex artery; drains into the great cardiac vein.

posterior interventricular artery (also posterior descending artery): Branch of the right coronary artery that runs along the posterior portion of the interventricular sulcus toward the apex of the heart and gives rise to branches that supply the interventricular septum and portions of both ventricles.

posterior interventricular sulcus: Sulcus located between the left and right ventricles on the posterior surface of the heart.

preload (also end diastolic volume): Amount of blood in the ventricles at the end of atrial systole just prior to ventricular contraction.

prepotential depolarization (also spontaneous depolarization): Mechanism that accounts for the autorhythmic property of cardiac muscle; the membrane potential increases as sodium ions diffuse through the always-open sodium ion channels and causes the electrical potential to rise.

pulmonary arteries: Left and right branches of the pulmonary trunk that carry deoxygenated blood from the heart to each of the lungs.

pulmonary capillaries: Capillaries surrounding the alveoli of the lungs where gas exchange occurs: Carbon dioxide exits the blood and oxygen enters.

pulmonary circuit: Blood flow to and from the lungs.

pulmonary trunk: Large arterial vessel that carries blood ejected from the right ventricle; divides into the left and right pulmonary arteries.

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pulmonary valve (also pulmonary semilunar valve, pulmonic valve, or right semilunar valve): Valve at the base of the pulmonary trunk that prevents backflow of blood into the right ventricle; consists of three flaps.

pulmonary veins: Veins that carry highly oxygenated blood into the left atrium, which pumps the blood into the left ventricle, which in turn pumps oxygenated blood into the aorta and to the many branches of the systemic circuit.

Purkinje fibres: Specialized myocardial conduction fibres that arise from the bundle branches and spread the impulse to the myocardial contraction fibres of the ventricles.

P wave: Component of the electrocardiogram that represents the depolarization of the atria.

QRS complex: Component of the electrocardiogram that represents the depolarization of the ventricles and includes, as a component, the repolarization of the atria.

right atrioventricular valve (also tricuspid valve): Valve located between the right atrium and ventricle; consists of three flaps of tissue.

semilunar valves: Valves located at the base of the pulmonary trunk and at the base of the aorta.

septum (plural = septa): Walls or partitions that divide the heart into chambers.

serous pericardium: Delicate layer that also consists of two layers: the parietal pericardium and the visceral pericardium (epicardium).

sinoatrial (SA) node: Known as the pacemaker, a specialized clump of myocardial conducting cells located in the superior portion of the right atrium that has the highest inherent rate of depolarization that then spreads throughout the heart.

sinus rhythm: Normal electrical pattern followed by contraction of the heart.

small cardiac vein: Parallels the right coronary artery and drains blood from the posterior surfaces of the right atrium and ventricle; drains into the coronary sinus, middle cardiac vein, or right atrium.

spontaneous depolarization (also prepotential depolarization): The mechanism that accounts for the autorhythmic property of cardiac muscle; the membrane potential increases as sodium ions diffuse through the always-open sodium ion channels and causes the electrical potential to rise.

stroke volume (SV): Amount of blood pumped by each ventricle per contraction; also the difference between EDV and ESV.

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sulcus (plural = sulci): Fat-filled groove visible on the surface of the heart; coronary vessels are also located in these areas.

superior vena cava: Large systemic vein that returns blood to the heart from the superior portion of the body.

systemic circuit: Blood flow to and from virtually all of the tissues of the body.

systole: Period of time when the heart muscle is contracting.

target heart rate: Range in which both the heart and the lungs receive the maximum benefit from an aerobic workout.

trabeculae carneae: Ridges of muscle covered by endocardium located in the ventricles.

tricuspid valve: Term used most often in clinical settings for the right atrioventricular valve.

T wave: Component of the electrocardiogram that represents the repolarization of the ventricles.

valve: In the cardiovascular system, a specialized structure located within the heart or vessels that ensures one-way flow of blood.

ventricle: One of the primary pumping chambers of the heart located in the lower portion of the heart; the left ventricle is the major pumping chamber on the lower left side of the heart that ejects blood into the systemic circuit via the aorta and receives blood from the left atrium; the right ventricle is the major pumping chamber on the lower right side of the heart that ejects blood into the pulmonary circuit via the pulmonary trunk and receives blood from the right atrium.

ventricular ejection phase: Second phase of ventricular systole during which blood is pumped from the ventricle.

visceral pericardium (epicardium): Layer of serous pericardium that is fused to the heart and is part of the heart wall.

Chapter Review

18.1 Heart Anatomy

The heart resides within the pericardial sac and is located in the mediastinal space within the thoracic cavity. The pericardial sac consists of two fused layers: an outer fibrous capsule and an inner parietal pericardium lined with a serous membrane. Between the pericardial sac and the heart is the pericardial cavity, which is filled with lubricating serous fluid. The walls of the heart are composed of an outer epicardium, a thick myocardium, and an inner lining layer of endocardium. The human heart consists of a pair of atria, which receive blood and pump it into a pair of ventricles, which pump blood into

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the vessels. The right atrium receives systemic blood relatively low in oxygen and pumps it into the right ventricle, which pumps it into the pulmonary circuit. Exchange of oxygen and carbon dioxide occurs in the lungs, and blood high in oxygen returns to the left atrium, which pumps blood into the left ventricle, which in turn pumps blood into the aorta and the remainder of the systemic circuit. The septa are the partitions that separate the chambers of the heart. They include the interatrial septum, the interventricular septum, and the atrioventricular septum. Two of these openings are guarded by the atrioventricular valves, the right tricuspid valve and the left mitral valve, which prevent the backflow of blood. Each is attached to chordae tendineae that extend to the papillary muscles, which are extensions of the myocardium, to prevent the valves from being blown back into the atria. The pulmonary valve is located at the base of the pulmonary trunk, and the left semilunar valve is located at the base of the aorta. The right and left coronary arteries are the first to branch off the aorta and arise from two of the three sinuses located near the base of the aorta and are generally located in the sulci. Cardiac veins parallel the small cardiac arteries and generally drain into the coronary sinus.

18.2 Cardiac Muscle and Electrical Activity

The heart is regulated by both neural and endocrine control, yet it is capable of initiating its own action potential followed by muscular contraction. The conductive cells within the heart establish the heart rate and transmit it through the myocardium. The contractile cells contract and propel the blood. The normal path of transmission for the conductive cells is the sinoatrial (SA) node, internodal pathways, atrioventricular (AV) node, atrioventricular (AV) bundle of His, bundle branches, and Purkinje fibres. The action potential for the conductive cells consists of a prepotential phase with a slow influx of Na^+ followed by a rapid influx of Ca^{2+} and an outflux of K^+. Contractile cells have an action potential with an extended plateau phase that results in an extended refractory period to allow complete contraction for the heart to pump blood effectively. Recognizable points on the ECG include the P wave that corresponds to atrial depolarization, the QRS complex that corresponds to ventricular depolarization, and the T wave that corresponds to ventricular repolarization.

18.3 Cardiac Cycle

The cardiac cycle comprises a complete relaxation and contraction of both the atria and the ventricles and lasts approximately 0.8 seconds. Beginning with all chambers in diastole, blood flows passively from the veins into the atria and past the atrioventricular valves into the ventricles. The atria begin to contract (atrial systole) following depolarization of the atria and pump blood into the

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ventricles. The ventricles begin to contract (ventricular systole), raising pressure within the ventricles. When ventricular pressure rises above the pressure in the atria, blood flows toward the atria, producing the first heart sound, S_1 or lub. As pressure in the ventricles rises above two major arteries, blood pushes open the two semilunar valves and moves into the pulmonary trunk and aorta in the ventricular ejection phase. Following ventricular repolarization, the ventricles begin to relax (ventricular diastole), and pressure within the ventricles drops. As ventricular pressure drops, there is a tendency for blood to flow back into the atria from the major arteries, producing the dicrotic notch in the ECG and closing the two semilunar valves. The second heart sound, S_2 or dub, occurs when the semilunar valves close. When the pressure falls below that of the atria, blood moves from the atria into the ventricles, opening the atrioventricular valves and marking one complete heart cycle. The valves prevent backflow of blood. Failure of the valves to operate properly produces turbulent blood flow within the heart; the resulting heart murmur can often be heard with a stethoscope.

18.4 Cardiac Physiology

Many factors affect HR and SV, and together, they contribute to cardiac function. HR is largely determined and regulated by autonomic stimulation and hormones. There are several feedback loops that contribute to maintaining homeostasis dependent on activity levels, such as the atrial reflex, which is determined by venous return.

SV is regulated by autonomic innervation and hormones but also by filling time and venous return. Venous return is determined by the activity of the skeletal muscles, blood volume, and changes in peripheral circulation. Venous return determines preload and the atrial reflex. Filling time directly related to HR also determines preload. Preload then impacts both EDV and ESV. Autonomic innervation and hormones largely regulate contractility. Contractility impacts EDV, as does afterload. CO is the product of HR multiplied by SV. SV is the difference between EDV and ESV.

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19

The Cardiovascular System: Blood Vessels and Circulation

Chapter Objectives

After studying this chapter, you will be able to:

- Compare and contrast the anatomical structure of arteries, arterioles, capillaries, venules, and veins
- Accurately describe the forces that account for capillary exchange
- List the major factors affecting blood flow, blood pressure, and resistance
- Describe how blood flow, blood pressure, and resistance interrelate
- Discuss how the neural and endocrine mechanisms maintain homeostasis within the blood vessels
- Describe the interaction of the cardiovascular system with other body systems
- Label the major blood vessels of the pulmonary and systemic circulations
- Identify and describe the hepatic portal system
- Describe the development of blood vessels and fetal circulation
- Compare fetal circulation to that of an individual after birth

In this chapter, you will learn about the vascular part of the cardiovascular system—that is, the vessels that transport blood throughout the body and provide the physical site where gases, nutrients, and other substances are exchanged with body cells. When vessel functioning is reduced, blood-borne substances do

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not circulate effectively throughout the body. As a result, tissue injury occurs, metabolism is impaired, and the functions of every bodily system are threatened.

19.1 Structure and Function of Blood Vessels

Learning Objectives

By the end of this section, you will be able to:

- Compare and contrast the three tunics that make up the walls of most blood vessels
- Distinguish between elastic arteries, muscular arteries, and arterioles on the basis of structure, location, and function
- Describe the basic structure of a capillary bed, from the supplying metarteriole to the venule into which it drains
- Explain the structure and function of venous valves in the large veins of the extremities

Blood is carried through the body via blood vessels. An **artery** is a blood vessel that carries blood away from the heart, where it branches into ever-smaller vessels. Eventually, the smallest arteries, vessels called **arterioles**, further branch into tiny **capillaries**, where nutrients and wastes are exchanged, and then combine with other vessels that exit capillaries to form **venules**, small blood vessels that carry blood to a **vein**, a larger blood vessel that returns blood to the heart.

Arteries and veins transport blood in two distinct circuits: the **systemic circuit** and the **pulmonary circuit** (Figure 19.1). Systemic arteries provide blood rich in oxygen to the body's tissues. The blood returned to the heart through systemic veins has less oxygen, since much of the oxygen carried by the arteries has been delivered to the cells. In contrast, in the pulmonary circuit, arteries carry blood low in oxygen exclusively to the lungs for gas exchange.

Pulmonary veins then return freshly oxygenated blood from the lungs to the heart to be pumped back out into systemic circulation. Although arteries and veins differ structurally and functionally, they share certain features.

Shared Structures

Different types of blood vessels vary slightly in their structures, but they share the same general features. Arteries and arterioles have thicker walls than veins and venules because they receive blood that is surging at a far greater pressure (Figure 19.2). Each type of vessel has a **lumen**—a hollow passageway through which blood flows. Arteries have smaller lumens than veins, a characteristic

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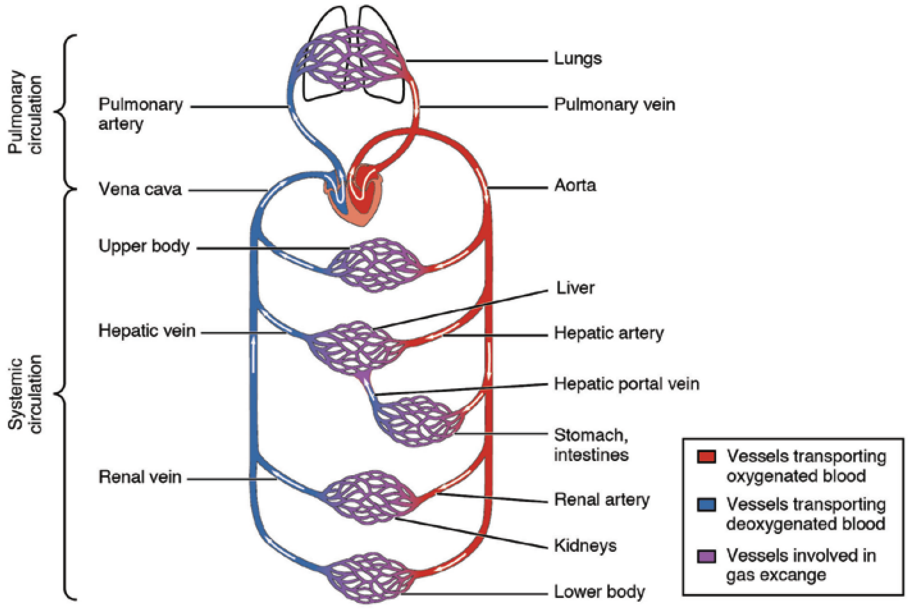


Figure 19.1 Cardiovascular Circulation. The pulmonary circuit moves blood from the right side of the heart to the lungs and back to the heart. The systemic circuit moves blood from the left side of the heart to the head and body and returns it to the right side of the heart to repeat the cycle. The arrows indicate the direction of blood flow, and the colours show the relative levels of oxygen concentration.

that helps maintain the pressure of blood moving through the system. Together, their thicker walls and smaller diameters give arterial lumens a more rounded appearance in cross section than the lumens of veins.

By the time blood has passed through capillaries and entered venules, the pressure initially exerted on it by heart contractions has diminished. In other words, in comparison to arteries, venules and veins withstand a much lower pressure from the blood that flows through them. Their walls are considerably thinner, and their lumens are correspondingly larger in diameter, allowing more blood to flow with less vessel resistance. In addition, many veins of the body, particularly those of the limbs, contain **vein valves** that assist the unidirectional flow of blood toward the heart. This is critical because blood flow becomes sluggish in the extremities as a result of the lower pressure and the effects of gravity.

The walls of arteries and veins are largely composed of living cells and their products (including collagenous and elastic fibres); the cells require nourishment and produce waste. Since blood passes through the larger vessels relatively quickly, there is limited opportunity for blood in the lumen of the vessel to provide nourishment to or remove waste from the vessel's cells. Further, the walls of the larger vessels are too thick for nutrients to diffuse through to all of the

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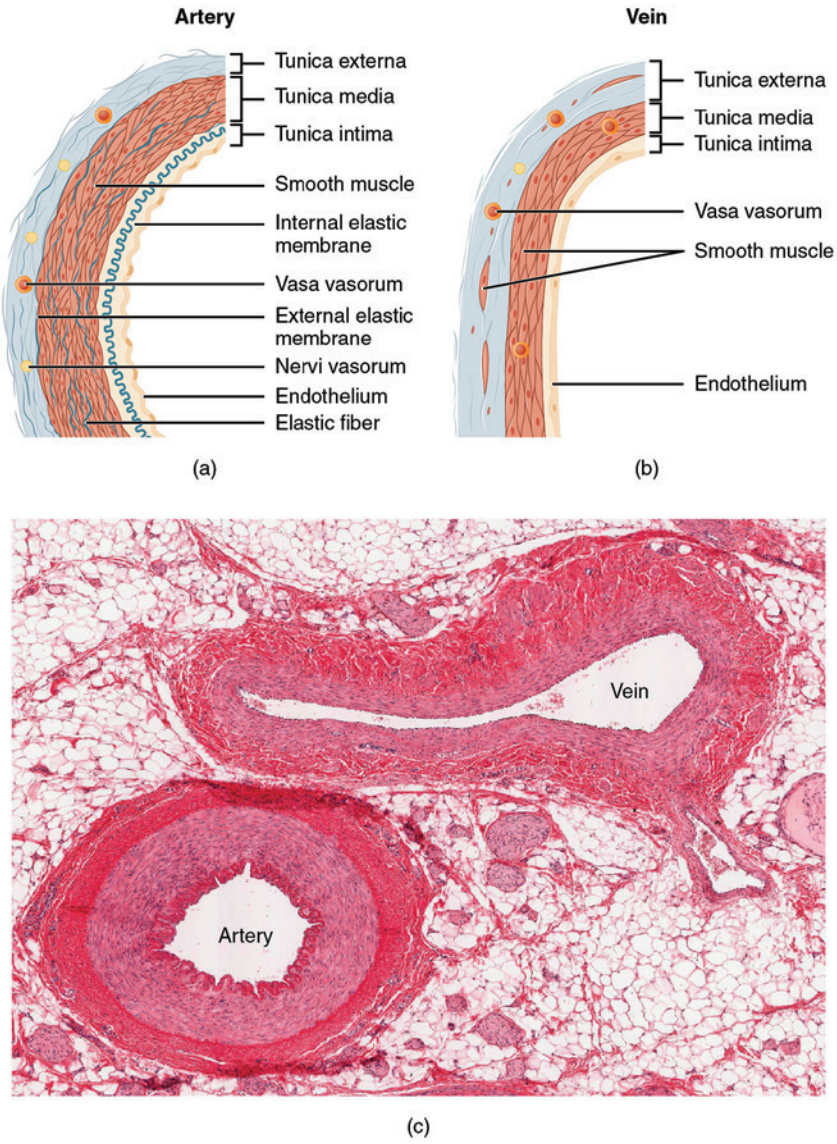


Figure 19.2 Structure of Blood Vessels. (a) Arteries and (b) veins share the same general features, but the walls of arteries are much thicker because of the higher pressure of the blood that flows through them. (c) A micrograph shows the relative differences in thickness. LM × 160. (Micrograph provided by the Regents of the University of Michigan Medical School © 2012)

cells. Larger arteries and veins contain small blood vessels within their walls known as the **vasa vasorum**—literally "vessels of the vessel"—to provide them with this critical exchange. Since the pressure within arteries is relatively high, the vasa vasorum must function in the outer layers of the vessel (see Figure 19.2) or the pressure exerted by the blood passing through the vessel would collapse it, preventing any exchange from occurring. The lower pressure within veins

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allows the vasa vasorum to be located closer to the lumen. The restriction of the vasa vasorum to the outer layers of arteries is thought to be one reason that arterial diseases are more common than venous diseases, since its location makes it more difficult to nourish the cells of the arteries and remove waste products. There are also minute nerves within the walls of both types of vessels that control the contraction and dilation of smooth muscle. These minute nerves are known as the nervi vasorum.

Both arteries and veins have the same three distinct tissue layers called tunics (from the Latin term *tunica*) for the garments first worn by ancient Romans; the term *tunic* is also used for some modern garments. From the most interior layer to the outer, these tunics are the **tunica intima**, the **tunica media**, and the **tunica externa** (see Figure 19.2). Table 19.1 compares and contrasts the tunics of the arteries and veins.

Table 19.1 Comparison of Tunics in Arteries and Veins

	Arteries	Veins
General appearance	Thick walls with small lumens Generally, appear rounded	Thin walls with large lumens Generally, appear flattened
Tunica intima	Endothelium usually appears wavy due to constriction of smooth muscle Internal elastic membrane present in larger vessels	Endothelium appears smooth Internal elastic membrane absent
Tunica media	Normally the thickest layer in arteries Smooth muscle cells and elastic fibres predominate (the proportions of these vary with distance from the heart) External elastic membrane present in larger vessels	Normally thinner than the tunica externa Smooth muscle cells and collagenous fibres predominate Nervi vasorum and vasa vasorum present External elastic membrane absent
Tunica externa	Normally thinner than the tunica media in all but the largest arteries Collagenous and elastic fibres Nervi vasorum and vasa vasorum present	Normally the thickest layer in veins Collagenous and smooth fibres predominate Some smooth muscle fibres Nervi vasorum and vasa vasorum present

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Tunica Intima

The **tunica intima** (also called the tunica interna) is composed of epithelial and connective tissue layers. Lining the tunica intima is the specialized simple squamous epithelium called the endothelium, which is continuous throughout the entire vascular system, including the lining of the chambers of the heart. Damage to this endothelial lining and exposure of blood to the collagenous fibres beneath is one of the primary causes of clot formation. Until recently, the endothelium was viewed simply as the boundary between the blood in the lumen and the walls of the vessels. Recent studies, however, have shown that it is physiologically critical to such activities as helping regulate capillary exchange and altering blood flow. The endothelium releases local chemicals called endothelins that can constrict the smooth muscle within the walls of the vessel to increase blood pressure. Uncompensated overproduction of endothelins may contribute to hypertension (high blood pressure) and cardiovascular disease.

Next to the endothelium is the basement membrane, or basal lamina, that effectively binds the endothelium to the connective tissue. The basement membrane provides strength while maintaining flexibility, and it is permeable, allowing materials to pass through it. The thin outer layer of the tunica intima contains a small amount of areolar connective tissue that consists primarily of elastic fibres to provide the vessel with additional flexibility; it also contains some collagenous fibres to provide additional strength.

In larger arteries, there is also a thick, distinct layer of elastic fibres known as the **internal elastic membrane** (also called the internal elastic lamina) at the boundary with the tunica media. Like the other components of the tunica intima, the internal elastic membrane provides structure while allowing the vessel to stretch. It is permeated with small openings that allow exchange of materials between the tunics. The internal elastic membrane is not apparent in veins. In addition, many veins, particularly in the lower limbs, contain valves formed by sections of thickened endothelium that are reinforced with connective tissue, extending into the lumen.

Under the microscope, the lumen and the entire tunica intima of a vein will appear smooth, whereas those of an artery will normally appear wavy because of the partial constriction of the smooth muscle in the tunica media, the next layer of blood vessel walls.

Tunica Media

The **tunica media** is the substantial middle layer of the vessel wall (see Figure 19.2). It is generally the thickest layer in arteries, and it is much thicker in arteries than it is in veins. The tunica media consists of layers of smooth

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muscle supported by connective tissue that is primarily made up of elastic fibres, most of which are arranged in circular sheets. Toward the outer portion of the tunic, there are also layers of longitudinal muscle. Contraction and relaxation of the circular muscles decrease and increase the diameter of the vessel lumen, respectively. Specifically in arteries, **vasoconstriction** decreases blood flow as the smooth muscle in the walls of the tunica media contracts, making the lumen narrower and increasing blood pressure. Similarly, **vasodilation** increases blood flow as the smooth muscle relaxes, allowing the lumen to widen and blood pressure to drop. Both vasoconstriction and vasodilation are regulated in part by small vascular nerves known as **nervi vasorum**, or "nerves of the vessel," that run within the walls of blood vessels. These are generally all sympathetic fibres, although some trigger vasodilation and others induce vasoconstriction, depending on the nature of the neurotransmitter and receptors located on the target cell. Parasympathetic stimulation does trigger vasodilation as well as erection during sexual arousal in the external genitalia of both sexes. Nervous control over vessels tends to be more generalized than the specific targeting of individual blood vessels. Local controls, discussed later, account for this phenomenon. Hormones and local chemicals also control blood vessels. Together, these neural and chemical mechanisms reduce or increase blood flow in response to changing body conditions, from exercise to hydration. Regulation of both blood flow and blood pressure is discussed in detail later in this chapter.

The smooth muscle layers of the tunica media are supported by a framework of collagenous fibres that also binds the tunica media to the inner and outer tunics. Along with the collagenous fibres are large numbers of elastic fibres that appear as wavy lines in prepared slides. Separating the tunica media from the outer tunica externa in larger arteries is the **external elastic membrane** (also called the external elastic lamina), which also appears wavy in slides. This structure is not usually seen in smaller arteries, nor is it seen in veins.

Tunica Externa

The outer tunic, the **tunica externa** (also called the tunica adventitia), is a substantial sheath of connective tissue composed primarily of collagenous fibres. Some bands of elastic fibres are found here as well. The tunica externa in veins also contains groups of smooth muscle fibres. This is normally the thickest tunic in veins and may be thicker than the tunica media in some larger arteries. The outer layers of the tunica externa are not distinct but rather blend with the surrounding connective tissue outside the vessel, helping hold the vessel in relative position. If you are able to palpate some of the superficial

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veins on your upper limbs and try to move them, you will find that the tunica externa prevents this. If the tunica externa did not hold the vessel in place, any movement would likely result in disruption of blood flow.

Arteries

An **artery** is a blood vessel that conducts blood away from the heart. All arteries have relatively thick walls that can withstand the high pressure of blood ejected from the heart. However, those close to the heart have the thickest walls, containing a high percentage of elastic fibres in all three of their tunics. This type of artery is known as an **elastic artery** (Figure 19.3). Vessels larger than 10 mm in diameter are typically elastic. Their abundant elastic fibres allow them to expand as blood pumped from the ventricles passes through them and then to recoil after the surge has passed. If artery walls were rigid and unable to expand and recoil, their resistance to blood flow would greatly increase and blood pressure would rise to even higher levels, which would in turn require the heart to pump harder to increase the volume of blood expelled by each pump (the stroke volume) and maintain adequate pressure and flow. Artery walls would have to become even thicker in response to this increased pressure. The elastic recoil of the vascular wall helps maintain the pressure gradient that drives the blood through the arterial system. An elastic artery is also known as a conducting artery, because the large diameter of the lumen enables it to accept a large volume of blood from the heart and conduct it to smaller branches.

Farther from the heart, where the surge of blood has dampened, the percentage of elastic fibres in an artery's tunica intima decreases and the amount of smooth muscle in its tunica media increases. The artery at this point is described as a **muscular artery**. The diameter of muscular arteries typically ranges from 0.1 mm to 10 mm. Their thick tunica media allows muscular arteries to play a leading role in vasoconstriction. In contrast, their decreased quantity of elastic fibres limits their ability to expand. Fortunately, because

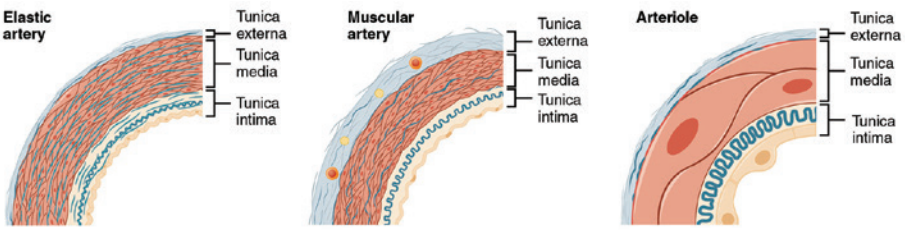


Figure 19.3 Types of Arteries and Arterioles. Comparison of the walls of an elastic artery, a muscular artery, and an arteriole is shown. In terms of scale, the diameter of an arteriole is measured in micrometres compared to millimetres for elastic and muscular arteries.

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the blood pressure has eased by the time it reaches these more distant vessels, elasticity has become less important.

Notice that although the distinctions between elastic and muscular arteries are important, there is no "line of demarcation" where an elastic artery suddenly becomes muscular. Rather, there is a gradual transition as the vascular tree repeatedly branches. In turn, muscular arteries branch to distribute blood to the vast network of arterioles. For this reason, a muscular artery is also known as a distributing artery.

Arterioles

An **arteriole** is a very small artery that leads to a capillary. Arterioles have the same three tunics as the larger vessels, but the thickness of each is greatly diminished. The critical endothelial lining of the tunica intima is intact. The tunica media is restricted to one or two smooth muscle cell layers in thickness. The tunica externa remains but is very thin (see Figure 19.3).

With a lumen averaging 30 μm or less in diameter, arterioles are critical in slowing down—or resisting—blood flow and thus causing a substantial drop in blood pressure. Because of this, you may see them referred to as resistance vessels. The muscle fibres in arterioles are normally slightly contracted, causing arterioles to maintain a consistent muscle tone—in this case referred to as vascular tone—in a similar manner to the muscular tone of skeletal muscle. In reality, all blood vessels exhibit vascular tone due to the partial contraction of smooth muscle. The importance of the arterioles is that they will be the primary site of both resistance and regulation of blood pressure. The precise diameter of the lumen of an arteriole at any given moment is determined by neural and chemical controls, and vasoconstriction and vasodilation in the arterioles are the primary mechanisms for distribution of blood flow.

Capillaries

A **capillary** is a microscopic channel that supplies blood to the tissue in a process called **perfusion**. Exchange of gases and other substances occurs between the blood in capillaries and the surrounding cells and their tissue fluid (interstitial fluid). The diameter of a capillary lumen ranges from 5–10 μm; the smallest are just barely wide enough for an erythrocyte to squeeze through. Flow through capillaries is often described as **microcirculation**.

The wall of a capillary consists of the endothelial layer surrounded by a basement membrane with occasional smooth muscle fibres. There is some variation in wall structure: In a large capillary, several endothelial cells bordering each other may line the lumen; in a small capillary, there may be only a single cell layer that wraps around to contact itself.

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For capillaries to function, their walls must be leaky, allowing substances to pass through. There are three major types of capillaries, which differ according to their degree of "leakiness": continuous, fenestrated, and sinusoid capillaries (Figure 19.4).

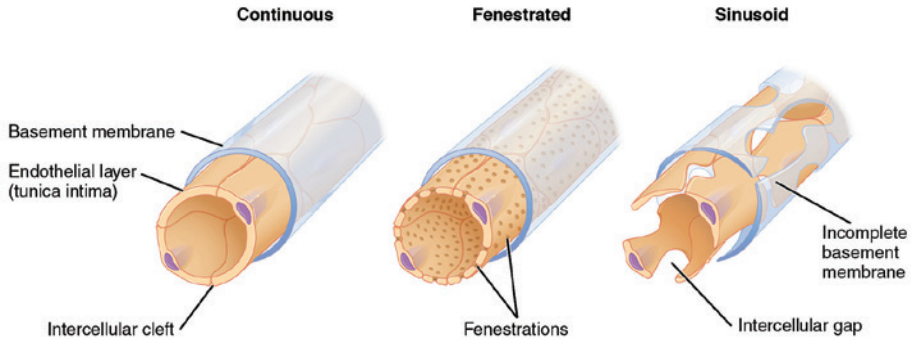


Figure 19.4 Types of Capillaries. The three major types of capillaries: continuous, fenestrated, and sinusoid.

Continuous Capillaries

The most common type of capillary, the **continuous capillary**, is found in almost all vascularized tissues. Continuous capillaries are characterized by a complete endothelial lining with tight junctions between endothelial cells.

Although tight junctions are usually impermeable and only allow for the passage of water and ions, they are often incomplete in capillaries, leaving intercellular clefts that allow for exchange of water and other very small molecules between the blood plasma and the interstitial fluid. Substances that can pass between cells include metabolic products, such as glucose, water, and small hydrophobic molecules like gases and hormones, as well as various leukocytes. Continuous capillaries not associated with the brain are rich in transport vesicles, contributing to either endocytosis or exocytosis. Those in the brain are part of the blood-brain barrier. Here, there are tight junctions and no intercellular clefts, plus a thick basement membrane and astrocyte extensions called end feet; these structures combine to prevent the movement of nearly all substances.

Fenestrated Capillaries

A **fenestrated capillary** is one that has pores (or fenestrations) in addition to tight junctions in the endothelial lining. These make the capillary permeable to larger molecules. The number of fenestrations and their degree of permeability vary, however, according to their location. Fenestrated capillaries are

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common in the small intestine, which is the primary site of nutrient absorption, as well as in the kidneys, which filter the blood. They are also found in the choroid plexus of the brain and many endocrine structures, including the hypothalamus, pituitary, pineal, and thyroid glands.

Sinusoid Capillaries

A **sinusoid capillary** (or sinusoid) is the least common type of capillary. Sinusoid capillaries are flattened, and they have extensive intercellular gaps and incomplete basement membranes in addition to intercellular clefts and fenestrations. This gives them an appearance not unlike Swiss cheese. These very large openings allow for the passage of the largest molecules, including plasma proteins and even cells. Blood flow through sinusoids is very slow, allowing more time for exchange of gases, nutrients, and wastes. Sinusoids are found in the liver and spleen, bone marrow, lymph nodes (where they carry lymph, not blood), and many endocrine glands, including the pituitary and adrenal glands. Without these specialized capillaries, these organs would not be able to provide their myriad functions.

For example, when bone marrow forms new blood cells, the cells must enter the blood supply and can only do so through the large openings of a sinusoid capillary; they cannot pass through the small openings of continuous or fenestrated capillaries.

The liver also requires extensive specialized sinusoid capillaries in order to process the materials brought to it by the hepatic portal vein from both the digestive tract and the spleen and to release plasma proteins into circulation.

Metarterioles and Capillary Beds

A **metarteriole** is a type of vessel that has structural characteristics of both an arteriole and a capillary. Slightly larger than the typical capillary, the smooth muscle of the tunica media of the metarteriole is not continuous but forms rings of smooth muscle (sphincters) prior to the entrance to the capillaries. Each metarteriole arises from a terminal arteriole and branches to supply blood to a **capillary bed** that may consist of 10–100 capillaries.

The **precapillary sphincters**, circular smooth muscle cells that surround the capillary at its origin with the metarteriole, tightly regulate the flow of blood from a metarteriole to the capillaries it supplies. Their function is critical: If all of the capillary beds in the body were to open simultaneously, they would collectively hold every drop of blood in the body, and there would be none in the arteries, arterioles, venules, veins, or the heart itself. Normally, the precapillary sphincters are closed. When the surrounding tissues need oxygen and have excess waste products, the precapillary sphincters open, allowing blood

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to flow through and exchange to occur before closing once more (Figure 19.5). If all of the precapillary sphincters in a capillary bed are closed, blood will flow from the metarteriole directly into a **thoroughfare channel** and then into the venous circulation, bypassing the capillary bed entirely. This creates what is known as a **vascular shunt**. In addition, an **arteriovenous anastomosis** may bypass the capillary bed and lead directly to the venous system.

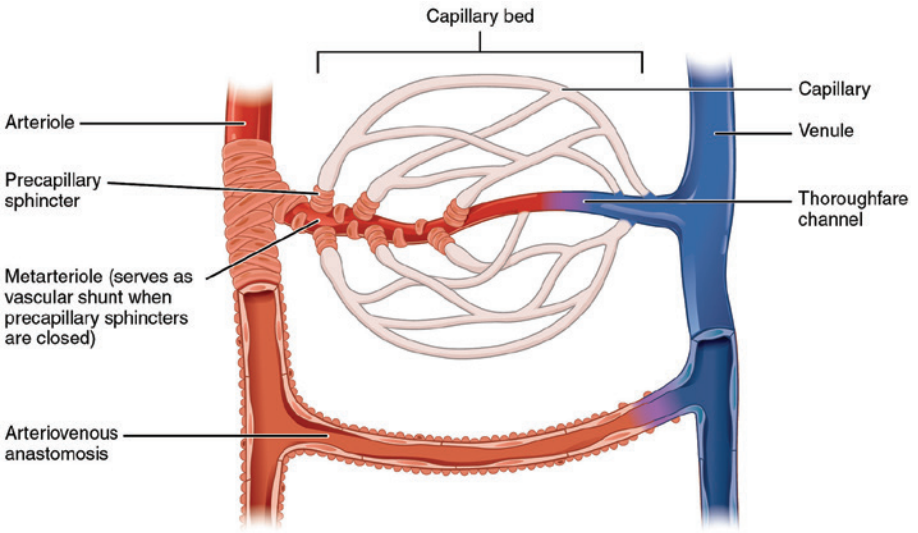


Figure 19.5 Capillary Bed. In a capillary bed, arterioles give rise to metarterioles. Precapillary sphincters located at the junction of a metarteriole with a capillary regulate blood flow. A thoroughfare channel connects the metarteriole to a venule. An arteriovenous anastomosis, which directly connects the arteriole with the venule, is shown at the bottom.

Although you might expect blood flow through a capillary bed to be smooth, in reality, it moves with an irregular, pulsating flow. This pattern is called **vasomotion** and is regulated by chemical signals that are triggered in response to changes in internal conditions, such as oxygen, carbon dioxide, hydrogen ion, and lactic acid levels.

For example, during strenuous exercise, when oxygen levels decrease and carbon dioxide, hydrogen ion, and lactic acid levels all increase, the capillary beds in skeletal muscle are open, as they would be in the digestive system when nutrients are present in the digestive tract.

During sleep or rest periods, vessels in both areas are largely closed; they open only occasionally to allow oxygen and nutrient supplies to travel to the tissues to maintain basic life processes.

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Venules

A **venule** is an extremely small vein, generally 8–100 μm in diameter. Postcapillary venules join multiple capillaries exiting from a capillary bed. Multiple venules join to form veins. The walls of venules consist of endothelium, a thin middle layer with a few muscle cells and elastic fibres, plus an outer layer of connective tissue fibres that constitute a very thin tunica externa (Figure 19.6). Venules and capillaries are the primary sites of emigration or diapedesis, in which the white blood cells adhere to the endothelial lining of the vessels and then squeeze through adjacent cells to enter the tissue fluid.

Veins

A **vein** is a blood vessel that conducts blood toward the heart. Compared to arteries, veins are thin-walled vessels with large and irregular lumens (see Figure 19.6). Because they are low-pressure vessels, larger veins are commonly equipped with valves that promote the unidirectional flow of blood toward the heart and prevent backflow toward the capillaries caused by the inherent low blood pressure in veins as well as the pull of gravity. Table 19.2 compares the features of arteries and veins.

Veins as Blood Reservoirs

In addition to their primary function of returning blood to the heart, veins may be considered blood reservoirs, since systemic veins contain approximately 64 percent of the blood volume at any given time (Table 19.3). Their ability to hold this much blood is due to their high **capacitance**—that is, their capacity to distend (expand) readily to store a high volume of blood, even at a low pressure. The large lumens and relatively thin walls of veins make them far more distensible than arteries; thus, they are said to be **capacitance vessels**.

When blood flow needs to be redistributed to other portions of the body, the vasomotor centre located in the medulla oblongata sends sympathetic stimulation to the smooth muscles in the walls of the veins, causing constriction—or in this case, venoconstriction. Less dramatic than the vasoconstriction seen in smaller arteries and arterioles, venoconstriction may be likened to a "stiffening" of the vessel wall. This increases pressure on the blood within the veins, speeding its return to the heart. As you will note in Table 19.3, approximately 21 percent of the venous blood is located in venous networks within the liver, bone marrow, and integument. This volume of blood is referred to as **venous reserve**. Through venoconstriction, this "reserve" volume of blood can get back to the heart more quickly for redistribution to other parts of the circulation.

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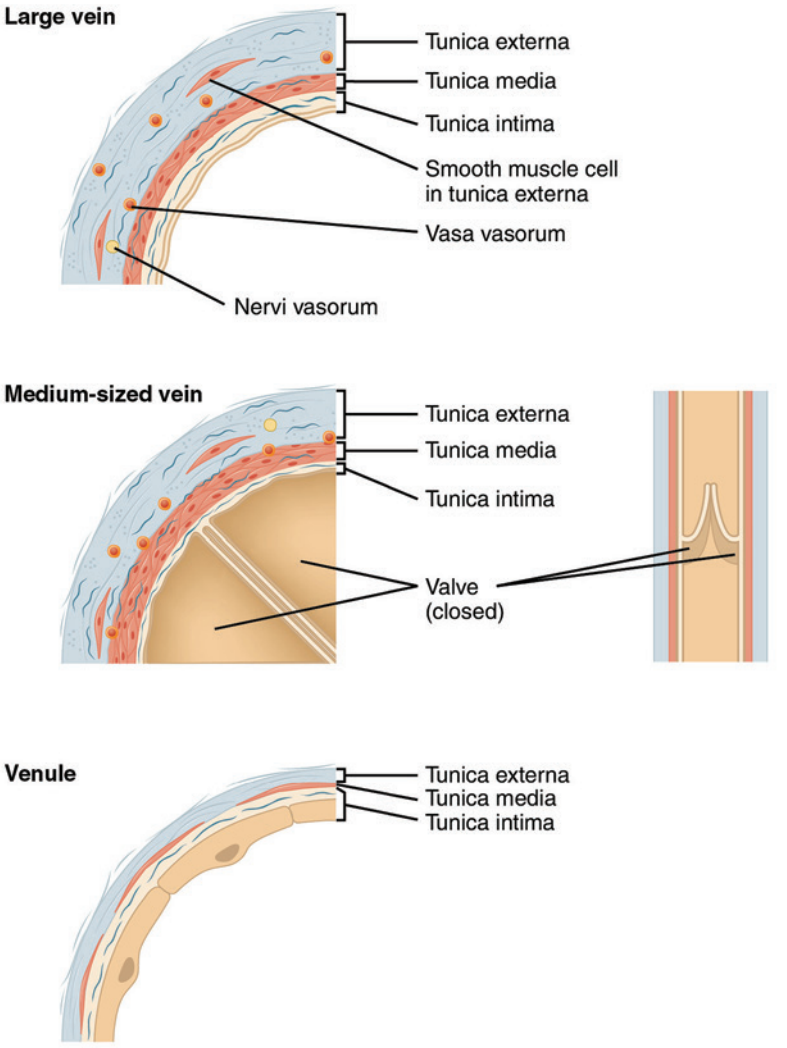


Figure 19.6 Comparison of Veins and Venules. Many veins have valves to prevent backflow of blood, whereas venules do not. In terms of scale, the diameter of a venule is measured in micrometres compared to millimetres for veins.

Interactive Link 19.1

Visit this site (http://oer.aupress.ca/oer-202505/19.1) to learn more about vascular surgery.

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Table 19.2 Comparison of Arteries and Veins

	Arteries	Veins
Direction of blood flow	Conducts blood away from the heart	Conducts blood toward the heart
General appearance	Rounded	Irregular, often collapsed
Pressure	High	Low
Wall thickness	Thick	Thin
Relative oxygen concentration	Higher in systemic arteries Lower in pulmonary arteries	Lower in systemic veins Higher in pulmonary veins
Valves	Not present	Present most commonly in limbs and in veins inferior to the heart

Table 19.3 Distribution of Blood Flow

Systemic circulation 84%	Systemic veins 64%	Large veins 18%
		Large venous networks (liver, bone marrow, and integument) 21%
		Venules and medium-sized veins 25%
	Systemic arteries 13%	Arterioles 2%
		Muscular arteries 5%
		Elastic arteries 4%
		Aorta 2%
	Systemic capillaries 7%	Systemic capillaries 7%
Pulmonary circulation 9%	Pulmonary veins 4%	
	Pulmonary capillaries 2%	
	Pulmonary arteries 3%	
Heart 7%		

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19.2 Blood Flow, Blood Pressure, and Resistance

Learning Objectives

By the end of this section, you will be able to:

- Distinguish between systolic pressure, diastolic pressure, pulse pressure, and mean arterial pressure
- Describe the clinical measurement of pulse and blood pressure
- Identify and discuss five variables affecting arterial blood flow and blood pressure
- Discuss several factors affecting blood flow in the venous system

Blood flow refers to the movement of blood through a vessel, tissue, or organ and is usually expressed in terms of volume of blood per unit of time. It is initiated by the contraction of the ventricles of the heart. Ventricular contraction ejects blood into the major arteries, resulting in flow from regions of higher pressure to regions of lower pressure as blood encounters smaller arteries and arterioles, then capillaries, then the venules and veins of the venous system. This section discusses a number of critical variables that contribute to blood flow throughout the body. It also discusses the factors that impede or slow blood flow, a phenomenon known as **resistance**.

As noted earlier, hydrostatic pressure is the force exerted by a fluid due to gravitational pull, usually against the wall of the container in which it is located. One form of hydrostatic pressure is **blood pressure**, the force exerted by blood upon the walls of the blood vessels or the chambers of the heart. Blood pressure may be measured in capillaries and veins as well as the vessels of the pulmonary circulation; however, the term *blood pressure* without any specific descriptors typically refers to systemic arterial blood pressure—that is, the pressure of blood flowing in the arteries of the systemic circulation. In clinical practice, this pressure is measured in mm Hg and is usually obtained using the brachial artery of the arm.

Components of Arterial Blood Pressure

Arterial blood pressure in the larger vessels consists of several distinct components (Figure 19.7): systolic and diastolic pressures, pulse pressure, and mean arterial pressure.

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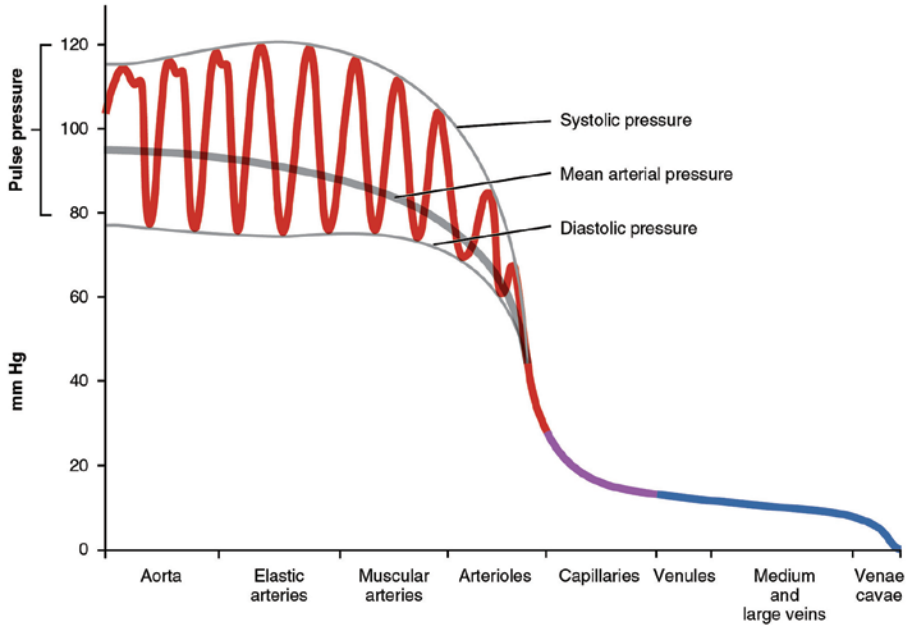


Figure 19.7 Systemic Blood Pressure. The graph shows the components of blood pressure throughout the blood vessels, including systolic, diastolic, mean arterial, and pulse pressures.

Systolic and Diastolic Pressures

When systemic arterial blood pressure is measured, it is recorded as a ratio of two numbers (e.g., 120/80 is a normal adult blood pressure) expressed as systolic pressure over diastolic pressure. The **systolic pressure** is the higher value (typically around 120 mm Hg) and reflects the arterial pressure resulting from the ejection of blood during ventricular contraction, or systole. The **diastolic pressure** is the lower value (usually about 80 mm Hg) and represents the arterial pressure of blood during ventricular relaxation, or diastole.

Pulse Pressure

As shown in Figure 19.7, the difference between the systolic pressure and the diastolic pressure is the **pulse pressure**. For example, an individual with a systolic pressure of 120 mm Hg and a diastolic pressure of 80 mm Hg would have a pulse pressure of 40 mm Hg.

Generally, a pulse pressure should be at least 25 percent of the systolic pressure. A pulse pressure below this level is described as low or narrow. This may occur, for example, in patients with a low stroke volume, which may be seen in congestive heart failure, stenosis of the aortic valve, or significant blood loss following trauma. In contrast, a high or wide pulse pressure is common in healthy people following strenuous exercise, when their resting pulse pressure

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of 30–40 mm Hg may increase temporarily to 100 mm Hg as stroke volume increases. A persistently high pulse pressure at or above 100 mm Hg may indicate excessive resistance in the arteries and can be caused by a variety of disorders. Chronic high resting pulse pressures can degrade the heart, brain, and kidneys and warrant medical treatment.

Mean Arterial Pressure

Mean arterial pressure (**MAP**) represents the "average" pressure of blood in the arteries—that is, the average force driving blood into vessels that serve the tissues. Mean is a statistical concept and is calculated by taking the sum of the values divided by the number of values. Although complicated to measure directly and complicated to calculate, MAP can be approximated by adding the diastolic pressure to one-third of the pulse pressure or systolic pressure minus the diastolic pressure:

$$\text{MAP} = \text{diastolic BP} + \frac{(\text{systolic} - \text{diastolic BP})}{3}$$

In Figure 19.7, this value is approximately 80 + (120 − 80) / 3, or 93.33. Normally, the MAP falls within the range of 70–110 mm Hg. If the value falls below 60 mm Hg for an extended time, blood pressure will not be high enough to ensure circulation to and through the tissues, which results in **ischemia**, or insufficient blood flow. A condition called **hypoxia**, inadequate oxygenation of tissues, commonly accompanies ischemia. The term *hypoxemia* refers to low levels of oxygen in systemic arterial blood. Neurons are especially sensitive to hypoxia and may die or be damaged if blood flow and oxygen supplies are not quickly restored.

Pulse

After blood is ejected from the heart, elastic fibres in the arteries help maintain a high-pressure gradient as they expand to accommodate the blood, then recoil. This expansion and recoiling effect, known as the **pulse**, can be palpated manually or measured electronically. Although the effect diminishes over distance from the heart, elements of the systolic and diastolic components of the pulse are still evident down to the level of the arterioles.

Because pulse indicates heart rate, it is measured clinically to provide clues to a patient's state of health. It is recorded as beats per minute. Both the rate and the strength of the pulse are important clinically. A high or irregular pulse rate can be caused by physical activity or other temporary factors, but it may also indicate a heart condition. The pulse strength indicates the strength of

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ventricular contraction and cardiac output. If the pulse is strong, then systolic pressure is high. If it is weak, systolic pressure has fallen, and medical intervention may be warranted.

Pulse can be palpated manually by placing the tips of the fingers across an artery that runs close to the body surface and pressing lightly. While this procedure is normally performed using the radial artery in the wrist or the common carotid artery in the neck, any superficial artery that can be palpated may be used (Figure 19.8). Common sites to find a pulse include temporal and facial arteries in the head, brachial arteries in the upper arm, femoral arteries in the thigh, popliteal arteries behind the knees, posterior tibial arteries near the medial tarsal regions, and dorsalis pedis arteries in the feet. A variety of commercial electronic devices are also available to measure pulse.

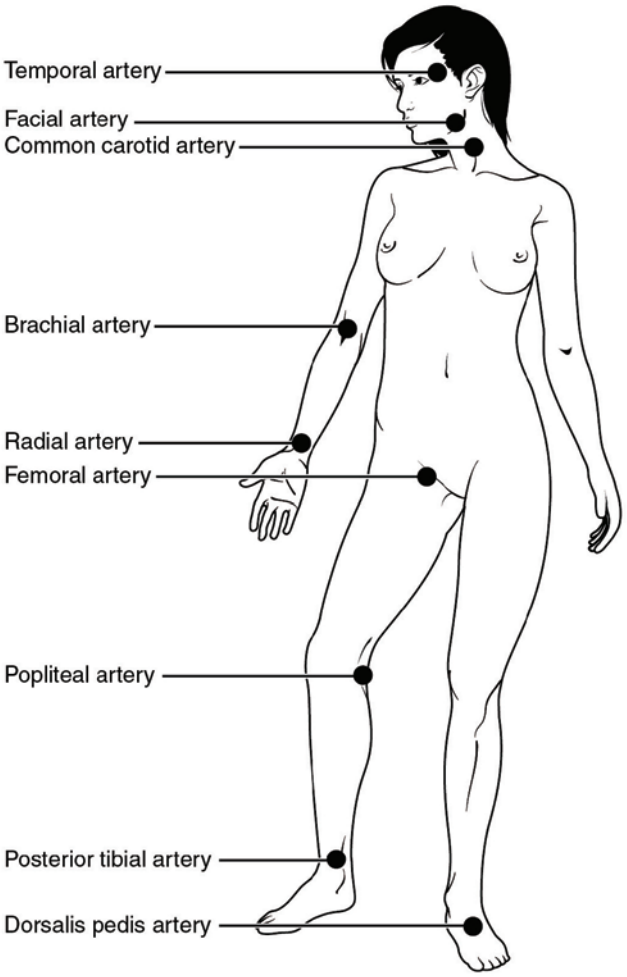


Figure 19.8 Pulse Sites. The pulse is most readily measured at the radial artery but can be measured at any of the pulse points shown.

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Measurement of Blood Pressure

Blood pressure is one of the critical parameters measured on virtually every patient in every health care setting. The technique used today was developed more than 100 years ago by a pioneering Russian physician, Dr. Nikolai Korotkoff. Turbulent blood flow through the vessels can be heard as a soft ticking while measuring blood pressure; these sounds are known as **Korotkoff sounds**. The technique of measuring blood pressure requires the use of a **sphygmomanometer** (a blood pressure cuff attached to a measuring device) and a stethoscope. The technique is as follows:

- The clinician wraps an inflatable cuff tightly around the patient's arm at about the level of the heart.
- The clinician squeezes a rubber pump to inject air into the cuff, raising pressure around the artery and temporarily cutting off blood flow into the patient's arm.
- The clinician places the stethoscope on the patient's antecubital region and, while gradually allowing air within the cuff to escape, listens for the Korotkoff sounds.

Although there are five recognized Korotkoff sounds, only two are normally recorded. Initially, no sounds are heard, since there is no blood flow through the vessels, but as air pressure drops, the cuff relaxes and blood flow returns to the arm. As shown in Figure 19.9, the first sound heard through the stethoscope—the first Korotkoff sound—indicates systolic pressure. As more air is released from the cuff, blood is able to flow freely through the brachial artery, and all sounds disappear. The point at which the last sound is heard is recorded as the patient's diastolic pressure.

The majority of hospitals and clinics have automated equipment for measuring blood pressure that works on the same principles. An even more recent innovation is a small instrument that wraps around a patient's wrist. The patient then holds the wrist over the heart while the device measures blood flow and records pressure.

Variables Affecting Blood Flow and Blood Pressure

Five variables influence blood flow and blood pressure:

- Cardiac output
- Compliance
- Volume of the blood
- Viscosity of the blood
- Blood vessel length and diameter

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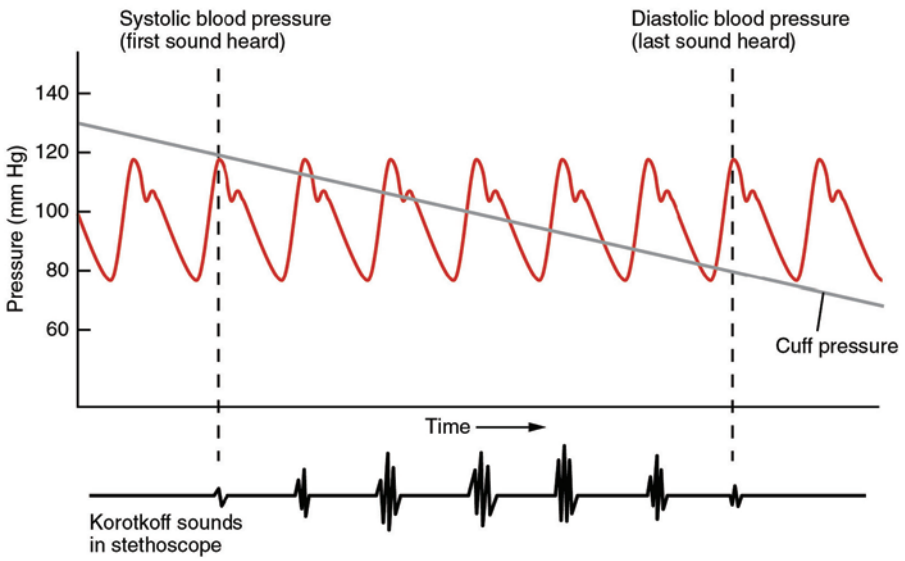


Figure 19.9 Blood Pressure Measurement. When pressure in a sphygmomanometer cuff is released, a clinician can hear the Korotkoff sounds. In this graph, a blood pressure tracing is aligned to a measurement of systolic and diastolic pressures.

Recall that blood moves from higher pressure to lower pressure. It is pumped from the heart into the arteries at high pressure. If you increase pressure in the arteries (afterload) and cardiac function does not compensate, blood flow will actually decrease. In the venous system, the opposite relationship is true. Increased pressure in the veins does not decrease flow as it does in arteries but actually increases flow. Since pressure in the veins is normally relatively low, for blood to flow back into the heart, the pressure in the atria during atrial diastole must be even lower. It normally approaches zero, except when the atria contract (see Figure 19.7).

Cardiac Output

Cardiac output is the measurement of blood flow from the heart through the ventricles and is usually measured in litres per minute. Any factor that causes cardiac output to increase, by elevating heart rate or stroke volume or both, will elevate blood pressure and promote blood flow. These factors include sympathetic stimulation, the catecholamines epinephrine and norepinephrine, thyroid hormones, and increased calcium ion levels. Conversely, any factor that decreases cardiac output, by decreasing heart rate or stroke volume or both, will decrease arterial pressure and blood flow. These factors include parasympathetic stimulation, elevated or decreased potassium ion levels, decreased calcium levels, anoxia, and acidosis.

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Compliance

Compliance is the ability of any compartment to expand to accommodate increased content. A metal pipe, for example, is not compliant, whereas a balloon is. The greater the compliance of an artery, the more effectively it is able to expand to accommodate surges in blood flow without increased resistance or blood pressure. Veins are more compliant than arteries and can expand to hold more blood. When vascular disease causes stiffening of arteries, compliance is reduced and resistance to blood flow is increased. The result is more turbulence, higher pressure within the vessel, and reduced blood flow. This increases the work of the heart.

Blood Volume

The relationship between blood volume, blood pressure, and blood flow is intuitively obvious. Water may merely trickle along a creek bed in a dry season but rush quickly and under great pressure after a heavy rain. Similarly, as blood volume decreases, pressure and flow decrease. As blood volume increases, pressure and flow increase.

Under normal circumstances, blood volume varies little. Low blood volume, called **hypovolemia**, may be caused by bleeding, dehydration, vomiting, severe burns, or some medications used to treat hypertension. It is important to recognize that other regulatory mechanisms in the body are so effective at maintaining blood pressure that an individual may be asymptomatic until 10–20 percent of the blood volume has been lost. Treatment typically includes intravenous fluid replacement.

Hypervolemia, or excessive fluid volume, may be caused by retention of water and sodium, as seen in patients with heart failure, liver cirrhosis, some forms of kidney disease, hyperaldosteronism, and some glucocorticoid steroid treatments. Restoring homeostasis in these patients depends on reversing the condition that triggered the hypervolemia.

Blood Viscosity

Viscosity is the thickness of fluids that affects their ability to flow. Clean water, for example, is less viscous than mud. The viscosity of blood is directly proportional to resistance and inversely proportional to flow; therefore, any condition that causes viscosity to increase will also increase resistance and decrease flow.

For example, imagine sipping milk, then a milkshake, through the same size straw. You experience more resistance and therefore less flow from the milkshake. Conversely, any condition that causes viscosity to decrease (such as when the milkshake melts) will decrease resistance and increase flow.

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Normally the viscosity of blood does not change over short periods of time. The two primary determinants of blood viscosity are the formed elements and plasma proteins. Since the vast majority of formed elements are erythrocytes, any condition affecting erythropoiesis, such as polycythemia or anemia, can alter viscosity. Since most plasma proteins are produced by the liver, any condition affecting liver function can also change the viscosity slightly and therefore alter blood flow. Liver abnormalities such as hepatitis, cirrhosis, alcohol damage, and drug toxicities result in decreased levels of plasma proteins, which decrease blood viscosity. While leukocytes and platelets are normally a small component of the formed elements, there are some rare conditions in which severe overproduction can impact viscosity as well.

Vessel Length and Diameter

The length of a vessel is directly proportional to its resistance: the longer the vessel, the greater the resistance and the lower the flow. As with blood volume, this makes intuitive sense, since the increased surface area of the vessel will impede the flow of blood. Likewise, if the vessel is shortened, the resistance will decrease and flow will increase.

The length of our blood vessels increases throughout childhood as we grow, of course, but is unchanging in adults under normal physiological circumstances. Further, the distribution of vessels is not the same in all tissues. Adipose tissue does not have an extensive vascular supply. One pound of adipose tissue contains approximately 200 miles of vessels, whereas skeletal muscle contains more than twice that. Overall, vessels decrease in length only during loss of mass or amputation. An individual weighing 150 pounds has approximately 60,000 miles of vessels in the body. Gaining about 10 pounds adds from 2,000 to 4,000 miles of vessels, depending on the nature of the gained tissue. One of the great benefits of weight reduction is the reduced stress to the heart, which does not have to overcome the resistance of as many miles of vessels.

In contrast to length, the diameter of blood vessels changes throughout the body according to the type of vessel, as we discussed earlier. The diameter of any given vessel may also change frequently throughout the day in response to neural and chemical signals that trigger vasodilation and vasoconstriction. The **vascular tone** of the vessel is the contractile state of the smooth muscle and the primary determinant of diameter and thus of resistance and flow.

The effect of vessel diameter on resistance is inverse: Given the same volume of blood, an increased diameter means there is less blood contacting the vessel wall, thus lower friction and lower resistance, subsequently increasing

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flow. A decreased diameter means more of the blood contacts the vessel wall, and resistance increases, subsequently decreasing flow.

The influence of lumen diameter on resistance is dramatic: A slight increase or decrease in diameter causes a huge decrease or increase in resistance. This is because resistance is inversely proportional to the radius of the blood vessel (one-half of the vessel's diameter) raised to the fourth power ($R = 1/r^4$).

This means, for example, that if an artery or arteriole constricts to one-half of its original radius, the resistance to flow will increase 16 times. And if an artery or arteriole dilates to twice its initial radius, then resistance in the vessel will decrease to 1/16 of its original value, and flow will increase 16 times.

The Roles of Vessel Diameter and Total Area in Blood Flow and Blood Pressure

Recall that we classified arterioles as resistance vessels, because given their small lumen, they dramatically slow the flow of blood from arteries. In fact, arterioles are the site of greatest resistance in the entire vascular network. This may seem surprising, given that capillaries have a smaller size. How can this phenomenon be explained?

Figure 19.10 compares vessel diameter, total cross-sectional area, average blood pressure, and blood velocity through the systemic vessels. Notice in parts (a) and (b) that the total cross-sectional area of the body's capillary beds is far greater than any other type of vessel. Although the diameter of an individual capillary is significantly smaller than the diameter of an arteriole, there are vastly more capillaries in the body than there are of other types of blood vessels. Part (c) shows that blood pressure drops unevenly as blood travels from arteries to arterioles, capillaries, venules, and veins and encounters greater resistance. However, the site of the most precipitous drop, and the site of greatest resistance, is the arterioles. This explains why vasodilation and vasoconstriction of arterioles play more significant roles in regulating blood pressure than do the vasodilation and vasoconstriction of other vessels.

Part (d) shows that the velocity (speed) of blood flow decreases dramatically as the blood moves from arteries to arterioles to capillaries. This slow flow rate allows more time for exchange processes to occur. As blood flows through the veins, the rate of velocity increases as blood is returned to the heart.

Venous System

The pumping action of the heart propels the blood into the arteries from an area of higher pressure toward an area of lower pressure. If blood is to flow from the veins back into the heart, the pressure in the veins must be greater than the pressure in the atria of the heart. Two factors help maintain this pressure gradient

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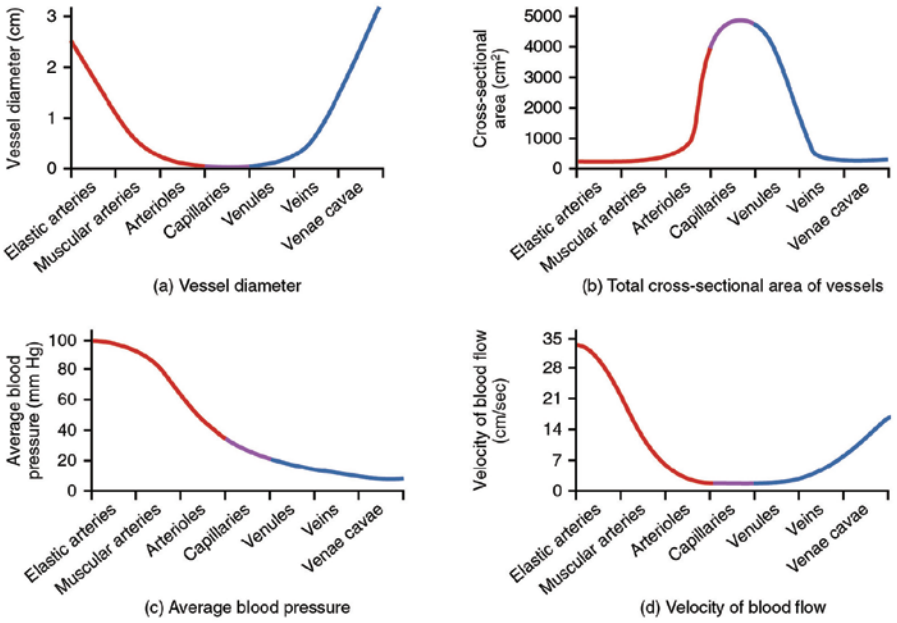


Figure 19.10 Relationships Among Vessels in the Systemic Circuit. The relationships among blood vessels that can be compared include (a) vessel diameter, (b) total cross-sectional area, (c) average blood pressure, and (d) velocity of blood flow.

between the veins and the heart. First, the pressure in the atria during diastole is very low, often approaching zero when the atria are relaxed (atrial diastole). Second, two physiologic "pumps" increase pressure in the venous system. The use of the term *pump* implies a physical device that speeds flow. These physiological pumps are less obvious.

Skeletal Muscle Pump

In many body regions, the pressure within the veins can be increased by the contraction of the surrounding skeletal muscle. This mechanism, known as the **skeletal muscle pump** (Figure 19.11), helps the lower-pressure veins counteract the force of gravity, increasing pressure to move blood back to the heart. As leg muscles contract—for example, during walking or running—they exert pressure on nearby veins with their numerous one-way valves. This increased pressure causes blood to flow upward, opening valves superior to the contracting muscles so blood flows through. Simultaneously, valves inferior to the contracting muscles close; thus, blood should not seep back downward toward the feet. Military recruits are trained to flex their legs slightly while standing at attention for prolonged periods. Failure to do so may allow blood to pool in the lower limbs rather than returning to the heart. Consequently, the brain will not receive enough oxygenated blood, and the individual may lose consciousness.

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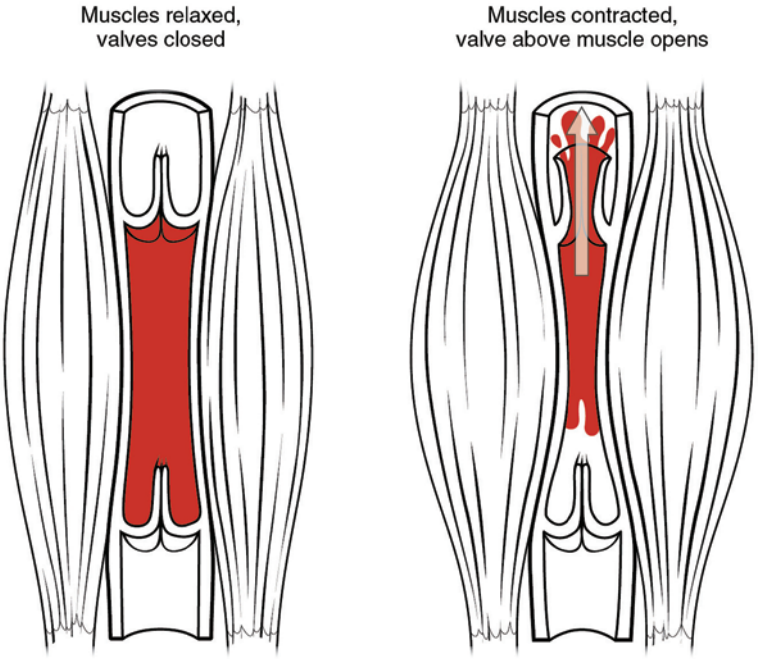


Figure 19.11 Skeletal Muscle Pump. The contraction of skeletal muscles surrounding a vein compresses the blood and increases the pressure in that area. This action forces blood closer to the heart, where venous pressure is lower. Note the importance of the one-way valves to ensure that blood flows only in the proper direction.

Respiratory Pump

The **respiratory pump** aids blood flow through the veins of the thorax and abdomen. During inhalation, the volume of the thorax increases, largely through the contraction of the diaphragm, which moves downward and compresses the abdominal cavity. The elevation of the chest caused by the contraction of the external intercostal muscles also contributes to the increased volume of the thorax. The volume increase causes air pressure within the thorax to decrease, allowing us to inhale. Additionally, as air pressure within the thorax drops, blood pressure in the thoracic veins also decreases, falling below the pressure in the abdominal veins. This causes blood to flow along its pressure gradient from veins outside the thorax, where pressure is higher, into the thoracic region, where pressure is now lower. This in turn promotes the return of blood from the thoracic veins to the atria. During exhalation, when air pressure increases within the thoracic cavity, pressure in the thoracic veins increases, speeding blood flow into the heart while valves in the veins prevent blood from flowing backward from the thoracic and abdominal veins.

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Pressure Relationships in the Venous System

Although vessel diameter increases from the smaller venules to the larger veins and eventually to the venae cavae (singular = vena cava), the total cross-sectional area actually decreases (see Figure 19.11a and Figure 19.11b). The individual veins are larger in diameter than the venules, but their total number is much lower, so their total cross-sectional area is also lower.

Also notice that as blood moves from venules to veins, the average blood pressure drops (see Figure 19.11c), but the blood velocity actually increases (see Figure 19.11). This pressure gradient drives blood back toward the heart. Again, the presence of one-way valves and the skeletal muscle and respiratory pumps contribute to this increased flow. Since approximately 64 percent of the total blood volume resides in systemic veins, any action that increases the flow of blood through the veins will increase venous return to the heart. Maintaining vascular tone within the veins prevents the veins from merely distending, dampening the flow of blood, and as you will see, vasoconstriction actually enhances the flow.

The Role of Venoconstriction in Resistance, Blood Pressure, and Flow

As previously discussed, vasoconstriction of an artery or arteriole decreases the radius, increasing resistance and pressure but decreasing flow. Venoconstriction, on the other hand, has a very different outcome. The walls of veins are thin but irregular; thus, when the smooth muscle in those walls constricts, the lumen becomes more rounded. The more rounded the lumen, the less surface area the blood encounters and the less resistance the vessel offers. Vasoconstriction increases pressure within a vein as it does in an artery, but in veins, the increased pressure increases flow. Recall that the pressure in the atria, into which the venous blood will flow, is very low, approaching zero for at least part of the relaxation phase of the cardiac cycle. Thus, venoconstriction increases the return of blood to the heart. Another way of stating this is that venoconstriction increases the preload or stretch of the cardiac muscle and increases contraction.

19.3 Capillary Exchange

Learning Objectives

By the end of this section, you will be able to:

- Identify the primary mechanisms of capillary exchange

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- Distinguish between capillary hydrostatic pressure and blood colloid osmotic pressure, explaining the contribution of each to net filtration pressure
- Compare filtration and reabsorption
- Explain the fate of fluid that is not reabsorbed from the tissues into the vascular capillaries

The primary purpose of the cardiovascular system is to circulate gases, nutrients, wastes, and other substances to and from the cells of the body. Small molecules, such as gases, lipids, and lipid-soluble molecules, can diffuse directly through the membranes of the endothelial cells of the capillary wall. Glucose, amino acids, and ions—including sodium, potassium, calcium, and chloride—use transporters to move through specific channels in the membrane by facilitated diffusion. Glucose, ions, and larger molecules may also leave the blood through intercellular clefts. Larger molecules can pass through the pores of fenestrated capillaries, and even large plasma proteins can pass through the great gaps in the sinusoids. Some large proteins in blood plasma can move into and out of the endothelial cells packaged within vesicles by endocytosis and exocytosis. Water moves by osmosis.

Bulk Flow

The mass movement of fluids into and out of capillary beds requires a transport mechanism far more efficient than mere diffusion. This movement, often referred to as bulk flow, involves two pressure-driven mechanisms: Volumes of fluid move from an area of higher pressure in a capillary bed to an area of lower pressure in the tissues via **filtration**. In contrast, the movement of fluid from an area of higher pressure in the tissues into an area of lower pressure in the capillaries is **reabsorption**. Two types of pressure interact to drive each of these movements: hydrostatic pressure and osmotic pressure.

Hydrostatic Pressure

The primary force driving fluid transport between the capillaries and tissues is hydrostatic pressure, which can be defined as the pressure of any fluid enclosed in a space. **Blood hydrostatic pressure** is the force exerted by the blood confined within blood vessels or heart chambers. Even more specifically, the pressure exerted by blood against the wall of a capillary is called **capillary hydrostatic pressure** (**CHP**) and is the same as capillary blood pressure. CHP is the force that drives fluid out of capillaries and into the tissues.

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As fluid exits a capillary and moves into tissues, the hydrostatic pressure in the interstitial fluid correspondingly rises. This opposing hydrostatic pressure is called the **interstitial fluid hydrostatic pressure** (**IFHP**). Generally, the CHP originating from the arterial pathways is considerably higher than the IFHP, because lymphatic vessels are continually absorbing excess fluid from the tissues. Thus, fluid generally moves out of the capillary and into the interstitial fluid. This process is called filtration.

Osmotic Pressure

The net pressure that drives reabsorption—the movement of fluid from the interstitial fluid back into the capillaries—is called osmotic pressure (sometimes referred to as oncotic pressure). Whereas hydrostatic pressure forces fluid out of the capillary, osmotic pressure draws fluid back in. Osmotic pressure is determined by osmotic concentration gradients—that is, the difference in the solute-to-water concentrations in the blood and tissue fluid. A region higher in solute concentration (and lower in water concentration) draws water across a semipermeable membrane from a region higher in water concentration (and lower in solute concentration).

As we discuss osmotic pressure in blood and tissue fluid, it is important to recognize that the formed elements of blood do not contribute to osmotic concentration gradients. Rather, it is the plasma proteins that play the key role. Solutes also move across the capillary wall according to their concentration gradient, but overall, the concentrations should be similar and not have a significant impact on osmosis. Because of their large size and chemical structure, plasma proteins are not truly solutes—that is, they do not dissolve but are dispersed or suspended in their fluid medium, forming a colloid rather than a solution.

The pressure created by the concentration of colloidal proteins in the blood is called the **blood colloidal osmotic pressure** (**BCOP**). Its effect on capillary exchange accounts for the reabsorption of water. The plasma proteins suspended in blood cannot move across the semipermeable capillary cell membrane, and so they remain in the plasma. As a result, blood has a higher colloidal concentration and a lower water concentration than tissue fluid. It therefore attracts water. We can also say that the BCOP is higher than the **interstitial fluid colloidal osmotic pressure** (**IFCOP**), which is always very low because interstitial fluid contains few proteins. Thus, water is drawn from the tissue fluid back into the capillary, carrying dissolved molecules with it. This difference in colloidal osmotic pressure accounts for reabsorption.

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Interaction of Hydrostatic and Osmotic Pressures

The normal unit used to express pressures within the cardiovascular system is millimetres of mercury (mm Hg). When blood leaving an arteriole first enters a capillary bed, the CHP is quite high—about 35 mm Hg. Gradually, this initial CHP declines as the blood moves through the capillary so that by the time the blood has reached the venous end, the CHP has dropped to approximately 18 mm Hg. In comparison, the plasma proteins remain suspended in the blood, so the BCOP remains fairly constant at about 25 mm Hg throughout the length of the capillary and considerably above the osmotic pressure in the interstitial fluid.

The **net filtration pressure** (**NFP**) represents the interaction of the hydrostatic and osmotic pressures, driving fluid out of the capillary. It is equal to the difference between the CHP and the BCOP. Since filtration is, by definition, the movement of fluid out of the capillary, when reabsorption is occurring, the NFP is a negative number.

NFP changes at different points in a capillary bed (Figure 19.12). Close to the arterial end of the capillary, it is approximately 10 mm Hg, because the CHP of 35 mm Hg minus the BCOP of 25 mm Hg equals 10 mm Hg. Recall that the hydrostatic and osmotic pressures of the interstitial fluid are essentially negligible. Thus, the NFP of 10 mm Hg drives a net movement of fluid out of the capillary at the arterial end. At approximately the middle of the capillary, the CHP is about the same as the BCOP of 25 mm Hg, so the NFP drops to zero. At this point, there is no net change of volume: Fluid moves out of the capillary at the same rate as it moves into the capillary. Near the venous

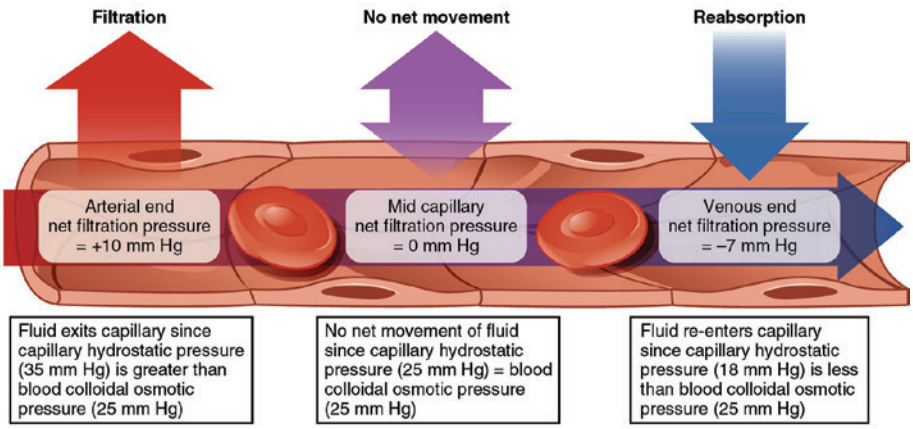


Figure 19.12 Capillary Exchange. Net filtration occurs near the arterial end of the capillary since capillary hydrostatic pressure (CHP) is greater than blood colloidal osmotic pressure (BCOP). There is no net movement of fluid near the midpoint, since CHP = BCOP. Net reabsorption occurs near the venous end, since BCOP is greater than CHP.

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end of the capillary, the CHP has dwindled to about 18 mm Hg due to loss of fluid. Because the BCOP remains steady at 25 mm Hg, water is drawn into the capillary—that is, reabsorption occurs. Another way of expressing this is to say that at the venous end of the capillary, there is an NFP of −7 mm Hg.

The Role of Lymphatic Capillaries

Since overall CHP is higher than BCOP, it is inevitable that more net fluid will exit the capillary through filtration at the arterial end than enters through reabsorption at the venous end. Considering all capillaries over the course of a day, this can be quite a substantial amount of fluid: Approximately 24 L per day are filtered, whereas 20.4 L are reabsorbed. This excess fluid is picked up by capillaries of the lymphatic system. These extremely thin-walled vessels have a copious number of valves that ensure unidirectional flow through ever-larger lymphatic vessels that eventually drain into the subclavian veins in the neck. An important function of the lymphatic system is to return the fluid, called **lymph**, to the blood. Lymph may be thought of as recycled blood plasma.

Interactive Link 19.2

Watch this video (http://oer.aupress.ca/oer-202505/19.2) to explore capillaries and how they function in the body. Capillaries are never more than 100 µm away. What is the main component of interstitial fluid?

19.4 Homeostatic Regulation of the Vascular System

Learning Objectives

By the end of this section, you will be able to:

- Discuss the mechanisms involved in the neural regulation of vascular homeostasis
- Describe the contribution of a variety of hormones to the renal regulation of blood pressure
- Identify the effects of exercise on vascular homeostasis
- Discuss how hypertension, hemorrhage, and circulatory shock affect vascular health

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In order to maintain homeostasis in the cardiovascular system and provide adequate blood to the tissues, blood flow must be redirected continually to the tissues as they become more active. In a very real sense, the cardiovascular system engages in resource allocation, because there is not enough blood flow to distribute blood equally to all tissues simultaneously.

For example, when an individual is exercising, more blood will be directed to skeletal muscles, the heart, and the lungs. Following a meal, more blood is directed to the digestive system. Only the brain receives a more or less constant supply of blood whether you are active, resting, thinking, or engaged in any other activity.

Table 19.4 provides the distribution of systemic blood at rest and during exercise. Although most of the data appears logical, the values for the distribution of blood to the integument may seem surprising. During exercise, the body distributes more blood to the body surface, where it can dissipate the excess heat generated by increased activity into the environment.

Three homeostatic mechanisms ensure adequate blood flow, blood pressure, distribution, and ultimately perfusion: neural, endocrine, and autoregulatory mechanisms. They are summarized in Figure 19.13.

Neural Regulation

The nervous system plays a critical role in the regulation of vascular homeostasis. The primary regulatory sites include the cardiovascular centres in the

Table 19.4 Systemic Blood Flow During Rest, Mild Exercise, and Maximal Exercise in a Healthy Young Individual

Organ	Resting (mL/min)	Mild exercise (mL/min)	Maximal exercise (mL/min)
Skeletal muscle	1200	4500	12,500
Heart	250	350	750
Brain	750	750	750
Integument	500	1500	1900
Kidney	1100	900	600
Gastrointestinal	1400	1100	600
Others (i.e., liver, spleen)	600	400	400
Total	5800	9500	17,500

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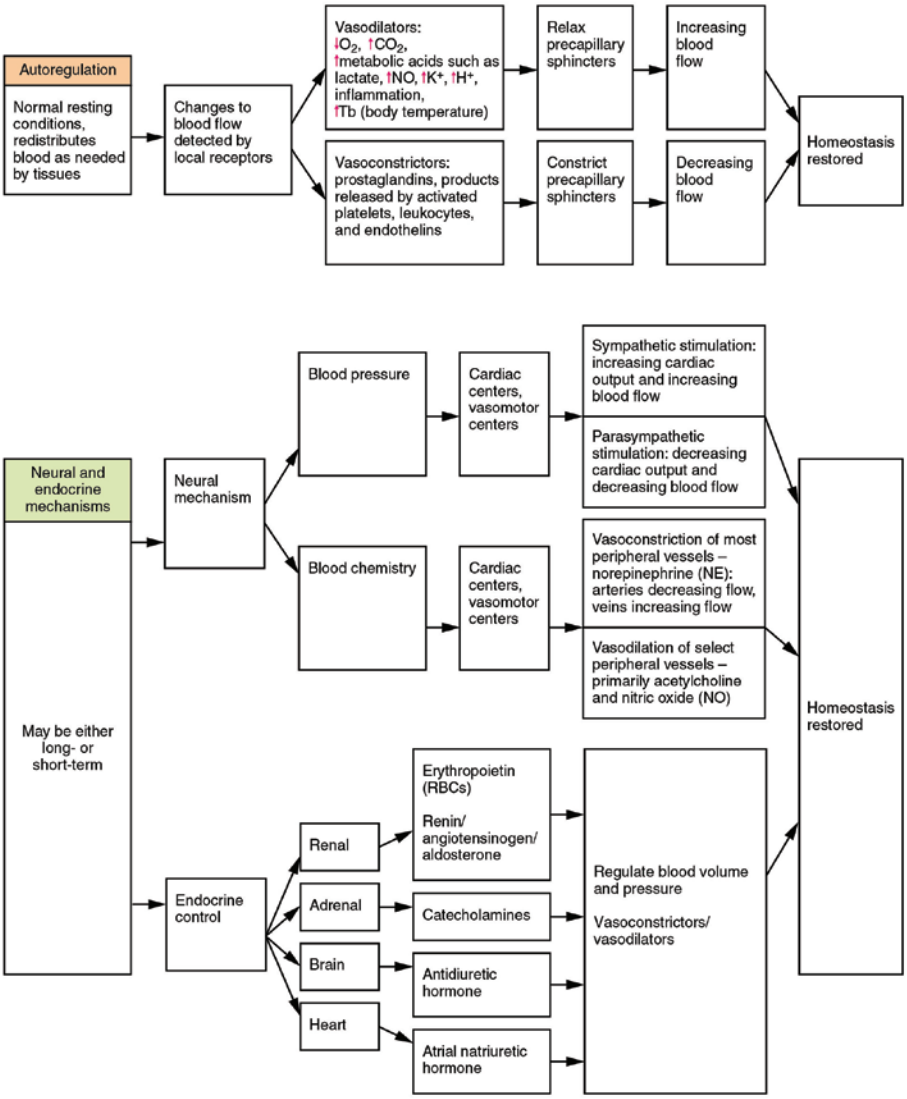


Figure 19.13 Summary of Factors Maintaining Vascular Homeostasis. Adequate blood flow, blood pressure, distribution, and perfusion involve autoregulatory, neural, and endocrine mechanisms.

brain that control both cardiac and vascular functions. In addition, more generalized neural responses from the limbic system and the autonomic nervous system are factors.

The Cardiovascular Centres in the Brain

Neurological regulation of blood pressure and flow depends on the cardiovascular centres located in the medulla oblongata. This cluster of neurons responds to changes in blood pressure as well as blood concentrations of oxygen, carbon

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dioxide, and hydrogen ions. The cardiovascular centre contains three distinct paired components:

- The **cardioaccelerator centres** stimulate cardiac function by regulating heart rate and stroke volume via sympathetic stimulation from the cardiac accelerator nerve.
- The **cardioinhibitor centres** slow cardiac function by decreasing heart rate and stroke volume via parasympathetic stimulation from the vagus nerve.
- The **vasomotor centres** control vessel tone or contraction of the smooth muscle in the tunica media. Changes in diameter affect peripheral resistance, pressure, and flow, which affect cardiac output. The majority of these neurons act via the release of the neurotransmitter norepinephrine from sympathetic neurons.

Although each centre functions independently, they are not anatomically distinct.

There is also a small population of neurons that control vasodilation in the vessels of the brain and skeletal muscles by relaxing the smooth muscle fibres in the vessel tunics. Many of these are cholinergic neurons—that is, they release acetylcholine, which in turn stimulates the vessels' endothelial cells to release nitric oxide (NO), which causes vasodilation. Others release norepinephrine that binds to β_2 receptors. A few neurons release NO directly as a neurotransmitter.

Recall that mild stimulation of the skeletal muscles maintains muscle tone. A similar phenomenon occurs with vascular tone in vessels. As noted earlier, arterioles are normally partially constricted: With maximal stimulation, their radius may be reduced to one-half of the resting state. Full dilation of most arterioles requires that this sympathetic stimulation be suppressed. When it is, an arteriole can expand by as much as 150 percent. Such a significant increase can dramatically affect resistance, pressure, and flow.

Baroreceptor Reflexes

Baroreceptors are specialized stretch receptors located within thin areas of blood vessels and heart chambers that respond to the degree of stretch caused by the presence of blood. They send impulses to the cardiovascular centre to regulate blood pressure. Vascular baroreceptors are found primarily in sinuses (small cavities) within the aorta and carotid arteries: The **aortic sinuses** are found in the walls of the ascending aorta just superior to the aortic valve, whereas the **carotid sinuses** are in the base of the internal carotid arteries. There are also low-pressure baroreceptors located in the walls of the venae cavae and right atrium.

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When blood pressure increases, the baroreceptors are stretched more tightly and initiate action potentials at a higher rate. At lower blood pressures, the degree of stretch is lower, and the rate of firing is slower. When the cardiovascular centre in the medulla oblongata receives this input, it triggers a reflex that maintains homeostasis (Figure 19.14):

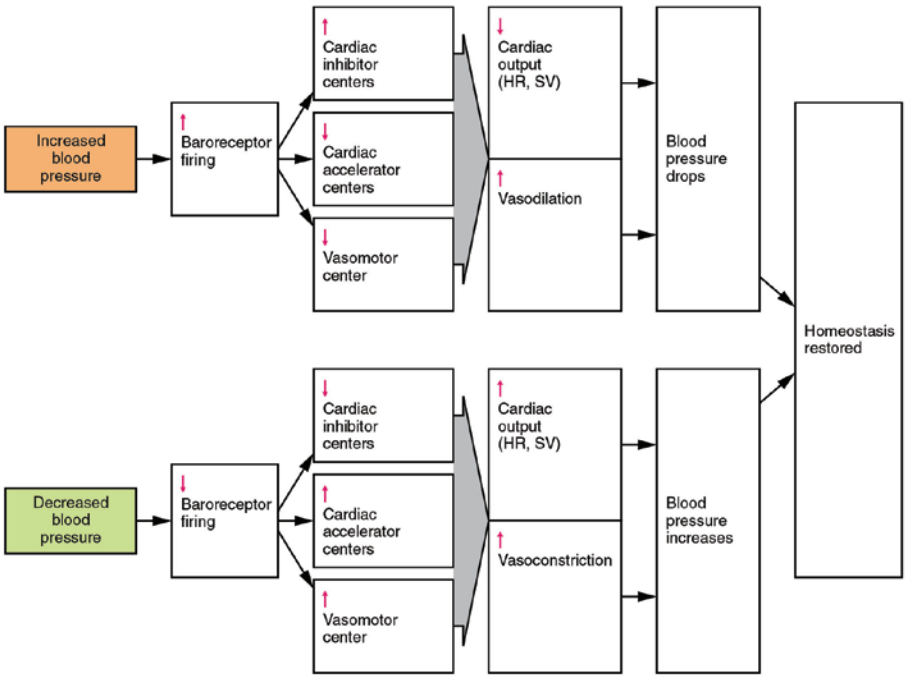


Figure 19.14 Baroreceptor Reflexes for Maintaining Vascular Homeostasis. Increased blood pressure results in increased rates of baroreceptor firing, whereas decreased blood pressure results in slower rates of firing, both initiating the homeostatic mechanism to restore blood pressure.

- When blood pressure rises too high, the baroreceptors fire at a higher rate and trigger parasympathetic stimulation of the heart. As a result, cardiac output falls. Sympathetic stimulation of the peripheral arterioles will also decrease, resulting in vasodilation. Combined, these activities cause blood pressure to fall.
- When blood pressure drops too low, the rate of baroreceptor firing decreases. This will trigger an increase in sympathetic stimulation of the heart, causing cardiac output to increase. It will also trigger sympathetic stimulation of the peripheral vessels, resulting in vasoconstriction. Combined, these activities cause blood pressure to rise.

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The baroreceptors in the venae cavae and right atrium monitor blood pressure as the blood returns to the heart from the systemic circulation. Normally, blood flow into the aorta is the same as blood flow back into the right atrium. If blood is returning to the right atrium more rapidly than it is being ejected from the left ventricle, the atrial receptors will stimulate the cardiovascular centres to increase sympathetic firing and increase cardiac output until homeostasis is achieved. The opposite is also true. This mechanism is referred to as the **atrial reflex**.

Chemoreceptor Reflexes

In addition to the baroreceptors are chemoreceptors that monitor levels of oxygen, carbon dioxide, and hydrogen ions (pH) and thereby contribute to vascular homeostasis. Chemoreceptors monitoring the blood are located in close proximity to the baroreceptors in the aortic and carotid sinuses. They signal the cardiovascular centre as well as the respiratory centres in the medulla oblongata.

Since tissues consume oxygen and produce carbon dioxide and acids as waste products, when the body is more active, oxygen levels fall and carbon dioxide levels rise as cells undergo cellular respiration to meet the energy needs of activities. This causes more hydrogen ions to be produced, causing the blood pH to drop. When the body is resting, oxygen levels are higher, carbon dioxide levels are lower, more hydrogen is bound, and pH rises.

The chemoreceptors respond to increasing carbon dioxide and hydrogen ion levels (falling pH) by stimulating the cardioaccelerator and vasomotor centres, increasing cardiac output and constricting peripheral vessels. The cardioinhibitor centres are suppressed. With falling carbon dioxide and hydrogen ion levels (increasing pH), the cardioinhibitor centres are stimulated, and the cardioaccelerator and vasomotor centres are suppressed, decreasing cardiac output and causing peripheral vasodilation. In order to maintain adequate supplies of oxygen to the cells and remove waste products such as carbon dioxide, it is essential that the respiratory system respond to changing metabolic demands. In turn, the cardiovascular system will transport these gases to the lungs for exchange, again in accordance with metabolic demands. This interrelationship of cardiovascular and respiratory control cannot be overemphasized.

Other neural mechanisms can also have a significant impact on cardiovascular function. These include the limbic system that links physiological responses to psychological stimuli as well as generalized sympathetic and parasympathetic stimulation.

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Endocrine Regulation

Endocrine control over the cardiovascular system involves the catecholamines, epinephrine and norepinephrine, as well as several hormones that interact with the kidneys in the regulation of blood volume.

Epinephrine and Norepinephrine

The catecholamines epinephrine and norepinephrine are released by the adrenal medulla and enhance and extend the body's sympathetic or "fight-or-flight" response (see Figure 19.13). They increase heart rate and force of contraction while temporarily constricting blood vessels to organs not essential for flight-or-fight responses and redirecting blood flow to the liver, muscles, and heart.

Antidiuretic Hormone

Antidiuretic hormone (ADH), also known as vasopressin, is secreted by the cells in the hypothalamus and transported via the hypothalamic-hypophyseal tracts to the posterior pituitary, where it is stored until released upon nervous stimulation. The primary trigger prompting the hypothalamus to release ADH is increasing osmolarity of tissue fluid, usually in response to significant loss of blood volume. ADH signals its target cells in the kidneys to reabsorb more water, thus preventing the loss of additional fluid in the urine. This will increase overall fluid levels and help restore blood volume and pressure. In addition, ADH constricts peripheral vessels.

Renin-Angiotensin-Aldosterone Mechanism

The renin-angiotensin-aldosterone mechanism has a major effect on the cardiovascular system (Figure 19.15). Renin is an enzyme, although because of its importance in the renin-angiotensin-aldosterone pathway, some sources identify it as a hormone. Specialized cells in the kidneys, called juxtaglomerular (JG) cells, respond to decreased blood pressure by secreting renin into the blood. Renin converts the plasma protein angiotensinogen, which is produced by the liver, into its active form—angiotensin I. Angiotensin I circulates in the blood and is then converted into angiotensin II in the lungs. This reaction is catalyzed by the angiotensin-converting enzyme (ACE).

Angiotensin II is a powerful vasoconstrictor, greatly increasing blood pressure. It also stimulates the release of ADH and aldosterone, a hormone produced by the adrenal cortex. Aldosterone increases the reabsorption of sodium into the blood by the kidneys. Since water follows sodium, this increases the reabsorption of water. This in turn increases blood volume, raising blood pressure.

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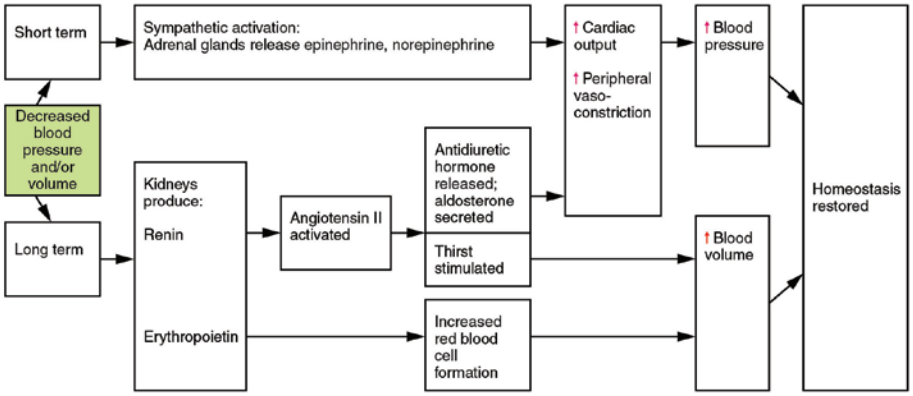


Figure 19.15 Hormones Involved in Renal Control of Blood Pressure. In the renin-angiotensin-aldosterone mechanism, increasing angiotensin II will stimulate the production of antidiuretic hormone and aldosterone. In addition to renin, the kidneys produce erythropoietin, which stimulates the production of red blood cells, further increasing blood volume.

Angiotensin II also stimulates the thirst centre in the hypothalamus, so an individual will likely consume more fluids, again increasing blood volume and pressure.

Erythropoietin

Erythropoietin (EPO) is released by the kidneys when blood flow and/or oxygen levels decrease. EPO stimulates the production of erythrocytes within the bone marrow. Erythrocytes are the major formed element of the blood and may contribute 40 percent or more to blood volume, a significant factor of viscosity, resistance, pressure, and flow. In addition, EPO is a vasoconstrictor. Overproduction of EPO or excessive intake of synthetic EPO, often to enhance athletic performance, will increase viscosity, resistance, and pressure and decrease flow in addition to its contribution as a vasoconstrictor.

Atrial Natriuretic Hormone

Secreted by cells in the atria of the heart, atrial natriuretic hormone (ANH; also known as atrial natriuretic peptide) is secreted when blood volume is high enough to cause extreme stretching of the cardiac cells. Cells in the ventricle produce a hormone with similar effects called B-type natriuretic hormone. Natriuretic hormones are antagonists to angiotensin II. They promote loss of sodium and water from the kidneys and suppress renin, aldosterone, and ADH production and release. All of these actions promote loss of fluid from the body, so blood volume and blood pressure drop.

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Autoregulation of Perfusion

As the name would suggest, autoregulation mechanisms require neither specialized nervous stimulation nor endocrine control. Rather, these are local, self-regulatory mechanisms that allow each region of tissue to adjust its blood flow—and thus its perfusion. These local mechanisms include chemical signals and myogenic controls.

Chemical Signals Involved in Autoregulation

Chemical signals work at the level of the precapillary sphincters to trigger either constriction or relaxation. As you know, opening a precapillary sphincter allows blood to flow into that particular capillary, whereas constricting a precapillary sphincter temporarily shuts off blood flow to that region. The factors involved in regulating the precapillary sphincters include the following:

- Opening of the sphincter is triggered in response to decreased oxygen concentrations, increased carbon dioxide concentrations, increasing levels of lactic acid or other by-products of cellular metabolism, increasing concentrations of potassium ions or hydrogen ions (falling pH), inflammatory chemicals such as histamines, and increased body temperature. These conditions in turn stimulate the release of NO, a powerful vasodilator, from endothelial cells (see Figure 19.13).
- Contraction of the precapillary sphincter is triggered by the opposite levels of the regulators, which prompt the release of endothelins, powerful vasoconstricting peptides secreted by endothelial cells. Platelet secretions and certain prostaglandins may also trigger constriction.

Again, these factors alter tissue perfusion via their effects on the precapillary sphincter mechanism, which regulates blood flow to capillaries. Since the amount of blood is limited, not all capillaries can fill at once, so blood flow is allocated based on the needs and metabolic state of the tissues as reflected in these parameters. Bear in mind, however, that dilation and constriction of the arterioles feeding the capillary beds is the primary control mechanism.

The Myogenic Response

The **myogenic response** is a reaction to the stretching of the smooth muscle in the walls of arterioles as changes in blood flow occur through the vessel. This may be viewed as a largely protective function against dramatic fluctuations in blood pressure and blood flow to maintain homeostasis. If perfusion of an organ is too low (ischemia), the tissue will experience low levels of oxygen (hypoxia). In contrast, excessive perfusion could damage the organ's smaller

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and more fragile vessels. The myogenic response is a localized process that serves to stabilize blood flow in the capillary network that follows that arteriole.

When blood flow is low, the vessel's smooth muscle will be only minimally stretched. In response, it relaxes, allowing the vessel to dilate and thereby increase the movement of blood into the tissue. When blood flow is too high, the smooth muscle will contract in response to the increased stretch, prompting vasoconstriction that reduces blood flow.

Effect of Exercise on Vascular Homeostasis

The heart is a muscle, and like any muscle, it responds dramatically to exercise. For a healthy young adult, cardiac output (heart rate × stroke volume) increases in the nonathlete from approximately 5.0 L per minute to a maximum of about 20 L per minute. Accompanying this will be an increase in blood pressure from about 120/80 to 185/75. However, well-trained aerobic athletes can increase these values substantially. For these individuals, cardiac output soars from approximately 5.3 L per minute resting to more than 30 L per minute during maximal exercise. Along with this increase in cardiac output, blood pressure increases from 120/80 at rest to 200/90 at maximum values.

In addition to improved cardiac function, exercise increases the size and mass of the heart. The average weight of the heart for the nonathlete is about 300 g, whereas in an athlete it will increase to 500 g. This increase in size generally makes the heart stronger and more efficient at pumping blood, increasing both stroke volume and cardiac output.

Tissue perfusion also increases as the body transitions from a resting state to light exercise and eventually to heavy exercise. These changes result in selective vasodilation in the skeletal muscles, heart, lungs, liver, and integument. Simultaneously, vasoconstriction occurs in the vessels leading to the kidneys and most of the digestive and reproductive organs. The flow of blood to the brain remains largely unchanged whether at rest or exercising, since the vessels in the brain largely do not respond to regulatory stimuli, in most cases, because they lack the appropriate receptors.

As vasodilation occurs in selected vessels, resistance drops and more blood rushes into the organs they supply. This blood eventually returns to the venous system. Venous return is further enhanced by both the skeletal muscle and respiratory pumps. As blood returns to the heart more quickly, preload rises, and the Frank-Starling principle tells us that contraction of the cardiac muscle in the atria and ventricles will be more forceful. Eventually, even the best-trained athletes will fatigue and must undergo a period of rest following exercise. Cardiac output and distribution of blood then return to normal.

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Regular exercise promotes cardiovascular health in a variety of ways. Because an athlete's heart is larger than a nonathlete's, stroke volume increases, so the athletic heart can deliver the same amount of blood as the nonathletic heart but with a lower heart rate. This increased efficiency allows the athlete to exercise for longer periods of time before muscles fatigue and places less stress on the heart. Exercise also lowers overall cholesterol levels by removing from the circulation a complex form of cholesterol, triglycerides, and proteins known as low-density lipoproteins (LDLs), which are widely associated with increased risk of cardiovascular disease. Although there is no way to remove deposits of plaque from the walls of arteries other than specialized surgery, exercise does promote the health of vessels by decreasing the rate of plaque formation and reducing blood pressure so the heart does not have to generate as much force to overcome resistance.

Generally, as little as 30 minutes of noncontinuous exercise over the course of each day has beneficial effects and has been shown to lower the rate of heart attack by nearly 50 percent. While it is always advisable to follow a healthy diet, stop smoking, and lose weight, studies have clearly shown that fit, overweight people may actually be healthier overall than sedentary slender people. Thus, the benefits of moderate exercise are undeniable.

Clinical Considerations in Vascular Homeostasis

Any disorder that affects blood volume, vascular tone, or any other aspect of vascular functioning is likely to affect vascular homeostasis as well. That includes hypertension, hemorrhage, and shock.

Hypertension

Guidelines list normal blood pressure (BP) as less than 120/80 mm Hg and elevated BP as systolic pressure between 120–129 and diastolic pressure less than 80 mm Hg. Chronically elevated blood pressure is known clinically as **hypertension**. The new guidelines list hypertension that should be treated as 130/80 mm Hg. Tens of millions of Americans currently suffer from hypertension. Unfortunately, hypertension is typically a silent disorder; therefore, hypertensive patients may fail to recognize the seriousness of their condition and fail to follow their treatment plan. The result is often a heart attack or stroke. Hypertension may also lead to an aneurysm (ballooning of a blood vessel caused by a weakening of the wall), peripheral arterial disease (obstruction of vessels in peripheral regions of the body), chronic kidney disease, or heart failure.

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Interactive Link 19.3

Listen to this CDC podcast (http://oer.aupress.ca/oer-202505/19.3) to learn about hypertension, often described as a "silent killer." What steps can you take to reduce your risk of a heart attack or stroke?

Hemorrhage

Minor blood loss is managed by hemostasis and repair. Hemorrhage is a loss of blood that cannot be controlled by hemostatic mechanisms. Initially, the body responds to hemorrhage by initiating mechanisms aimed at increasing blood pressure and maintaining blood flow. Ultimately, however, blood volume will need to be restored either through physiological processes or through medical intervention.

In response to blood loss, stimuli from the baroreceptors trigger the cardiovascular centres to stimulate sympathetic responses to increase cardiac output and vasoconstriction. This typically prompts the heart rate to increase to about 180–200 contractions per minute, restoring cardiac output to normal levels. Vasoconstriction of the arterioles increases vascular resistance, whereas constriction of the veins increases venous return to the heart. Both of these steps will help increase blood pressure. Sympathetic stimulation also triggers the release of epinephrine and norepinephrine, which enhance both cardiac output and vasoconstriction. If blood loss were less than 20 percent of total blood volume, these responses together would usually return blood pressure to normal and redirect the remaining blood to the tissues.

Additional endocrine involvement is necessary, however, to restore the lost blood volume. The angiotensin-renin-aldosterone mechanism stimulates the thirst centre in the hypothalamus, which increases fluid consumption to help restore the lost blood. More importantly, it increases renal reabsorption of sodium and water, reducing water loss in urine output. The kidneys also increase the production of EPO, stimulating the formation of erythrocytes that not only deliver oxygen to the tissues but also increase overall blood volume. Figure 19.16 summarizes the responses to loss of blood volume.

Circulatory Shock

The loss of too much blood may lead to **circulatory shock**, a life-threatening condition in which the circulatory system is unable to maintain blood flow to adequately supply sufficient oxygen and other nutrients to the tissues to maintain cellular metabolism. It should not be confused with emotional or psychological shock. Typically, the patient in circulatory shock will demonstrate

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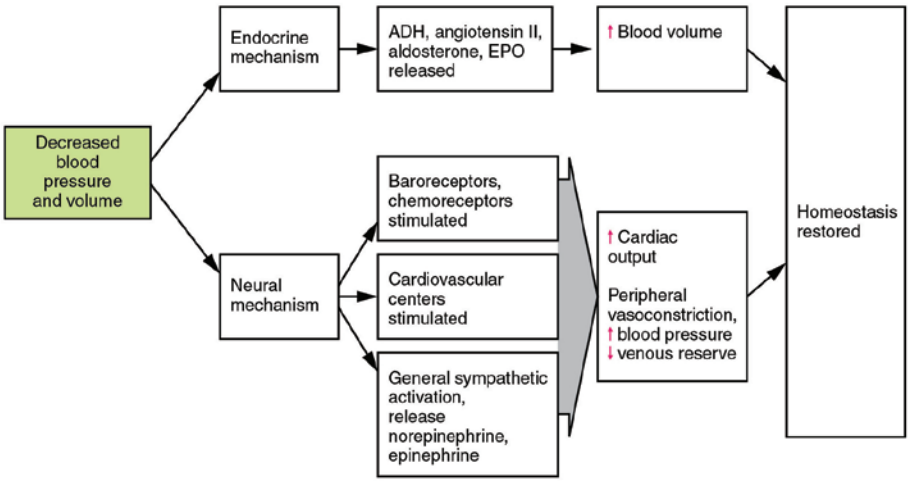


Figure 19.16 Homeostatic Responses to Loss of Blood Volume.

an increased heart rate but decreased blood pressure, but there are cases in which blood pressure will remain normal. Urine output will fall dramatically, and the patient may appear confused or lose consciousness. Urine output of less than 1 mL/kg body weight per hour is cause for concern.

Unfortunately, shock is an example of a positive feedback loop that, if uncorrected, may lead to the death of the patient.

There are several recognized forms of shock:

- **Hypovolemic shock** in adults is typically caused by hemorrhage, although in children it may be caused by fluid losses related to severe vomiting or diarrhea. Other causes for hypovolemic shock include extensive burns, exposure to some toxins, and excessive urine loss related to diabetes insipidus or ketoacidosis. Typically, patients present with a rapid, almost tachycardic heart rate; a weak pulse often described as "thready"; cool, clammy skin, particularly in the extremities, due to restricted peripheral blood flow; rapid, shallow breathing; hypothermia; thirst; and dry mouth. Treatments generally involve providing intravenous fluids to restore the patient to normal function and various drugs such as dopamine, epinephrine, and norepinephrine to raise blood pressure.
- **Cardiogenic shock** results from the inability of the heart to maintain cardiac output. Most often, it results from a myocardial infarction (heart attack), but it may also be caused by arrhythmias, valve disorders, cardiomyopathies, cardiac failure, or simply insufficient flow of blood through the cardiac vessels. Treatment involves repairing the damage to the heart or its vessels to resolve the underlying cause rather than treating cardiogenic shock directly.

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- **Vascular shock** occurs when arterioles lose their normal muscular tone and dilate dramatically. It may arise from a variety of causes, and treatments almost always involve fluid replacement and medications called inotropic or pressor agents, which restore tone to the muscles of the vessels. In addition, eliminating or at least alleviating the underlying cause of the condition is required. This might include antibiotics and antihistamines, or select steroids, which may aid in the repair of nerve damage. A common cause is **sepsis** (or septicemia), also called "blood poisoning," which is a widespread bacterial infection that results in an organismal-level inflammatory response known as **septic shock**. **Neurogenic shock** is a form of vascular shock that occurs with cranial or spinal injuries that damage the cardiovascular centres in the medulla oblongata or the nervous fibres originating from this region. **Anaphylactic shock** is a severe allergic response that causes the widespread release of histamines, triggering vasodilation throughout the body.
- **Obstructive shock**, as the name would suggest, occurs when a significant portion of the vascular system is blocked. It is not always recognized as a distinct condition and may be grouped with cardiogenic shock, including pulmonary embolism and cardiac tamponade. Treatments depend on the underlying cause and, in addition to administering fluids intravenously, often include the administration of anticoagulants, removal of fluid from the pericardial cavity or air from the thoracic cavity, and surgery as required. The most common cause is a pulmonary embolism, a clot that lodges in the pulmonary vessels and interrupts blood flow. Other causes include stenosis of the aortic valve; cardiac tamponade, in which excess fluid in the pericardial cavity interferes with the ability of the heart to fully relax and fill with blood (resulting in decreased preload); and a pneumothorax, in which an excessive amount of air is present in the thoracic cavity, outside of the lungs, which interferes with venous return, pulmonary function, and delivery of oxygen to the tissues.

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19.5 Circulatory Pathways

Learning Objectives

By the end of this section, you will be able to:

- Identify the vessels through which blood travels within the pulmonary circuit, beginning from the right ventricle of the heart and ending at the left atrium
- Create a flowchart showing the major systemic arteries through which blood travels from the aorta and its major branches to the most significant arteries feeding into the right and left upper and lower limbs
- Create a flowchart showing the major systemic veins through which blood travels from the feet to the right atrium of the heart

Virtually every cell, tissue, organ, and system in the body is impacted by the circulatory system. This includes the generalized and more specialized functions of transport of materials, capillary exchange, maintaining health by transporting white blood cells and various immunoglobulins (antibodies), hemostasis, regulation of body temperature, and helping maintain acid-base balance. In addition to these shared functions, many systems enjoy a unique relationship with the circulatory system. Table 19.5 summarizes these relationships.

As you read about circular pathways, notice that there is an occasional, very large artery referred to as a **trunk**, a term indicating that the vessel gives rise to several smaller arteries. For example, the celiac trunk gives rise to the left gastric, common hepatic, and splenic arteries.

Interactive Link 19.4

Visit this site (http://oer.aupress.ca/oer-202505/19.4) for a brief summary of the arteries.

Systemic Circulation

Students are not expected to learn all the blood vessels described in this chapter. However, students need to learn the blood vessels outlined in the Arteries and Veins sections.

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Table 19.5 Interaction of the Circulatory System with Other Body Systems

System	Role of circulatory system
Digestive	Absorbs nutrients and water; delivers nutrients (except most lipids) to liver for processing by hepatic portal vein; provides nutrients essential for hematopoiesis and building hemoglobin
Endocrine	Delivers hormones: atrial natriuretic hormone (peptide) secreted by the heart atrial cells to help regulate blood volumes and pressures; epinephrine, ANH, angiotensin II, ADH, and thyroxine to help regulate blood pressure; estrogen to promote vascular health in women and men
Integumentary	Carries clotting factors, platelets, and white blood cells for hemostasis, fighting infection, and repairing damage; regulates temperature by controlling blood flow to the surface, where heat can be dissipated; provides some colouration of integument; acts as a blood reservoir
Lymphatic	Transports various white blood cells, including those produced by lymphatic tissue, and immunoglobulins (antibodies) throughout the body to maintain health; carries excess tissue fluid not able to be reabsorbed by the vascular capillaries back to the lymphatic system for processing
Muscular	Provides nutrients and oxygen for contraction; removes lactic acid and distributes heat generated by contraction; muscular pumps aid in venous return; exercise contributes to cardiovascular health and helps prevent atherosclerosis
Nervous	Produces cerebrospinal fluid (CSF) within choroid plexuses; contributes to blood-brain barrier; cardiac and vasomotor centres regulate cardiac output and blood flow through vessels via autonomic system
Reproductive	Aids in erection of genitalia in both sexes during sexual arousal; transports gonadotropic hormones that regulate reproductive functions
Respiratory	Provides blood for critical exchange of gases to carry oxygen needed for metabolic reactions and carbon dioxide generated as by-products of these processes
Skeletal	Provides calcium, phosphate, and other minerals critical for bone matrix; transports hormones regulating buildup and absorption of matrix, including growth hormone (somatotropin), thyroid hormone, calcitonin, and parathyroid hormone; erythropoietin stimulates myeloid cell hematopoiesis; some level of protection for select vessels by bony structures
Urinary	Delivers 20% of resting circulation to kidneys for filtering, reabsorption of useful products, and excretion of excesses; regulates blood volume and pressure by regulating fluid loss in the form of urine and by releasing the enzyme renin that is essential in the renin-angiotensin-aldosterone mechanism

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Arteries

Oxygenated blood from the left ventricle is pumped into the aorta, which has three regions:

- Ascending aorta → delivers blood to the right and left coronary arteries.
- Arch of the aorta → delivers blood to three branches:
  - Brachiocephalic trunk → right common carotid artery and right subclavian artery
  - Left common carotid artery → internal and external carotid arteries
  - Left subclavian artery: axillary artery → brachial artery → radial and ulnar arteries
- Descending aorta, which has two regions:
  - Thoracic aorta → bronchial, esophageal, intercostal, and phrenic arteries
  - Abdominal aorta → left gastric, splenic, common hepatic, renal, suprarenal, and gonadal arteries
    → right and left common iliac arteries → internal and external iliac arteries → femoral artery → anterior and posterior arteries.

Veins

The right atrium receives deoxygenated blood directly from three major veins:

- Coronary sinus ← cardiac veins
- Superior vena cava ← right and left brachiocephalic veins ← internal and external jugular veins and subclavian vein ← axillary vein
  - Axillary vein ← cephalic vein
    ← brachial vein ← radial and ulnar veins
- Inferior vena cava ← hepatic veins, right and left renal veins, gonadal veins, and common iliac veins
  - Common iliac veins ← internal and external iliac veins
    - External iliac veins ← femoral vein
      - Femoral vein ← great saphenous vein
        ← anterior and posterior veins

Hepatic Portal System

Nutrient-rich, deoxygenated blood from the digestive organs is carried to the liver by the hepatic portal vein.

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Pulmonary Circulation

Deoxygenated blood from the right ventricle is pumped into the pulmonary trunk, to the right and left pulmonary arteries, to the alveoli of the lungs, to the four pulmonary veins (oxygenated blood), and to the left atrium.

Recall that blood returning from the systemic circuit enters the right atrium (Figure 19.17) via the superior and inferior venae cavae and the coronary sinus, which drains the blood supply of the heart muscle. These vessels will be described more fully later in this section. This blood is relatively low in oxygen and relatively high in carbon dioxide, since much of the oxygen has been extracted for use by the tissues, and the waste gas carbon dioxide was picked up to be transported to the lungs for elimination. From the right atrium, blood moves into the right ventricle, which pumps it to the lungs for gas exchange. This system of vessels is referred to as the **pulmonary circuit**.

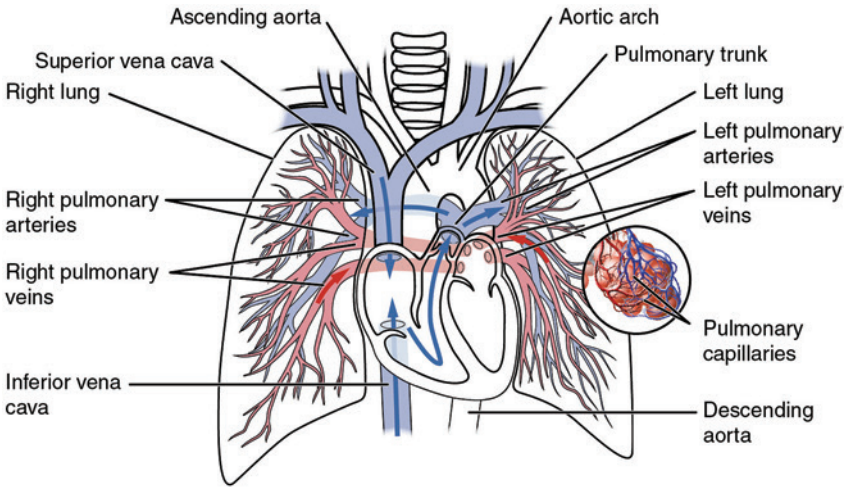


Figure 19.17 Pulmonary Circuit. Blood exiting from the right ventricle flows into the pulmonary trunk, which bifurcates into the two pulmonary arteries. These vessels branch to supply blood to the pulmonary capillaries, where gas exchange occurs within the lung alveoli. Blood returns via the pulmonary veins to the left atrium.

The single vessel exiting the right ventricle is the **pulmonary trunk**. At the base of the pulmonary trunk is the pulmonary semilunar valve, which prevents backflow of blood into the right ventricle during ventricular diastole. As the pulmonary trunk reaches the superior surface of the heart, it curves posteriorly and rapidly bifurcates (divides) into two branches, a left and a right **pulmonary artery**. To prevent confusion between these vessels, it is important to refer to the vessel exiting the heart as the pulmonary trunk rather than also calling it a pulmonary artery. The pulmonary arteries in turn branch many times within

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the lung, forming a series of smaller arteries and arterioles that eventually lead to the pulmonary capillaries. The pulmonary capillaries surround lung structures known as alveoli that are the sites of oxygen and carbon dioxide exchange.

Once gas exchange is completed, oxygenated blood flows from the pulmonary capillaries into a series of pulmonary venules that eventually lead to a series of larger **pulmonary veins**. Four pulmonary veins, two on the left and two on the right, return blood to the left atrium. At this point, the pulmonary circuit is complete. Table 19.6 defines the major arteries and veins of the pulmonary circuit discussed in the text.

Table 19.6 Pulmonary Arteries and Veins

Vessel	Description
Pulmonary trunk	Single large vessel exiting the right ventricle that divides to form the right and left pulmonary arteries
Pulmonary arteries	Left and right vessels that form from the pulmonary trunk and lead to smaller arterioles and eventually to the pulmonary capillaries
Pulmonary veins	Two sets of paired vessels—one pair on each side—that are formed from the small venules, leading away from the pulmonary capillaries to flow into the left atrium

Overview of Systemic Arteries

Blood relatively high in oxygen concentration is returned from the pulmonary circuit to the left atrium via the four pulmonary veins. From the left atrium, blood moves into the left ventricle, which pumps blood into the aorta. The aorta and its branches—the systemic arteries—send blood to virtually every organ of the body (Figure 19.18).

The Aorta

The **aorta** is the largest artery in the body (Figure 19.19). It arises from the left ventricle and eventually descends to the abdominal region, where it bifurcates at the level of the fourth lumbar vertebra into the two common iliac arteries. The aorta consists of the ascending aorta, the aortic arch, and the descending aorta, which passes through the diaphragm and a landmark that divides into the superior thoracic and inferior abdominal components. Arteries originating from the aorta ultimately distribute blood to virtually all tissues of the body. At the base of the aorta is the aortic semilunar valve that prevents backflow of blood into the left ventricle while the heart is relaxing. After exiting the heart,

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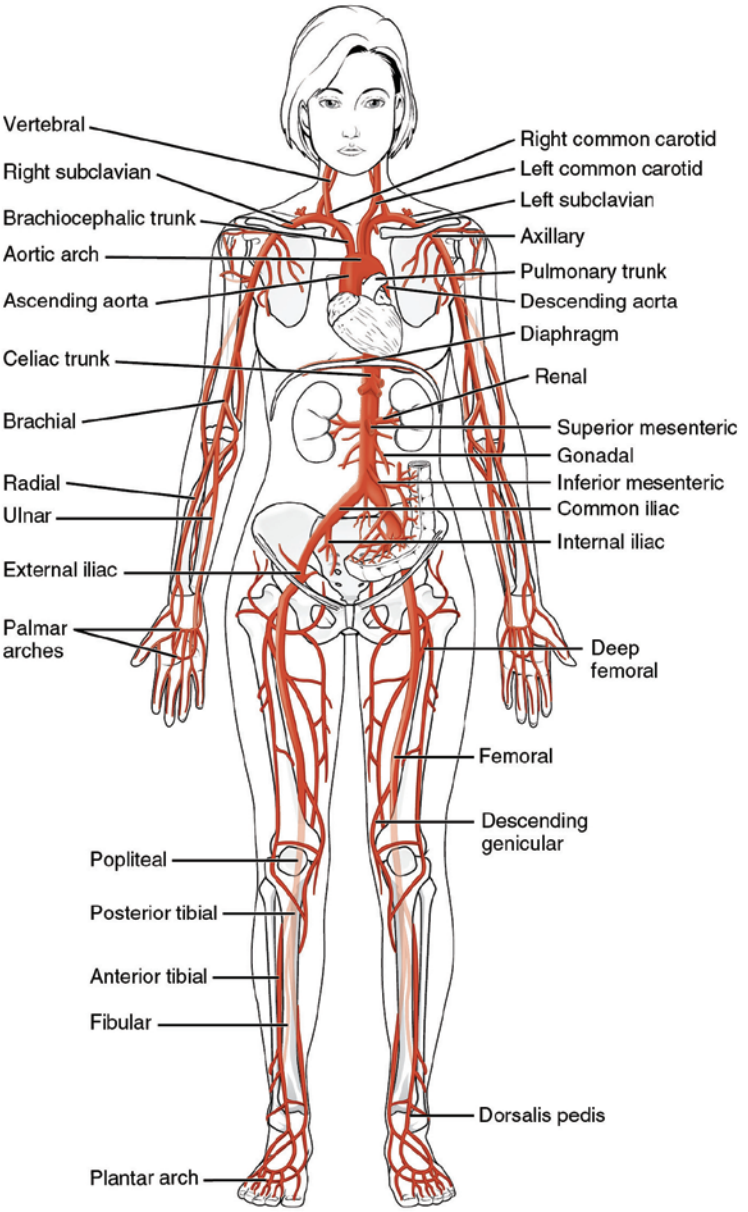


Figure 19.18 Systemic Arteries. The major systemic arteries shown here deliver oxygenated blood throughout the body.

the **ascending aorta** moves in a superior direction for approximately 5 cm and ends at the sternal angle. Following this ascent, it reverses direction, forming a graceful arc to the left called the **aortic arch**. The aortic arch descends toward the inferior portions of the body and ends at the level of the intervertebral disk between the fourth and fifth thoracic vertebrae. Beyond this point, the **descending aorta** continues close to the bodies of the vertebrae and passes

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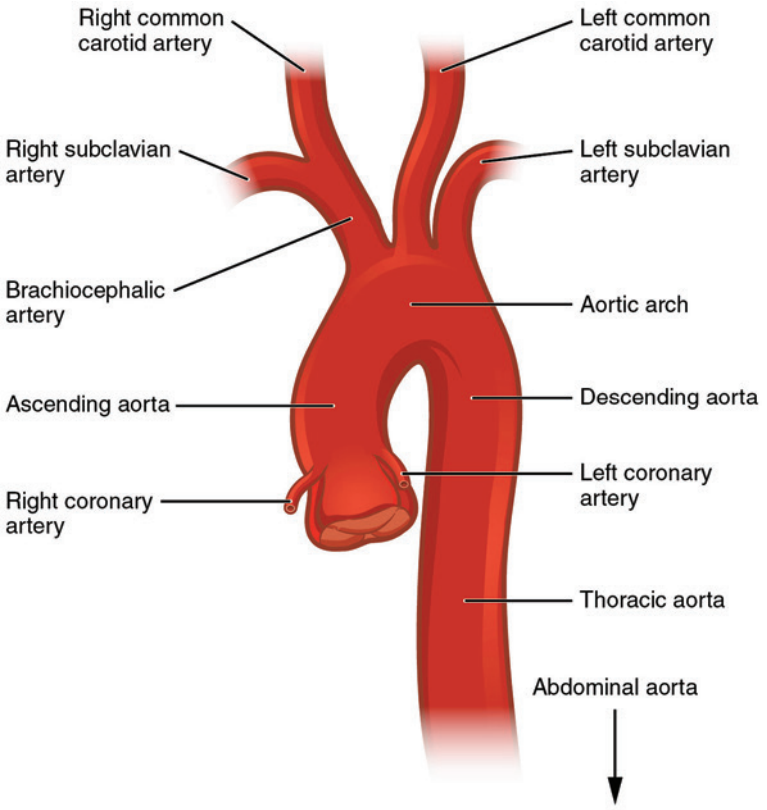


Figure 19.19 Aorta. The aorta has distinct regions, including the ascending aorta, the aortic arch, and the descending aorta, which includes the thoracic and abdominal regions.

through an opening in the diaphragm known as the **aortic hiatus**. Superior to the diaphragm, the aorta is called the **thoracic aorta**, and inferior to the diaphragm, it is called the **abdominal aorta**. The abdominal aorta terminates when it bifurcates into the two common iliac arteries at the level of the fourth lumbar vertebra. See Figure 19.19 for an illustration of the ascending aorta, the aortic arch, and the initial segment of the descending aorta plus major branches; Table 19.7 summarizes the structures of the aorta.

Coronary Circulation

The first vessels that branch from the ascending aorta are the paired coronary arteries (see Figure 19.19), which arise from two of the three sinuses in the ascending aorta just superior to the aortic semilunar valve. These sinuses contain the aortic baroreceptors and chemoreceptors critical to maintaining cardiac function. The left coronary artery arises from the left posterior aortic sinus. The right coronary artery arises from the anterior aortic sinus. Normally, the right posterior aortic sinus does not give rise to a vessel.

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Table 19.7 Components of the Aorta

Vessel	Description
Aorta	Largest artery in the body, originating from the left ventricle and descending to the abdominal region, where it bifurcates into the common iliac arteries at the level of the fourth lumbar vertebra; arteries originating from the aorta distribute blood to virtually all tissues of the body
Ascending aorta	Initial portion of the aorta, rising superiorly from the left ventricle for a distance of approximately 5 cm
Aortic arch	Graceful arc to the left that connects the ascending aorta to the descending aorta; ends at the intervertebral disk between the fourth and fifth thoracic vertebrae
Descending aorta	Portion of the aorta that continues inferiorly past the end of the aortic arch; subdivided into the thoracic aorta and the abdominal aorta
Thoracic aorta	Portion of the descending aorta superior to the aortic hiatus
Abdominal aorta	Portion of the aorta inferior to the aortic hiatus and superior to the common iliac arteries

The coronary arteries encircle the heart, forming a ring-like structure that divides into the next level of branches that supplies blood to the heart tissues. (Seek additional content for more detail on cardiac circulation.)

Aortic Arch Branches

There are three major branches of the aortic arch: the brachiocephalic artery, the left common carotid artery, and the left subclavian (literally "under the clavicle") artery. As you would expect based on proximity to the heart, each of these vessels is classified as an elastic artery.

The **brachiocephalic artery** is located only on the right side of the body; there is no corresponding artery on the left. The brachiocephalic artery branches into the right subclavian artery and the right common carotid artery. The left subclavian and left common carotid arteries arise independently from the aortic arch but otherwise follow a similar pattern and distribution to the corresponding arteries on the right side (see Figure 19.17).

Each **subclavian artery** supplies blood to the arms, chest, shoulders, back, and central nervous system. It then gives rise to three major branches: the internal thoracic artery, the vertebral artery, and the thyrocervical artery.

The **common carotid artery** divides into internal and external carotid arteries. The right common carotid artery arises from the brachiocephalic artery, and the left common carotid artery arises directly from the aortic arch. The

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external carotid artery supplies blood to numerous structures within the face, lower jaw, neck, esophagus, and larynx. These branches include the lingual, facial, occipital, maxillary, and superficial temporal arteries. The **internal carotid artery** initially forms an expansion known as the carotid sinus, containing the carotid baroreceptors and chemoreceptors. Like their counterparts in the aortic sinuses, the information provided by these receptors is critical to maintaining cardiovascular homeostasis (see Figure 19.20).

The internal carotid arteries along with the vertebral arteries are the two primary suppliers of blood to the human brain. Given the central role and vital importance of the brain to life, it is critical that blood supply to this organ remains uninterrupted. Recall that blood flow to the brain is remarkably

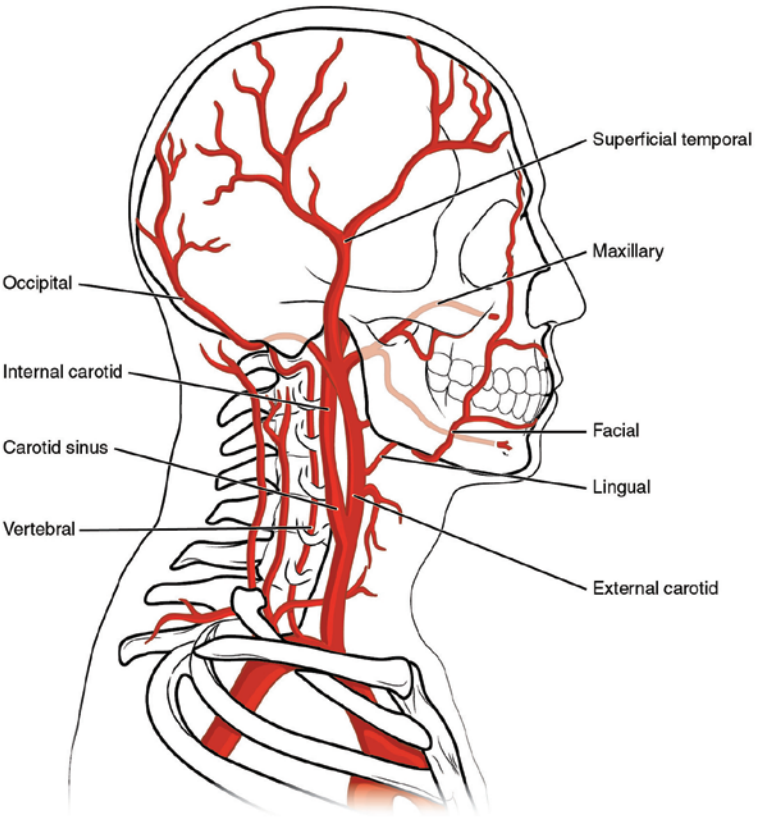


Figure 19.20 Arteries Supplying the Head and Neck. The common carotid artery gives rise to the external and internal carotid arteries. The external carotid artery remains superficial and gives rise to many arteries of the head. The internal carotid artery first forms the carotid sinus and then reaches the brain via the carotid canal and carotid foramen, emerging into the cranium via the foramen lacerum. The vertebral artery branches from the subclavian artery and passes through the transverse foramen in the cervical vertebrae, entering the base of the skull at the vertebral foramen. The subclavian artery continues toward the arm as the axillary artery.

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Table 19.8 Aortic Arch Branches and Brain Circulation

Vessel	Description
Brachiocephalic artery	Single vessel located on the right side of the body; the first vessel branching from the aortic arch; gives rise to the right subclavian artery and the right common carotid artery; supplies blood to the head, neck, upper limbs, and wall of the thoracic region
Subclavian artery	The right subclavian artery arises from the brachiocephalic artery, while the left subclavian artery arises from the aortic arch; gives rise to the internal thoracic, vertebral, and thyrocervical arteries; supplies blood to the arms, chest, shoulders, back, and central nervous system
Common carotid artery	The right common carotid artery arises from the brachiocephalic artery, and the left common carotid artery arises from the aortic arch; each gives rise to the external and internal carotid arteries; supplies the respective sides of the head and neck
External carotid artery	Arises from the common carotid artery; supplies blood to numerous structures within the face, lower jaw, neck, esophagus, and larynx
Internal carotid artery	Arises from the common carotid artery and begins with the carotid sinus; goes through the carotid canal of the temporal bone to the base of the brain; combines with the branches of the vertebral artery, forming the arterial circle; supplies blood to the brain

constant, with approximately 20 percent of blood flow directed to this organ at any given time. When blood flow is interrupted, even for just a few seconds, a **transient ischemic attack** (**TIA**), or ministroke, may occur, resulting in loss of consciousness or temporary loss of neurological function. In some cases, the damage may be permanent. Loss of blood flow for longer periods, typically between 3 and 4 minutes, will likely produce irreversible brain damage or a stroke, also called a **cerebrovascular accident** (**CVA**). The locations of the arteries in the brain not only provide blood flow to the brain tissue but also prevent interruption in the flow of blood.

Thoracic Aorta and Major Branches

The thoracic aorta begins at the level of vertebra T5 and continues through to the diaphragm at the level of T12, initially travelling within the mediastinum to the left of the vertebral column. As it passes through the thoracic region, the thoracic aorta gives rise to several branches, which are collectively referred to as visceral branches and parietal branches (Figure 19.21). Those branches that supply blood primarily to visceral organs are known as the **visceral branches**

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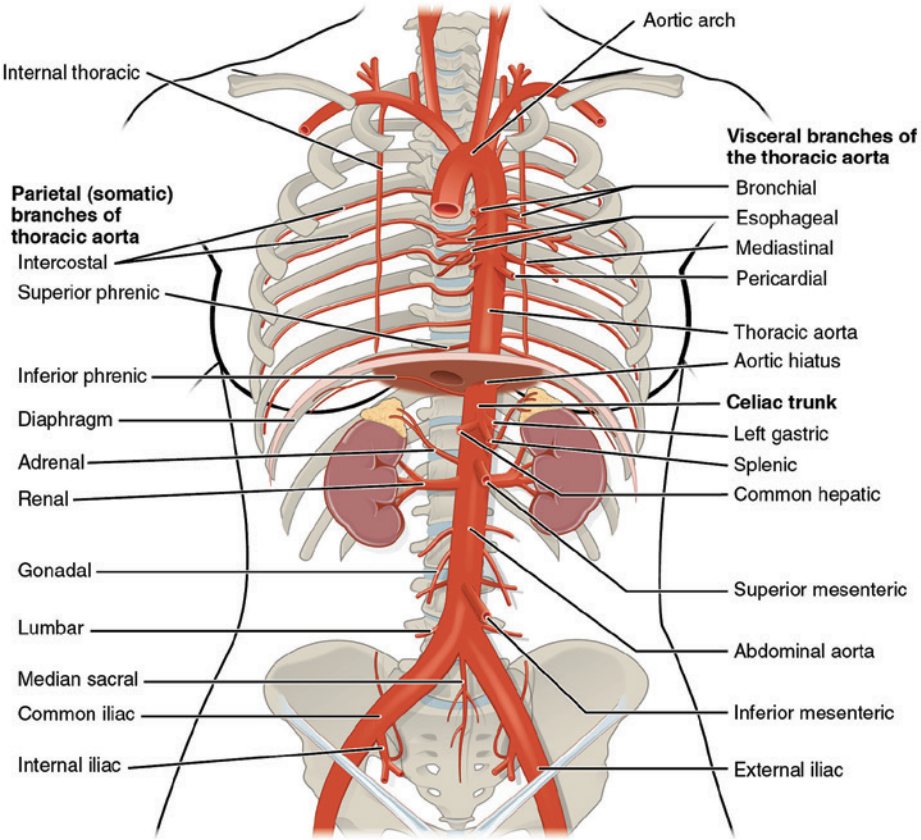


Figure 19.21 Arteries of the Thoracic and Abdominal Regions. The thoracic aorta gives rise to the arteries of the visceral and parietal branches.

and include the bronchial arteries, pericardial arteries, esophageal arteries, and mediastinal arteries, each named after the tissues they supply. Each **bronchial artery** (typically two on the left and one on the right) supplies systemic blood to the lungs and visceral pleura, in addition to the blood pumped to the lungs for oxygenation via the pulmonary circuit. The bronchial arteries follow the same path as the respiratory branches, beginning with the bronchi and ending with the bronchioles. There is considerable, but not total, intermingling of the systemic and pulmonary blood at anastomoses in the smaller branches of the lungs. This may sound incongruous—that is, the mixing of systemic arterial blood high in oxygen with the pulmonary arterial blood lower in oxygen—but the systemic vessels also deliver nutrients to the lung tissue just as they do elsewhere in the body. The mixed blood drains into typical pulmonary veins, whereas the bronchial artery branches remain separate and drain into bronchial veins described later. The **mediastinal artery** provides blood to the mediastinum. The remaining thoracic aorta branches are collectively

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referred to as **parietal branches** or somatic branches and include the intercostal and superior phrenic arteries. Each **intercostal artery** provides blood to the muscles of the thoracic cavity and vertebral column. Table 19.9 lists the arteries of the thoracic region.

Table 19.9 Arteries of the Thoracic Region

Vessel	Description
Visceral branches	A group of arterial branches of the thoracic aorta; supply blood to the viscera (i.e., organs) of the thorax
Bronchial artery	Systemic branch from the aorta that provides oxygenated blood to the lungs; this blood supply is in addition to the pulmonary circuit that brings blood for oxygenation
Mediastinal artery	Branch of the thoracic aorta; supplies blood to the mediastinum
Parietal branches	Also called somatic branches, a group of arterial branches of the thoracic aorta; include those that supply blood to the thoracic wall, the vertebral column, and the superior surface of the diaphragm
Intercostal artery	Branch of the thoracic aorta; supplies blood to the muscles of the thoracic cavity and vertebral column

Abdominal Aorta and Major Branches

After crossing through the diaphragm at the aortic hiatus, the thoracic aorta is called the abdominal aorta (see Figure 19.21). This vessel remains to the left of the vertebral column and is embedded in adipose tissue behind the peritoneal cavity. It formally ends at approximately the level of vertebra L4, where it bifurcates to form the common iliac arteries. Before this division, the abdominal aorta gives rise to several important branches. A single **celiac trunk** (artery) emerges and divides into the **left gastric artery** to supply blood to the stomach and esophagus, the **splenic artery** to supply blood to the spleen, and the **common hepatic artery**.

The **adrenal artery** supplies blood to the adrenal (suprarenal) glands and arises near the superior mesenteric artery. Each **renal artery** branches approximately 2.5 cm inferior to the superior mesenteric arteries and supplies a kidney. The right renal artery is longer than the left, since the aorta lies to the left of the vertebral column and the vessel must travel a greater distance to reach its target. Renal arteries branch repeatedly to supply blood to the kidneys. Each **gonadal artery** supplies blood to the gonads, or reproductive organs, and is also described as either an ovarian artery or a testicular artery (internal spermatic) depending on the sex of the individual.

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The aorta divides at approximately the level of vertebra L4 into a left and a right **common iliac artery**. The common iliac arteries provide blood to the pelvic region and ultimately to the lower limbs. They split into external and internal iliac arteries approximately at the level of the lumbar-sacral articulation. Each **internal iliac artery** sends branches to the urinary bladder, the walls of the pelvis, the external genitalia, and the medial portion of the femoral region. In females, they also provide blood to the uterus and vagina. The much larger **external iliac artery** supplies blood to each of the lower limbs. Figure 19.22 shows the distribution of the major branches of the aorta into the thoracic and abdominal regions. Figure 19.23 shows the distribution of the major branches of the common iliac arteries. Table 19.10 summarizes the major branches of the abdominal aorta.

Table 19.10 Vessels of the Abdominal Aorta

Vessel	Description
Celiac trunk	Also called the celiac artery; a major branch of the abdominal aorta; gives rise to the left gastric artery, the splenic artery, and the common hepatic artery that forms the hepatic artery to the liver, the right gastric artery to the stomach, and the cystic artery to the gall bladder
Left gastric artery	Branch of the celiac trunk; supplies blood to the stomach
Splenic artery	Branch of the celiac trunk; supplies blood to the spleen
Common hepatic artery	Branch of the celiac trunk that forms the hepatic artery, the right gastric artery, and the cystic artery
Adrenal artery	Branch of the abdominal aorta; supplies blood to the adrenal (suprarenal) glands
Renal artery	Branch of the abdominal aorta; supplies each kidney
Gonadal artery	Branch of the abdominal aorta; supplies blood to the gonads or reproductive organs; also described as ovarian arteries or testicular arteries, depending on the sex of the individual
Common iliac artery	Branch of the aorta that leads to the internal and external iliac arteries
Internal iliac artery	Branch from the common iliac arteries; supplies blood to the urinary bladder, walls of the pelvis, external genitalia, and the medial portion of the femoral region; in females, also provides blood to the uterus and vagina
External iliac artery	Branch of the common iliac artery that leaves the body cavity and becomes a femoral artery; supplies blood to the lower limbs

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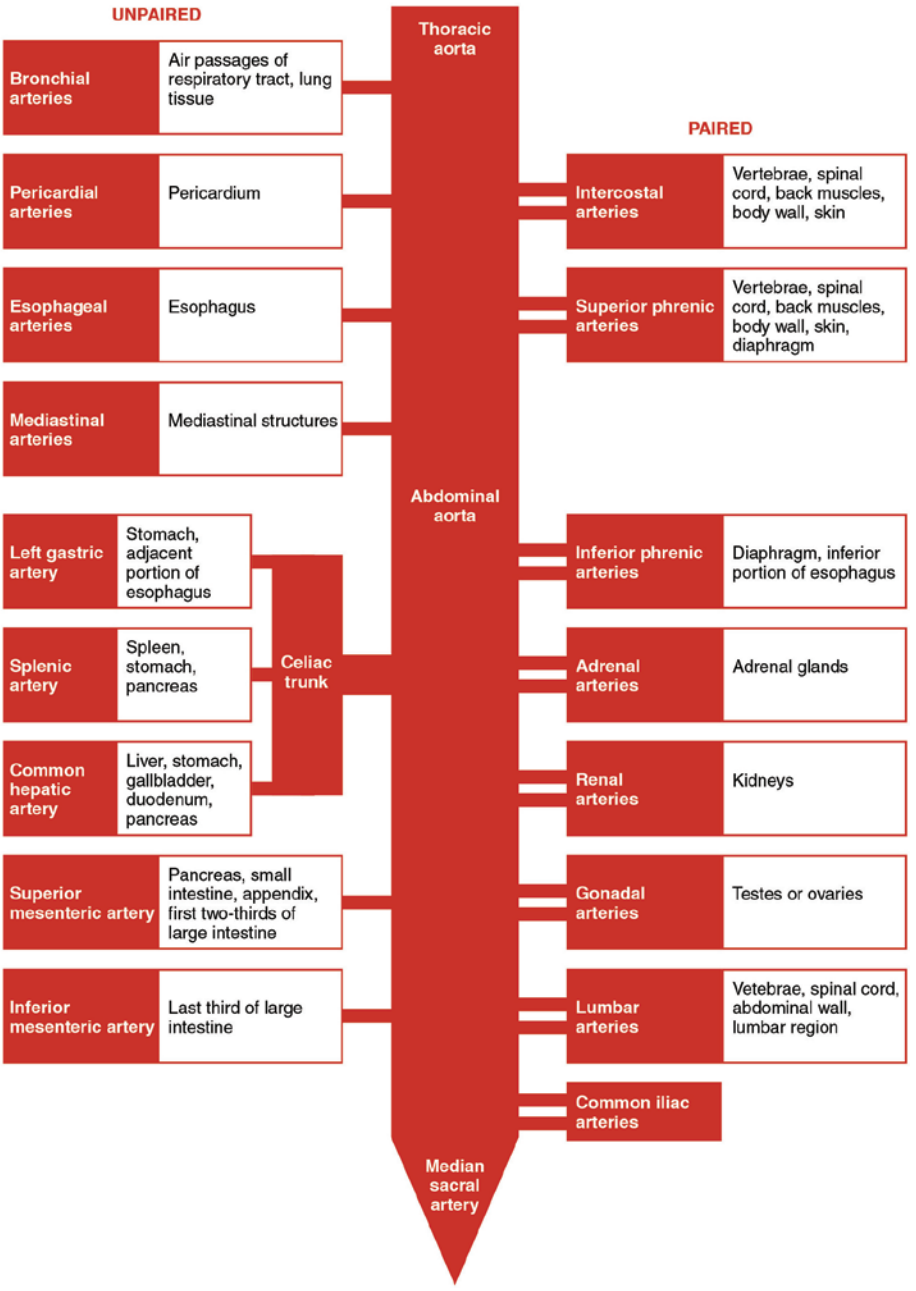


Figure 19.22 Major Branches of the Aorta. The flowchart summarizes the distribution of the major branches of the aorta into the thoracic and abdominal regions.

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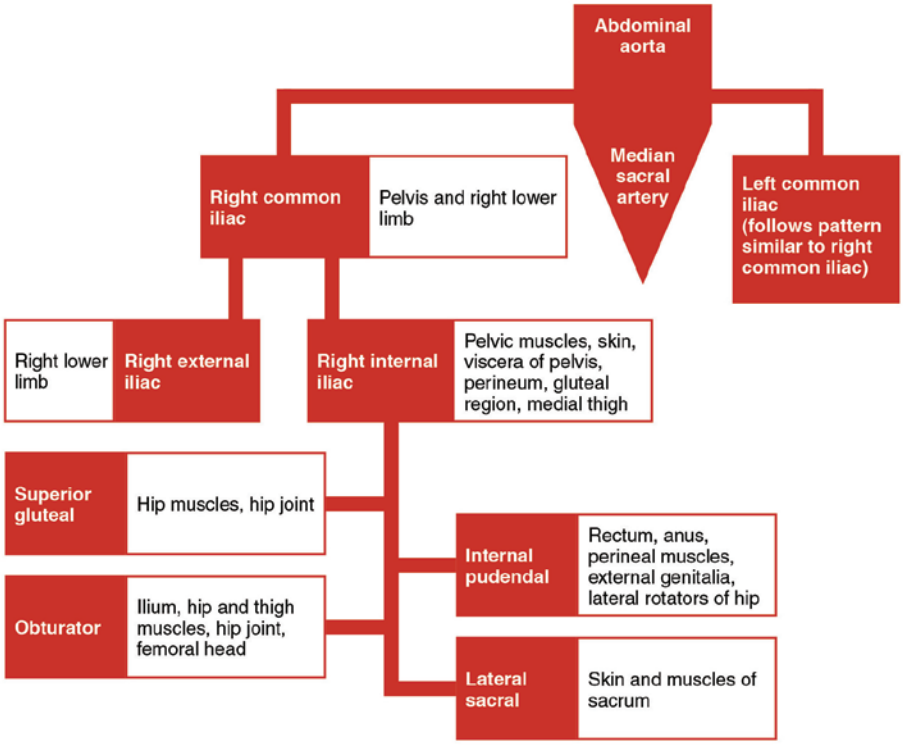


Figure 19.23 Major Branches of the Iliac Arteries. The flowchart summarizes the distribution of the major branches of the common iliac arteries into the pelvis and lower limbs. The left side follows a similar pattern to the right.

Arteries Serving the Upper Limbs

As the subclavian artery exits the thorax into the axillary region, it is renamed the **axillary artery**. Although it does branch and supply blood to the region near the head of the humerus (via the humeral circumflex arteries), the majority of the vessel continues into the upper arm, or brachium, and becomes the brachial artery (Figure 19.24). The **brachial artery** supplies blood to much of the brachial region and divides at the elbow into several smaller branches, including the deep brachial arteries, which provide blood to the posterior surface of the arm, and the ulnar collateral arteries, which supply blood to the region of the elbow. As the brachial artery approaches the coronoid fossa, it bifurcates into the radial and ulnar arteries, which continue into the forearm, or antebrachium. The **radial artery** and **ulnar artery** parallel their namesake bones, giving off smaller branches until they reach the wrist, or carpal region. Figure 19.25 shows the distribution of systemic arteries from the heart into the upper limb. Table 19.11 summarizes the arteries serving the upper limbs.

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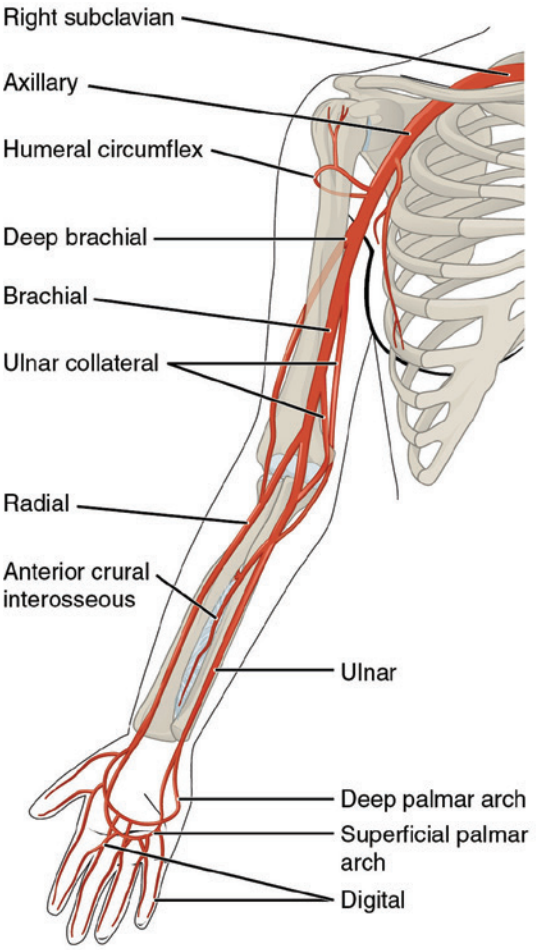


Figure 19.24 Major Arteries Serving the Thorax and Upper Limb. The arteries that supply blood to the arms and hands are extensions of the subclavian arteries.

Arteries Serving the Lower Limbs

The external iliac artery exits the body cavity and enters the femoral region of the lower leg (Figure 19.26). As it passes through the body wall, it is renamed the **femoral artery**.

The **anterior tibial artery** is located between the tibia and fibula and supplies blood to the muscles and integument of the anterior tibial region. Figure 19.27 shows the distribution of the major systemic arteries in the lower limb. Table 19.12 summarizes the major systemic arteries discussed in the text.

Overview of Systemic Veins

Systemic veins return blood to the right atrium. Since the blood has already passed through the systemic capillaries, it will be relatively low in oxygen

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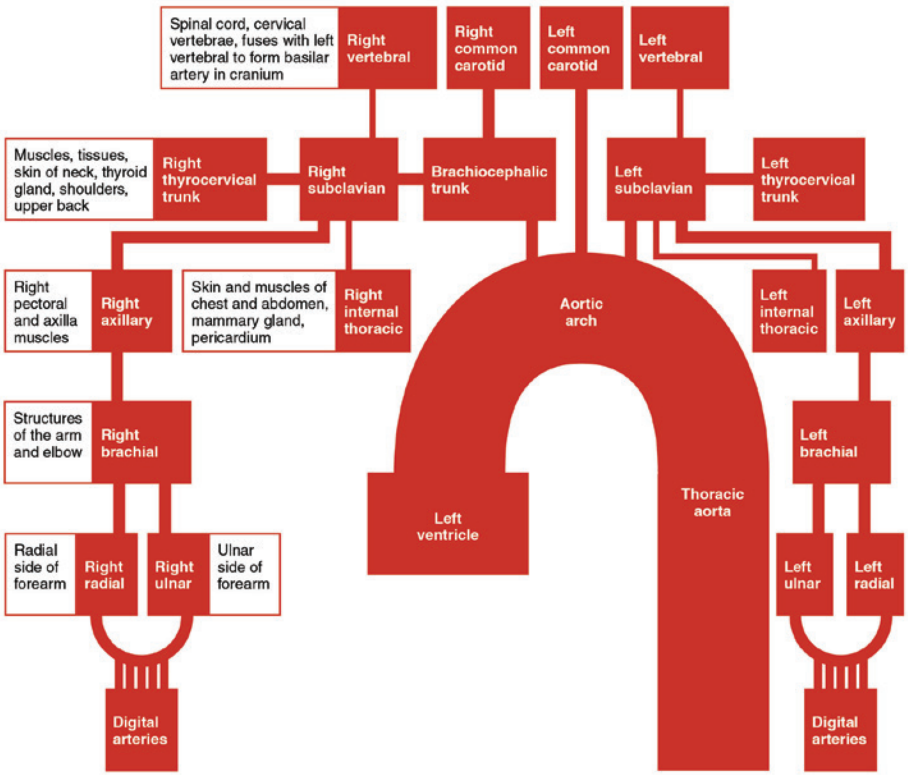


Figure 19.25 Major Arteries of the Upper Limb. The flowchart summarizes the distribution of the major arteries from the heart into the upper limb.

Table 19.11 Arteries Serving the Upper Limbs

Vessel	Description
Axillary artery	Continuation of the subclavian artery as it penetrates the body wall and enters the axillary region; supplies blood to the region near the head of the humerus (humeral circumflex arteries); the majority of the vessel continues into the brachium and becomes the brachial artery
Brachial artery	Continuation of the axillary artery in the brachium; supplies blood to much of the brachial region; gives off several smaller branches that provide blood to the posterior surface of the arm in the region of the elbow; bifurcates into the radial and ulnar arteries at the coronoid fossa
Radial artery	Formed at the bifurcation of the brachial artery; parallels the radius; gives off smaller branches until it reaches the carpal region, where it fuses with the ulnar artery to form the superficial and deep palmar arches; supplies blood to the lower arm and carpal region
Ulnar artery	Formed at the bifurcation of the brachial artery; parallels the ulna; gives off smaller branches until it reaches the carpal region, where it fuses with the radial artery to form the superficial and deep palmar arches; supplies blood to the lower arm and carpal region

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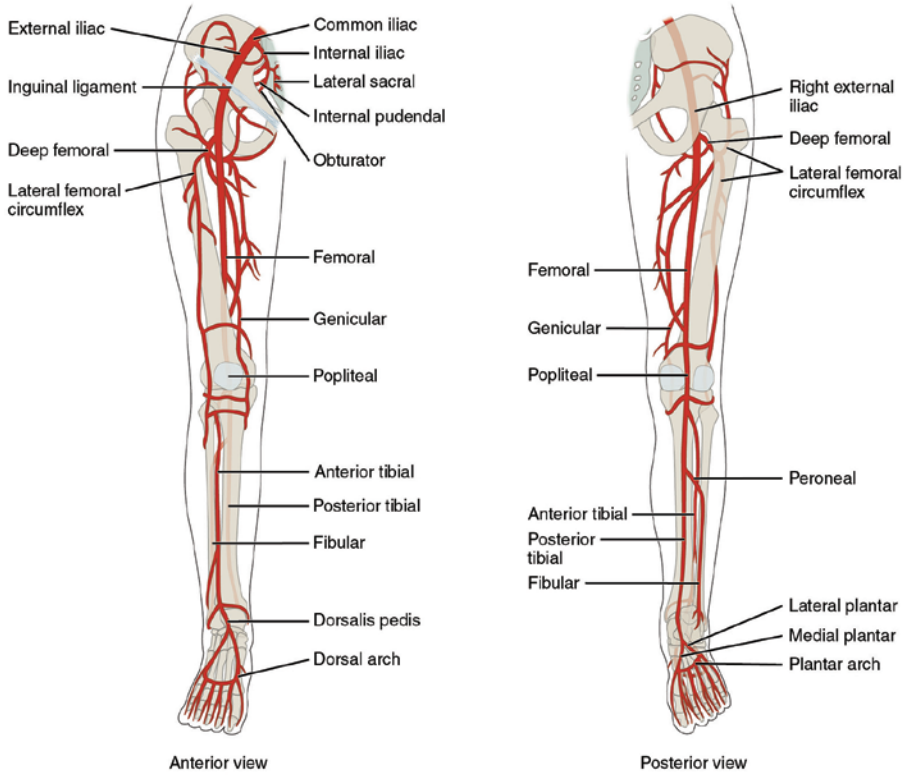


Figure 19.26 Major Arteries Serving the Lower Limb. Major arteries serving the lower limb are shown in anterior and posterior views.

Table 19.12 Arteries Serving the Lower Limbs

Vessel	Description
Femoral artery	Continuation of the external iliac artery after it passes through the body cavity; divides into several smaller branches, the lateral deep femoral artery, and the genicular artery; becomes the popliteal artery as it passes posterior to the knee
Anterior tibial artery	Branches from the popliteal artery; supplies blood to the anterior tibial region; becomes the dorsalis pedis artery

concentration. In many cases, there will be veins draining organs and regions of the body with the same name as the arteries that supplied these regions, and the two often parallel one another. This is often described as a "complementary" pattern. However, there is a great deal more variability in the venous circulation than normally occurs in the arteries. For the sake of brevity and clarity, this text will discuss only the most commonly encountered patterns.

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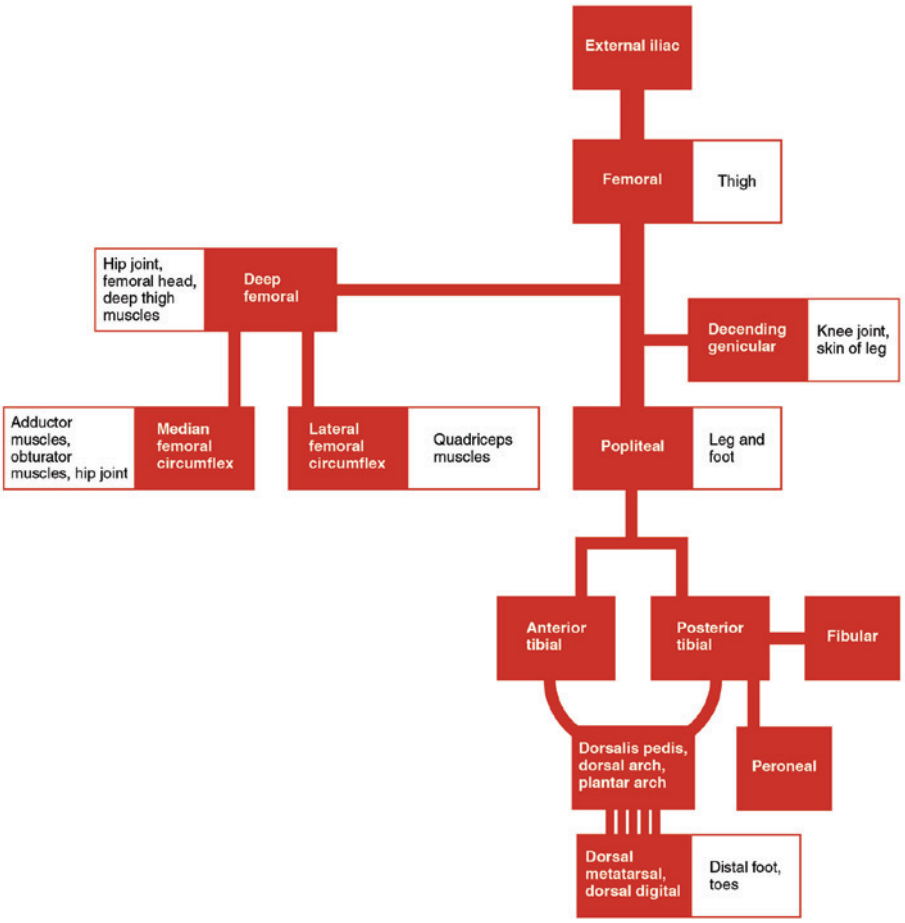


Figure 19.27 Systemic Arteries of the Lower Limb. The flowchart summarizes the distribution of the systemic arteries from the external iliac artery into the lower limb.

However, keep this variation in mind when you move from the classroom to clinical practice.

In both the neck and limb regions, there are often both superficial and deeper levels of veins. The deeper veins generally correspond to the complementary arteries. The superficial veins do not normally have direct arterial counterparts, but in addition to returning blood, they also make contributions to the maintenance of body temperature. When the ambient temperature is warm, more blood is diverted to the superficial veins, where heat can be more easily dissipated to the environment. In colder weather, there is more constriction of the superficial veins, and blood is diverted deeper, where the body can retain more of the heat. From the capillaries, we move into the smallest veins and follow the direction of blood flow into larger veins and back to the heart. Figure 19.28 outlines the path of the major systemic veins.

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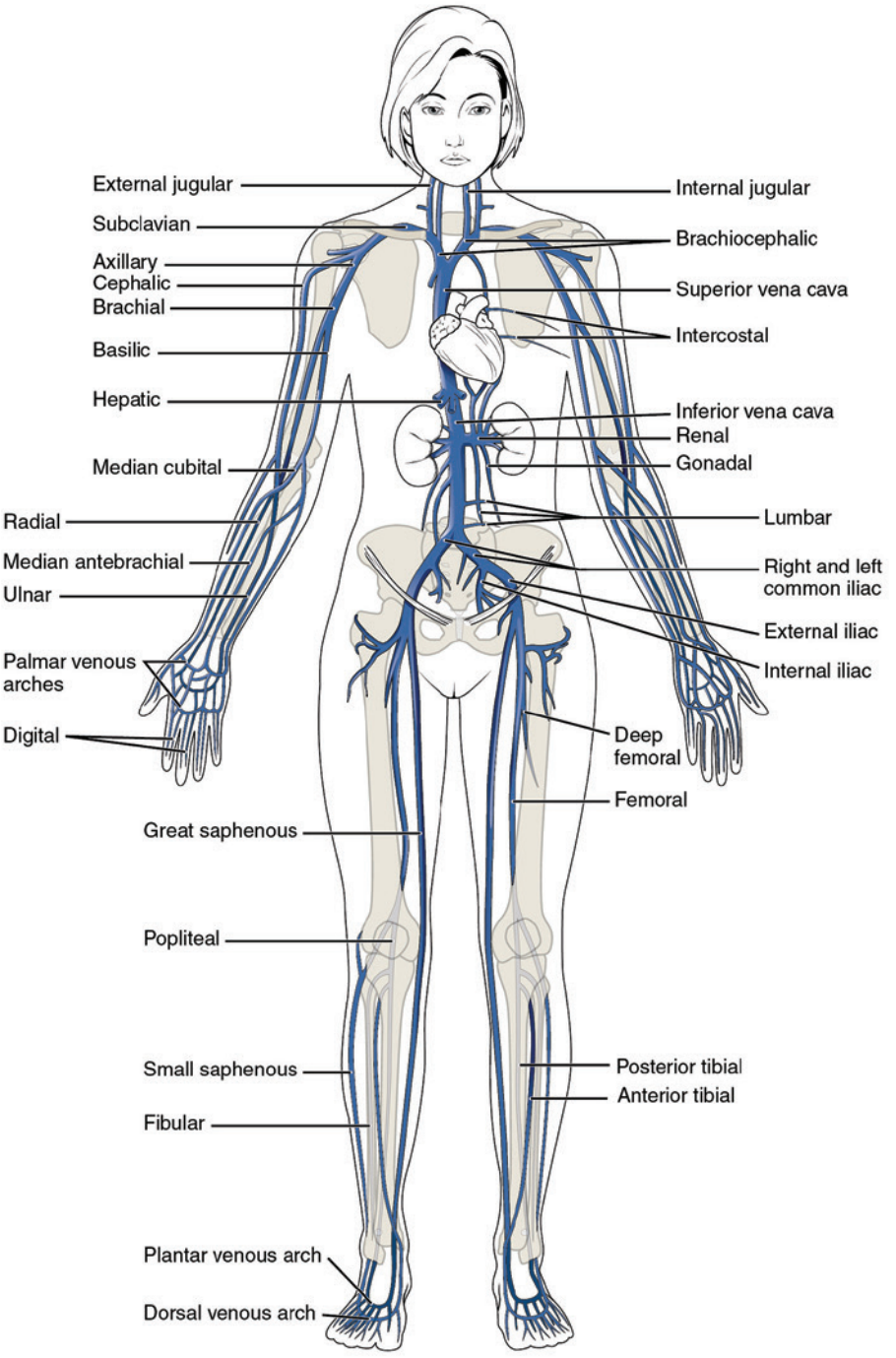


Figure 19.28 Major Systemic Veins of the Body. The major systemic veins of the body are shown here in an anterior view.

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Interactive Link 19.5

Visit this site (http://oer.aupress.ca/oer-202505/19.5) for a brief online summary of the veins.

The right atrium receives all of the systemic venous return. Most of the blood flows into either the superior vena cava or inferior vena cava. If you draw an imaginary line at the level of the diaphragm, systemic venous circulation from above that line will generally flow into the superior vena cava; this includes blood from the head, neck, chest, shoulders, and upper limbs. The exception to this is that most venous blood flow from the coronary veins passes directly into the coronary sinus and from there directly into the right atrium. Beneath the diaphragm, systemic venous flow enters the inferior vena cava—that is, blood from the abdominal and pelvic regions and the lower limbs.

The Superior Vena Cava

The **superior vena cava** drains most of the body superior to the diaphragm (Figure 19.29). On both the left and right sides, the **subclavian vein** forms when the axillary vein passes through the body wall from the axillary region. It fuses with the external and internal jugular veins from the head and neck to form the **brachiocephalic vein**. Each **internal thoracic vein**, also known as an internal mammary vein, drains the anterior surface of the chest wall and flows into the brachiocephalic vein.

The remainder of the blood supply from the thorax drains into the azygos vein. **Bronchial veins** carry approximately 13 percent of the blood that flows into the bronchial arteries; the remainder intermingles with the pulmonary circulation and returns to the heart via the pulmonary veins. These veins flow into the **azygos vein**, which drains blood from the thoracic region. The hemiazygos vein does not drain directly into the superior vena cava but enters the brachiocephalic vein via the superior intercostal vein.

The azygos vein passes through the diaphragm from the thoracic cavity on the right side of the vertebral column and begins in the lumbar region of the thoracic cavity. It flows into the superior vena cava at approximately the level of T2, making a significant contribution to the flow of blood. It combines with the two large left and right brachiocephalic veins to form the superior vena cava.

Table 19.13 summarizes the veins of the thoracic region that flow into the superior vena cava.

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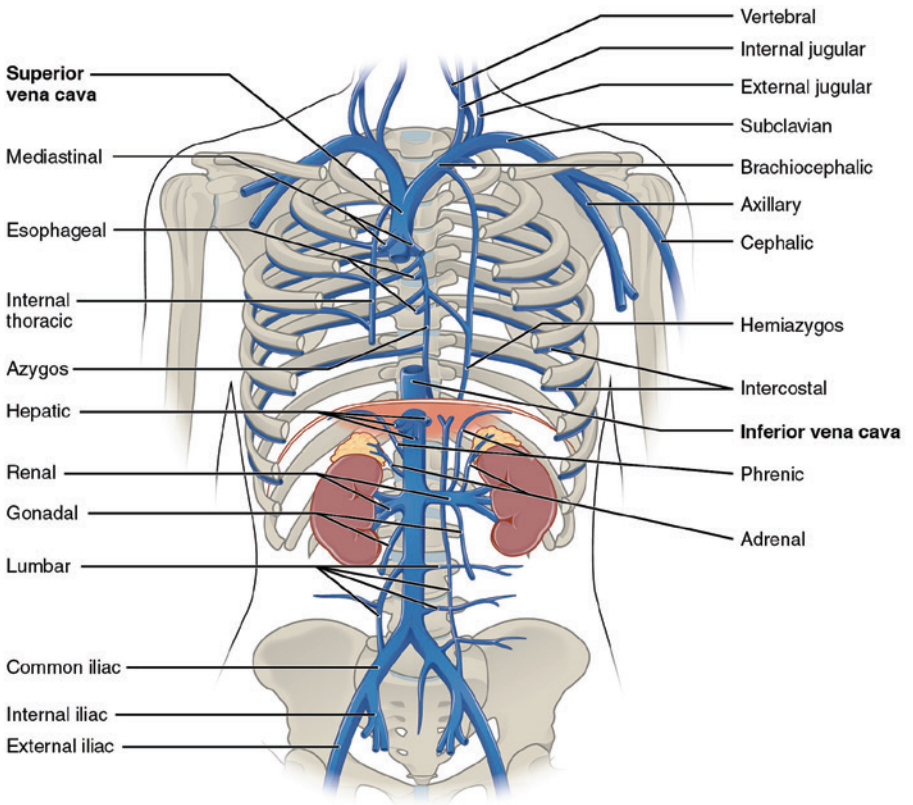


Figure 19.29 Veins of the Thoracic and Abdominal Regions. Veins of the thoracic and abdominal regions drain blood from the area above the diaphragm, returning it to the right atrium via the superior vena cava.

Veins of the Head and Neck

Blood from the brain and the superficial facial vein flow into each **internal jugular vein** (Figure 19.30). Blood from the more superficial portions of the head, scalp, and cranial regions flows into each **external jugular vein**. Although the external and internal jugular veins are separate vessels, there are anastomoses between them close to the thoracic region. Blood from the external jugular vein empties into the subclavian vein. Table 19.14 summarizes the major veins of the head and neck.

Venous Drainage of the Brain

Circulation to the brain is both critical and complex (see Figure 19.30). Many smaller veins of the brain stem and the superficial veins of the cerebrum lead to larger vessels referred to as intracranial sinuses. Ultimately, sinuses will lead back to either the inferior jugular vein or the vertebral vein.

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Table 19.13 Veins of the Thoracic Region

Vessel	Description
Superior vena cava	Large systemic vein; drains blood from most areas superior to the diaphragm; empties into the right atrium
Subclavian vein	Located deep in the thoracic cavity; formed by the axillary vein as it enters the thoracic cavity from the axillary region; drains the axillary and smaller local veins near the scapular region and leads to the brachiocephalic vein
Brachiocephalic veins	Pair of veins that forms from a fusion of the external and internal jugular veins and the subclavian vein; subclavian, external and internal jugular, vertebral, and internal thoracic veins flow into it; drain the upper thoracic region and lead to the superior vena cava
Internal thoracic veins	Also called internal mammary veins; drain the anterior surface of the chest wall and lead to the brachiocephalic vein
Bronchial vein	Drains the systemic circulation from the lungs and leads to the azygos vein
Azygos vein	Originates in the lumbar region and passes through the diaphragm into the thoracic cavity on the right side of the vertebral column; drains blood from the intercostal veins, esophageal veins, bronchial veins, and other veins draining the mediastinal region and leads to the superior vena cava

Table 19.14 Major Veins of the Head and Neck

Vessel	Description
Internal jugular vein	Parallel to the common carotid artery, which is more or less its counterpart, and passes through the jugular foramen and canal; primarily drains blood from the brain, receives the superficial facial vein, and empties into the subclavian vein
External jugular vein	Drains blood from the more superficial portions of the head, scalp, and cranial regions and leads to the subclavian vein

Most of the veins on the superior surface of the cerebrum flow into the largest of the sinuses, the **superior sagittal sinus**. It is located midsagittally between the meningeal and periosteal layers of the dura mater within the falx cerebri and, at first glance in images or models, can be mistaken for the subarachnoid space. Most reabsorption of cerebrospinal fluid occurs via the chorionic villi (arachnoid granulations) into the superior sagittal sinus. Blood from most of the smaller vessels originating from the inferior cerebral veins flows into the **great**

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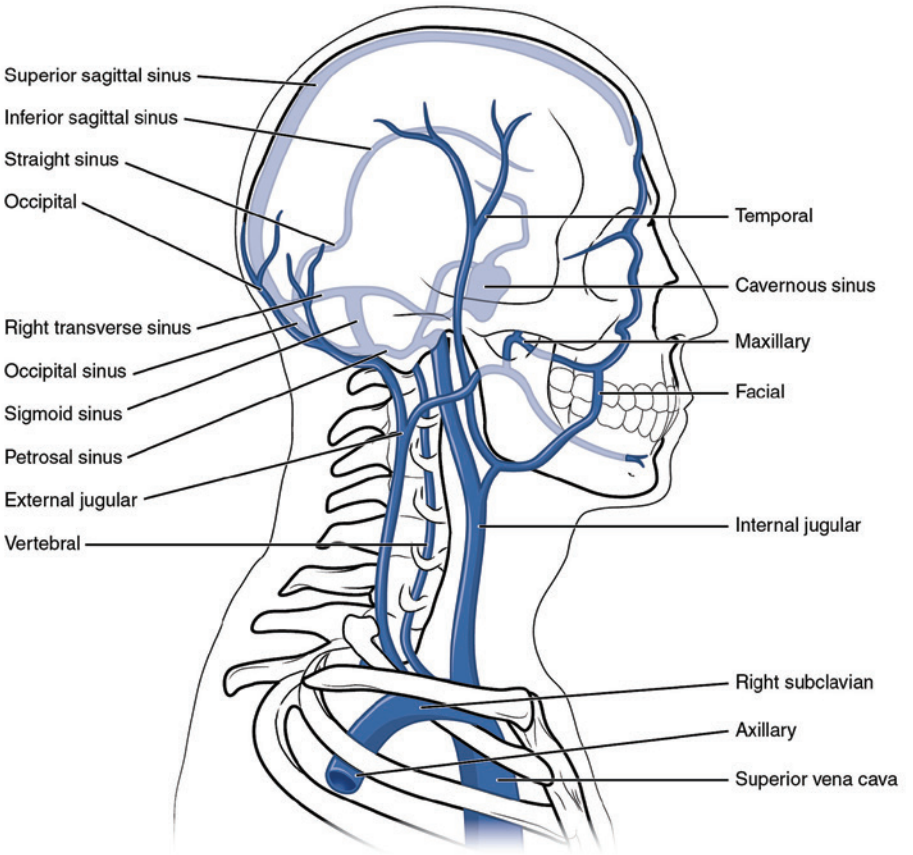


Figure 19.30 Veins of the Head and Neck. This left lateral view shows the veins of the head and neck, including the intracranial sinuses.

cerebral vein and into the **straight sinus**. The **occipital sinus**, sagittal sinus, and straight sinuses all flow into the left and right transverse sinuses near the lambdoid suture. Table 19.15 summarizes the major veins of the brain.

Veins Draining the Upper Limbs

The **digital veins** in the fingers come together in the hand to form the **palmar venous arches** (Figure 19.31). From here, the veins come together to form the radial vein, the ulnar vein, and the median antebrachial vein. The **radial vein** and the **ulnar vein** parallel the bones of the forearm and join together at the antebrachium to form the **brachial vein**, a deep vein that flows into the axillary vein in the brachium.

Many of the larger veins of the thoracic and abdominal region and upper limb are further represented in the flowchart in Figure 19.32. Table 19.16 summarizes the veins of the upper limbs.

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Table 19.15 Major Veins of the Brain

Vessel	Description
Superior sagittal sinus	Enlarged vein located midsagittally between the meningeal and periosteal layers of the dura mater within the falx cerebri; receives most of the blood drained from the superior surface of the cerebrum and leads to the inferior jugular vein and the vertebral vein
Great cerebral vein	Receives most of the smaller vessels from the inferior cerebral veins and leads to the straight sinus
Straight sinus	Enlarged vein that drains blood from the brain; receives most of the blood from the great cerebral vein and leads to the left or right transverse sinus
Occipital sinus	Enlarged vein that drains the occipital region near the falx cerebelli and leads to the left and right transverse sinuses and also the vertebral veins

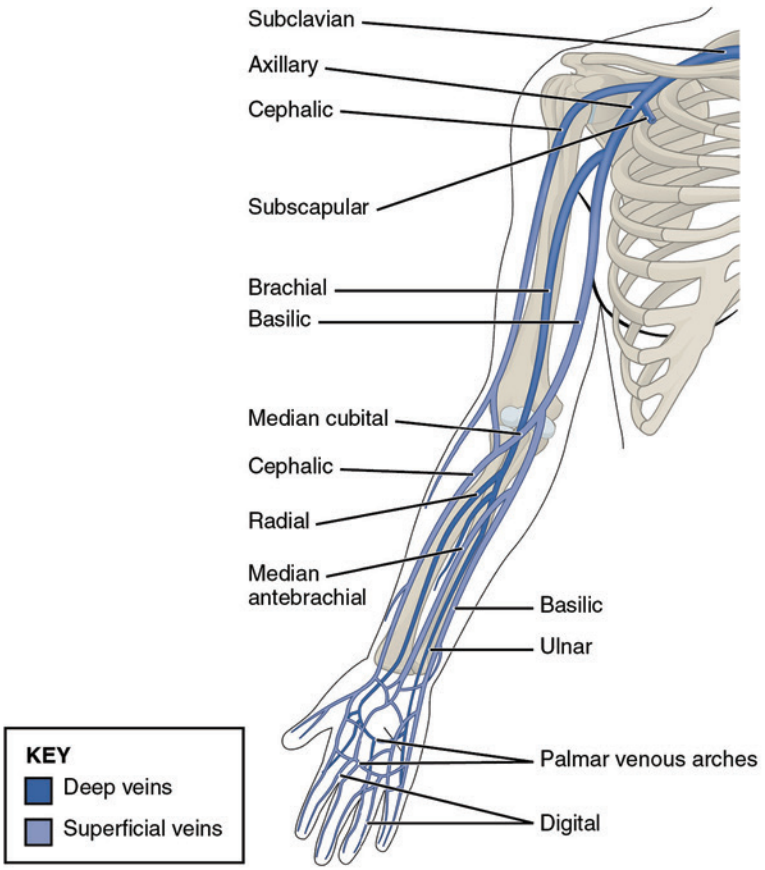


Figure 19.31 Veins of the Upper Limb. This anterior view shows the veins that drain the upper limb.

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Table 19.16 Veins of the Upper Limbs

Vessel	Description
Digital veins	Drain the digits and lead to the palmar arches of the hand and dorsal venous arch of the foot
Palmar venous arches	Drain the hand and digits and lead to the radial vein, ulnar veins, and the median antebrachial vein
Radial vein	Parallels the radius and radial artery; arises from the palmar venous arches and leads to the brachial vein
Ulnar vein	Parallels the ulna and ulnar artery; arises from the palmar venous arches and leads to the brachial vein
Brachial vein	Deeper vein of the arm; forms from the radial and ulnar veins in the lower arm; leads to the axillary vein
Cephalic vein	Superficial vessel in the upper arm; leads to the axillary vein
Subscapular vein	Drains blood from the subscapular region and leads to the axillary vein
Axillary vein	Major vein in the axillary region; drains the upper limb and becomes the subclavian vein

The **cephalic vein** begins in the antebrachium and drains blood from the superficial surface of the arm into the axillary vein. It is extremely superficial and easily seen along the surface of the biceps brachii muscle in individuals with good muscle tone and in those without excessive subcutaneous adipose tissue in the arms.

The **subscapular vein** drains blood from the subscapular region and joins the cephalic vein to form the **axillary vein**. As it passes through the body wall and enters the thorax, the axillary vein becomes the subclavian vein.

The Inferior Vena Cava

Other than the small amount of blood drained by the azygos and hemiazygos veins, most of the blood inferior to the diaphragm drains into the inferior vena cava before it is returned to the heart (see Figure 19.29). Lying just beneath the parietal peritoneum in the abdominal cavity, the **inferior vena cava** parallels the abdominal aorta, where it can receive blood from abdominal veins.

Blood supply from the kidneys flows into each **renal vein**, normally the largest veins entering the inferior vena cava. A number of other, smaller veins empty into the left renal vein. Each **adrenal vein** drains the adrenal or suprarenal glands located immediately superior to the kidneys. The right

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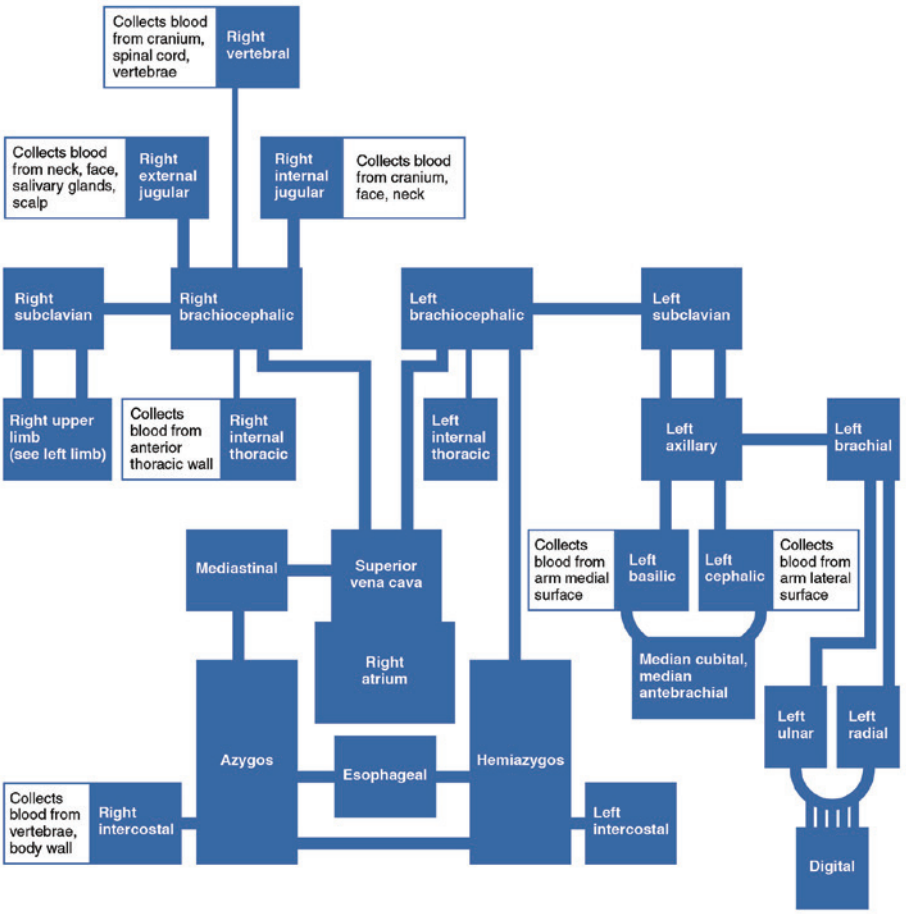


Figure 19.32 Veins Flowing into the Superior Vena Cava. The flowchart summarizes the distribution of the veins flowing into the superior vena cava.

adrenal vein enters the inferior vena cava directly, whereas the left adrenal vein enters the left renal vein.

On the reproductive organs, veins are generically called **gonadal veins**. The right gonadal vein empties directly into the inferior vena cava, and the left gonadal vein empties into the left renal vein.

Blood supply from the liver drains into each **hepatic vein** and directly into the inferior vena cava. Since the inferior vena cava lies primarily to the right of the vertebral column and aorta, the left renal vein is longer, as are the left phrenic, adrenal, and gonadal veins. The longer length of the left renal vein makes the left kidney the primary target of surgeons removing this organ for donation. Figure 19.33 provides a flowchart of the veins flowing into the inferior vena cava. Table 19.17 summarizes the major veins of the abdominal region.

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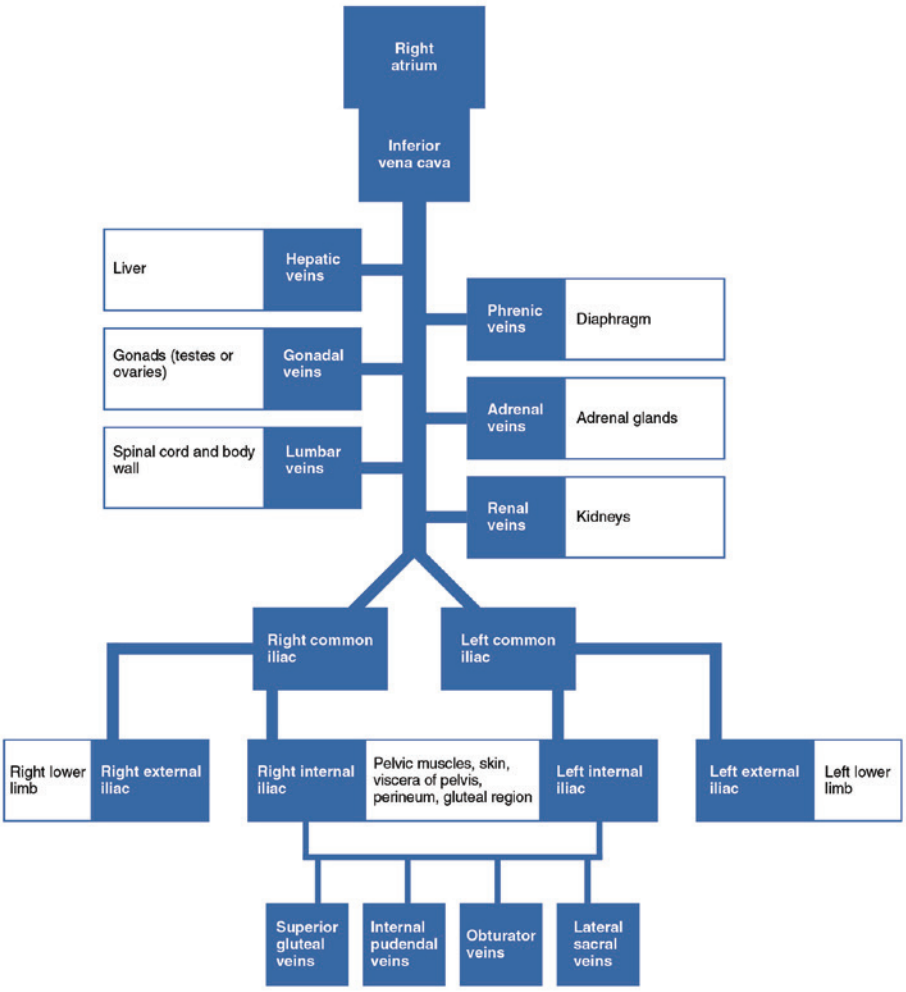


Figure 19.33 Venous Flow into Inferior Vena Cava. The flowchart summarizes veins that deliver blood to the inferior vena cava.

Veins Draining the Lower Limbs

Close to the body wall, the great saphenous vein, the deep femoral vein, and the femoral circumflex vein drain into the femoral vein. The **great saphenous vein** is a prominent surface vessel located on the medial surface of the leg and thigh that collects blood from the superficial portions of these areas (Figure 19.34).

As the **femoral vein** penetrates the body wall from the femoral portion of the upper limb, it becomes the **external iliac vein**, a large vein that drains blood from the leg to the common iliac vein. Blood from the pelvic organs and integument drain into the **internal iliac vein**, which forms from several smaller veins in the region, including the umbilical veins that run on either side of the

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Table 19.17 Major Veins of the Abdominal Region

Vessel	Description
Inferior vena cava	Large systemic vein; drains blood from areas mostly inferior to the diaphragm; empties into the right atrium
Renal vein	Largest vein entering the inferior vena cava; drains the kidneys and flows into the inferior vena cava
Adrenal vein	Drains the adrenal or suprarenal; the right adrenal vein enters the inferior vena cava directly, and the left adrenal vein enters the left renal vein
Gonadal vein	Generic term for a vein draining a reproductive organ; may be either an ovarian vein or a testicular vein, depending on the sex of the individual
Hepatic vein	Drains systemic blood from the liver and flows into the inferior vena cava

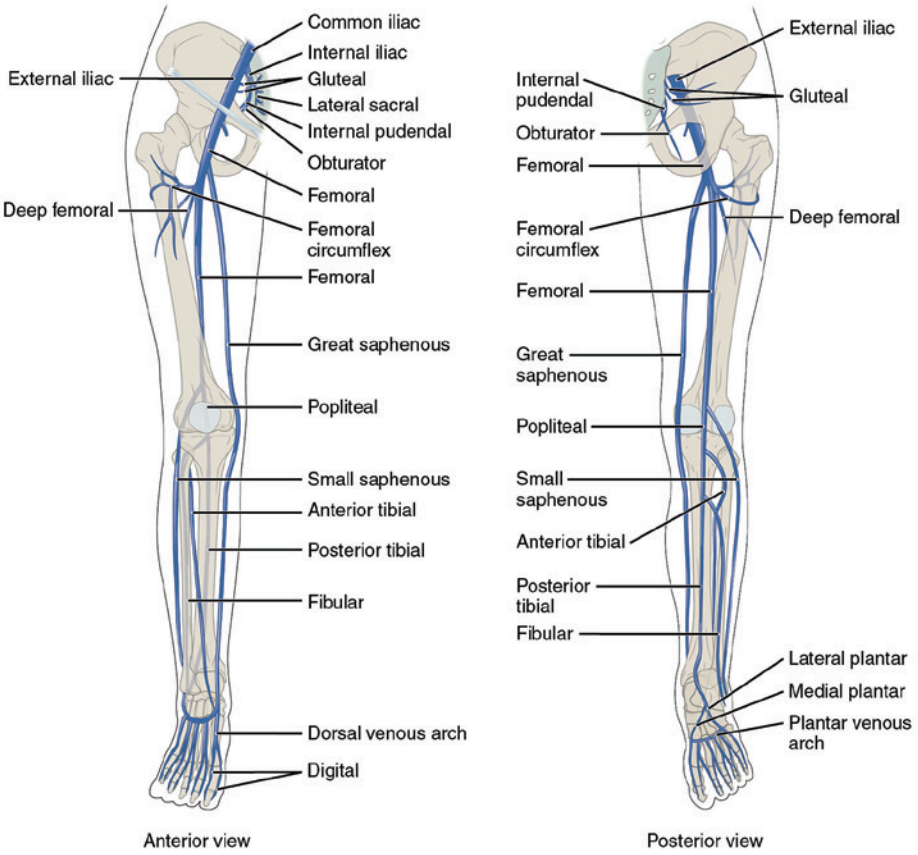


Figure 19.34 Major Veins Serving the Lower Limbs. Anterior and posterior views show the major veins that drain the lower limb into the inferior vena cava.

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bladder. The external and internal iliac veins combine near the inferior portion of the sacroiliac joint to form the **common iliac vein**. Similar to the common iliac arteries, the common iliac veins come together at the level of L5 to form the inferior vena cava.

Figure 19.35 is a flowchart of veins flowing into the lower limb. Table 19.18 summarizes the major veins of the lower limbs.

Hepatic Portal System

The liver is a complex biochemical processing plant. It packages nutrients absorbed by the digestive system; produces plasma proteins, clotting factors, and bile; and disposes of worn-out cell components and waste products. Instead of entering the circulation directly, absorbed nutrients and certain wastes (for

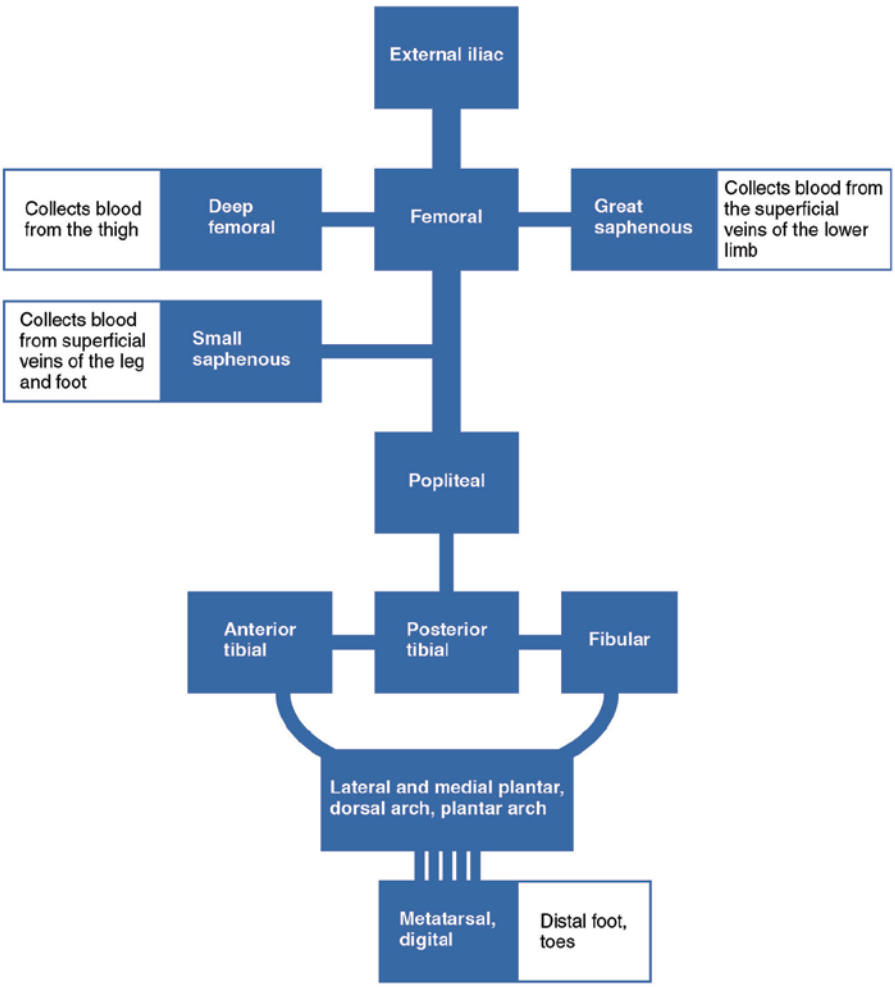


Figure 19.35 Major Veins of the Lower Limb. The flowchart summarizes venous flow from the lower limb.

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Table 19.18 Veins of the Lower Limbs

Vessel	Description
Great saphenous vein	Prominent surface vessel located on the medial surface of the leg and thigh; drains the superficial portions of these areas and flows into the femoral vein
Femoral vein	Drains the upper leg; receives blood from the great saphenous vein, the deep femoral vein, and the femoral circumflex vein; becomes the external iliac vein when it crosses the body wall
External iliac vein	Formed when the femoral vein passes into the body cavity; drains the legs and flows into the common iliac vein
Internal iliac vein	Drains the pelvic organs and integument; formed from several smaller veins in the region; flows into the common iliac vein
Common iliac vein	Flows into the inferior vena cava at the level of L5; left common iliac vein drains the sacral region; formed from the union of the external and internal iliac veins near the inferior portion of the sacroiliac joint

example, materials produced by the spleen) travel to the liver for processing. They do so via the **hepatic portal system** (Figure 19.36). Portal systems begin and end in capillaries. In this case, the initial capillaries from the stomach, small intestine, large intestine, and spleen lead to the hepatic portal vein and end in specialized capillaries within the liver, the hepatic sinusoids. You saw the only other portal system with the hypothalamic-hypophyseal portal vessel in chapter 16 on the endocrine system.

The hepatic portal system consists of the hepatic portal vein and the veins that drain into it. The hepatic portal vein itself is relatively short, beginning at the level of L2 with the confluence of the superior mesenteric and splenic veins. It also receives branches from the inferior mesenteric vein, plus the splenic veins and all their tributaries. The superior mesenteric vein receives blood from the small intestine, two-thirds of the large intestine, and the stomach. The inferior mesenteric vein drains the distal third of the large intestine, including the descending colon, the sigmoid colon, and the rectum. The splenic vein is formed by branches from the spleen and receives blood from the pancreas, portions of the stomach, and the inferior mesenteric vein. After its formation, the hepatic portal vein also receives branches from the gastric veins of the stomach and cystic veins from the gall bladder. The hepatic portal vein delivers materials from these digestive and circulatory organs directly to the liver for processing.

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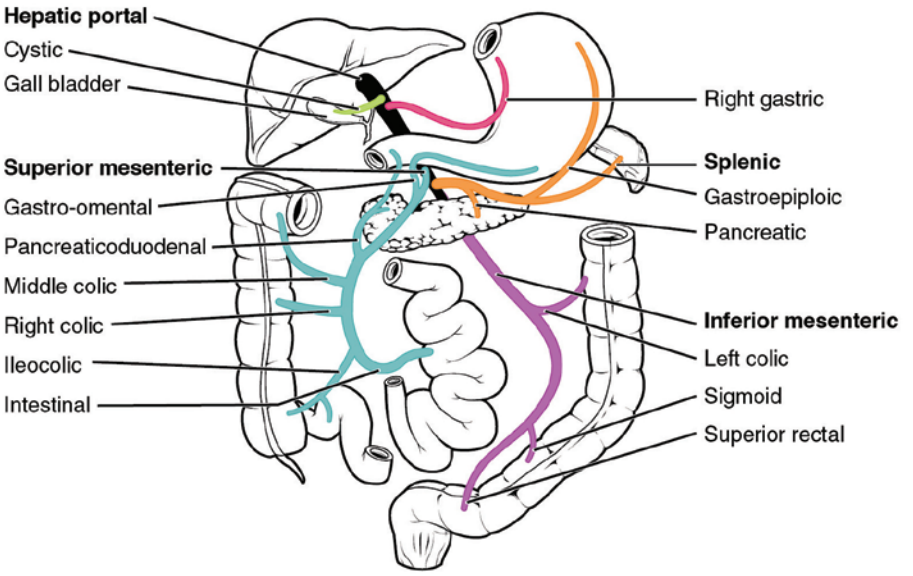


Figure 19.36 Hepatic Portal System. The liver receives blood from the normal systemic circulation via the hepatic artery. It also receives and processes blood from other organs, delivered via the veins of the hepatic portal system. All blood exits the liver via the hepatic vein, which delivers the blood to the inferior vena cava. (Different colours are used to help distinguish among the different vessels in the system.)

Because of the hepatic portal system, the liver receives its blood supply from two different sources: from normal systemic circulation via the hepatic artery and from the hepatic portal vein. The liver processes the blood from the portal system to remove certain wastes and excess nutrients, which are stored for later use. This processed blood, as well as the systemic blood that came from the hepatic artery, exits the liver via the right, left, and middle hepatic veins and flows into the inferior vena cava. Overall systemic blood composition remains relatively stable, since the liver is able to metabolize the absorbed digestive components.

19.6 Development of Blood Vessels and Fetal Circulation

Learning Objectives

By the end of this section, you will be able to:

- Describe the development of blood vessels
- Describe the fetal circulation

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As the embryo grows within the mother's uterus, its requirements for nutrients and gas exchange also grow. The placenta—a circulatory organ unique to pregnancy—develops jointly from the embryo and uterine wall structures to fill this need. Emerging from the placenta is the **umbilical vein**, which carries oxygen-rich blood from the pregnant person to the fetal inferior vena cava via the ductus venosus to the heart that pumps it into fetal circulation. Two **umbilical arteries** carry oxygen-depleted fetal blood, including wastes and carbon dioxide, to the placenta.

Remnants of the umbilical arteries remain in the adult. (Seek additional content for more information on the role of the placenta in fetal circulation.)

There are three major shunts—alternate paths for blood flow—found in the circulatory system of the fetus. Two of these shunts divert blood from the pulmonary to the systemic circuit, whereas the third connects the umbilical vein to the inferior vena cava. The first two shunts are critical during fetal life, when the lungs are compressed, filled with amniotic fluid, and nonfunctional, and gas exchange is provided by the placenta. These shunts close shortly after birth, however, when the newborn begins to breathe. The third shunt persists a bit longer but becomes nonfunctional once the umbilical cord is severed. The three shunts are as follows (Figure 19.37):

- The **foramen ovale** is an opening in the interatrial septum that allows blood to flow from the right atrium to the left atrium. A valve associated with this opening prevents backflow of blood during the fetal period. As the newborn begins to breathe and blood pressure in the atria increases, this shunt closes. The fossa ovalis remains in the interatrial septum after birth, marking the location of the former foramen ovale.
- The **ductus arteriosus** is a short, muscular vessel that connects the pulmonary trunk to the aorta. Most of the blood pumped from the right ventricle into the pulmonary trunk is thereby diverted into the aorta. Only enough blood reaches the fetal lungs to maintain the developing lung tissue. When the newborn takes the first breath, pressure within the lungs drops dramatically, and both the lungs and the pulmonary vessels expand. As the amount of oxygen increases, the smooth muscles in the wall of the ductus arteriosus constrict, sealing off the passage. Eventually, the muscular and endothelial components of the ductus arteriosus degenerate, leaving only the connective tissue component of the ligamentum arteriosum.
- The **ductus venosus** is a temporary blood vessel that branches from the umbilical vein, allowing much of the freshly oxygenated blood from

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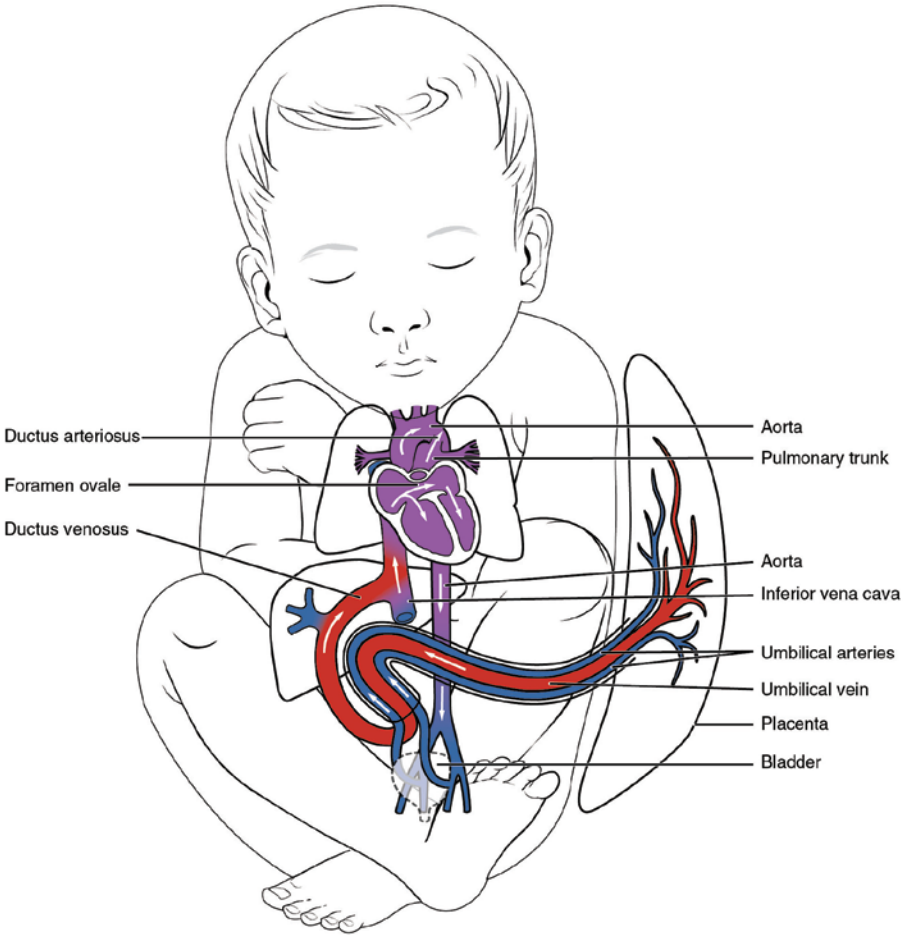


Figure 19.37 Fetal Shunts. The foramen ovale in the interatrial septum allows blood to flow from the right atrium to the left atrium. The ductus arteriosus is a temporary vessel connecting the aorta to the pulmonary trunk. The ductus venosus links the umbilical vein to the inferior vena cava largely through the liver.

the placenta—the organ of gas exchange between the pregnant person and fetus—to bypass the fetal liver and go directly to the fetal heart. The ductus venosus closes slowly during the first weeks of infancy and degenerates to become the ligamentum venosum.

Key Terms

abdominal aorta: Portion of the aorta inferior to the aortic hiatus and superior to the common iliac arteries.

adrenal artery: Branch of the abdominal aorta; supplies blood to the adrenal (suprarenal) glands.

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adrenal vein: Drains the adrenal or suprarenal glands that are immediately superior to the kidneys; the right adrenal vein enters the inferior vena cava directly, and the left adrenal vein enters the left renal vein.

anaphylactic shock: Type of shock that follows a severe allergic reaction and results from massive vasodilation.

anterior tibial artery: Branches from the popliteal artery; supplies blood to the anterior tibial region; becomes the dorsalis pedis artery.

aorta: Largest artery in the body, originating from the left ventricle and descending to the abdominal region, where it bifurcates into the common iliac arteries at the level of the fourth lumbar vertebra; arteries originating from the aorta distribute blood to virtually all tissues of the body.

aortic arch: Arch that connects the ascending aorta to the descending aorta; ends at the intervertebral disk between the fourth and fifth thoracic vertebrae.

aortic hiatus: Opening in the diaphragm that allows passage of the thoracic aorta into the abdominal region, where it becomes the abdominal aorta.

aortic sinuses: Small pockets in the ascending aorta near the aortic valve that are the locations of the baroreceptors (stretch receptors) and chemoreceptors that trigger a reflex that aids in the regulation of vascular homeostasis.

arteriole (also resistance vessel): Very small artery that leads to a capillary.

arteriovenous anastomosis: Short vessel connecting an arteriole directly to a venule and bypassing the capillary beds.

artery: Blood vessel that conducts blood away from the heart; may be a conducting or distributing vessel.

ascending aorta: Initial portion of the aorta, rising from the left ventricle for a distance of approximately 5 cm.

atrial reflex: Mechanism for maintaining vascular homeostasis involving atrial baroreceptors: If blood is returning to the right atrium more rapidly than it is being ejected from the left ventricle, the atrial receptors will stimulate the cardiovascular centres to increase sympathetic firing and increase cardiac output until the situation is reversed; the opposite is also true.

axillary artery: Continuation of the subclavian artery as it penetrates the body wall and enters the axillary region; supplies blood to the region near the head of the humerus (humeral circumflex arteries); the majority of the vessel continues into the brachium and becomes the brachial artery.

axillary vein: Major vein in the axillary region; drains the upper limb and becomes the subclavian vein.

azygos vein: Originates in the lumbar region and passes through the diaphragm into the thoracic cavity on the right side of the vertebral

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column; drains blood from the intercostal veins, esophageal veins, bronchial veins, and other veins draining the mediastinal region; leads to the superior vena cava.

blood colloidal osmotic pressure (BCOP): Pressure exerted by colloids suspended in blood within a vessel; a primary determinant is the presence of plasma proteins.

blood flow: Movement of blood through a vessel, tissue, or organ that is usually expressed in terms of volume per unit of time.

blood hydrostatic pressure: Force blood exerts against the walls of a blood vessel or heart chamber.

blood pressure: Force exerted by the blood against the wall of a vessel or heart chamber; can be described with the more generic term *hydrostatic pressure*.

brachial artery: Continuation of the axillary artery in the brachium; supplies blood to much of the brachial region; gives off several smaller branches that provide blood to the posterior surface of the arm in the region of the elbow; bifurcates into the radial and ulnar arteries at the coronoid fossa.

brachial vein: A deep vein that flows into the axillary vein in the brachium formed by joining of the radial vein with the ulnar vein.

brachiocephalic artery: Single vessel located on the right side of the body; the first vessel branching from the aortic arch; gives rise to the right subclavian artery and the right common carotid artery; supplies blood to the head, neck, upper limb, and wall of the thoracic region.

brachiocephalic vein: One of a pair of veins that form from a fusion of the external and internal jugular veins and the subclavian vein; subclavian, external and internal jugulars, vertebral, and internal thoracic veins lead to it; drains the upper thoracic region and flows into the superior vena cava.

bronchial artery: Systemic branch from the aorta that provides oxygenated blood to the lungs in addition to the pulmonary circuit.

bronchial vein: Drains the systemic circulation from the lungs and leads to the azygos vein.

capacitance: Ability of a vein to distend and store blood.

capacitance vessels: Veins; more distensible than arteries.

capillary: Smallest of blood vessels where physical exchange occurs between the blood and tissue cells surrounded by interstitial fluid.

capillary bed: Network of 10–100 capillaries connecting arterioles to venules.

capillary hydrostatic pressure (CHP): Force blood exerts against a capillary.

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cardioaccelerator centres: Stimulate cardiac function by regulating heart rate and stroke volume via sympathetic stimulation from the cardiac accelerator nerve.

cardiogenic shock: Type of shock that results from the inability of the heart to maintain cardiac output.

cardioinhibitor centres: Slow cardiac function by decreasing heart rate and stroke volume via parasympathetic stimulation from the vagus nerve.

carotid sinuses: Small pockets near the base of the internal carotid arteries that are the locations of the baroreceptors and chemoreceptors that trigger a reflex that aids in the regulation of vascular homeostasis.

celiac trunk (also celiac artery): Major branch of the abdominal aorta; gives rise to the left gastric artery, the splenic artery, and the common hepatic artery that forms the hepatic artery to the liver, the right gastric artery to the stomach, and the cystic artery to the gall bladder.

cephalic vein: Superficial vessel in the upper arm; leads to the axillary vein.

cerebrovascular accident (CVA): Blockage of blood flow to the brain; also called a stroke.

circulatory shock: Also simply called shock; a life-threatening medical condition in which the circulatory system is unable to supply enough blood flow to provide adequate oxygen and other nutrients to the tissues to maintain cellular metabolism.

common carotid artery: Right common carotid artery arises from the brachiocephalic artery, and the left common carotid arises from the aortic arch; gives rise to the external and internal carotid arteries; supplies the respective sides of the head and neck.

common hepatic artery: Branch of the celiac trunk that forms the hepatic artery, the right gastric artery, and the cystic artery.

common iliac artery: Branch of the aorta that leads to the internal and external iliac arteries.

common iliac vein: One of a pair of veins that flows into the inferior vena cava at the level of L5; the left common iliac vein drains the sacral region; divides into external and internal iliac veins near the inferior portion of the sacroiliac joint.

compliance: Degree to which a blood vessel can stretch as opposed to being rigid.

continuous capillary: Most common type of capillary, found in virtually all tissues except epithelia and cartilage; contains very small gaps in the endothelial lining that permit exchange.

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descending aorta: Portion of the aorta that continues downward past the end of the aortic arch; subdivided into the thoracic aorta and the abdominal aorta.

diastolic pressure: Lower number recorded when measuring arterial blood pressure; represents the minimal value corresponding to the pressure that remains during ventricular relaxation.

digital veins: Drain the digits and feed into the palmar arches of the hand and dorsal venous arch of the foot.

ductus arteriosus: Shunt in the fetal pulmonary trunk that diverts oxygenated blood back to the aorta.

ductus venosus: Shunt that causes oxygenated blood to bypass the fetal liver on its way to the inferior vena cava.

elastic artery (also conducting artery): Artery with abundant elastic fibres located closer to the heart, which maintains the pressure gradient and conducts blood to smaller branches.

external carotid artery: Arises from the common carotid artery; supplies blood to numerous structures within the face, lower jaw, neck, esophagus, and larynx.

external elastic membrane: Membrane composed of elastic fibres that separates the tunica media from the tunica externa; seen in larger arteries.

external iliac artery: Branch of the common iliac artery that leaves the body cavity and becomes a femoral artery; supplies blood to the lower limbs.

external iliac vein: Formed when the femoral vein passes into the body cavity; drains the legs and leads to the common iliac vein.

external jugular vein: One of a pair of major veins located in the superficial neck region that drains blood from the more superficial portions of the head, scalp, and cranial regions and leads to the subclavian vein.

femoral artery: Continuation of the external iliac artery after it passes through the body cavity; divides into several smaller branches, the lateral deep femoral artery, and the genicular artery; becomes the popliteal artery as it passes posterior to the knee.

femoral vein: Drains the upper leg; receives blood from the great saphenous vein, the deep femoral vein, and the femoral circumflex vein; becomes the external iliac vein when it crosses the body wall.

fenestrated capillary: Type of capillary with pores or fenestrations in the endothelium that allow for rapid passage of certain small materials.

filtration: In the cardiovascular system, the movement of material from a capillary into the interstitial fluid, moving from an area of higher pressure to lower pressure.

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foramen ovale: Shunt that directly connects the right and left atria and helps divert oxygenated blood from the fetal pulmonary circuit.

gonadal artery: Branch of the abdominal aorta; supplies blood to the gonads or reproductive organs; also described as ovarian arteries or testicular arteries, depending on the sex of the individual.

gonadal vein: Generic term for a vein draining a reproductive organ; may be either an ovarian vein or a testicular vein, depending on the sex of the individual.

great cerebral vein: Receives most of the smaller vessels from the inferior cerebral veins and leads to the straight sinus.

great saphenous vein: Prominent surface vessel located on the medial surface of the leg and thigh; drains the superficial portions of these areas and leads to the femoral vein.

hepatic portal system: Specialized circulatory pathway that carries blood from digestive organs to the liver for processing before being sent to the systemic circulation.

hepatic vein: Drains systemic blood from the liver and flows into the inferior vena cava.

hypertension: Chronic and persistent blood pressure measurements of 140/90 mm Hg or above.

hypervolemia: Abnormally high levels of fluid and blood within the body.

hypovolemia: Abnormally low levels of fluid and blood within the body.

hypovolemic shock: Type of circulatory shock caused by excessive loss of blood volume due to hemorrhage or possibly dehydration.

hypoxia: Lack of oxygen supply to the tissues.

inferior vena cava: Large systemic vein that drains blood from areas largely inferior to the diaphragm; empties into the right atrium.

intercostal artery: Branch of the thoracic aorta; supplies blood to the muscles of the thoracic cavity and vertebral column.

internal carotid artery: Arises from the common carotid artery and begins with the carotid sinus; goes through the carotid canal of the temporal bone to the base of the brain; combines with branches of the vertebral artery forming the arterial circle; supplies blood to the brain.

internal elastic membrane: Membrane composed of elastic fibres that separates the tunica intima from the tunica media; seen in larger arteries.

internal iliac artery: Branch from the common iliac arteries; supplies blood to the urinary bladder, walls of the pelvis, external genitalia, and the medial portion of the femoral region; in females, also provides blood to the uterus and vagina.

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internal iliac vein: Drains the pelvic organs and integument; formed from several smaller veins in the region; leads to the common iliac vein.

internal jugular vein: One of a pair of major veins located in the neck region that passes through the jugular foramen and canal and flows parallel to the common carotid artery that is more or less its counterpart; primarily drains blood from the brain, receives the superficial facial vein, and empties into the subclavian vein.

internal thoracic vein (also internal mammary vein): Drains the anterior surface of the chest wall and leads to the brachiocephalic vein.

interstitial fluid colloidal osmotic pressure (IFCOP): Pressure exerted by the colloids within the interstitial fluid.

interstitial fluid hydrostatic pressure (IFHP): Force exerted by the fluid in the tissue spaces.

ischemia: Insufficient blood flow to the tissues.

Korotkoff sounds: Noises created by turbulent blood flow through the vessels.

left gastric artery: Branch of the celiac trunk; supplies blood to the stomach.

lumen: Interior of a tubular structure such as a blood vessel or a portion of the alimentary canal through which blood, chyme, or other substances travel.

lymph: Liquid of the lymphatic system that is returned to the blood.

mean arterial pressure (MAP): Average driving force of blood to the tissues; approximated by taking diastolic pressure and adding one-third of pulse pressure.

mediastinal artery: Branch of the thoracic aorta; supplies blood to the mediastinum.

metarteriole: Short vessel arising from a terminal arteriole that branches to supply a capillary bed.

microcirculation: Blood flow through the capillaries.

muscular artery (also distributing artery): Artery with abundant smooth muscle in the tunica media that branches to distribute blood to the arteriole network.

myogenic response: Constriction or dilation in the walls of arterioles in response to pressures related to blood flow; reduces high blood flow or increases low blood flow to help maintain consistent flow to the capillary network.

nervi vasorum: Small nerve fibres found in arteries and veins that trigger contraction of the smooth muscle in their walls.

net filtration pressure (NFP): Force driving fluid out of the capillary and into the tissue spaces; equal to the difference of the capillary hydrostatic pressure and the blood colloidal osmotic pressure.

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neurogenic shock: Type of shock that occurs with cranial or high spinal injuries that damage the cardiovascular centres in the medulla oblongata or the nervous fibres originating from this region.

obstructive shock: Type of shock that occurs when a significant portion of the vascular system is blocked.

occipital sinus: Enlarged vein that drains the occipital region near the falx cerebelli and flows into the left and right transverse sinuses and also into the vertebral veins.

palmar venous arches: Drain the hand and digits and feed into the radial and ulnar veins.

parietal branches (also somatic branches): Group of arterial branches of the thoracic aorta; include those that supply blood to the thoracic cavity, the vertebral column, and the superior surface of the diaphragm.

perfusion: Distribution of blood into the capillaries so the tissues can be supplied.

precapillary sphincters: Circular rings of smooth muscle that surround the entrance to a capillary and regulate blood flow into that capillary.

pulmonary artery: One of two branches, left and right, that divides off from the pulmonary trunk and leads to smaller arterioles and eventually to the pulmonary capillaries.

pulmonary circuit: System of blood vessels that provides gas exchange via a network of arteries, veins, and capillaries that run from the heart, through the body, and back to the lungs.

pulmonary trunk: Single large vessel exiting the right ventricle that divides to form the right and left pulmonary arteries.

pulmonary veins: Two sets of paired vessels, one pair on each side, that are formed from the small venules leading away from the pulmonary capillaries that flow into the left atrium.

pulse: Alternating expansion and recoil of an artery as blood moves through the vessel; an indicator of heart rate.

pulse pressure: Difference between the systolic and diastolic pressures.

radial artery: Formed at the bifurcation of the brachial artery; parallels the radius; gives off smaller branches until it reaches the carpal region, where it fuses with the ulnar artery to form the superficial and deep palmar arches; supplies blood to the lower arm and carpal region.

radial vein: Parallels the radius and radial artery; arises from the palmar venous arches and leads to the brachial vein.

reabsorption: In the cardiovascular system, the movement of material from the interstitial fluid into the capillaries.

renal artery: Branch of the abdominal aorta; supplies each kidney.

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renal vein: Largest vein entering the inferior vena cava; drains the kidneys and leads to the inferior vena cava.

resistance: Any condition or parameter that slows or counteracts the flow of blood.

respiratory pump: Increase in the volume of the thorax during inhalation that decreases air pressure, enabling venous blood to flow into the thoracic region; then exhalation increases pressure, moving blood into the atria.

sepsis (also septicemia): Organismal-level inflammatory response to a massive infection.

septic shock (also blood poisoning): Type of shock that follows a massive infection resulting in organism-wide inflammation.

sinusoid capillary: Rarest type of capillary, which has extremely large intercellular gaps in the basement membrane in addition to clefts and fenestrations; found in areas such as the bone marrow and liver, where passage of large molecules occurs.

skeletal muscle pump: Effect on increasing blood pressure within veins by compression of the vessel caused by the contraction of nearby skeletal muscle.

sphygmomanometer: Blood pressure cuff attached to a device that measures blood pressure.

splenic artery: Branch of the celiac trunk; supplies blood to the spleen.

straight sinus: Enlarged vein that drains blood from the brain; receives most of the blood from the great cerebral vein and flows into the left or right transverse sinus.

subclavian artery: Right subclavian arises from the brachiocephalic artery, whereas the left subclavian artery arises from the aortic arch; gives rise to the internal thoracic, vertebral, and thyrocervical arteries; supplies blood to the arms, chest, shoulders, back, and central nervous system.

subclavian vein: Located deep in the thoracic cavity; becomes the axillary vein as it enters the axillary region; drains the axillary and smaller local veins near the scapular region; leads to the brachiocephalic vein.

subscapular vein: Drains blood from the subscapular region and leads to the axillary vein.

superior sagittal sinus: Enlarged vein located midsagittally between the meningeal and periosteal layers of the dura mater within the falx cerebri; receives most of the blood drained from the superior surface of the cerebrum and leads to the inferior jugular vein and the vertebral vein.

superior vena cava: Large systemic vein; drains blood from most areas superior to the diaphragm; empties into the right atrium.

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systemic circuit: Provides blood rich in oxygen to the body's tissues, then returns the less oxygenated blood to the heart.

systolic pressure: Larger number recorded when measuring arterial blood pressure; represents the maximum value following ventricular contraction.

thoracic aorta: Portion of the descending aorta superior to the aortic hiatus.

thoroughfare channel: Continuation of the metarteriole that enables blood to bypass a capillary bed and flow directly into a venule, creating a vascular shunt.

transient ischemic attack (TIA): Temporary loss of neurological function caused by a brief interruption in blood flow; also known as a ministroke.

trunk: Large vessel that gives rise to smaller vessels.

tunica externa (also tunica adventitia): Outermost layer or tunic of a vessel (except capillaries).

tunica intima (also tunica interna): Innermost lining or tunic of a vessel.

tunica media: Middle layer or tunic of a vessel (except capillaries).

ulnar artery: Formed at the bifurcation of the brachial artery; parallels the ulna; gives off smaller branches until it reaches the carpal region, where it fuses with the radial artery to form the superficial and deep palmar arches; supplies blood to the lower arm and carpal region.

ulnar vein: Parallels the ulna and ulnar artery; arises from the palmar venous arches and leads to the brachial vein.

umbilical arteries: Pair of vessels that runs within the umbilical cord and carries fetal blood low in oxygen and high in waste to the placenta for exchange with maternal blood.

umbilical vein: Single vessel that originates in the placenta and runs within the umbilical cord, carrying oxygen- and nutrient-rich blood to the fetal heart.

vasa vasorum: Small blood vessels located within the walls or tunics of larger vessels that supply nourishment to and remove wastes from the cells of the vessels.

vascular shock: Type of shock that occurs when arterioles lose their normal muscular tone and dilate dramatically.

vascular shunt: Continuation of the metarteriole and thoroughfare channel that allows blood to bypass the capillary beds to flow directly from the arterial to the venous circulation.

vascular tone: Contractile state of smooth muscle in a blood vessel.

vasoconstriction: Constriction of the smooth muscle of a blood vessel, resulting in a decreased vascular diameter.

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vasodilation: Relaxation of the smooth muscle in the wall of a blood vessel, resulting in an increased vascular diameter.

vasomotion: Irregular, pulsating flow of blood through capillaries and related structures.

vasomotor centres: Control vessel tone or contraction of the smooth muscle in the tunica media.

vein: Blood vessel that conducts blood toward the heart.

vein valves: Assist the unidirectional flow of blood toward the heart; particularly those of the limbs.

venous reserve: Volume of blood contained within systemic veins in the integument, bone marrow, and liver that can be returned to the heart for circulation if needed.

venule: Small vessel leading from the capillaries to veins.

visceral branches: Branches of the descending aorta that supply blood to the viscera.

Chapter Review

19.1 Structure and Function of Blood Vessels

Blood pumped by the heart flows through a series of vessels known as arteries, arterioles, capillaries, venules, and veins before returning to the heart.

Arteries transport blood away from the heart and branch into smaller vessels, forming arterioles. Arterioles distribute blood to capillary beds, the sites of exchange with the body tissues. Capillaries lead back to small vessels known as venules that flow into the larger veins and eventually back to the heart.

The arterial system is a relatively high-pressure system, so arteries have thick walls that appear round in cross section. The venous system is a lower-pressure system, containing veins that have larger lumens and thinner walls. They often appear flattened. Arteries, arterioles, venules, and veins are composed of three tunics known as the tunica intima, tunica media, and tunica externa. Capillaries have only a tunica intima layer. The tunica intima is a thin layer composed of a simple squamous epithelium known as endothelium and a small amount of connective tissue. The tunica media is a thicker area composed of variable amounts of smooth muscle and connective tissue. It is the thickest layer in all but the largest arteries. The tunica externa is primarily a layer of connective tissue, although in veins, it also contains some smooth muscle. Blood flow through vessels can be dramatically influenced by vasoconstriction and vasodilation in their walls.

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19.2 Blood Flow, Blood Pressure, and Resistance

Blood flow is the movement of blood through a vessel, tissue, or organ. The slowing or blocking of blood flow is called resistance. Blood pressure is the force that blood exerts on the walls of the blood vessels or chambers of the heart. The components of blood pressure include systolic pressure, which results from ventricular contraction, and diastolic pressure, which results from ventricular relaxation. Pulse pressure is the difference between systolic and diastolic measures, and mean arterial pressure is the "average" pressure of blood in the arterial system, driving blood into the tissues. Pulse, the expansion and recoiling of an artery, reflects the heartbeat. The variables affecting blood flow and blood pressure in the systemic circulation are cardiac output, compliance, blood volume, blood viscosity, and the length and diameter of the blood vessels. In the arterial system, vasodilation and vasoconstriction of the arterioles are significant factors in systemic blood pressure: Slight vasodilation greatly decreases resistance and increases flow, whereas slight vasoconstriction greatly increases resistance and decreases flow. In the arterial system, as resistance increases, blood pressure increases and flow decreases. In the venous system, constriction increases blood pressure as it does in arteries; the increasing pressure helps return blood to the heart. In addition, constriction causes the vessel lumen to become more rounded, decreasing resistance and increasing blood flow. Venoconstriction, while less important than arterial vasoconstriction, works with the skeletal muscle pump, the respiratory pump, and their valves to promote venous return to the heart.

19.3 Capillary Exchange

Small molecules can cross into and out of capillaries via simple or facilitated diffusion. Some large molecules can cross in vesicles or through clefts, fenestrations, or gaps between cells in capillary walls. However, the bulk flow of capillary and tissue fluid occurs via filtration and reabsorption. Filtration, the movement of fluid out of the capillaries, is driven by the CHP. Reabsorption, the influx of tissue fluid into the capillaries, is driven by the BCOP. Filtration predominates in the arterial end of the capillary; in the middle section, the opposing pressures are virtually identical, so there is no net exchange, whereas reabsorption predominates at the venule end of the capillary. The hydrostatic and colloid osmotic pressures in the interstitial fluid are negligible in healthy circumstances.

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19.4 Homeostatic Regulation of the Vascular System

Neural, endocrine, and autoregulatory mechanisms affect blood flow, blood pressure, and eventually perfusion of blood to body tissues. Neural mechanisms include the cardiovascular centres in the medulla oblongata, baroreceptors in the aorta and carotid arteries and right atrium, and associated chemoreceptors that monitor blood levels of oxygen, carbon dioxide, and hydrogen ions. Endocrine controls include epinephrine and norepinephrine, as well as ADH, the renin-angiotensin-aldosterone mechanism, ANH, and EPO. Autoregulation is the local control of vasodilation and constriction by chemical signals and the myogenic response. Exercise greatly improves cardiovascular function and reduces the risk of cardiovascular diseases, including hypertension, a leading cause of heart attacks and strokes. Significant hemorrhage can lead to a form of circulatory shock known as hypovolemic shock. Sepsis, obstruction, and widespread inflammation can also cause circulatory shock.

19.5 Circulatory Pathways

The right ventricle pumps oxygen-depleted blood into the pulmonary trunk and right and left pulmonary arteries, which carry it to the right and left lungs for gas exchange. Oxygen-rich blood is transported by pulmonary veins to the left atrium. The left ventricle pumps this blood into the aorta. The main regions of the aorta are the ascending aorta, aortic arch, and descending aorta, which is further divided into the thoracic and abdominal aorta. The coronary arteries branch from the ascending aorta. After oxygenating tissues in the capillaries, systemic blood is returned to the right atrium from the venous system via the superior vena cava, which drains most of the veins superior to the diaphragm; the inferior vena cava, which drains most of the veins inferior to the diaphragm; and the coronary veins via the coronary sinus. The hepatic portal system carries blood to the liver for processing before it enters circulation. Review the figures provided in this section for circulation of blood through the blood vessels.

19.6 Development of Blood Vessels and Fetal Circulation

As the embryo grows within the mother's womb, the placenta develops to supply blood rich in oxygen and nutrients via the umbilical vein and to remove wastes in oxygen-depleted blood via the umbilical arteries. Three major shunts found in the fetus are the foramen ovale and ductus arteriosus, which divert blood from the pulmonary to the systemic circuit, and the ductus venosus, which carries freshly oxygenated blood high in nutrients to the fetal heart.

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20

The Lymphatic and Immune System

Chapter Objectives

After studying this chapter, you will be able to:

- Identify the components and anatomy of the lymphatic system
- Discuss the role of the innate immune response against pathogens
- Describe the power of the adaptive immune response to cure disease
- Describe the interaction of the immune and lymphatic systems with other body systems

Acquired immune deficiency syndrome, or AIDS, turned out to be a new disease caused by the previously unknown human immunodeficiency virus (HIV). Although nearly 100 percent fatal in those with active HIV infections in the early years, the development of anti-HIV drugs has transformed HIV infection into a chronic, manageable disease and not the certain death sentence it once was. One positive outcome resulting from the emergence of HIV disease was that the public's attention became focused as never before on the importance of having a functional and healthy immune system.

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20.1 Anatomy of the Lymphatic and Immune Systems

Learning Objectives

By the end of this section, you will be able to:

- Describe the structure and function of the lymphatic tissue (lymph fluid, vessels, ducts, and organs)
- Describe the structure and function of the primary and secondary lymphatic organs
- Discuss the cells of the immune system, how they function, and their relationship with the lymphatic system

The **immune system** is the complex collection of cells and organs that destroys or neutralizes pathogens that would otherwise cause disease or death. The lymphatic system, for most people, is associated with the immune system to such a degree that the two systems are virtually indistinguishable. The **lymphatic system** is the system of vessels, cells, and organs that carries excess fluids to the bloodstream and filters pathogens from the blood. The swelling of lymph nodes during an infection and the transport of lymphocytes via the lymphatic vessels are but two examples of the many connections between these critical organ systems.

Functions of the Lymphatic System

A major function of the lymphatic system is to drain body fluids and return them to the bloodstream. Blood pressure causes leakage of fluid from the capillaries, resulting in the accumulation of fluid in the interstitial space—that is, spaces between individual cells in the tissues. In humans, 20 L of plasma are released into the interstitial space of the tissues each day due to capillary filtration. Once this filtrate is out of the bloodstream and in the tissue spaces, it is referred to as interstitial fluid. Of this, 17 L are reabsorbed directly by the blood vessels. But what happens to the remaining 3 L? This is where the lymphatic system comes into play. It drains the excess fluid and empties it back into the bloodstream via a series of vessels, trunks, and ducts. **Lymph** is the term used to describe interstitial fluid once it has entered the lymphatic system. When the lymphatic system is damaged in some way, such as by being blocked by cancer cells or destroyed by injury, protein-rich interstitial fluid accumulates (sometimes "backs up" from the lymph vessels) in the tissue spaces. This inappropriate accumulation of fluid, referred to as lymphedema, may lead to serious medical consequences.

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As the vertebrate immune system evolved, the network of **lymphatic vessels** became a convenient avenue for transporting the cells of the immune system. Additionally, the transport of dietary lipids and fat-soluble vitamins absorbed in the gut uses this system.

Cells of the immune system not only use lymphatic vessels to make their way from interstitial spaces back into the circulation, but they also use lymph nodes as major staging areas for the development of critical immune responses. A **lymph node** is one of the small, bean-shaped organs located throughout the lymphatic system.

Interactive Link 20.1

Visit this website (http://oer.aupress.ca/oer-202505/20.1) for an overview of the lymphatic system. What are the three main components of the lymphatic system?

Structure of the Lymphatic System

The **lymphatic vessels** begin as blind ending capillaries (closed at one end), which feed into larger and larger lymphatic vessels and eventually empty into the bloodstream by a series of ducts. Along the way, the lymph travels through the lymph nodes, which are commonly found near the groin, armpits, neck, chest, and abdomen. Humans have about 500–600 lymph nodes throughout the body (Figure 20.1).

A major distinction between the lymphatic and cardiovascular systems in humans is that lymph is not actively pumped by the heart but forced through the vessels by the movements of the body, the contraction of skeletal muscles during body movements, and breathing. One-way valves (semilunar valves) in lymphatic vessels keep the lymph moving toward the heart. Lymph flows from the lymphatic capillaries, through lymphatic vessels, and then is dumped into the circulatory system via the lymphatic ducts located at the junction of the jugular and subclavian veins in the neck.

Lymphatic Capillaries

Lymphatic capillaries, also called the terminal lymphatics, are vessels where interstitial fluid enters the lymphatic system to become lymph fluid. Located in almost every tissue in the body, these vessels are interlaced among the arterioles and venules of the circulatory system in the soft connective tissues of the body (Figure 20.2). Exceptions are the central nervous system, bone marrow, bones, teeth, and the cornea of the eye, which do not contain lymph vessels.

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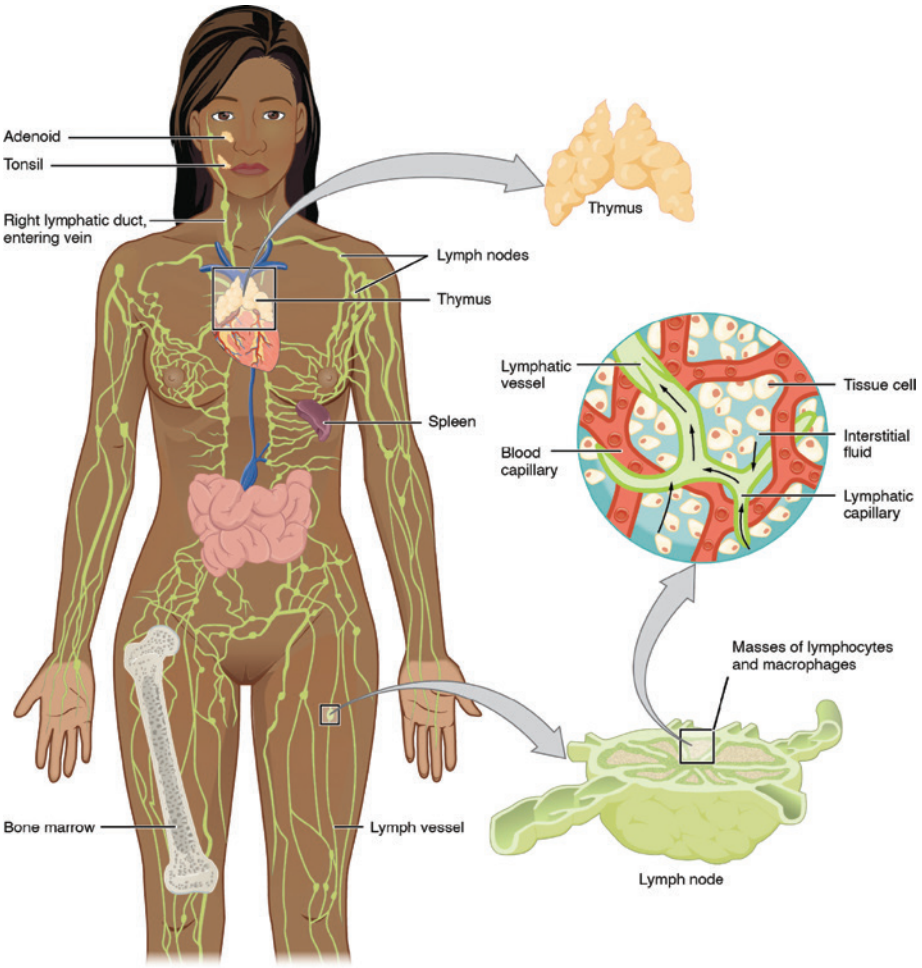


Figure 20.1 Anatomy of the Lymphatic System. Lymphatic vessels in the arms and legs convey lymph to the larger lymphatic vessels in the torso.

Lymphatic capillaries are formed by a one-cell-thick layer of endothelial cells and represent the open end of the system, allowing interstitial fluid to flow into them via overlapping cells (see Figure 20.2). When interstitial pressure is low, the endothelial flaps close to prevent "backflow." As interstitial pressure increases, the spaces between the cells open up, allowing the fluid to enter. Entry of fluid into lymphatic capillaries is also enabled by the collagen filaments that anchor the capillaries to surrounding structures. As interstitial pressure increases, the filaments pull on the endothelial cell flaps, opening them up even further to allow easy entry of fluid.

In the small intestine, lymphatic capillaries called **lacteals** are critical for the transport of dietary lipids and lipid-soluble vitamins to the bloodstream. In the small intestine, dietary triglycerides combine with other lipids and

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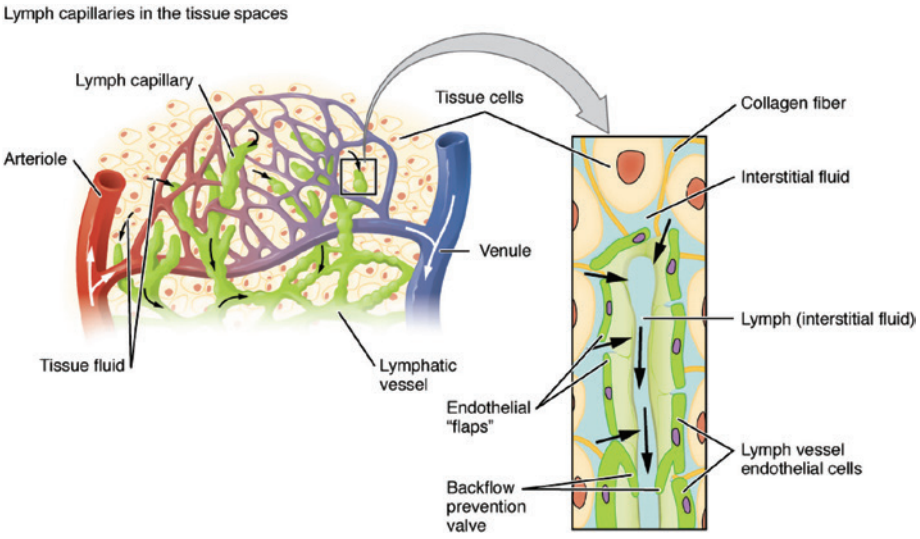


Figure 20.2 Lymphatic Capillaries. Lymphatic capillaries are interlaced with the arterioles and venules of the cardiovascular system. Collagen fibres anchor a lymphatic capillary in the tissue (inset). Interstitial fluid slips through spaces between the overlapping endothelial cells that compose the lymphatic capillary.

proteins and enter the lacteals to form a milky fluid called **chyle**. The chyle then travels through the lymphatic system, eventually entering the bloodstream.

Larger Lymphatic Vessels, Trunks, and Ducts

The lymphatic capillaries empty into larger lymphatic vessels, which are similar to veins in terms of their three-tunic structure and the presence of valves. These one-way valves are located fairly close to one another, and each one causes a bulge in the lymphatic vessel, giving the vessels a beaded appearance (see Figure 20.2).

The superficial and deep lymphatics eventually merge to form larger lymphatic vessels known as **lymphatic trunks**. On the right side of the body, the right sides of the head, thorax, and right upper limb drain lymph fluid into the right subclavian vein via the right lymphatic duct (Figure 20.3). The remaining portions of the left side of the body drain into the larger thoracic duct, which drains into the left subclavian vein. The thoracic duct itself begins just beneath the diaphragm in the **cisterna chyli**, a sac-like chamber that receives lymph from the lower abdomen, pelvis, and lower limbs by way of the left and right lumbar trunks and the intestinal trunk.

The overall drainage system of the body is asymmetrical (see Figure 20.3). The **right lymphatic duct** receives lymph from only the upper right side of the body. The lymph from the rest of the body enters the bloodstream through the **thoracic**

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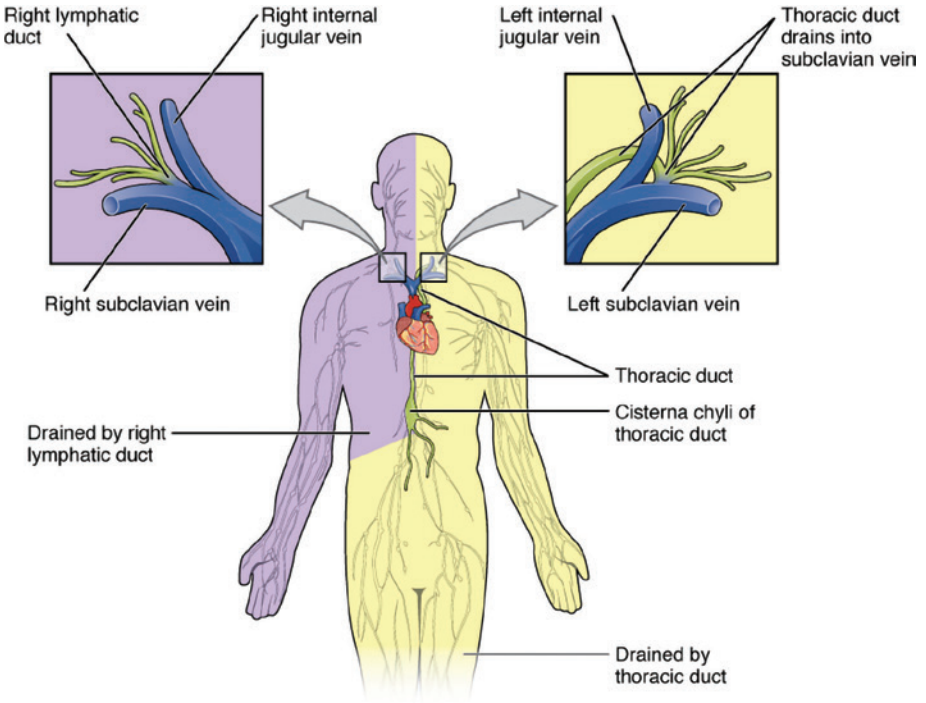


Figure 20.3 Major Trunks and Ducts of the Lymphatic System. The thoracic duct drains a much larger portion of the body than does the right lymphatic duct.

duct via all the remaining lymphatic trunks. In general, the lymphatic vessels of the subcutaneous tissues of the skin—that is, the superficial lymphatics—follow the same routes as veins, whereas the deep lymphatic vessels of the viscera generally follow the paths of arteries.

The Organization of Immune Function

The immune system is a collection of barriers, cells, and soluble proteins that interact and communicate with each other in extraordinarily complex ways. The modern model of immune function is organized into three phases based on the timing of their effects. The three temporal phases consist of the following:

- **Barrier defences** such as the skin and mucous membranes, which act instantaneously to prevent pathogenic invasion of the body tissues
- The rapid but nonspecific **innate immune response**, which consists of a variety of specialized cells and soluble factors
- The slower but more specific and effective **adaptive immune response**, which involves many cell types and soluble factors but is primarily

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controlled by white blood cells (leukocytes) known as **lymphocytes**, which help control immune responses

The cells of the blood, including all those involved in the immune response, arise in the bone marrow via various differentiation pathways from hematopoietic stem cells (Figure 20.4). In contrast with embryonic stem cells, hematopoietic stem cells are present throughout adulthood and allow for the continuous differentiation of blood cells to replace those lost to age or function. These cells can be divided into three classes based on function:

- Phagocytic cells, which ingest pathogens to destroy them
- Lymphocytes, which specifically coordinate the activities of adaptive immunity
- Cells containing cytoplasmic granules, which help mediate immune responses against parasites and intracellular pathogens such as viruses

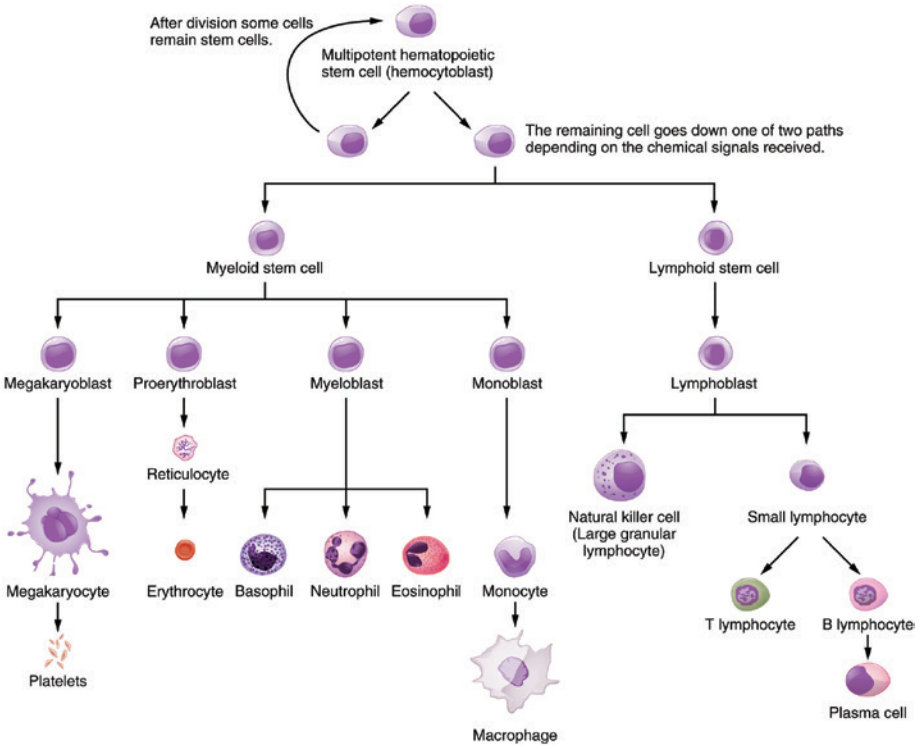


Figure 20.4 Hematopoietic System of the Bone Marrow. All the cells of the immune response as well as of the blood arise by differentiation from hematopoietic stem cells. Platelets are cell fragments involved in the clotting of blood.

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Lymphocytes: B Cells, T Cells, Plasma Cells, and Natural Killer Cells

As stated in the previous section, lymphocytes are the primary cells of adaptive immune responses (Table 20.1). The two basic types of lymphocytes, B cells and T cells, are identical morphologically, with a large central nucleus surrounded by a thin layer of cytoplasm. They are distinguished from each other by their surface protein markers as well as by the molecules they secrete. While B cells mature in red bone marrow and T cells mature in the thymus, they both initially develop from bone marrow. T cells migrate from bone marrow to the thymus gland, where they further mature. B cells and T cells are found in many parts of the body, circulating in the bloodstream and lymph and residing in secondary lymphoid organs, including the spleen and lymph nodes, which will be described later in this section. The human body contains approximately 1,012 lymphocytes.

Table 20.1 Lymphocytes

Type of lymphocyte	Primary function
B lymphocyte	Generates diverse antibodies
T lymphocyte	Secretes chemical messengers
Plasma cell	Secretes antibodies
NK cell	Destroys virally infected cells

B Cells

B cells are immune cells that function primarily by producing antibodies. An **antibody** is any of the group of proteins that binds specifically to pathogen-associated molecules known as antigens. An **antigen** is a chemical structure on the surface of a pathogen that binds to T or B lymphocyte antigen receptors. Once activated by binding to an antigen, B cells differentiate into cells that secrete a soluble form of their surface antibodies. These activated B cells are known as plasma cells.

T Cells

The **T cell**, on the other hand, does not secrete antibodies but performs a variety of functions in the adaptive immune response. Different T cell types have the ability to either secrete soluble factors that communicate with other cells of the adaptive immune response or destroy cells infected with intracellular pathogens. The roles of T and B lymphocytes in the adaptive immune response will be discussed further in this chapter.

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Plasma Cells

Another type of lymphocyte of importance is the plasma cell. A **plasma cell** is a B cell that has differentiated in response to antigen binding and has thereby gained the ability to secrete soluble antibodies. These cells differ in morphology from standard B and T cells in that they contain a large amount of cytoplasm packed with the protein-synthesizing machinery known as rough endoplasmic reticulum.

Natural Killer Cells

A fourth important lymphocyte is the natural killer cell, a participant in the innate immune response. A **natural killer** (**NK**) **cell** is a circulating blood cell that contains cytotoxic (cell-killing) granules in its extensive cytoplasm. It shares this mechanism with the **cytotoxic T cells** (**Tc**) of the adaptive immune response. NK cells are among the body's first lines of defence against viruses and certain types of cancer.

Interactive Link 20.2

Visit this website (http://oer.aupress.ca/oer-202505/20.2) to learn about the many different cell types in the immune system and their very specialized jobs. What is the role of the dendritic cell in an HIV infection?

Primary Lymphoid Organs and Lymphocyte Development

Knowledge of B and T cell differentiation and development is fundamental to understanding the adaptive immune response. It is through this process that the body (ideally) learns to destroy only pathogens and leaves the body's own cells relatively intact. The **primary lymphoid organs** are the bone marrow and thymus gland. The lymphoid organs are where lymphocytes mature, proliferate, and are selected, which enables them to attack pathogens without harming the cells of the body.

Bone Marrow

In the embryo, blood cells are made in the yolk sac. As development proceeds, this function is taken over by the spleen, lymph nodes, and liver. Later, the bone marrow takes over most hematopoietic functions, although the final stages of the differentiation of some cells may take place in other organs. The red **bone marrow** is a loose collection of cells where hematopoiesis occurs, and the yellow bone marrow is a site of energy storage, which consists largely of fat cells (Figure 20.5).

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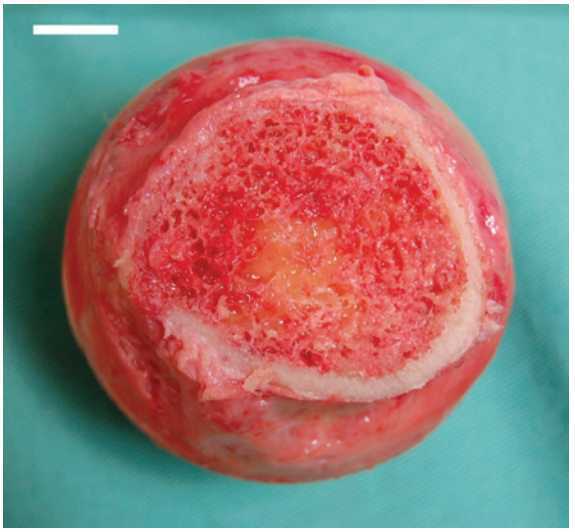


Figure 20.5 Bone Marrow. Red bone marrow fills the head of the femur, and a spot of yellow bone marrow is visible in the centre. The white reference bar is 1 cm.

The B cell undergoes nearly all of its development in the red bone marrow, whereas the immature T cell, called a **thymocyte**, leaves the bone marrow and matures largely in the thymus gland.

Thymus

The **thymus**, also called the thymus gland, is a bilobed organ found in the space between the sternum and the aorta of the heart (Figure 20.6). Connective tissue holds the lobes closely together but also separates them and forms a capsule.

Interactive Link 20.3

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/20.3) to explore the tissue sample in greater detail.

The connective tissue capsule further divides the thymus into lobules via extensions called trabeculae. The outer region of the organ is known as the cortex and contains large numbers of thymocytes with some epithelial cells, macrophages, and **dendritic cells** (two types of phagocytic cells that are derived from monocytes). The cortex is densely packed, so it stains more intensely than the rest of the thymus (see Figure 20.6). The medulla, where thymocytes migrate before leaving the thymus, contains a less dense collection of thymocytes, epithelial cells, and dendritic cells.

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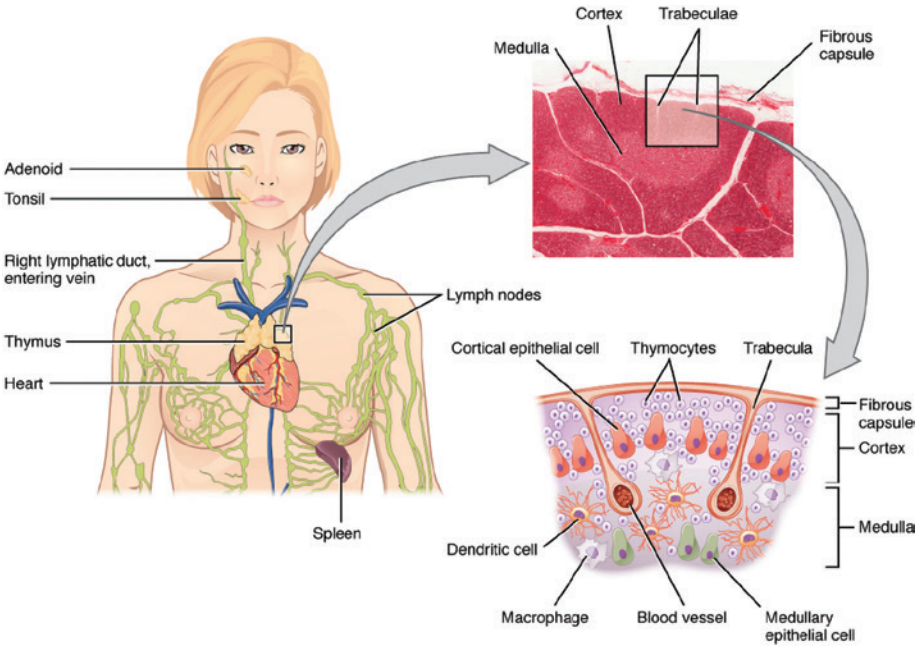


Figure 20.6 Location, Structure, and Histology of the Thymus. The thymus lies above the heart. The trabeculae and lobules, including the darkly staining cortex and the lighter-staining medulla of each lobule, are clearly visible in the light micrograph of the thymus of a newborn. LM × 100. (Micrograph provided by the Regents of the University of Michigan Medical School © 2012)

Secondary Lymphoid Organs and Their Roles in Active Immune Responses

Lymphocytes develop and mature in the primary lymphoid organs, but they mount immune responses from the **secondary lymphoid organs**. A **naive lymphocyte** is one that has left the primary organ and entered a secondary lymphoid organ. Naive lymphocytes are fully functional immunologically but have yet to encounter an antigen to respond to. In addition to circulating in the blood and lymph, lymphocytes concentrate in secondary lymphoid organs, which include the lymph nodes, spleen, and lymphoid nodules. All of these tissues have many features in common, including the following:

- The presence of **lymphoid follicles**, the sites of the formation of lymphocytes, with specific B cell–rich and T cell–rich areas
- An internal structure of reticular fibres with associated fixed macrophages
- **Germinal centres**, which are the sites of rapidly dividing and differentiating B lymphocytes

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- Specialized postcapillary vessels known as high endothelial venules; the cells lining these venules are thicker and more columnar than normal endothelial cells, which allow cells from the blood to directly enter these tissues

Lymph Nodes

Lymph nodes function to remove debris and pathogens from the lymph and are thus sometimes referred to as the "filters of the lymph" (Figure 20.7). Any bacteria that infect the interstitial fluid are taken up by the lymphatic capillaries and transported to a regional lymph node. Dendritic cells and macrophages within this organ internalize and kill many of the pathogens that pass through, thereby removing them from the body. The lymph node is also the site of adaptive immune responses mediated by T cells, B cells, and accessory cells of the adaptive immune system. Like the thymus, the bean-shaped lymph nodes are surrounded by a tough capsule of connective tissue and are separated into compartments by trabeculae, the extensions of the capsule. In addition to the structure provided by the capsule and trabeculae, the structural support of the lymph node is provided by a series of reticular fibres laid down by fibroblasts.

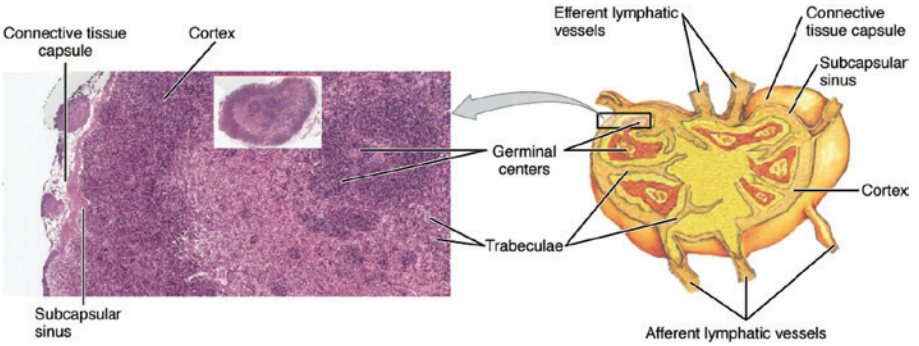


Figure 20.7 Structure and Histology of a Lymph Node. Lymph nodes are masses of lymphatic tissue located along the larger lymph vessels. The micrograph of the lymph nodes shows a germinal centre, which consists of rapidly dividing B cells surrounded by a layer of T cells and other accessory cells. LM × 128. (Micrograph provided by the Regents of the University of Michigan Medical School © 2012)

Interactive Link 20.4

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/20.4) to explore the tissue sample in greater detail.

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The major routes into the lymph node are via **afferent lymphatic vessels** (see Figure 20.7). Cells and lymph fluid that leave the lymph node may do so by another set of vessels known as the **efferent lymphatic vessels**. Lymph from afferent lymphatic vessels enters the lymph node via the subcapsular sinus, which is occupied by dendritic cells, macrophages, and reticular fibres. Within the cortex of the lymph node are lymphoid follicles, which consist of germinal centres of rapidly dividing B cells surrounded by a layer of T cells and other accessory cells. As the lymph continues to flow through the node, it enters the medulla, which consists of medullary cords of B cells and plasma cells, and the medullary sinuses, where the lymph collects before leaving the node via the efferent lymphatic vessels.

Spleen

In addition to the lymph nodes, the **spleen** is a major secondary lymphoid organ (Figure 20.8). It is about 12 cm long and is attached to the lateral border of the stomach via the gastrosplenic ligament. The spleen is a fragile organ without a strong capsule and is dark red due to its extensive vascularization. The spleen is sometimes called the "filter of the blood" because of its extensive vascularization and the presence of macrophages and dendritic cells that remove microbes and other materials from the blood, including dying red blood cells. The spleen also functions as the location of immune responses to blood-borne pathogens.

The spleen is also divided by trabeculae of connective tissue, and within each splenic nodule is an area of **red pulp**, consisting of mostly red blood cells, and **white pulp**, which resembles the lymphoid follicles of the lymph nodes.

Upon entering the spleen, the splenic artery splits into several arterioles (surrounded by white pulp) and eventually into sinusoids. Blood from the capillaries subsequently collects in the venous sinuses and leaves via the splenic vein. The red pulp consists of reticular fibres with fixed macrophages attached, free macrophages, and all of the other cells typical of the blood, including some lymphocytes. The white pulp surrounds a central arteriole and consists of germinal centres of dividing B cells surrounded by T cells and accessory cells, including macrophages and dendritic cells. Thus, the red pulp primarily functions as a filtration system of the blood, using cells of the relatively nonspecific immune response, and white pulp is where adaptive T and B cell responses are mounted.

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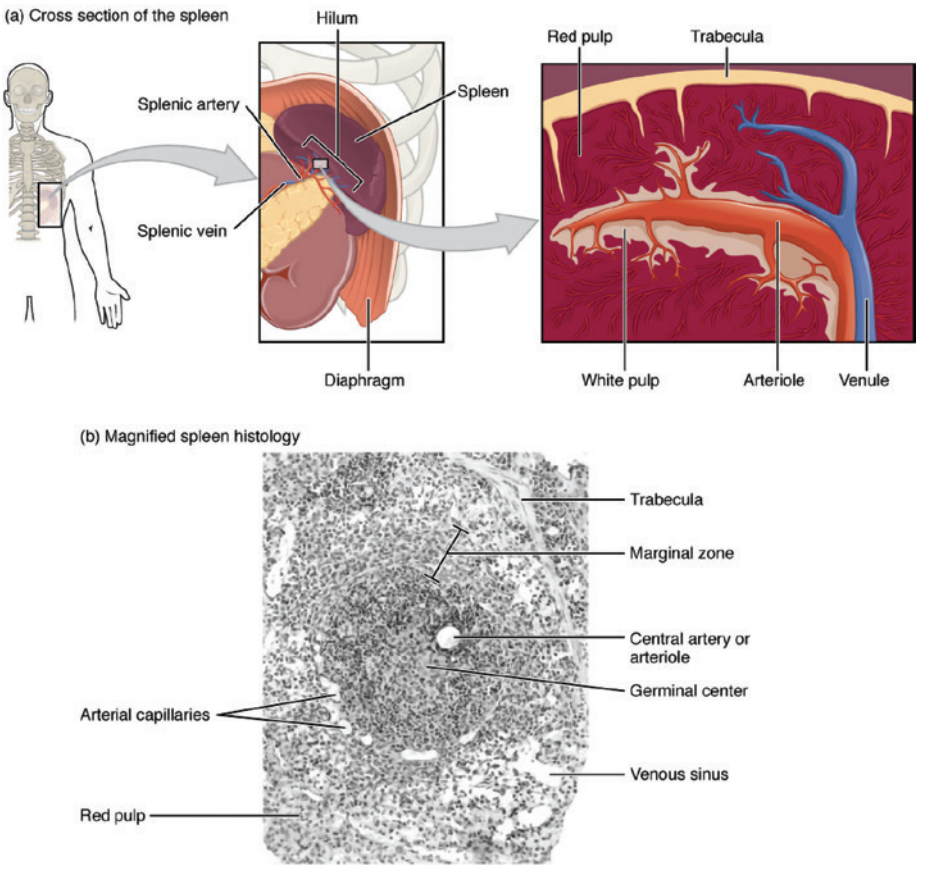


Figure 20.8 Spleen. (a) The spleen is attached to the stomach. (b) A micrograph of spleen tissue shows the germinal centre. The marginal zone is the region between the red pulp and white pulp, which sequesters particulate antigens from the circulation and presents these antigens to lymphocytes in the white pulp. EM × 660. (Micrograph provided by the Regents of the University of Michigan Medical School © 2012)

Lymphoid Nodules

The other lymphoid tissues, the **lymphoid nodules**, have a simpler architecture than the spleen and lymph nodes in that they consist of a dense cluster of lymphocytes without a surrounding fibrous capsule. These nodules are located in the respiratory and digestive tracts, areas routinely exposed to environmental pathogens.

Tonsils (specifically named the **palatine, pharyngeal, and lingual tonsils**) are lymphoid nodules located along the inner surface of the pharynx and are important in developing immunity to oral pathogens (Figure 20.9). The tonsil located at the back of the throat, the pharyngeal tonsil, is sometimes referred to as the adenoid when swollen. Such swelling is an indication of an active

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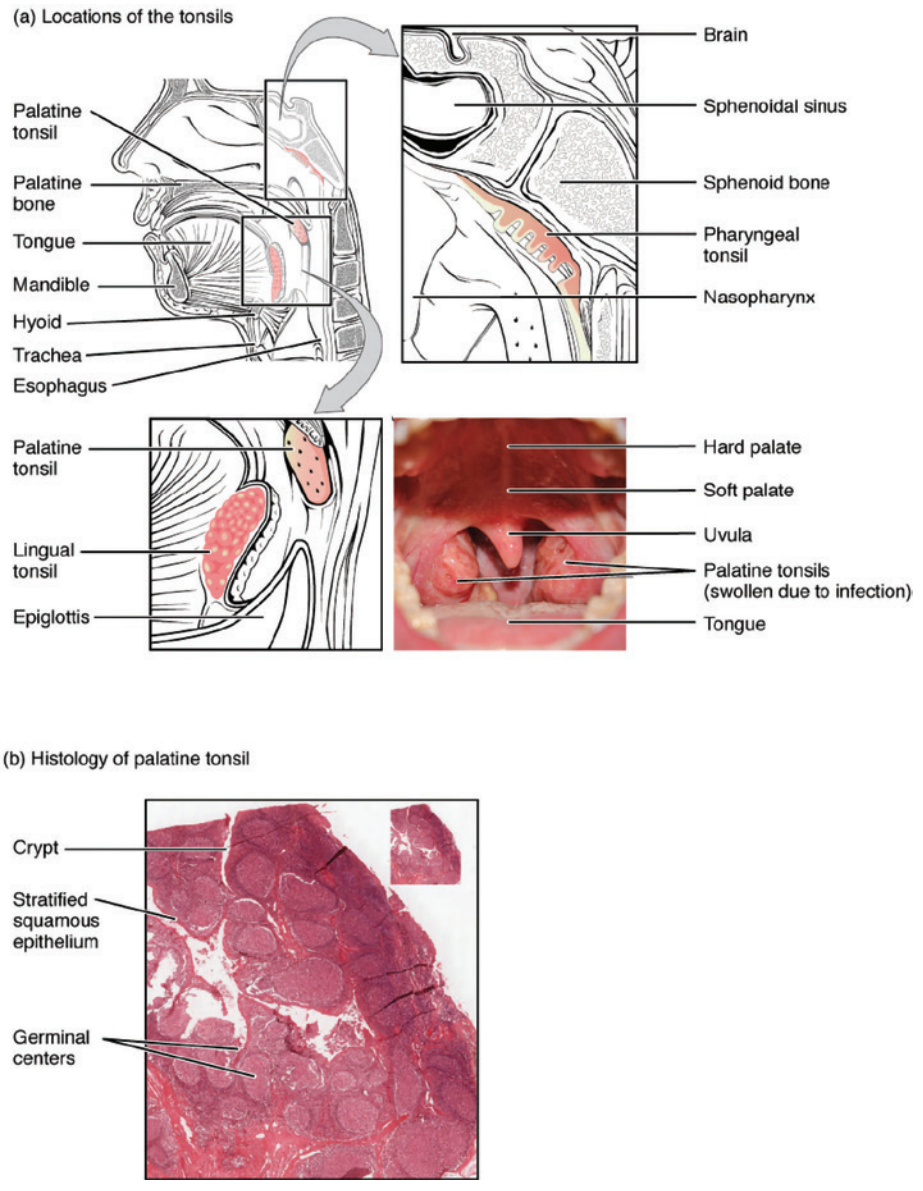


Figure 20.9 Locations and Histology of the Tonsils. (a) The pharyngeal tonsil is located on the roof of the posterior superior wall of the nasopharynx. The palatine tonsils lay on each side of the pharynx. (b) A micrograph shows the palatine tonsil tissue. LM × 40. (Micrograph provided by the Regents of the University of Michigan Medical School © 2012)

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immune response to infection. Histologically, tonsils do not contain a complete capsule, and the epithelial layer invaginates deeply into the interior of the tonsil to form tonsillar crypts. These structures, which accumulate all sorts of materials taken into the body through eating and breathing, actually "encourage" pathogens to penetrate deep into the tonsillar tissues, where they are acted upon by numerous lymphoid follicles and eliminated. This seems to be the major function of tonsils—to help children's bodies recognize, destroy, and develop immunity to common environmental pathogens so that they will be protected in their later lives. Tonsils are often removed in those children who have recurring throat infections, especially those involving the palatine tonsils on either side of the throat, whose swelling may interfere with their breathing and/or swallowing.

Interactive Link 20.5

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/20.5) to explore the tissue sample in greater detail.

Mucosa-associated lymphoid tissue (**MALT**) consists of an aggregate of lymphoid follicles directly associated with the mucous membrane epithelia. MALT makes up dome-shaped structures found underlying the mucosa of the gastrointestinal tract, breast tissue, lungs, and eyes. **Peyer's patches**, a type of MALT in the small intestine, are especially important for immune responses against ingested substances (Figure 20.10). Peyer's patches contain specialized endothelial cells called M (or microfold) cells that sample material from the intestinal lumen and transport it to nearby follicles so that adaptive immune responses to potential pathogens can be mounted. A similar process occurs involving MALT in the mucosa and submucosa of the appendix. A blockage of the lumen triggers these cells to elicit an inflammatory response that can lead to appendicitis.

Bronchus-associated lymphoid tissue (**BALT**) consists of lymphoid follicular structures with an overlying epithelial layer found along the bifurcations of the bronchi and between bronchi and arteries. They also have the typically less-organized structure of other lymphoid nodules. These tissues, in addition to the tonsils, are effective against inhaled pathogens.

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Figure 20.10 Mucosa-Associated Lymphoid Tissue (MALT) Nodule. LM × 40. (Micrograph provided by the Regents of the University of Michigan Medical School © 2012)

20.2 Barrier Defences and the Innate Immune Response

Learning Objectives

By the end of this section, you will be able to:

- Describe the barrier defences of the body
- Show how the innate immune response is important and how it helps guide and prepare the body for adaptive immune responses
- Describe various soluble factors that are part of the innate immune response
- Explain the steps of inflammation and how they lead to destruction of a pathogen
- Discuss early induced immune responses and their level of effectiveness

The immune system can be divided into two overlapping mechanisms to destroy pathogens: the innate immune response, which is relatively rapid but non-specific and thus not always effective, and the adaptive immune response,

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which is slower in its development during an initial infection with a pathogen but is highly specific and effective at attacking a wide variety of pathogens (Figure 20.11).

Any discussion of the innate immune response usually begins with the physical barriers that prevent pathogens from entering the body, destroy them after they enter, or flush them out before they can establish themselves in the hospitable environment of the body's soft tissues. Barrier defences are part of the body's most basic defence mechanisms. The barrier defences are not a response to infections, but they are continuously working to protect against a broad range of pathogens.

The different modes of barrier defences are associated with the external surfaces of the body, where pathogens may try to enter (Table 20.2). The primary barrier to the entrance of microorganisms into the body is the skin. Not only is the skin covered with a layer of dead, keratinized epithelium that is too dry for bacteria to grow in, but as these cells are continuously sloughed off from the skin, they carry bacteria and other pathogens with them.

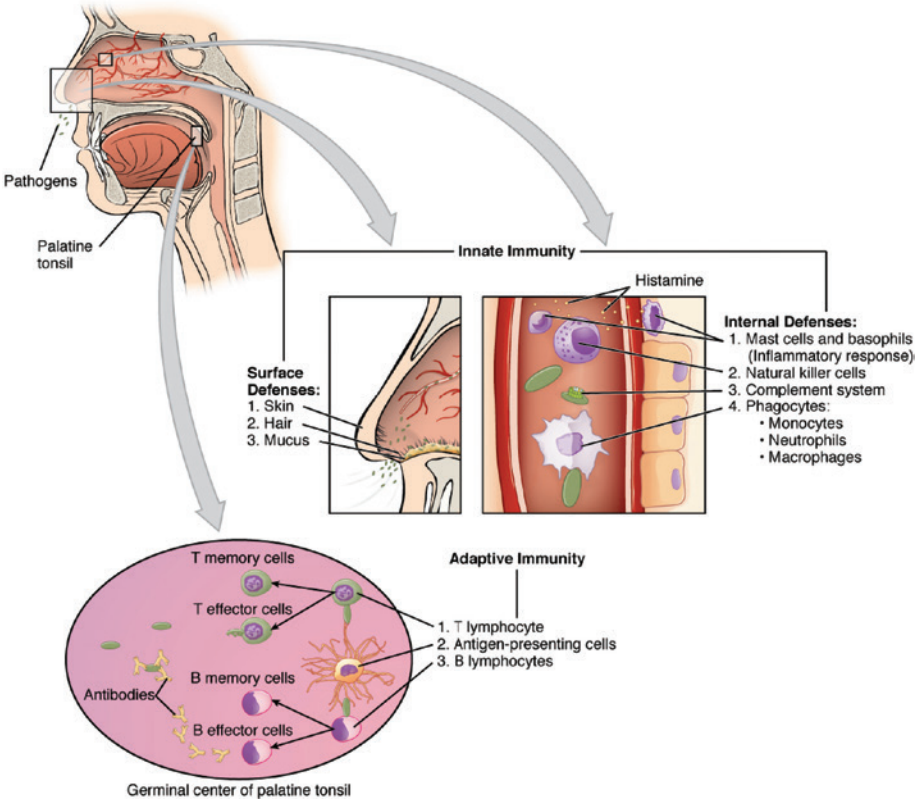


Figure 20.11 Cooperation Between Innate and Adaptive Immune Responses. The innate immune system enhances adaptive immune responses so they can be more effective.

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Additionally, sweat and other skin secretions may lower pH, contain toxic lipids, and physically wash microbes away.

Table 20.2 Barrier Defences

Site	Specific defence	Protective aspect
Skin	Epidermal surface	Keratinized cells of surface, Langerhans cells
Skin (sweat/secretions)	Sweat glands, sebaceous glands	Low pH, washing action
Oral cavity	Salivary glands	Lysozyme
Stomach	Gastrointestinal tract	Low pH
Mucosal surfaces	Mucosal epithelium	Nonkeratinized epithelial cells
Normal flora (nonpathogenic bacteria)	Mucosal tissues	Prevent pathogens from growing on mucosal surfaces

Another barrier is the saliva in the mouth, which is rich in lysozyme—an enzyme that destroys bacteria by digesting their cell walls. The acidic environment of the stomach, which is fatal to many pathogens, is also a barrier.

Additionally, the mucus layer of the gastrointestinal tract, respiratory tract, reproductive tract, eyes, ears, and nose traps both microbes and debris and facilitates their removal. In the case of the upper respiratory tract, ciliated epithelial cells move potentially contaminated mucus upward to the mouth, where it is then swallowed into the digestive tract, ending up in the harsh acidic environment of the stomach. Considering how often you breathe compared to how often you eat or perform other activities that expose you to pathogens, it is not surprising that multiple barrier mechanisms have evolved to work in concert to protect this vital area.

Cells of the Innate Immune Response

A phagocyte is a cell that is able to surround and engulf a particle or cell, a process called **phagocytosis**. Phagocytes of the immune system engulf particles or cells to remove debris, such as dead or damaged cells, or to destroy pathogens like bacteria. Phagocytes are the body's fast-acting, first line of immunological defence against organisms that have breached barrier defences and have entered the vulnerable tissues of the body.

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Phagocytes: Macrophages and Neutrophils

Many of the cells of the immune system have a phagocytic ability, at least at some point during their life cycles. Phagocytosis is an important and effective mechanism of destroying pathogens during innate immune responses. The phagocyte takes the organism inside itself as a phagosome, which subsequently fuses with a lysosome and its digestive enzymes, effectively killing many pathogens. On the other hand, some bacteria, including *Mycobacterium tuberculosis*, the cause of tuberculosis, may be resistant to these enzymes and are therefore much more difficult to clear from the body. Macrophages, neutrophils, and dendritic cells are the major phagocytes of the immune system.

A **macrophage** is an irregularly shaped phagocyte that is amoeboid in nature and is the most versatile of the phagocytes in the body. Macrophages move through tissues and squeeze through capillary walls using pseudopodia. They not only participate in innate immune responses but have also evolved to cooperate with lymphocytes as part of the adaptive immune response. Macrophages exist in many tissues of the body, either freely roaming through connective tissues or fixed to reticular fibres within specific tissues such as lymph nodes. When pathogens breach the body's barrier defences, macrophages are the first line of defence (Table 20.3). They are called different names, depending on the tissue: Kupffer cells in the liver, histiocytes in connective tissue, and alveolar macrophages in the lungs.

A **neutrophil** is a phagocytic cell that is attracted via chemotaxis from the bloodstream to infected tissues. These spherical cells are granulocytes. A granulocyte contains cytoplasmic granules, which in turn contain a variety of vasoactive mediators such as histamine. In contrast, macrophages are agranulocytes. An agranulocyte has few or no cytoplasmic granules. Whereas macrophages act like sentries, always on guard against infection, neutrophils can be thought of as military reinforcements that are called into a battle to hasten the destruction of the enemy. Although usually thought of as

Table 20.3 Phagocytic Cells of the Innate Immune System

Cell	Cell type	Primary location	Function in the innate immune response
Macrophage	Agranulocyte	Body cavities/organs	Phagocytosis
Neutrophil	Granulocyte	Blood	Phagocytosis
Monocyte	Agranulocyte	Blood	Precursor of macrophage/ dendritic cell

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the primary pathogen-killing cell of the inflammatory process of the innate immune response, new research has suggested that neutrophils play a role in the adaptive immune response as well, just as macrophages do.

A **monocyte** is a circulating precursor cell that differentiates into either a macrophage or a dendritic cell, which can be rapidly attracted to areas of infection by signal molecules of inflammation.

Natural Killer Cells

NK cells are a type of lymphocyte that have the ability to induce apoptosis—that is, programmed cell death—in cells infected with intracellular pathogens such as obligate intracellular bacteria and viruses. NK cells recognize these cells by mechanisms that are still not well understood but that presumably involve their surface receptors. NK cells can induce apoptosis, in which a cascade of events inside the cell causes its own death by either of two mechanisms:

1. NK cells are able to respond to chemical signals and express the fas ligand. The fas ligand is a surface molecule that binds to the fas molecule on the surface of the infected cell, sending it apoptotic signals, thus killing the cell and the pathogen within it; or
2. The granules of the NK cells release perforins and granzymes. A **perforin** is a protein that forms pores in the membranes of infected cells. A **granzyme** is a protein-digesting enzyme that enters the cell via the perforin pores and triggers apoptosis intracellularly.

Both mechanisms are especially effective against virally infected cells. If apoptosis is induced before the virus has the ability to synthesize and assemble all its components, no infectious virus will be released from the cell, thus preventing further infection.

Recognition of Pathogens

Cells of the innate immune response, the phagocytic cells, and the cytotoxic NK cells recognize patterns of pathogen-specific molecules, such as bacterial cell wall components or bacterial flagellar proteins, using pattern recognition receptors. A pattern recognition receptor (PRR) is a membrane-bound receptor that recognizes characteristic features of a pathogen and molecules released by stressed or damaged cells.

These receptors, which are thought to have evolved prior to the adaptive immune response, are present on the cell surface whether they are needed or not. Their variety, however, is limited by two factors. First, the fact that each receptor type must be encoded by a specific gene requires the cell to allocate

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most or all of its DNA to make receptors able to recognize all pathogens. Second, the variety of receptors is limited by the finite surface area of the cell membrane. Thus, the innate immune system must "get by" using only a limited number of receptors that are active against as wide a variety of pathogens as possible. This strategy is in stark contrast to the approach used by the adaptive immune system, which uses large numbers of different receptors, each highly specific to a particular pathogen.

Should the cells of the innate immune system come into contact with a species of pathogen they recognize, the cell will bind to the pathogen and initiate phagocytosis (or cellular apoptosis in the case of an intracellular pathogen) in an effort to destroy the offending microbe. Receptors vary somewhat according to cell type, but they usually include receptors for bacterial components and for complement, discussed below.

Soluble Mediators of the Innate Immune Response

The previous discussions have alluded to chemical signals that can induce cells to change various physiological characteristics, such as the expression of a particular receptor. These soluble factors are secreted during innate or early induced responses and later during adaptive immune responses.

Cytokines and Chemokines

A **cytokine** is a signalling molecule that allows cells to communicate with each other over short distances. Cytokines are secreted into the intercellular space, and the action of the cytokine induces the receiving cell to change its physiology. A **chemokine** is a soluble chemical mediator similar to cytokines except that its function is to attract cells (chemotaxis) from longer distances.

Interactive Link 20.6

Visit this website (http://oer.aupress.ca/oer-202505/20.6) to learn about phagocyte chemotaxis. Phagocyte chemotaxis is the movement of phagocytes according to the secretion of chemical messengers in the form of interleukins and other chemokines. By what means does a phagocyte destroy a bacterium that it has ingested?

Early Induced Proteins

Early induced proteins are those that are not constitutively present in the body but are made as they are needed early during the innate immune response.

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Interferons are an example of early induced proteins. Cells infected with viruses secrete interferons that travel to adjacent cells and induce them to make antiviral proteins. Thus, even though the initial cell is sacrificed, the surrounding cells are protected. Other early induced proteins specific for bacterial cell wall components are mannose-binding protein and C-reactive protein, made in the liver, which bind specifically to polysaccharide components of the bacterial cell wall. Phagocytes such as macrophages have receptors for these proteins, and they are thus able to recognize them as they are bound to the bacteria. This brings the phagocyte and bacterium into close proximity and enhances the phagocytosis of the bacterium by the process known as opsonization. **Opsonization** is the tagging of a pathogen for phagocytosis by the binding of an antibody or an antimicrobial protein.

Complement System

The **complement** system is a series of proteins constitutively found in the blood plasma. As such, these proteins are not considered part of the early induced immune response, even though they share features with some of the antibacterial proteins of this class. Made in the liver, they have a variety of functions in the innate immune response, using what is known as the "alternate pathway" of complement activation. Additionally, the complement system functions in the adaptive immune response as well in what is called the classical pathway. The complement system consists of several proteins that enzymatically alter and fragment later proteins in a series, which is why it is termed *cascade*. Once activated, the series of reactions is irreversible and releases fragments that have the following actions:

- Bind to the cell membrane of the pathogen that activates it, labelling it for phagocytosis (opsonization)
- Diffuse away from the pathogen and act as chemotactic agents to attract phagocytic cells to the site of inflammation
- Form damaging pores in the plasma membrane of the pathogen.

Inflammatory Response

The hallmark of the innate immune response is **inflammation**. Inflammation is something everyone has experienced. Stub a toe, cut a finger, or do any activity that causes tissue damage and inflammation will result, with its four characteristics: heat, redness, pain, and swelling ("loss of function" is sometimes mentioned as a fifth characteristic). It is important to note that inflammation does not have to be initiated by an infection but can also be caused by tissue

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injuries. The release of damaged cellular contents into the site of injury is enough to stimulate the response, even in the absence of breaks in physical barriers that would allow pathogens to enter (by hitting your thumb with a hammer, for example). The inflammatory reaction brings phagocytic cells to the damaged area to clear cellular debris and to set the stage for wound repair (Figure 20.12).

This reaction also brings in the cells of the innate immune system, allowing them to get rid of the sources of a possible infection. Inflammation is part of a very basic form of immune response. The process not only brings fluid and cells into the site to destroy the pathogen and remove it and debris from the site but also helps isolate the site, limiting the spread of the pathogen. **Acute inflammation** is a short-term inflammatory response to an insult to the body. If the cause of the inflammation is not resolved, however, it can lead to chronic inflammation, which is associated with major tissue destruction and fibrosis. **Chronic inflammation** is ongoing inflammation. It can be caused by foreign bodies, persistent pathogens, and autoimmune diseases such as rheumatoid arthritis.

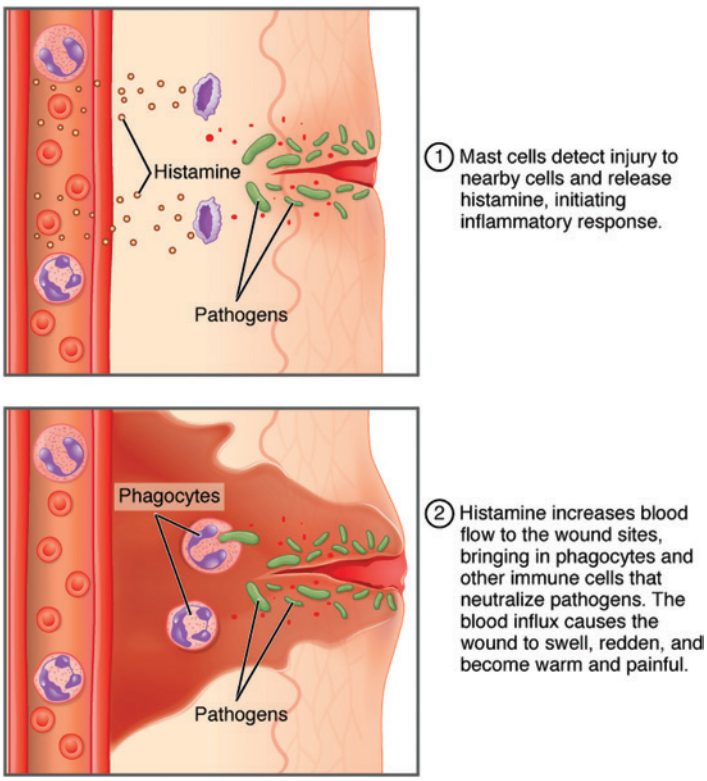


Figure 20.12 The Inflammatory Reaction.

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There are four important parts to the inflammatory response:

- *Tissue Injury.* The released contents of injured cells stimulate the release of **mast cell** granules and their potent inflammatory mediators, such as histamine, leukotrienes, and prostaglandins. **Histamine** increases the diameter of local blood vessels (vasodilation), causing an increase in blood flow. Histamine also increases the permeability of local capillaries, causing plasma to leak out and form interstitial fluid. This causes the swelling associated with inflammation.

  Additionally, injured cells, phagocytes, and basophils are sources of inflammatory mediators, including prostaglandins and leukotrienes. Leukotrienes attract neutrophils from the blood by chemotaxis and increase vascular permeability. Prostaglandins cause vasodilation by relaxing vascular smooth muscle and are a major cause of the pain associated with inflammation. Nonsteroidal anti-inflammatory drugs such as aspirin and ibuprofen relieve pain by inhibiting prostaglandin production.
- *Vasodilation.* Many inflammatory mediators such as histamine are vasodilators that increase the diameters of local capillaries. This causes increased blood flow and is responsible for the heat and redness of inflamed tissue. It allows greater access of the blood to the site of inflammation.
- *Increased Vascular Permeability.* At the same time, inflammatory mediators increase the permeability of the local vasculature, causing leakage of fluid into the interstitial space, resulting in the swelling, or edema, associated with inflammation.
- *Recruitment of Phagocytes.* Leukotrienes are particularly good at attracting neutrophils from the blood to the site of infection by chemotaxis. Following an early neutrophil infiltrate stimulated by macrophage cytokines, more macrophages are recruited to clean up the debris left over at the site. When local infections are severe, neutrophils are attracted to the sites of infections in large numbers, and as they phagocytose the pathogens and subsequently die, their accumulated cellular remains are visible as pus at the infection site.

Overall, inflammation is valuable for many reasons. Not only are the pathogens killed and debris removed, but the increase in vascular permeability encourages the entry of clotting factors, the first step toward wound repair.

Inflammation also facilitates the transport of antigen to lymph nodes by dendritic cells for the development of the adaptive immune response.

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20.3 The Adaptive Immune Response: T Lymphocytes and Their Functional Types

Learning Objectives

By the end of this section, you will be able to:

- Explain the advantages of the adaptive immune response over the innate immune response
- List the various characteristics of an antigen
- Describe the types of T cell antigen receptors
- Outline the steps of T cell development
- Describe the major T cell types and their functions

Innate immune responses (and early induced responses) are in many cases ineffective at completely controlling pathogen growth. However, they slow pathogen growth and allow time for the adaptive immune response to strengthen and either control or eliminate the pathogen. The innate immune system also sends signals to the cells of the adaptive immune system, guiding them in how to attack the pathogen. Thus, these are the two important arms of the immune response.

The Benefits of the Adaptive Immune Response

The specificity of the adaptive immune response—its ability to specifically recognize and make a response against a wide variety of pathogens—is its great strength. Antigens, the small chemical groups often associated with pathogens, are recognized by receptors on the surface of B and T lymphocytes. The adaptive immune response to these antigens is so versatile that it can respond to nearly any pathogen. This increase in specificity comes because the adaptive immune response has a unique way to develop as many as 1011, or 100 trillion, different receptors to recognize nearly every conceivable pathogen.

Primary Disease and Immunological Memory

The immune system's first exposure to a pathogen is called a **primary adaptive response**. Symptoms of a first infection, called primary disease, are always relatively severe because it takes time for an initial adaptive immune response to a pathogen to become effective.

Upon reexposure to the same pathogen, a secondary adaptive immune response is generated, which is stronger and faster than the primary response. The **secondary adaptive response** often eliminates a pathogen before it can

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cause significant tissue damage or any symptoms. Without symptoms, there is no disease, and the individual is not even aware of the infection. This secondary response is the basis of **immunological memory**, which protects us from getting diseases repeatedly from the same pathogen. By this mechanism, an individual's exposure to pathogens early in life spares the person from these diseases later in life.

Self-Recognition

A third important feature of the adaptive immune response is its ability to distinguish between self-antigens, those that are normally present in the body, and foreign antigens, those that might be on a potential pathogen. As T and B cells mature, there are mechanisms in place that prevent them from recognizing self-antigens, preventing a damaging immune response against the body. These mechanisms are not 100 percent effective, however, and their breakdown leads to autoimmune diseases, which will be discussed later in this chapter.

T Cell–Mediated Immune Responses

The primary cells that control the adaptive immune response are the lymphocytes, the T and B cells. T cells are particularly important, as they not only control a multitude of immune responses directly but also control B cell immune responses in many cases as well. Thus, many of the decisions about how to attack a pathogen are made at the T cell level, and knowledge of their functional types is crucial to understanding the functioning and regulation of adaptive immune responses as a whole.

T lymphocytes recognize antigens based on a two-chain protein receptor. The most common and important of these are the alpha-beta T cell receptors (Figure 20.13).

Antigens

Antigens on pathogens are usually large and complex and consist of many antigenic determinants. An **antigenic determinant** (epitope) is one of the small regions within an antigen to which a receptor can bind, and antigenic determinants are limited by the size of the receptor itself. They usually consist of six or fewer amino acid residues in a protein, or one or two sugar moieties in a carbohydrate antigen. Antigenic determinants on a carbohydrate antigen are usually less diverse than on a protein antigen. Carbohydrate antigens are found on bacterial cell walls and on red blood cells (the ABO blood group antigens). Protein antigens are complex because of the variety of three-dimensional shapes that proteins can assume and are especially important for the immune responses to viruses and worm parasites. It is the interaction of the shape of

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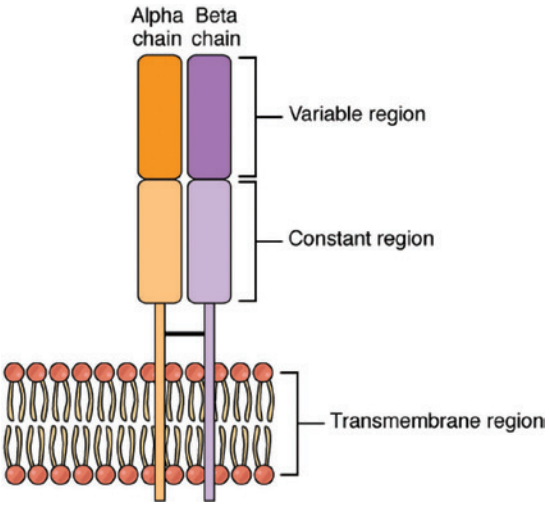


Figure 20.13 Alpha-Beta T Cell Receptor. Notice the constant and variable regions of each chain, anchored by the transmembrane region.

the antigen and the complementary shape of the amino acids of the antigen-binding site that accounts for the chemical basis of specificity.

Antigen Processing and Presentation

The mechanism that T cells use to recognize antigens is complex. T cells do not recognize free-floating or cell-bound antigens as they appear on the surface of the pathogen. They only recognize antigens on the surface of specialized cells called antigen-presenting cells. Antigens are internalized by these cells. **Antigen processing** is a mechanism that enzymatically cleaves the antigen into smaller pieces. The antigen fragments are then brought to the cell's surface and associated with a specialized type of antigen-presenting protein known as a **major histocompatibility complex** (**MHC**) molecule. The MHC proteins are encoded by a cluster of genes that encode these antigen-presenting molecules. The association of the antigen fragments with an MHC molecule on the surface of a cell is known as **antigen presentation** and results in the recognition of antigen by a T cell. This association of antigen and MHC occurs inside the cell, and it is the complex of the two that is brought to the surface. The peptide-binding cleft is a small indentation at the end of the MHC molecule that is farthest away from the cell membrane; it is here that the processed fragment of antigen sits. MHC molecules (which are specifically named **class I MHC** and **class II MHC** molecules) are capable of presenting a variety of antigens, depending on the amino acid sequence, in their peptide-binding clefts. It is the combination of the MHC molecule and the fragment of the original peptide or carbohydrate that is actually physically recognized by the T cell receptor (Figure 20.14).

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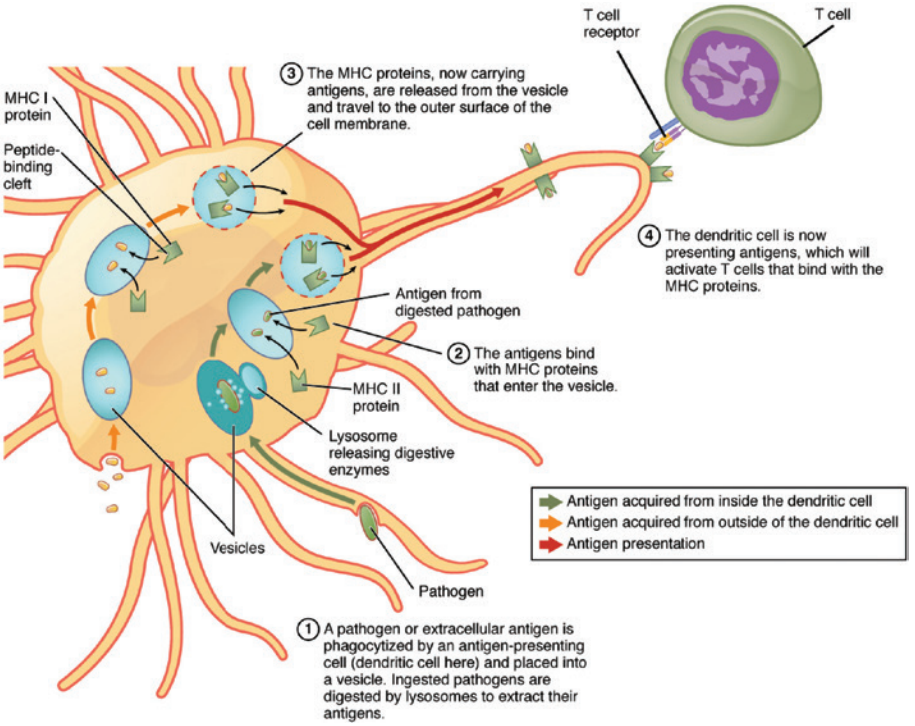


Figure 20.14 Antigen Processing and Presentation.

Professional Antigen-Presenting Cells

Many cell types express class I molecules for the presentation of intracellular antigens. These MHC molecules may then stimulate a cytotoxic T cell immune response, eventually destroying the cell and the pathogen within. This is especially important when it comes to the most common class of intracellular pathogens, the virus. Viruses infect nearly every tissue of the body, so all these tissues must necessarily be able to express class I MHC or no T cell response can be made.

On the other hand, class II MHC molecules are expressed only on the cells of the immune system, specifically cells that affect other arms of the immune response. Thus, these cells are called "professional" antigen-presenting cells to distinguish them from those that bear class I MHC. The three types of professional antigen presenters are macrophages, dendritic cells, and B cells (Table 20.4).

Macrophages stimulate T cells to release cytokines that enhance phagocytosis. Dendritic cells also kill pathogens by phagocytosis (see Figure 20.14), but their major function is to bring antigens to regional draining lymph nodes. The lymph nodes are the locations in which most T cell responses against pathogens of the interstitial tissues are mounted. Macrophages are found in the skin and

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Table 20.4 Classes of Antigen-Presenting Cells

MHC	Cell type	Phagocytic?	Function
Class I	Many	No	Stimulates cytotoxic T cell immune response
Class II	Macrophage	Yes	Stimulates phagocytosis and presentation at primary infection site
Class II	Dendritic	Yes, in tissues	Brings antigens to regional lymph nodes
Class II	B cell	Yes, internalizes surface Ig and antigen	Stimulates antibody secretion by B cells

in the lining of mucosal surfaces, such as the nasopharynx, stomach, lungs, and intestines. B cells may also present antigens to T cells, which are necessary for certain types of antibody responses, to be covered later in this chapter.

Mechanisms of T Cell–Mediated Immune Responses

Mature T cells become activated by recognizing processed foreign antigen in association with a self-MHC molecule and begin dividing rapidly by mitosis. This proliferation of T cells is called **clonal expansion** and is necessary to make the immune response strong enough to effectively control a pathogen. How does the body select only those T cells that are needed against a specific pathogen? Again, the specificity of a T cell is based on the amino acid sequence and the three-dimensional shape of the antigen-binding site formed by the variable regions of the two chains of the T cell receptor (Figure 20.15). **Clonal selection** is the process of antigen binding only to those T cells that have receptors specific to that antigen. Each T cell that is activated has a specific receptor "hardwired" into its DNA, and all of its progeny will have identical DNA and T cell receptors, forming clones of the original T cell.

Clonal Selection and Expansion

The clonal selection theory was proposed by Frank Burnet in the 1950s. However, the term *clonal selection* is not a complete description of the theory, as clonal expansion goes hand in glove with the selection process. The main tenet of the theory is that a typical individual has a multitude of (1,011) different types of T cell clones based on their receptors. In this use, a **clone** is a group of lymphocytes that share the same **antigen receptor**. Each clone is necessarily present in the body in low numbers. Otherwise, the body would not have room for lymphocytes with so many specificities.

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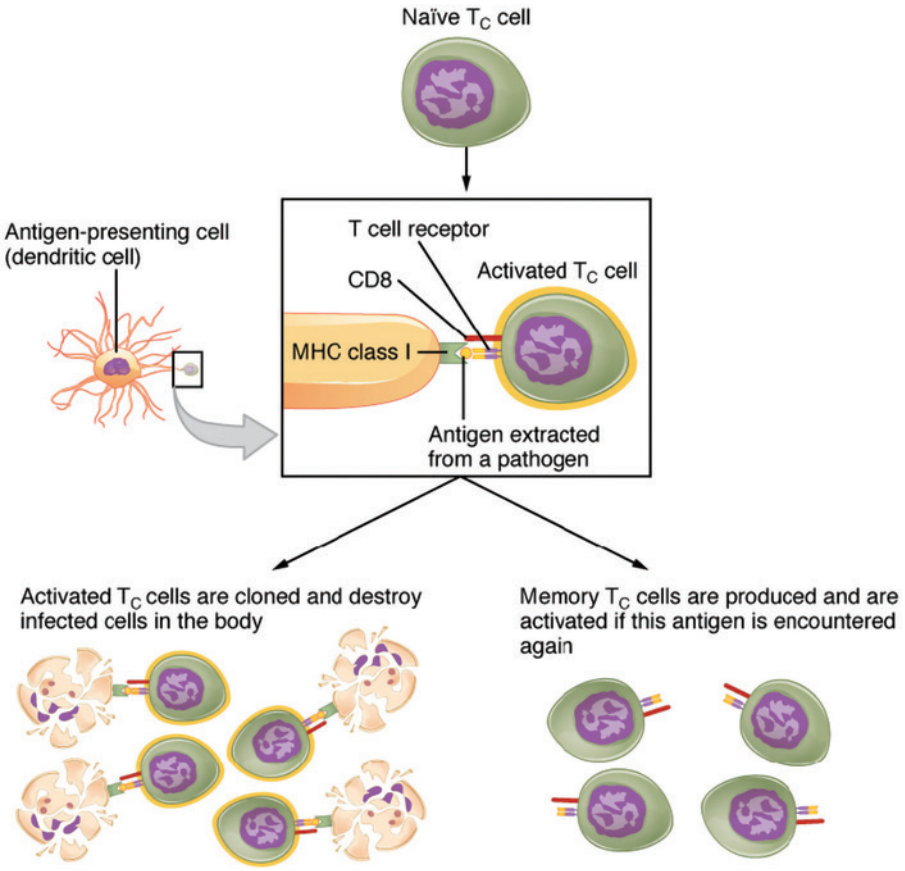


Figure 20.15 Clonal Selection and Expansion of T Lymphocytes. Stem cells differentiate into T cells with specific receptors called clones. The clones with receptors specific for antigens on the pathogen are selected for and expanded. The T_C cells are cytotoxic T cells, which are described later in this chapter.

Only those clones of lymphocytes whose receptors are activated by the antigen are stimulated to proliferate. Keep in mind that most antigens have multiple antigenic determinants, so a T cell response to a typical antigen involves a polyclonal response. A **polyclonal response** is the stimulation of multiple T cell clones. Once activated, the selected clones increase in number and make many copies of each cell type, each clone with its unique receptor. By the time this process is complete, the body will have large numbers of specific lymphocytes available to fight the infection (see Figure 20.15).

The Cellular Basis of Immunological Memory

As already discussed, one of the major features of an adaptive immune response is the development of immunological memory.

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During a primary adaptive immune response, both **memory T cells** and **effector T cells** are generated. Memory T cells are long lived and can even persist for a lifetime. Memory cells are primed to act rapidly. Thus, any subsequent exposure to the pathogen will elicit a very rapid T cell response. This rapid, secondary adaptive response generates large numbers of effector T cells so fast that the pathogen is often overwhelmed before it can cause any symptoms of disease. This is what is meant by immunity to a disease. The same pattern of primary and secondary immune responses occurs in B cells and the antibody response, as will be discussed later in the chapter.

T Cell Types and Their Functions

In T cell development, the mature T cells express specific markers (either the CD4 marker or the CD8 marker, but not both). These markers are cell adhesion molecules that keep the T cell in close contact with the antigen-presenting cell by directly binding to the MHC molecule (to a different part of the molecule than does the antigen). Thus, T cells and antigen-presenting cells are held together in two ways: by any marker attaching to MHC and by the T cell receptor binding to antigen.

Helper T Cells and Their Cytokines

Helper T cells (**Th**), bearing the CD4 molecule, function by secreting cytokines that act to enhance other immune responses. There are two classes of Th cells, and they act on different components of the immune response. These cells are distinguished not by their surface molecules but by the characteristic set of cytokines they secrete (Table 20.5).

Table 20.5 Functions of T Cell Types and Their Cytokines

T cell	Main target	Function	Pathogen	Surface marker	MHC	Cytokines or mediators
Tc	Infected cells	Cytotoxicity	Intracellular	CD8	Class I	Perforins, granzymes, and fas ligand
Th1	Macrophage	Helper inducer	Extracellular	CD4	Class II	Interferon-γ and TGF-β
Th2	B cell	Helper inducer	Extracellular	CD4	Class II	IL-4, IL-6, IL-10, and others
Treg	Th cell	Suppressor	None	CD4, CD25	?	TGF-β and IL-10

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Th1 cells are a type of helper T cell that secretes cytokines that regulate the immunological activity and development of a variety of cells, including macrophages and other types of T cells.

Th2 cells, on the other hand, are cytokine-secreting cells that act on B cells to drive their differentiation into plasma cells that make antibodies. In fact, T cell help is required for antibody responses to most protein antigens, and these are called T cell–dependent antigens.

Cytotoxic T cells

Cytotoxic T cells (**Tc**) are T cells that kill target cells by inducing apoptosis using the same mechanism as NK cells. They either express fas ligand, which binds to the fas molecule on the target cell, or act by using perforins and granzymes contained in their cytoplasmic granules. As was discussed earlier with NK cells, killing a virally infected cell before the virus can complete its replication cycle results in the production of no infectious particles. As more Tc cells are developed during an immune response, they overwhelm the ability of the virus to cause disease. In addition, each Tc cell can kill more than one target cell, making them especially effective. Tc cells are so important in the antiviral immune response that some speculate that this was the main reason the adaptive immune response evolved in the first place.

Regulatory T Cells

Regulatory T cells (**Treg**), or suppressor T cells, are the most recently discovered of the types listed here, so less is understood about them. In addition to CD4, they bear the molecules CD25 and FOXP3. Exactly how they function is still under investigation, but it is known that they suppress other T cell immune responses. This is an important feature of the immune response, because if clonal expansion during immune responses were allowed to continue uncontrolled, these responses could lead to autoimmune diseases and other medical issues.

Not only do T cells directly destroy pathogens, but they regulate nearly all other types of the adaptive immune response as well, as evidenced by the functions of the T cell types, their surface markers, the cells they work on, and the types of pathogens they work against (see Table 20.5).

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20.4 The Adaptive Immune Response: B Lymphocytes and Antibodies

Learning Objectives

By the end of this section, you will be able to:

- Explain how B cells mature and how B cell tolerance develops
- Discuss how B cells are activated and differentiate into plasma cells
- Describe the structure of the antibody classes and their functions

Antibodies were the first component of the adaptive immune response to be characterized by scientists working on the immune system. It was already known that individuals who survived a bacterial infection were immune to reinfection with the same pathogen. Early microbiologists took serum from an immune patient and mixed it with a fresh culture of the same type of bacteria, then observed the bacteria under a microscope. The bacteria became clumped in a process called agglutination. When a different bacterial species was used, the agglutination did not happen. Thus, there was something in the serum of immune individuals that could specifically bind to and agglutinate bacteria.

Scientists now know that the cause of the agglutination is an antibody molecule, also called an **immunoglobulin** (**Ig**). What is an antibody? An antibody protein is essentially a secreted form of a B cell receptor. (In fact, surface immunoglobulin is another name for the B cell receptor.) Not surprisingly, the same genes encode both the secreted antibodies and the surface immunoglobulins. One minor difference in the way these proteins are synthesized distinguishes a naive B cell with antibody on its surface from an antibody-secreting plasma cell with no antibodies on its surface. The antibodies of the plasma cell have the exact same antigen-binding site and specificity as their B cell precursors.

There are five different classes of antibody found in humans: IgM, IgD, IgG, IgA, and IgE. Each of these has specific functions in the immune response, so by learning about them, researchers can learn about the great variety of antibody functions critical to many adaptive immune responses.

B cells do not recognize antigen in the complex fashion of T cells. B cells can recognize native, unprocessed antigen and do not require the participation of MHC molecules and antigen-presenting cells.

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B Cell Differentiation and Activation

B cells differentiate in the bone marrow. During the process of maturation, up to 100 trillion different clones of B cells are generated, which is similar to the diversity of antigen receptors seen in T cells.

B cell differentiation and the development of tolerance are not quite as well understood as in T cells. **Central tolerance** is the destruction or inactivation of B cells that recognize self-antigens in the bone marrow, and its role is critical and well established. In the process of **clonal deletion**, immature B cells that bind strongly to self-antigens expressed on tissues are signalled to induce their own destruction by apoptosis, removing them from the population. In the process of **clonal anergy**, however, B cells exposed to soluble antigen in the bone marrow are not physically deleted but become unable to function.

Another mechanism called peripheral tolerance is a direct result of T cell tolerance. In **peripheral tolerance**, functional, mature B cells leave the bone marrow but have yet to be exposed to self-antigen. Most protein antigens require signals from helper T cells (Th2) to proceed to make antibody. When a B cell binds to a self-antigen but receives no signals from a nearby Th2 cell to produce antibody, the cell is signalled to undergo apoptosis and is destroyed. This is yet another example of the control that T cells have over the adaptive immune response.

After B cells' activation process by their binding to antigen, they differentiate into plasma cells. Plasma cells often leave the secondary lymphoid organs, where the response is generated, and migrate back to the bone marrow, where the whole differentiation process started. After secreting antibodies for a specific period, they die, as most of their energy is devoted to making antibodies and not to maintaining themselves. Thus, plasma cells are said to be terminally differentiated.

The final B cell of interest is the memory B cell, which results from the clonal expansion of an activated B cell. Memory B cells function in a way similar to memory T cells. They lead to a stronger and faster secondary response when compared to the primary response, as illustrated below.

Antibody Structure

Antibodies are glycoproteins consisting of two types of polypeptide chains with attached carbohydrates. The **heavy chain** and the **light chain** are the two polypeptides that form the antibody. The main differences between the classes of antibodies are in the differences between their heavy chains, but as you shall see, the light chains have an important role, forming part of the antigen-binding site on the antibody molecules.

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Four-Chain Models of Antibody Structures

All antibody molecules have two identical heavy chains and two identical light chains. (Some antibodies contain multiple units of this four-chain structure.) The **Fc region** of the antibody is formed by the two heavy chains coming together, usually linked by disulfide bonds (Figure 20.16).

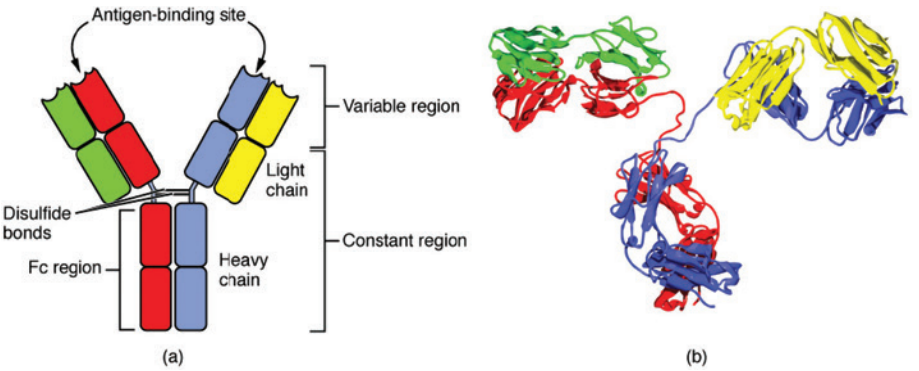


Figure 20.16 Antibody and IgG2 Structures. The typical four-chain structure of a generic antibody (a) and the corresponding three-dimensional structure of the antibody IgG2 (b). (credit b: modification of work by Tim Vickers)

The Fc portion of the antibody is important in that many effector cells of the immune system have Fc receptors. Cells having these receptors can then bind to antibody-coated pathogens, greatly increasing the specificity of the effector cells. At the other end of the molecule are two identical antigen-binding sites.

Five Classes of Antibodies and Their Functions

In general, antibodies have two basic functions. They can act as the B cell antigen receptor, or they can be secreted, circulate, and bind to a pathogen, often labelling it for identification by other forms of the immune response. Of the five antibody classes, notice that only two can function as the antigen receptor for naive B cells: IgM and **IgD** (Table 20.6). Mature B cells that leave the bone marrow express both IgM and IgD, but both antibodies have the same antigen specificity. Only IgM is secreted, however, and no other nonreceptor function for IgD has been discovered.

IgM consists of five four-chain structures (20 total chains with 10 identical antigen-binding sites) and is thus the largest of the antibody molecules. IgM is usually the first antibody made during a primary response. Its 10 antigen-binding sites and large shape allow it to bind well to many bacterial surfaces. It is excellent at binding complement proteins and activating the complement

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Table 20.6 Five Classes of Antibodies

Property	IgM (pentamer)	IgG (monomer)	Secretory IgA (dimer)	IgE (monomer)	IgD (monomer)
Heavy chains	μ	γ	α	ε	δ
Number of antigen-binding sites	10	2	4	2	2
Molecular weight (daltons)	900,000	150,000	385,000	200,000	180,000
Percentage of total antibody in serum	6	80	13	0.002	1
Crosses placenta	No	Yes	No	No	No
Fixes complement	Yes	Yes	No	No	No
Fc binds to	—	Phagocytes	—	Mast cells and basophils	—
Function	Main antibody of primary responses; best at fixing complement; the monomer form of IgM serves as the B cell receptor	Main blood antibody of secondary responses, neutralizes toxins, opsonization	Secreted into mucus, tears, saliva, colostrum	Antibody of allergy and antiparasitic activity	B cell receptor

cascade, consistent with its role in promoting chemotaxis, opsonization, and cell lysis. Thus, it is a very effective antibody against bacteria at early stages of a primary antibody response. As the primary response proceeds, the antibody produced in a B cell can change to IgG, IgA, or IgE by the process known as class switching. **Class switching** is the change of one antibody class to another. While the class of antibody changes, the specificity and the antigen-binding sites do not. Thus, the antibodies made are still specific to the pathogen that stimulated the initial IgM response.

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IgG is a major antibody of late primary responses and the main antibody of secondary responses in the blood. This is because class switching occurs during primary responses. IgG is a monomeric antibody that clears pathogens from the blood and can activate complement proteins (although not as well as IgM), taking advantage of its antibacterial activities. Furthermore, this class of antibody is the one that crosses the placenta to protect the developing fetus from disease and exits the blood to the interstitial fluid to fight extracellular pathogens.

IgA exists in two forms, a four-chain monomer in the blood and an eight-chain structure, or dimer, in exocrine gland secretions of the mucous membranes, including mucus, saliva, and tears. Thus, dimeric IgA is the only antibody to leave the interior of the body to protect body surfaces. IgA is also of importance to newborns, because this antibody is present in the mother's breast milk (colostrum), which serves to protect the infant from disease.

IgE is usually associated with allergies and anaphylaxis. It is present in the lowest concentration in the blood, because its Fc region binds strongly to an IgE-specific Fc receptor on the surfaces of mast cells. IgE makes mast cell degranulation very specific, such that if a person is allergic to peanuts, there will be peanut-specific IgE bound to their mast cells. In this person, eating peanuts will cause the mast cells to degranulate, sometimes causing severe allergic reactions, including anaphylaxis, a severe, systemic allergic response that can cause death.

Clonal Selection of B Cells

Clonal selection and expansion work in much the same way in B cells as in T cells. Only B cells with appropriate antigen specificity are selected for and expanded (Figure 20.17).

Eventually, the plasma cells secrete antibodies with antigenic specificity identical to those that were on the surfaces of the selected B cells. Notice in the figure that both plasma cells and memory B cells are generated simultaneously.

Primary Versus Secondary B Cell Responses

Primary and secondary responses as they relate to T cells were discussed in section 20.3 The Adaptive Immune Response: T Lymphocytes and Their Functional Types. This section will look at these responses with B cells and antibody production. Because antibodies are easily obtained from blood samples, they are easy to follow and graph (Figure 20.18). As you will see from the figure, the primary response to an antigen (representing a pathogen) is delayed by several days. This is the time it takes for the B cell clones to expand and differentiate into plasma cells. The level of antibody produced is low, but it is sufficient for immune protection. The second time a person encounters the same antigen, there is no time delay, and the amount of antibody made is much higher. Thus,

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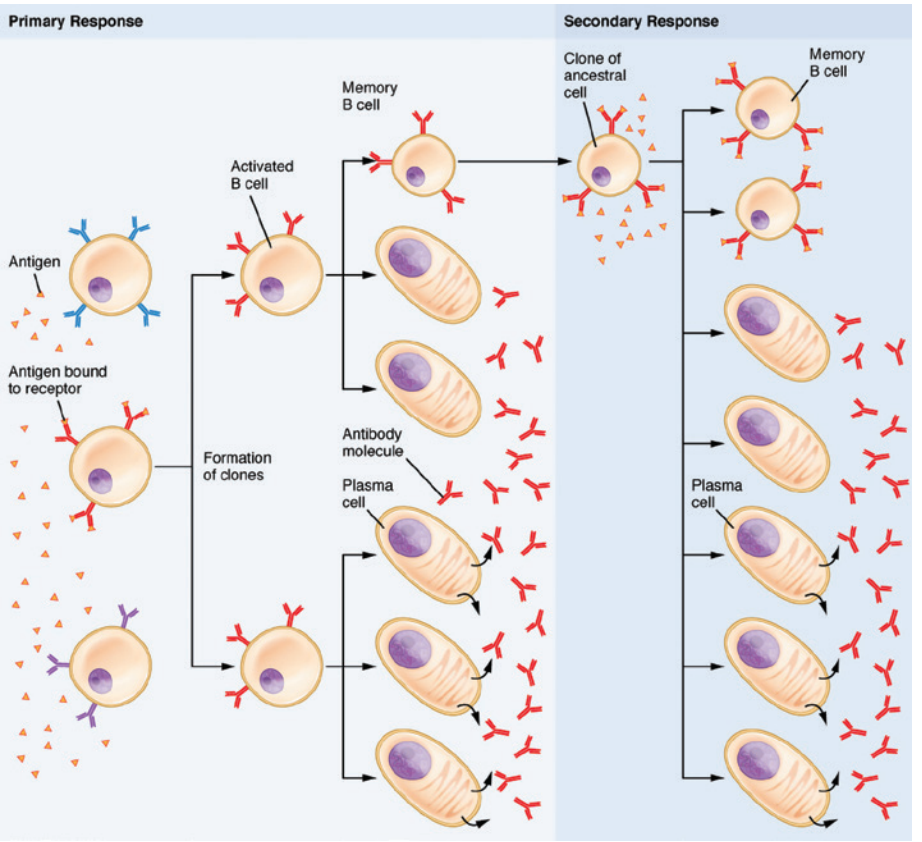


Figure 20.17 Clonal Selection of B Cells. During a primary B cell immune response, both antibody-secreting plasma cells and memory B cells are produced. These memory cells lead to the differentiation of more plasma cells and memory B cells during secondary responses.

the secondary antibody response overwhelms the pathogens quickly, and in most situations, no symptoms are felt. When a different antigen is used, another primary response is made with its low antibody levels and time delay.

Active Versus Passive Immunity

Immunity to pathogens and the ability to control pathogen growth so that damage to the tissues of the body is limited can be acquired by (1) the active development of an immune response in the infected individual or (2) the passive transfer of immune components from an immune individual to a non-immune one. Both active and passive immunity have examples in the natural world and as part of medicine.

Active immunity is the resistance to pathogens acquired during an adaptive immune response within an individual (Table 20.7). Naturally acquired active immunity, the response to a pathogen, is the focus of this chapter. Artificially acquired active immunity involves the use of vaccines. A vaccine is a killed or

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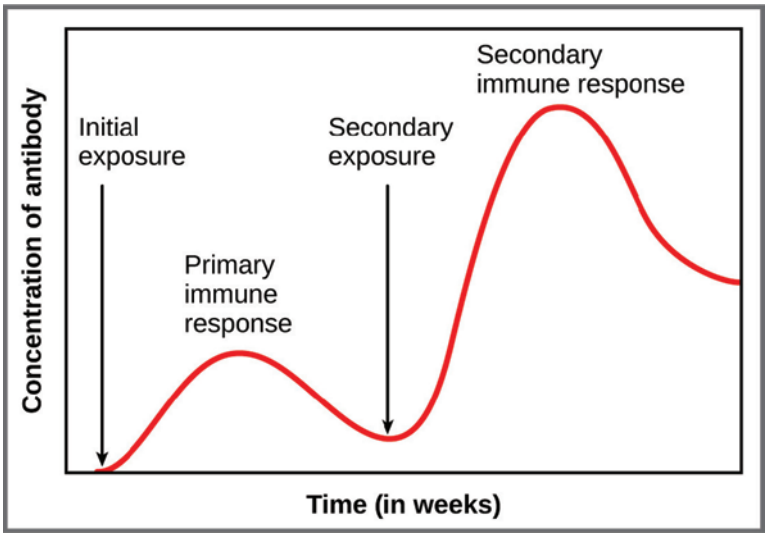


Figure 20.18 Primary and Secondary Antibody Responses. Antigen A is given once to generate a primary response and later to generate a secondary response. When a different antigen is given for the first time, a new primary response is made.

weakened pathogen or its components that, when administered to a healthy individual, leads to the development of immunological memory (a weakened primary immune response) without causing much in the way of symptoms. Thus, with the use of vaccines, one can avoid the damage from disease that results from the first exposure to the pathogen yet reap the benefits of protection from immunological memory. The advent of vaccines was one of the major medical advances of the twentieth century and led to the eradication of smallpox and the control of many infectious diseases, including polio, measles, and whooping cough.

Table 20.7 Active Versus Passive Immunity

	Natural	Artificial
Active	Adaptive immune response	Vaccine response
Passive	Transplacental antibodies / breastfeeding	Immune globulin injections

Passive immunity arises from the transfer of antibodies to an individual without requiring them to mount their own active immune response. Naturally acquired passive immunity is seen during fetal development. IgG is transferred from the maternal circulation to the fetus via the placenta, protecting the

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fetus from infection and protecting the newborn for the first few months of its life. As already stated, a newborn benefits from the IgA antibodies it obtains from milk during breastfeeding. The fetus and newborn thus benefit from the immunological memory based on the pathogens to which the pregnant person has been exposed. In medicine, artificially acquired passive immunity usually involves injections of immunoglobulins, taken from animals previously exposed to a specific pathogen. This treatment is a fast-acting method of temporarily protecting an individual who was possibly exposed to a pathogen. The downside to both types of passive immunity is the lack of the development of immunological memory. Once the antibodies are transferred, they are effective for only a limited time before they degrade.

Interactive Link 20.7

Immunity can be acquired in an active or passive way, and it can be natural or artificial. Watch this video (http://oer.aupress.ca/oer-202505/20.7) to see an animated discussion of passive and active immunity. What is an example of natural immunity acquired passively?

T Cell–Dependent Versus T Cell–Independent Antigens

As discussed previously, Th2 cells secrete cytokines that drive the production of antibodies in a B cell, responding to complex antigens such as those made by proteins. On the other hand, some antigens are T cell independent. A **T cell–independent antigen** usually is in the form of repeated carbohydrate moieties found on the cell walls of bacteria. Each antibody on the B cell surface has two binding sites, and the repeated nature of T cell–independent antigen leads to crosslinking of the surface antibodies on the B cell. The crosslinking is enough to activate it in the absence of T cell cytokines.

A **T cell–dependent antigen**, on the other hand, usually is not repeated to the same degree on the pathogen and thus does not crosslink surface antibody with the same efficiency. To elicit a response to such antigens, the B and T cells must come close together (Figure 20.19). The B cell must receive two signals to become activated. Its surface immunoglobulin must recognize native antigen. Some of this antigen is internalized, processed, and presented to the Th2 cells on a class II MHC molecule. The T cell then binds using its antigen receptor and is activated to secrete cytokines that diffuse to the B cell, finally activating it completely. Thus, the B cell receives signals from both its surface antibody and the T cell via its cytokines and acts as a professional antigen-presenting cell in the process.

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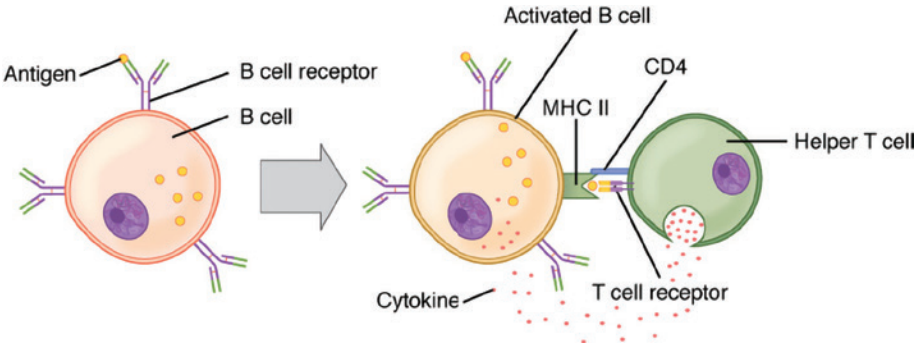


Figure 20.19 T and B Cell Binding. To elicit a response to a T cell–dependent antigen, the B and T cells must come close together. To become fully activated, the B cell must receive two signals from the native antigen and the T cell's cytokines.

Key Terms

active immunity: Immunity developed from an individual's own immune system.

acute inflammation: Inflammation occurring for a limited time period; rapidly developing.

adaptive immune response: Relatively slow but very specific and effective immune response controlled by lymphocytes.

afferent lymphatic vessels: Vessels that lead into a lymph node.

antibody: Antigen-specific protein secreted by plasma cells; immunoglobulin.

antigen: Molecule recognized by the receptors of B and T lymphocytes.

antigenic determinant (also epitope): One of the chemical groups recognized by a single type of lymphocyte antigen receptor.

antigen presentation: Binding of processed antigen to the protein-binding cleft of a major histocompatibility complex molecule.

antigen processing: Internalization and digestion of antigen in an antigen-presenting cell.

antigen receptor: Two-chain receptor by which lymphocytes recognize antigen.

barrier defences: Antipathogen defences deriving from a barrier that physically prevents pathogens from entering the body to establish an infection.

B cells: Lymphocytes that act by differentiating into an antibody-secreting plasma cell.

bone marrow: Tissue found inside bones; the site of all blood cell differentiation and maturation of B lymphocytes.

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bronchus-associated lymphoid tissue (BALT): Lymphoid nodule associated with the respiratory tract.

central tolerance: B cell tolerance induced in immature B cells of the bone marrow.

chemokine: Soluble, long-range, cell-to-cell communication molecule.

chronic inflammation: Inflammation occurring for long periods of time.

chyle: Lipid-rich lymph inside the lymphatic capillaries of the small intestine.

cisterna chyli: Bag-like vessel that forms the beginning of the thoracic duct.

class I MHC: Molecules for the presentation of intracellular antigens; may then stimulate a cytotoxic T cell immune response, eventually destroying the cell and the pathogen within.

class II MHC: Molecules expressed only on the cells of the immune system, specifically cells that affect other arms of the immune response.

class switching: Ability of B cells to change the class of antibody they produce without altering the specificity for antigen.

clonal anergy: Process whereby B cells that react to soluble antigens in bone marrow are made nonfunctional.

clonal deletion: Removal of self-reactive B cells by inducing apoptosis.

clonal expansion: Growth of a clone of selected lymphocytes.

clonal selection: Stimulating growth of lymphocytes that have specific receptors.

clone: Group of lymphocytes sharing the same antigen receptor.

complement: Enzymatic cascade of constitutive blood proteins that have antipathogen effects, including the direct killing of bacteria.

cytokine: Soluble, short-range, cell-to-cell communication molecule.

cytotoxic T cells (Tc): T lymphocytes with the ability to induce apoptosis in target cells.

dendritic cells: Two types of phagocytic cells in the thymus that are derived from monocytes.

effector T cells: Immune cells with a direct, adverse effect on a pathogen.

efferent lymphatic vessels: Vessels that lead out of a lymph node.

Fc region: In an antibody molecule, the site where the two termini of the heavy chains come together; many cells have receptors for this portion of the antibody, adding functionality to these molecules.

germinal centres: Clusters of rapidly proliferating B cells found in secondary lymphoid tissues.

granzyme: Apoptosis-inducing substance contained in granules of NK cells and cytotoxic T cells.

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heavy chain: Larger protein chain of an antibody.
helper T cells (Th): T cells that secrete cytokines to enhance other immune responses, involved in activation of both B and T cell lymphocytes.
histamine: Vasoactive mediator in granules of mast cells; the primary cause of allergies and anaphylactic shock.
IgA: Antibody whose dimer is secreted by exocrine glands, is especially effective against digestive and respiratory pathogens, and can pass immunity to an infant through breastfeeding.
IgD: Class of antibody whose only known function is as a receptor on naive B cells; important in B cell activation.
IgE: Antibody that binds to mast cells and causes antigen-specific degranulation during an allergic response.
IgG: Main blood antibody of late primary and early secondary responses; passed from carrier to unborn child via placenta.
IgM: Antibody whose monomer is a surface receptor of naive B cells; the pentamer is the first antibody made during primary responses.
immune system: Series of barriers, cells, and soluble mediators that combine in response to infections of the body by pathogenic organisms.
immunoglobulin (Ig): Protein antibody; occurs as one of five main classes.
immunological memory: Ability of the adaptive immune response to mount a stronger and faster immune response upon reexposure to a pathogen.
inflammation: Basic innate immune response characterized by heat, redness, pain, and swelling.
innate immune response: Rapid but relatively nonspecific immune response.
interferons: Early induced proteins made in virally infected cells that cause nearby cells to make antiviral proteins.
lacteals: Lymphatic capillaries in the small intestine critical for the transport of dietary lipids and lipid-soluble vitamins to the blood.
light chain: Small protein chain of an antibody.
lymph: Fluid contained within the lymphatic system.
lymphatic capillaries: Smallest of the lymphatic vessels and the origin of lymph flow.
lymphatic system: Network of lymphatic vessels, lymph nodes, and ducts that carries lymph from the tissues and back to the bloodstream.
lymphatic trunks: Large lymphatics that collect lymph from smaller lymphatic vessels and empty into the blood via lymphatic ducts.
lymphatic vessels: Vessels for transporting the cells of the immune system.

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lymph node: One of the bean-shaped organs associated with the lymphatic vessels.

lymphocytes: White blood cells characterized by a large nucleus and small rim of cytoplasm.

lymphoid follicles: The sites of the formation of lymphocytes, with specific B cell–rich and T cell–rich areas.

lymphoid nodules: Unencapsulated patches of lymphoid tissue found throughout the body.

macrophage: Amoeboid phagocyte found in several tissues throughout the body.

major histocompatibility complex (MHC): Gene cluster whose proteins present antigens to T cells.

mast cell: Cell found in the skin and the lining of body cells that contains cytoplasmic granules with vasoactive mediators such as histamine.

memory T cells: Long-lived immune cell reserved for future exposure to a pathogen.

monocyte: Precursor to macrophages and dendritic cells seen in the blood.

mucosa-associated lymphoid tissue (MALT): Lymphoid nodule associated with the mucosa.

naive lymphocyte: Mature B or T cell that has not yet encountered antigen for the first time.

natural killer (NK) cell: Cytotoxic lymphocyte of innate immune response.

neutrophil: Phagocytic white blood cell recruited from the bloodstream to the site of infection via the bloodstream.

opsonization: Enhancement of phagocytosis by the binding of antibody or antimicrobial protein.

passive immunity: Transfer of immunity to a pathogen to an individual that lacks immunity to this pathogen, usually by the injection of antibodies.

perforin: Molecule in NK cell and cytotoxic T cell granules that forms pores in the membrane of a target cell.

peripheral tolerance: Mature B cell made tolerant by lack of T cell help.

Peyer's patches: A type of MALT in the small intestine important for immune responses against ingested substances.

phagocytosis: Movement of material from the outside to the inside of the cells via vesicles made from invaginations of the plasma membrane.

plasma cell: Differentiated B cell that is actively secreting antibody.

polyclonal response: Response by multiple clones to a complex antigen with many determinants.

primary adaptive response: Immune system's response to the first exposure to a pathogen.

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primary lymphoid organ: Site where lymphocytes mature and proliferate; red bone marrow and thymus gland.
red pulp: Splenic nodule area consisting of mostly red blood cells.
regulatory T cells (Treg; also suppressor T cells): Class of CD4 T cells that regulates other T cell responses.
right lymphatic duct: Drains lymph fluid from the upper right side of the body into the right subclavian vein.
secondary adaptive response: Immune response observed upon reexposure to a pathogen, which is stronger and faster than a primary response.
secondary lymphoid organs: Sites where lymphocytes mount adaptive immune responses; examples include lymph nodes and spleen.
spleen: Secondary lymphoid organ that filters pathogens from the blood (white pulp) and removes degenerating or damaged blood cells (red pulp).
T cell: Lymphocyte that acts by secreting molecules that regulate the immune system or by causing the destruction of foreign cells, viruses, and cancer cells.
T cell–dependent antigen: Antigen that binds to B cells, which requires signals from T cells to make antibody.
T cell–independent antigen: Binds to B cells, which do not require signals from T cells to make antibody.
Th1 cells: Cells that secrete cytokines that enhance the activity of macrophages and other cells.
Th2 cells: Cells that secrete cytokines that induce B cells to differentiate into antibody-secreting plasma cells.
thoracic duct: Large duct that drains lymph from the lower limbs, left thorax, left upper limb, and the left side of the head.
thymocyte: Immature T cell found in the thymus.
thymus: Primary lymphoid organ; where T lymphocytes proliferate and mature.
tonsils (palatine, pharyngeal, and lingual): Lymphoid nodules associated with the nasopharynx.
white pulp: Splenic nodule area that resembles the lymphoid follicles of the lymph nodes.

Chapter Review

20.1 Anatomy of the Lymphatic and Immune Systems

The lymphatic system is a series of vessels, ducts, and trunks that removes interstitial fluid from the tissues and returns it to the blood. The lymphatics are

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also used to transport dietary lipids and cells of the immune system. Cells of the immune system all come from the hematopoietic system of the bone marrow. Primary lymphoid organs, the bone marrow and thymus gland, are the locations where lymphocytes of the adaptive immune system proliferate and mature. Secondary lymphoid organs are sites in which mature lymphocytes congregate to mount immune responses. Many immune system cells travel through the lymphatic and circulatory systems to patrol the body, destroy abnormal or infected cells, and protect against pathogens.

20.2 Barrier Defences and the Innate Immune Response

Innate immune responses are critical to the early control of infections. Whereas barrier defences are the body's first line of physical defence against pathogens, innate immune responses are the first line of physiological defence. Innate responses occur rapidly but with less specificity and effectiveness than the adaptive immune response. Innate responses can be caused by a variety of cells, mediators, and antibacterial proteins such as the complement system, a group of plasma proteins that work together to destroy pathogens, enhance phagocytosis, and promote inflammation. Within the first few days of an infection, another series of antibacterial proteins are induced, each with activities against certain bacteria, including opsonization of certain species. Additionally, interferons are induced that protect cells from viruses in their vicinity. Finally, the innate immune response does not stop when the adaptive immune response is developed. In fact, both can cooperate, and one can influence the other in their responses against pathogens.

20.3 The Adaptive Immune Response: T Lymphocytes and Their Functional Types

T cells recognize antigens with their antigen receptor, a complex of two protein chains on their surface. They do not recognize self-antigens, however, but only processed antigen presented on their surfaces in a binding groove of a major histocompatibility complex molecule. T cells develop in the thymus, where they learn to use self-MHC molecules to recognize only foreign antigens, thus making them tolerant to self-antigens. There are several functional types of T lymphocytes, the major ones being helper, regulatory, and cytotoxic T cells.

20.4 The Adaptive Immune Response: B Lymphocytes and Antibodies

B cells, which develop within the bone marrow, are responsible for making five different classes of antibodies, each with its own functions. B cells have their own mechanisms for tolerance, but in peripheral tolerance, the B cells that

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leave the bone marrow remain inactive due to T cell tolerance. Some B cells do not need T cell cytokines to make antibody, and they bypass this need by the crosslinking of their surface immunoglobulin by repeated carbohydrate residues found in the cell walls of many bacterial species.

Others require T cells to become activated.

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PART 5

Energy, Maintenance, and Environmental Exchange

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21

The Respiratory System

Chapter Objectives

After studying this chapter, you will be able to:

- List the structures of the respiratory system
- List the major functions of the respiratory system
- Outline the forces that allow for air movement into and out of the lungs
- Outline the process of gas exchange
- Summarize the process of oxygen and carbon dioxide transport within the respiratory system
- Create a flowchart illustrating how respiration is controlled
- Discuss how the respiratory system responds to exercise

A typical human cannot survive without breathing for more than 3 minutes, and even if you wanted to hold your breath longer, your autonomic nervous system would take control to force you to breathe. This is because every cell in the body needs to run the oxidative stages of cellular respiration, the process by which energy is produced in the form of adenosine triphosphate (ATP). For oxidative phosphorylation to occur, oxygen is used as a reactant, and carbon dioxide is released as a waste product. You may be surprised to learn that although oxygen is critical for cells, it is actually the accumulation of carbon dioxide that primarily drives your need to breathe. Carbon dioxide is exhaled and oxygen is inhaled through the respiratory system, which includes muscles to move air into and out of the lungs, passageways through which air moves, and microscopic gas exchange surfaces covered by capillaries. The circulatory system transports gases from the lungs to tissues throughout the body and vice versa.

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21.1 Organs and Structures of the Respiratory System

Learning Objectives

By the end of this section, you will be able to:

- List the structures that make up the respiratory system
- Describe how the respiratory system processes oxygen and CO_2
- Compare and contrast the functions of the upper respiratory tract with the lower respiratory tract

The major organs of the respiratory system function primarily to provide oxygen to body tissues for cellular respiration, remove the waste product carbon dioxide, and help maintain acid-base balance. Portions of the respiratory system are also used for nonvital functions, such as sensing odours, producing speech, and straining, such as during childbirth or coughing (Figure 21.1).

Functionally, the respiratory system can be divided into a conducting zone and a respiratory zone. The **conducting zone** of the respiratory system

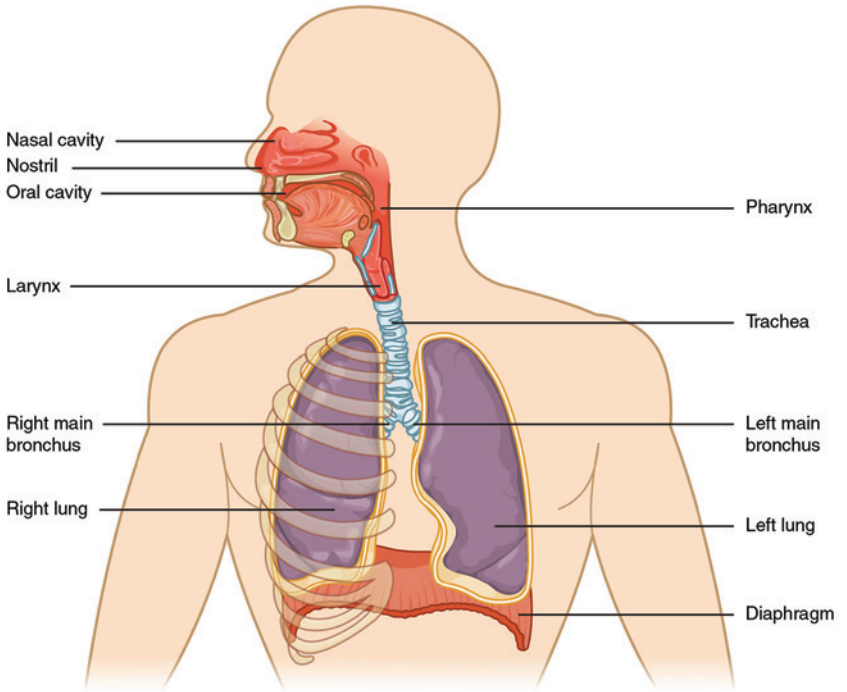


Figure 21.1 Major Respiratory Structures. The major respiratory structures span the nasal cavity to the diaphragm.

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includes the organs and structures not directly involved in gas exchange. The gas exchange occurs in the **respiratory zone**.

Conducting Zone

The major functions of the conducting zone are to provide a route for incoming and outgoing air, remove debris and pathogens from the incoming air, and warm and humidify the incoming air. Several structures within the conducting zone perform other functions as well.

Example: The epithelium of the nasal passages is essential to sensing odours, and the bronchial epithelium that lines the lungs can metabolize some airborne carcinogens.

The Nose and Its Adjacent Structures

The major entrance and exit for the respiratory system is through the nose. When discussing the nose, it is helpful to divide it into two major sections: the external nose and the nasal cavity or internal nose.

The **external nose** consists of the surface and skeletal structures that result in the outward appearance of the nose and contribute to its numerous functions (Figure 21.2). The **root** is the region of the nose located between the eyebrows. The **bridge** is the part of the nose that connects the root to the rest of the nose. The **dorsum nasi** is the length of the nose. The **apex** is the tip of the nose. On either side of the apex, the nostrils are formed by the alae (singular = ala). An **ala** is a cartilaginous structure that forms the lateral side of each **naris** (plural = nares), or nostril opening. The **philtrum** is the concave surface that connects the apex of the nose to the upper lip.

Underneath the thin skin of the nose are its skeletal features (see Figure 21.2, lower illustration). While the root and bridge of the nose consist of bone, the protruding portion of the nose is composed of cartilage. As a result, when looking at a skull, the nose is missing. The **nasal bone** is one of a pair of bones that lies under the root and bridge of the nose. The nasal bone articulates superiorly with the frontal bone and laterally with the maxillary bones. Septal cartilage is flexible hyaline cartilage connected to the nasal bone, forming the dorsum nasi. The **alar cartilage** consists of the apex of the nose; it surrounds the naris.

The nares open into the **nasal cavity**, which is separated into left and right sections by the nasal septum (Figure 21.3).

The **nasal septum** is formed anteriorly by a portion of the septal cartilage (the flexible portion you can touch with your fingers) and posteriorly by the perpendicular plate of the ethmoid bone (a cranial bone located just posterior to the nasal bones) and the thin vomer bones (whose name refers to its

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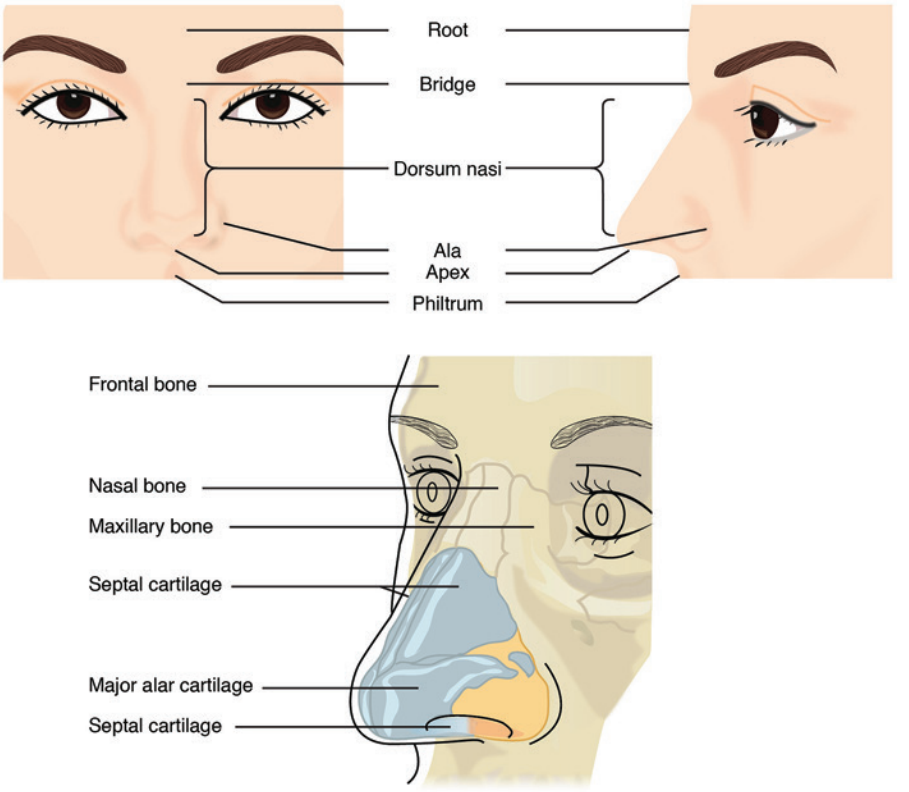


Figure 21.2 Nose. This illustration shows features of the external nose (top) and skeletal features of the nose (bottom).

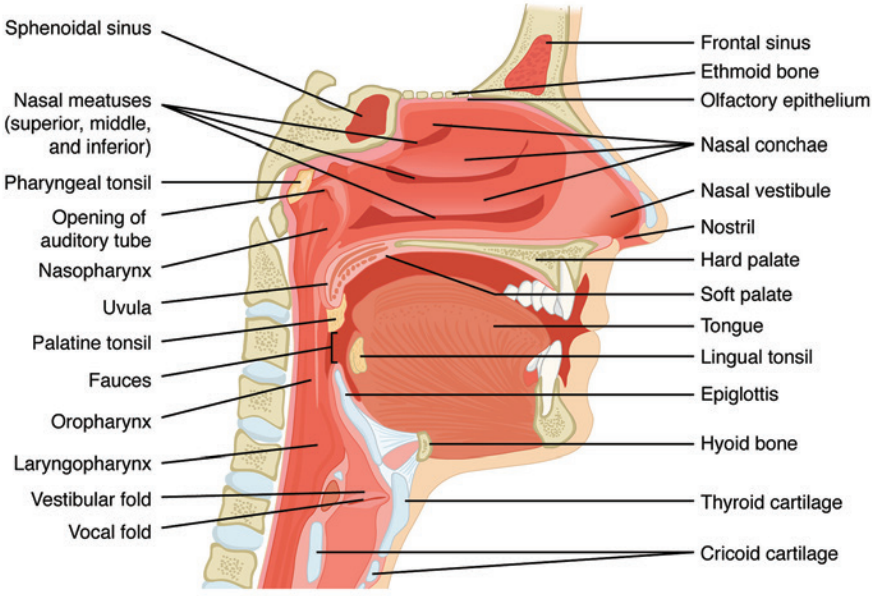


Figure 21.3 Upper Airway.

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plow shape). Each lateral wall of the nasal cavity has three bony projections, called the superior, middle, and inferior nasal conchae. The inferior conchae are separate bones, whereas the superior and middle conchae are portions of the ethmoid bone. Conchae serve to increase the surface area of the nasal cavity and to disrupt the flow of air as it enters the nose, causing air to bounce along the epithelium, where it is cleaned and warmed. The conchae and **meatuses**—groovelike air passageways, which are confined/located between the three conchae (superior, middle, and inferior nasal meatuses)—also conserve water and prevent dehydration of the nasal epithelium by trapping water during exhalation. The floor of the nasal cavity is composed of the palate. The hard palate at the anterior region of the nasal cavity is composed of bone. The soft palate at the posterior portion of the nasal cavity consists of muscle tissue. Air exits the nasal cavities via the internal nares and moves into the pharynx.

Several bones that help form the walls of the nasal cavity have air-containing spaces, called the paranasal sinuses, which open into the nasal cavity and serve to warm and humidify incoming air. Sinuses are lined with a mucosa. Each **paranasal sinus** is named for its associated bone: frontal sinus, maxillary sinus, sphenoidal sinus, and ethmoidal sinus. The sinuses produce mucus and lighten the weight of the skull.

The nares and anterior portion of the nasal cavities are lined with mucous membranes containing sebaceous glands and hair follicles that serve to prevent the passage of large debris, such as dirt, through the nasal cavity. An olfactory epithelium used to detect odours is found deeper in the nasal cavity.

The conchae, meatuses, and paranasal sinuses are lined by **respiratory epithelium** composed of pseudostratified ciliated columnar epithelium. The epithelium contains goblet cells, one of the specialized, columnar epithelial cells that produce mucus to trap debris. The cilia of the respiratory epithelium help remove the mucus and debris from the nasal cavity with a constant beating motion, sweeping materials toward the throat to be swallowed. Interestingly, cold air slows the movement of the cilia, resulting in accumulation of mucus that may in turn lead to a runny nose during cold weather. This moist epithelium functions to warm and humidify incoming air. Capillaries located just beneath the nasal epithelium warm the air by convection. Serous and mucus-producing cells also secrete the lysozyme enzyme and proteins called defensins, which have antibacterial properties. Immune cells that patrol the connective tissue deep to the respiratory epithelium provide additional protection.

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Interactive Link 21.1

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/21.1) to explore the tissue sample in greater detail.

Pharynx

The **pharynx** is a tube formed by skeletal muscle and lined by mucous membrane that is continuous with that of the nasal cavities (see Figure 21.3). The pharynx is divided into three major regions: the nasopharynx, the oropharynx, and the laryngopharynx (Figure 21.4).

The **nasopharynx** is flanked by the conchae of the nasal cavity, and it serves only as an airway. At the top of the nasopharynx are the pharyngeal tonsils. A **pharyngeal tonsil**, also called an adenoid, is an aggregate of lymphoid reticular tissue similar to a lymph node that lies at the superior portion of the nasopharynx. The function of the pharyngeal tonsil is not well understood, but it contains a rich supply of lymphocytes and is covered with ciliated epithelium that traps and destroys invading pathogens that enter during inhalation.

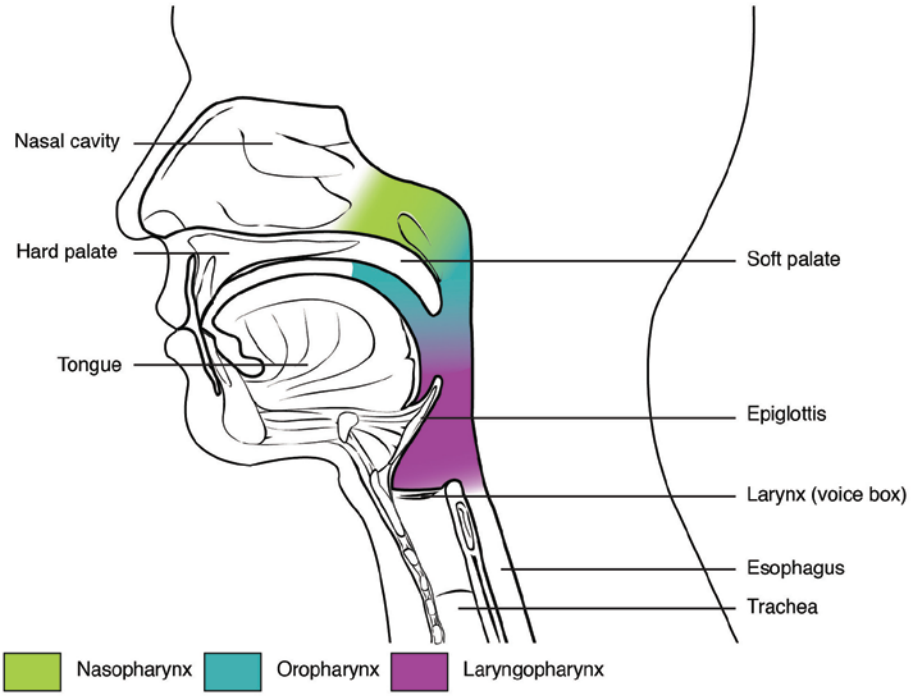


Figure 21.4 Divisions of the Pharynx. The pharynx is divided into three regions: the nasopharynx, the oropharynx, and the laryngopharynx.

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The pharyngeal tonsils are large in children but tend to regress with age and may even disappear. The uvula is a small bulbous, teardrop-shaped structure located at the apex of the soft palate. Both the uvula and the soft palate move like a pendulum during swallowing, swinging upward to close off the nasopharynx to prevent ingested materials from entering the nasal cavity. In addition, auditory (Eustachian) tubes that connect to each middle ear cavity open into the nasopharynx. This connection is why colds often lead to ear infections.

The **oropharynx** is a passageway for both air and food. The oropharynx is bordered superiorly by the nasopharynx and anteriorly by the oral cavity. The **fauces** is the opening at the connection between the oral cavity and the oropharynx. As the nasopharynx becomes the oropharynx, the epithelium changes from pseudostratified ciliated columnar epithelium to stratified squamous epithelium. The oropharynx contains two distinct sets of tonsils, the palatine and lingual tonsils. A **palatine tonsil** is one of a pair of structures located laterally in the oropharynx in the area of the fauces. The **lingual tonsil** is located at the base of the tongue. Similar to the pharyngeal tonsil, the palatine and lingual tonsils are composed of lymphoid tissue and trap and destroy pathogens entering the body through the oral or nasal cavities.

The **laryngopharynx** is inferior to the oropharynx and posterior to the larynx. It continues the route for ingested material and air until its inferior end, where the digestive and respiratory systems diverge. The stratified squamous epithelium of the oropharynx is continuous with the laryngopharynx. Anteriorly, the laryngopharynx opens into the larynx, whereas posteriorly, it enters the esophagus.

Larynx

The **larynx** is a cartilaginous structure inferior to the laryngopharynx that connects the pharynx to the trachea and helps regulate the volume of air that enters and leaves the lungs (Figure 21.5). The structure of the larynx is formed by several pieces of cartilage. Three large cartilage pieces—the thyroid cartilage (anterior), epiglottis (superior), and cricoid cartilage (inferior)—form the major structure of the larynx. The **thyroid cartilage** is the largest piece of cartilage that makes up the larynx. The thyroid cartilage consists of the **laryngeal prominence**, or "Adam's apple," which tends to be more prominent in males. The thick **cricoid cartilage** forms a ring, with a wide posterior region and a thinner anterior region. Three smaller, paired cartilages—the arytenoids, corniculates, and cuneiforms—attach to the epiglottis and the vocal cords and muscle that help move the vocal cords to produce speech.

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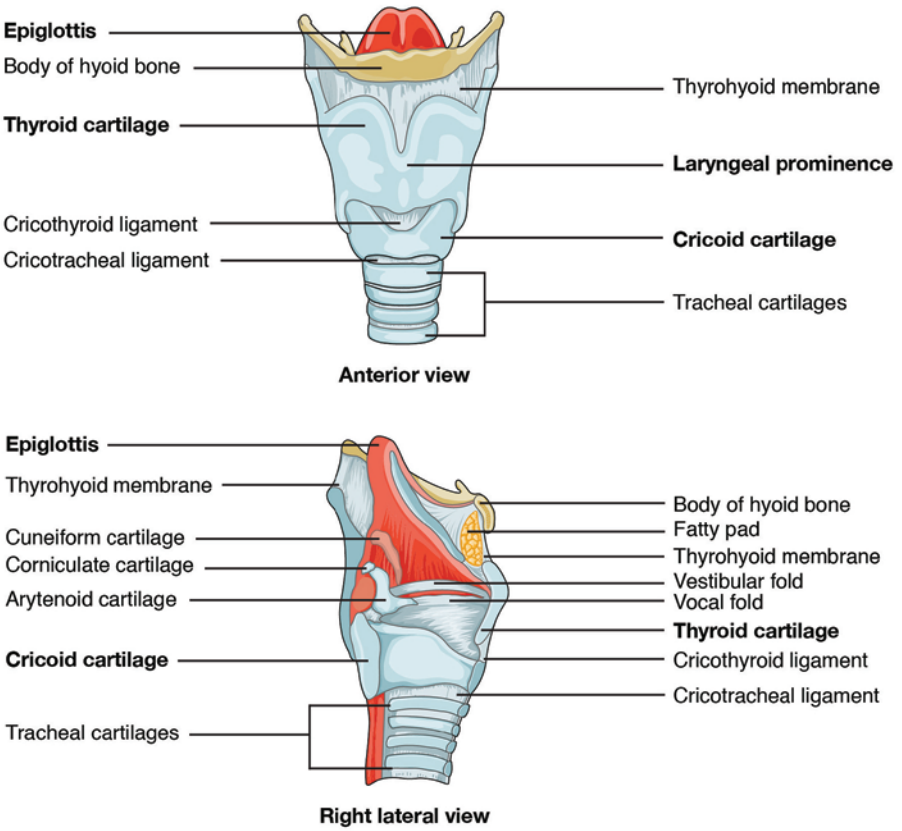


Figure 21.5 Larynx. The larynx extends from the laryngopharynx and the hyoid bone to the trachea.

The **epiglottis**, attached to the thyroid cartilage, is a very flexible piece of elastic cartilage that covers the opening of the larynx (see Figure 21.3). When in the "closed" position, the unattached end of the epiglottis rests on the glottis. The **glottis** is composed of the vestibular folds, the true vocal cords, and the space between these folds (Figure 21.6). A **vestibular fold**, or false vocal cord, is one of a pair of folded sections of mucous membrane. A **true vocal cord** is one of the white, membranous folds attached by muscle to the thyroid and arytenoid cartilages of the larynx on their outer edges. The inner edges of the true vocal cords are free, allowing oscillation to produce sound. The size of the membranous folds of the true vocal cords differs between individuals, producing voices with different pitch ranges. Folds in males tend to be larger than those in females, which create a deeper voice. The act of swallowing causes the pharynx and larynx to lift upward, allowing the pharynx to expand and the epiglottis of the larynx to swing downward, closing the opening to the trachea. These movements produce a larger area for food to pass through while preventing food and beverages from entering the trachea.

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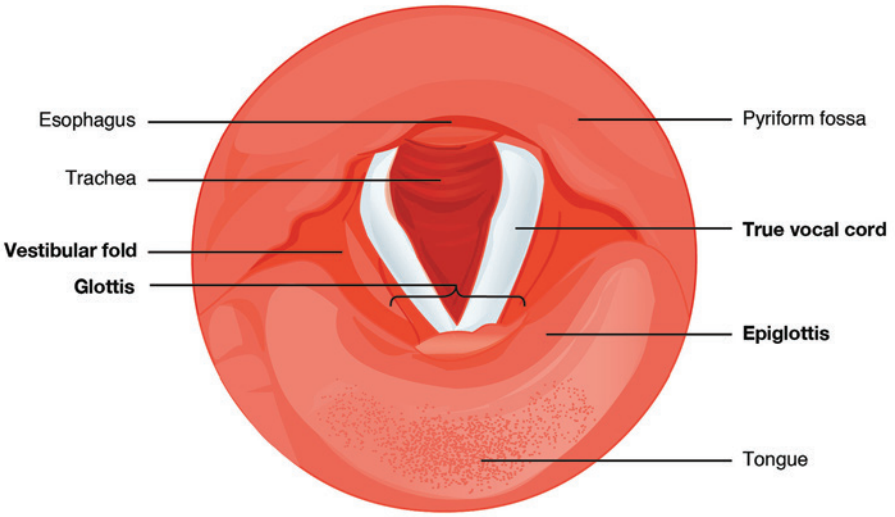


Figure 21.6 Vocal Cords. The true vocal cords and vestibular folds of the larynx are viewed inferiorly from the laryngopharynx.

Continuous with the laryngopharynx, the superior portion of the larynx is lined with stratified squamous epithelium, transitioning into pseudostratified ciliated columnar epithelium that contains goblet cells. Similar to the nasal cavity and nasopharynx, this specialized epithelium produces mucus to trap debris and pathogens as they enter the trachea. The cilia beat the mucus upward toward the laryngopharynx, where it can be swallowed down the esophagus.

Trachea

The trachea (windpipe) extends from the larynx toward the lungs (Figure 21.7a). The **trachea** is formed by 16 to 20 stacked, C-shaped pieces of hyaline cartilage that are connected by dense connective tissue. The **trachealis muscle** and elastic connective tissue together form the **fibroelastic membrane**, a flexible membrane that closes the posterior surface of the trachea, connecting the C-shaped cartilages. The fibroelastic membrane allows the trachea to stretch and expand slightly during inhalation and exhalation, whereas the rings of cartilage provide structural support and prevent the trachea from collapsing. In addition, the trachealis muscle can be contracted to force air through the trachea during exhalation. The trachea is lined with pseudostratified ciliated columnar epithelium, which is continuous with the larynx. The esophagus borders the trachea posteriorly.

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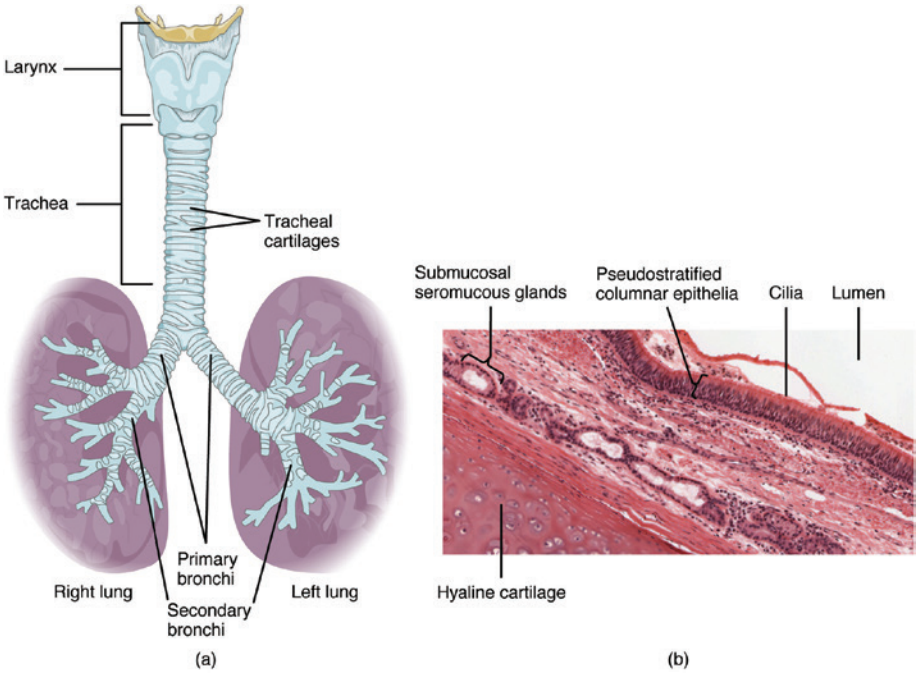


Figure 21.7 Trachea. (a) The tracheal tube is formed by stacked, C-shaped pieces of hyaline cartilage. (b) The layer visible in this cross section of tracheal wall tissue between the hyaline cartilage and the lumen of the trachea is the mucosa, which is composed of pseudostratified ciliated columnar epithelium that contains goblet cells. LM × 1220. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Bronchial Tree

The trachea branches into the right and left primary **bronchi** at the carina. These bronchi are also lined by pseudostratified ciliated columnar epithelium containing mucus-producing goblet cells (Figure 21.7b). The carina is a raised structure that contains specialized nervous tissue that induces violent coughing if a foreign body, such as food, is present. Rings of cartilage, similar to those of the trachea, support the structure of the bronchi and prevent their collapse. The **primary bronchi** enter the lungs at the **hilum**, a concave region where blood vessels, lymphatic vessels, and nerves also enter the lungs. The bronchi continue to branch into a bronchial tree. A **bronchial tree** (or respiratory tree) is the collective term used for these multiple-branched bronchi. The main function of the bronchi, like other conducting zone structures, is to provide a passageway for air to move into and out of each lung. In addition, the mucous membrane traps debris and pathogens.

A **bronchiole** branches from the tertiary bronchi. Bronchioles, which are about 1 mm in diameter, further branch until they become the tiny **terminal**

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bronchioles, which lead to the structures of gas exchange. There are more than 1,000 terminal bronchioles in each lung. The muscular walls of the bronchioles do not contain cartilage like those of the bronchi. This muscular wall can change the size of the tubing to increase or decrease airflow through the tube.

Respiratory Zone

In contrast to the conducting zone, the respiratory zone includes structures that are directly involved in gas exchange. The respiratory zone begins where the terminal bronchioles join a **respiratory bronchiole**, the smallest type of bronchiole (Figure 21.8), which then leads to an alveolar duct, opening into a cluster of alveoli.

Alveoli

An **alveolar duct** is a tube composed of smooth muscle and connective tissue, which opens into a cluster of alveoli. An **alveolus** is one of the many small, grape-like sacs that are attached to the alveolar ducts.

An **alveolar sac** is a cluster of many individual alveoli that are responsible for gas exchange. An alveolus is approximately 200 μm in diameter with

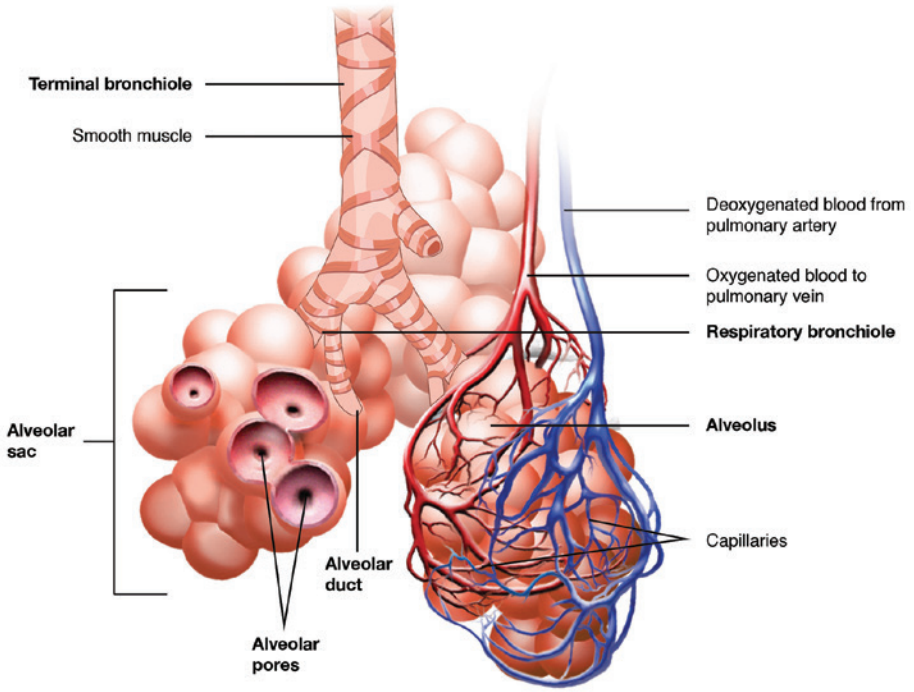


Figure 21.8 Respiratory Zone. Bronchioles lead to alveolar sacs in the respiratory zone, where gas exchange occurs.

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elastic walls that allow the alveolus to stretch during air intake, which greatly increases the surface area available for gas exchange. Alveoli are connected to their neighbours by **alveolar pores**, which help maintain equal air pressure throughout the alveoli and lung (Figure 21.9).

The alveolar wall consists of three major cell types: type I alveolar cells, type II alveolar cells, and alveolar macrophages. A **type I alveolar cell** is a squamous epithelial cell of the alveoli, which constitute up to 97 percent of the alveolar surface area. These cells are about 25 nm thick and are highly permeable to gases. A **type II alveolar cell** is interspersed among the type I cells and secretes **pulmonary surfactant**, a substance composed of phospholipids and proteins that reduces the surface tension of the alveoli. Roaming around the alveolar wall is the **alveolar macrophage**, a phagocytic cell of the immune system that removes debris and pathogens that have reached the alveoli. The simple squamous epithelium formed by type I alveolar cells is attached to a thin, elastic basement membrane. This epithelium is extremely thin and borders the endothelial membrane of capillaries. Taken together, the alveoli and capillary membranes form a **respiratory membrane** that is approximately 0.5 µm thick. The respiratory membrane allows gases to cross by simple diffusion, allowing oxygen to be picked up by the blood for transport and CO_2 to be released into the air of the alveoli.

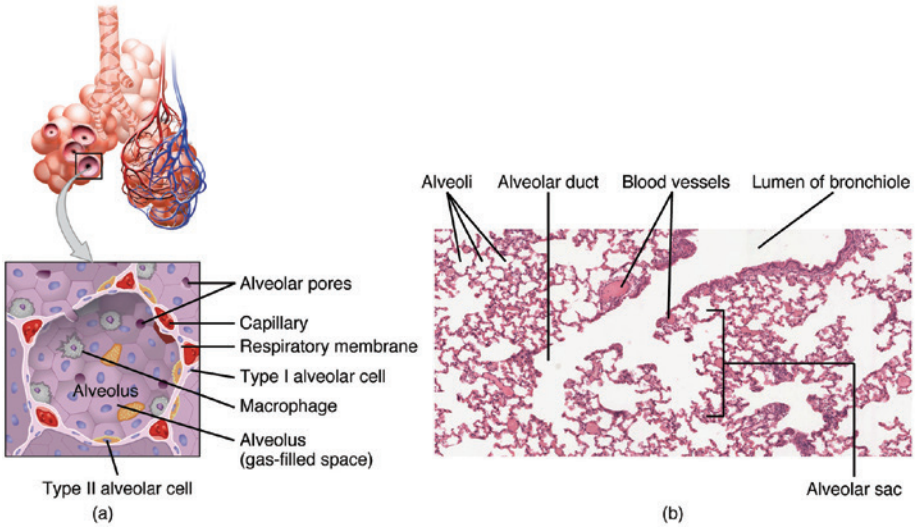


Figure 21.9 Structures of the Respiratory Zone. (a) The alveolus is responsible for gas exchange. (b) A micrograph shows the alveolar structures within lung tissue. LM × 178. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

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Interactive Link 21.2

Visit this site (http://oer.aupress.ca/oer-202505/21.2) to learn more about what happens during an asthma attack. What are the three changes that occur inside the airways during an asthma attack?

21.2 The Lungs

Learning Objectives

By the end of this section, you will be able to:

- Describe the overall function of the lungs
- Summarize the blood flow pattern associated with the lungs
- Outline the anatomy of the blood supply to the lungs
- Describe the pleura of the lungs and their function

A major organ of the respiratory system, each **lung** houses structures of both the conducting and respiratory zones. The main function of the lungs is to perform the exchange of oxygen and carbon dioxide with air from the atmosphere. To this end, the lungs exchange respiratory gases across a very large epithelial surface area—about 70 square metres—that is highly permeable to gases.

Gross Anatomy of the Lungs

The lungs are pyramid-shaped, paired organs that are connected to the trachea by the right and left primary bronchi; on the inferior surface, the lungs are bordered by the diaphragm. The diaphragm is a dome-shaped muscle located at the base of the lungs and thoracic cavity. The lungs are enclosed by the pleurae, which are attached to the mediastinum (which is the area between the lungs in which the heart is located). The right lung is shorter and wider than the left lung, and the left lung occupies a smaller volume than the right. The **cardiac notch** is an indentation on the surface of the left lung, and it allows space for the heart (Figure 21.10). The apex of the lung is the superior region, whereas the base is the opposite region near the diaphragm. The costal surface of the lung borders the ribs. The mediastinal surface faces the midline.

Each lung is composed of smaller units called **lobes**. **Fissures** separate these lobes from each other. The right lung consists of three lobes: the superior, middle, and inferior lobes. The left lung consists of two lobes: the superior and

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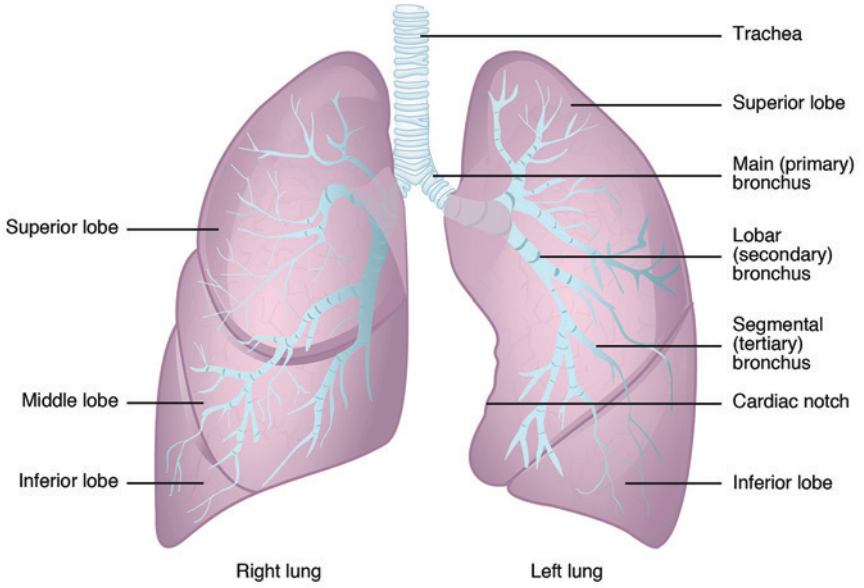


Figure 21.10 Gross Anatomy of the Lungs.

inferior lobes. A bronchopulmonary segment is a division of a lobe, and each lobe houses multiple bronchopulmonary segments. Each segment receives air from its own tertiary bronchus and is supplied with blood by its own artery. Some diseases of the lungs typically affect one or more bronchopulmonary segments, and in some cases, the diseased segments can be surgically removed with little influence on neighbouring segments. A pulmonary lobule is a subdivision formed as the bronchi branch into bronchioles. Each lobule receives its own large bronchiole that has multiple branches. An interlobular septum is a wall, composed of connective tissue, that separates lobules from one another.

Blood Supply and Nervous Innervation of the Lungs

The blood supply of the lungs plays an important role in gas exchange and serves as a transport system for gases throughout the body. In addition, innervation by both the parasympathetic and sympathetic nervous systems provides an important level of control through dilation and constriction of the airway.

Blood Supply

The major function of the lungs is to perform gas exchange, which requires blood from the pulmonary circulation. This blood supply contains deoxygenated blood and travels to the lungs, where erythrocytes, also known as red blood cells, pick up oxygen to be transported to tissues throughout the body.

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The **pulmonary artery** is an artery that arises from the pulmonary trunk and carries deoxygenated, arterial blood to the alveoli. The pulmonary artery enters a lung through the hilum (an opening on the medial side of a lung) and then branches multiple times as it follows the bronchi, and each branch becomes progressively smaller in diameter. One arteriole and an accompanying venule supply and drain one pulmonary lobule. As they near the alveoli, the pulmonary arteries become the pulmonary capillary network. The pulmonary capillary network consists of tiny vessels with very thin walls that lack smooth muscle fibres. The capillaries branch and follow the bronchioles and structure of the alveoli. It is at this point that the capillary wall meets the alveolar wall, creating the respiratory membrane. Once the blood is oxygenated, it drains from the alveoli by way of multiple pulmonary veins, which exit the lungs through the **hilum**.

Nervous Innervation

Dilation and constriction of the airway are achieved through nervous control by the parasympathetic and sympathetic nervous systems. The parasympathetic system causes **bronchoconstriction**, whereas the sympathetic nervous system stimulates **bronchodilation**. Reflexes such as coughing and the ability of the lungs to regulate oxygen and carbon dioxide levels also result from this autonomic nervous system control. Sensory nerve fibres arise from the vagus nerve and from the second to fifth thoracic ganglia. The pulmonary plexus is a region on the lung root formed by the entrance of the nerves at the hilum. The nerves then follow the bronchi in the lungs and branch to innervate muscle fibres, glands, and blood vessels.

Pleura of the Lungs

Each lung is enclosed within a cavity that is surrounded by the pleura. The pleura (plural = pleurae) is a serous membrane that surrounds the lung. The right and left pleurae, which enclose the right and left lungs, respectively, are separated by the mediastinum. The pleurae consist of two layers. The **visceral pleura** is the layer that is superficial to the lungs and extends into and lines the lung fissures (Figure 21.11). In contrast, the **parietal pleura** is the outer layer that connects to the thoracic wall, the mediastinum, and the diaphragm. The visceral and parietal pleurae connect to each other at the hilum. The **pleural cavity** is the space between the visceral and parietal layers.

The pleurae perform two major functions: They produce pleural fluid and create cavities that separate the major organs. **Pleural fluid** is secreted by mesothelial cells from both pleural layers and acts to lubricate their surfaces. This

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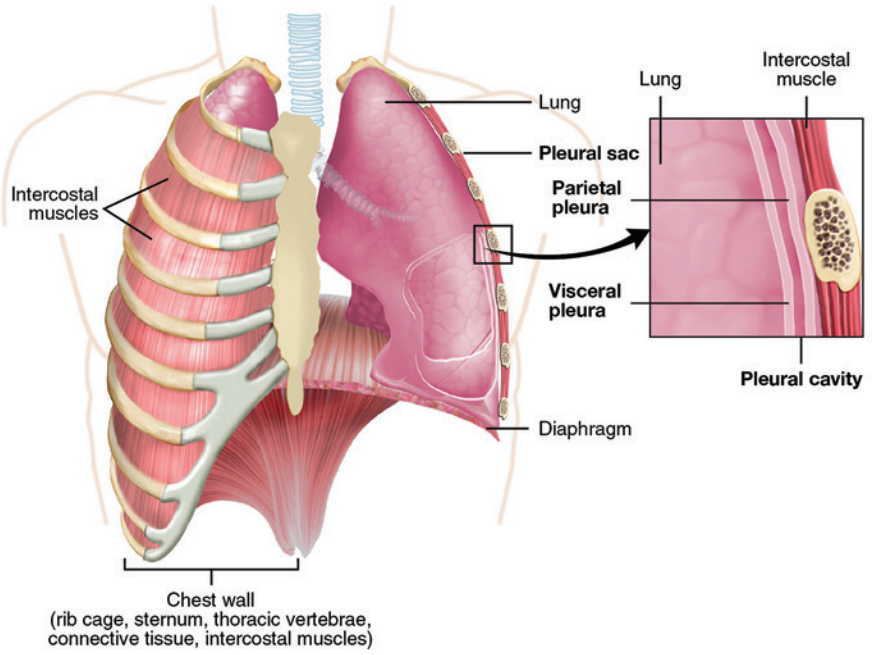


Figure 21.11 Parietal and Visceral Pleurae of the Lungs.

lubrication reduces friction between the two layers to prevent trauma during breathing and creates surface tension that helps maintain the position of the lungs against the thoracic wall. This adhesive characteristic of the pleural fluid causes the lungs to enlarge when the thoracic wall expands during ventilation, allowing the lungs to fill with air. The pleurae also create a division between major organs that prevents interference due to the movement of the organs while preventing the spread of infection.

21.3 The Process of Breathing

Learning Objectives

By the end of this section, you will be able to:

- Describe the mechanisms that drive breathing
- Discuss how pressure, volume, and resistance are related
- List the steps involved in pulmonary ventilation
- Discuss the physical factors related to breathing
- Discuss the meaning of respiratory volume and capacities
- Define respiratory rate
- Outline the mechanisms behind the control of breathing

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- Describe the respiratory centres of the medulla oblongata
- Describe the respiratory centres of the pons
- Discuss factors that can influence the respiratory rate

Pulmonary ventilation is the act of breathing, which can be described as the movement of air into and out of the lungs. The major mechanisms that drive pulmonary ventilation are atmospheric pressure (P_{atm}); the air pressure within the alveoli, called intra-alveolar pressure (P_{alv}); and the pressure within the pleural cavity, called intrapleural pressure (P_{ip}).

Mechanisms of Breathing

The intra-alveolar and intrapleural pressures are dependent on certain physical features of the lung. However, the ability to breathe, to have air enter the lungs during **inspiration** and air leave the lungs during **expiration**, is dependent on the air pressure of the atmosphere and the air pressure within the lungs.

Pressure Relationships

Inspiration (or inhalation) and expiration (or exhalation) are dependent on the differences in pressure between the atmosphere and the lungs. In a gas, pressure is a force created by the movement and collision of confined gas molecules.

For example, a certain number of gas molecules in a 2 L container have more room than the same number of gas molecules when volume decreases. So as volume decreases, the pressure of gas molecules increases (Figure 21.12).

In this case, the force exerted by the movement of the gas molecules against the walls of the 2 L container is lower than the force exerted by the gas molecules in a 1 L container. Therefore, the pressure is lower in the 2 L container and higher in the 1 L container. At a constant temperature, changing the volume occupied by the gas changes the pressure, as does changing the number of gas molecules. **Boyle's law** describes the relationship between volume and pressure in a gas at a constant temperature. Boyle discovered that the pressure of a gas is inversely proportional to its volume: If volume increases, pressure decreases. Likewise, if volume decreases, pressure increases. Pressure and volume are inversely related.

Pulmonary ventilation is dependent on three types of pressure: atmospheric, intra-alveolar, and intrapleural. **Atmospheric pressure** is the amount of force that is exerted by gases in the air surrounding any given surface, such as the body. Atmospheric pressure can be expressed in terms of the unit atmosphere (abbreviated atm) or in millimetres of mercury (mm Hg). One atm is equal to 760 mm Hg, which is the atmospheric pressure at sea level.

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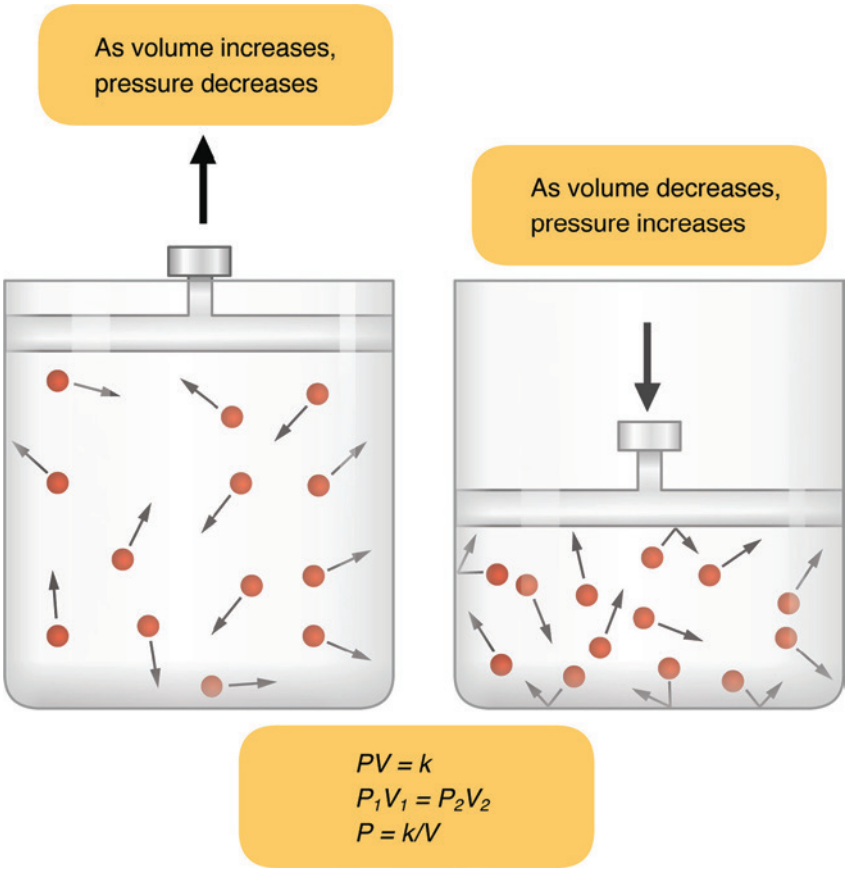


Figure 21.12 Boyle's Law. In a gas, pressure increases as volume decreases.

Typically, for respiration, other pressure values are discussed in relation to atmospheric pressure. Therefore, negative pressure is pressure lower than the atmospheric pressure, whereas positive pressure is pressure that is greater than the atmospheric pressure. A pressure that is equal to the atmospheric pressure is expressed as zero.

Intra-alveolar pressure (intrapulmonary pressure) is the pressure of the air within the alveoli, which changes during the different phases of breathing (Figure 21.13). Because the alveoli are connected to the atmosphere via the tubing of the airways (similar to the two- and one-litre containers in the previous example), the intrapulmonary pressure of the alveoli always equalizes with the atmospheric pressure.

Intrapleural pressure is the pressure within the pleural cavity, between the visceral and parietal pleurae. Similar to intra-alveolar pressure, intrapleural pressure also changes during the different phases of breathing.

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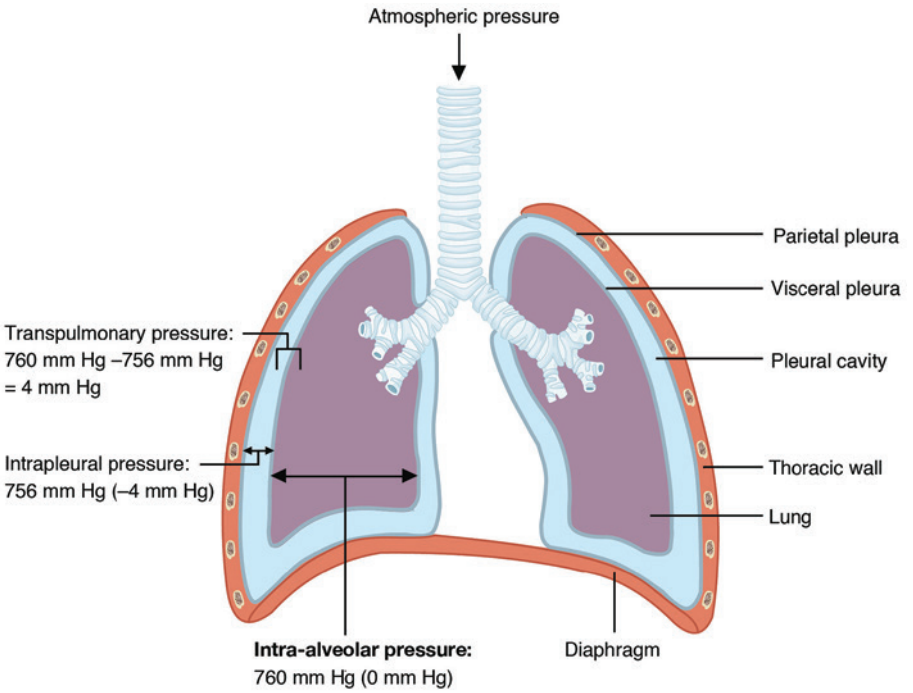


Figure 21.13 Intrapulmonary and Intrapleural Pressure Relationships. Intra-alveolar pressure changes during the different phases of the cycle. It equalizes at 760 mm Hg but does not remain at 760 mm Hg.

However, due to certain characteristics of the lungs, the intrapleural pressure is always lower than, or negative to, the intra-alveolar pressure (and therefore also to atmospheric pressure). Although it fluctuates during inspiration and expiration, intrapleural pressure remains lower than the atmospheric pressure with approximately −4 mm Hg throughout the breathing cycle.

Competing forces within the thorax cause the formation of the negative intrapleural pressure. One of these forces relates to the elasticity of the lungs themselves—elastic tissue pulls the lungs inward, away from the thoracic wall. Surface tension of alveolar fluid, which is mostly water, also creates an inward pull of the lung tissue. This inward tension from the lungs is countered by opposing forces from the pleural fluid and thoracic wall. Surface tension within the pleural cavity pulls the lungs outward. Too much or too little pleural fluid would hinder the creation of the negative intrapleural pressure; therefore, the level must be closely monitored by the mesothelial cells and drained by the lymphatic system. Since the parietal pleura is attached to the thoracic wall, the natural elasticity of the chest wall opposes the inward pull of the lungs. Ultimately, the outward pull is slightly greater than the inward pull, creating the −4 mm Hg

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intrapleural pressure relative to the intra-alveolar pressure. **Transpulmonary pressure** is the difference between the intrapleural and intra-alveolar pressures, and it determines the size of the lungs. A higher transpulmonary pressure corresponds to a larger lung.

Physical Factors Affecting Ventilation

In addition to the differences in pressures, breathing is also dependent on the contraction and relaxation of muscle fibres of both the diaphragm and the thorax. The lungs themselves are passive during breathing, meaning they are not involved in creating the movement that helps inspiration and expiration. This is because of the adhesive nature of the pleural fluid, which allows the lungs to be pulled outward when the thoracic wall moves during inspiration. The recoil of the thoracic wall during expiration causes compression of the lungs. Contraction and relaxation of the diaphragm and intercostals muscles (found between the ribs) cause most of the pressure changes that result in inspiration and expiration. These muscle movements and subsequent pressure changes cause air to either rush in or be forced out of the lungs.

Other characteristics of the lungs influence the effort that must be expended to ventilate. Resistance is a force that slows motion—in this case, the flow of gases. The size of the airway is the primary factor affecting resistance. A small tubular diameter forces air through a smaller space, causing more collisions of air molecules with the walls of the airways.

As noted earlier, there is surface tension within the alveoli caused by water present in the lining of the alveoli. This surface tension tends to inhibit expansion of the alveoli. However, pulmonary surfactant secreted by type II alveolar cells mixes with that water and helps reduce this surface tension. Without pulmonary surfactant, the alveoli would collapse during expiration.

Thoracic wall compliance is the ability of the thoracic wall to stretch while under pressure. This can also affect the effort expended in the process of breathing. In order for inspiration to occur, the thoracic cavity must expand. The expansion of the thoracic cavity directly influences the capacity of the lungs to expand. If the tissues of the thoracic wall are not very compliant, it will be difficult to expand the thorax to increase the size of the lungs.

Pulmonary Ventilation

The difference in pressures drives pulmonary ventilation because air flows down a pressure gradient—that is, air flows from an area of higher pressure to an area of lower pressure. Air flows into the lungs largely due to a difference in pressure; atmospheric pressure is greater than intra-alveolar pressure, and intra-alveolar pressure is greater than intrapleural pressure. Air flows out of

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the lungs during expiration based on the same principle; pressure within the lungs becomes greater than the atmospheric pressure.

Pulmonary ventilation comprises two major steps: inspiration and expiration. **Inspiration** is the process that causes air to enter the lungs, and **expiration** is the process that causes air to leave the lungs (Figure 21.14). A **respiratory cycle** is one sequence of inspiration and expiration. In general, two muscle groups are used during normal inspiration: the diaphragm and the external intercostal muscles.

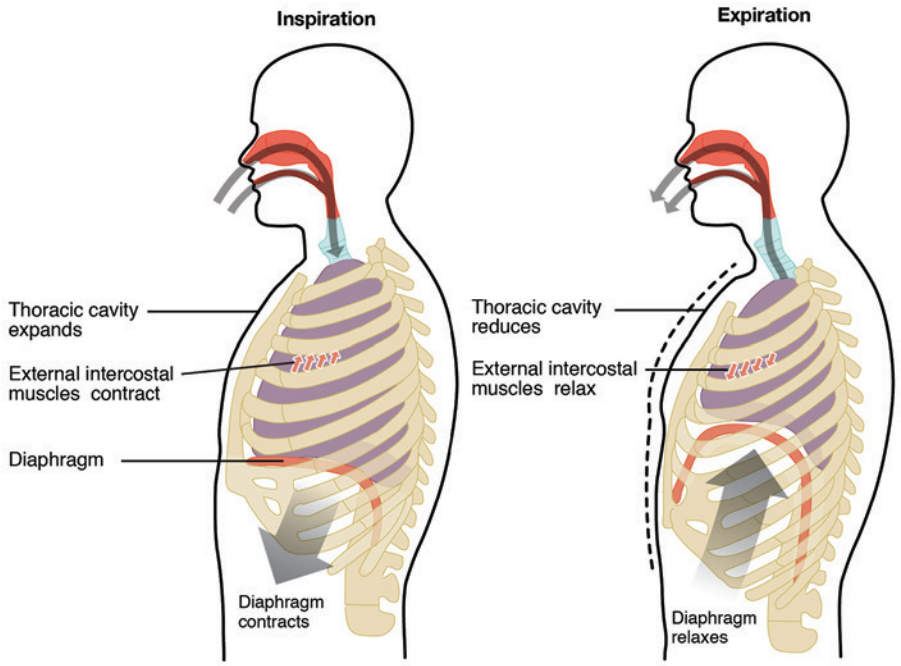


Figure 21.14 Inspiration and Expiration. Inspiration and expiration occur due to the expansion and contraction of the thoracic cavity, respectively.

Additional muscles can be used if a bigger breath is required. When the diaphragm contracts, it moves inferiorly toward the abdominal cavity, creating a larger thoracic cavity and more space for the lungs. Contraction of the external intercostal muscles moves the ribs upward and outward, causing the rib cage to expand, which increases the volume of the thoracic cavity. Due to the adhesive force of the pleural fluid, the expansion of the thoracic cavity forces the lungs to stretch and expand as well. This increase in volume leads to a decrease in intra-alveolar pressure, creating a pressure lower than atmospheric pressure. As a result, a pressure gradient is created that drives air into the lungs.

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The process of normal expiration is passive, meaning that energy is not required to push air out of the lungs. Instead, the elasticity of the lung tissue causes the lung to recoil as the diaphragm and intercostal muscles relax following inspiration. In turn, the thoracic cavity and lungs decrease in volume, causing an increase in intrapulmonary pressure. The intrapulmonary pressure rises above atmospheric pressure, creating a pressure gradient that causes air to leave the lungs.

There are different types, or modes, of breathing that require a slightly different process to allow inspiration and expiration. **Quiet breathing**, also known as eupnea, is a mode of breathing that occurs at rest and does not require the cognitive thought of the individual. During quiet breathing, the diaphragm and external intercostals must contract.

A deep breath, called diaphragmatic breathing, requires the diaphragm to contract. As the diaphragm relaxes, air passively leaves the lungs. A shallow breath, called costal breathing, requires contraction of the intercostal muscles. As the intercostal muscles relax, air passively leaves the lungs.

In contrast, **forced breathing**, also known as hyperpnea, is a mode of breathing that can occur during exercise or actions that require the active manipulation of breathing, such as singing. During forced breathing, inspiration and expiration both occur due to muscle contractions. In addition to the contraction of the diaphragm and intercostal muscles, other accessory muscles must also contract. During forced inspiration, muscles of the neck, including the scalenes, contract and lift the thoracic wall, increasing lung volume. During forced expiration, accessory muscles of the abdomen, including the obliques, contract, forcing abdominal organs upward against the diaphragm. This helps push the diaphragm further into the thorax, pushing more air out. In addition, accessory muscles (primarily the internal intercostals) help compress the rib cage, which also reduces the volume of the thoracic cavity.

Respiratory Volumes and Capacities

Respiratory volume is the term used for various volumes of air moved by or associated with the lungs at a given point in the respiratory cycle. There are four major types of respiratory volumes: tidal, residual, inspiratory reserve, and expiratory reserve (Figure 21.15). **Tidal volume** (**TV**) is the amount of air that normally enters the lungs during quiet breathing, which is about 500 mL. **Expiratory reserve volume** (**ERV**) is the amount of air you can forcefully exhale past a normal tidal expiration, up to 1,200 mL for males. **Inspiratory reserve volume** (**IRV**) is produced by a deep inhalation, past a tidal inspiration. This is the extra volume that can be brought into the lungs during a forced inspiration. **Residual volume** (**RV**) is the air left in the lungs if you exhale as much air as possible.

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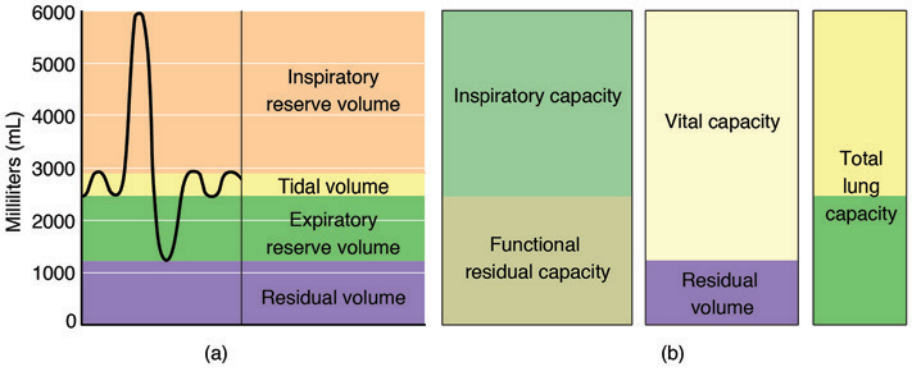


Figure 21.15 Respiratory Volumes and Capacities. These two graphs show (a) respiratory volumes and (b) the combination of volumes that results in respiratory capacity.

The residual volume makes breathing easier by preventing the alveoli from collapsing. Respiratory volume is dependent on a variety of factors, and measuring the different types of respiratory volumes can provide important clues about a person's respiratory health (Table 21.1).

Respiratory capacity is the combination of two or more selected volumes that further describes the amount of air in the lungs during a given time. For example, **total lung capacity** (**TLC**) is the sum of all of the lung volumes (TV, ERV, IRV, and RV), which represents the total amount of air a person can hold in the lungs after a forceful inhalation. TLC is about 6,000 mL air for males and about 4,200 mL for females. **Vital capacity** (**VC**) is the amount of air a person can move into or out of their lungs and is the sum of all of the volumes except residual volume (TV, ERV, and IRV), which is between 4,000 and 5,000 mL. **Inspiratory capacity** (**IC**), the maximum amount of air that can be inhaled past a normal tidal expiration, is the sum of the tidal volume and inspiratory reserve volume. On the other hand, the **functional residual capacity** (**FRC**) is the amount of air that remains in the lung after a normal tidal expiration; it is the sum of expiratory reserve volume and residual volume (see Figure 21.15).

Interactive Link 21.3

Watch this video (http://oer.aupress.ca/oer-202505/21.3) to learn more about lung volumes and spirometers. Explain how spirometry test results can be used to diagnose respiratory diseases or determine the effectiveness of disease treatment.

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Table 21.1 Pulmonary Function Testing

Pulmonary function test	Instrument	Measures	Function
Spirometry	Spirometer	Forced vital capacity (FVC)	Volume of air exhaled after maximum inhalation
		Forced expiratory volume (FEV)	Volume of air exhaled during one forced breath
		Forced expiratory flow, 25–75 percent	Airflow in the middle of exhalation
		Peak expiratory flow (PEF)	Rate of exhalation
		Maximum voluntary ventilation (MVV)	Volume of air that can be inspired and expired in 1 minute
		Slow vital capacity (SVC)	Volume of air that can be slowly exhaled after inhaling past the tidal volume
		Total lung capacity (TLC)	Volume of air in the lungs after maximum inhalation
		Functional residual capacity (FRC)	Volume of air left in the lungs after normal expiration
		Residual volume (RV)	Volume of air in the lungs after maximum exhalation
		Total lung capacity (TLC)	Maximum volume of air that the lungs can hold
		Expiratory reserve volume (ERV)	Volume of air that can be exhaled beyond normal exhalation
Gas diffusion	Blood gas analyzer	Arterial blood gases	Concentration of oxygen and carbon dioxide in the blood

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In addition to the air that creates respiratory volumes, the respiratory system also contains **anatomical dead space**, which is air that is present in the airway that never reaches the alveoli and therefore never participates in gas exchange. **Alveolar dead space** involves air found within alveoli that are unable to function, such as those affected by disease or abnormal blood flow. **Total dead space** is the anatomical dead space and alveolar dead space together and represents all of the air in the respiratory system that is not being used in the gas exchange process.

Respiratory Rate and Control of Ventilation

Breathing usually occurs without thought, although at times you can consciously control it, such as when you swim underwater, sing a song, or blow bubbles. The **respiratory rate** is the total number of breaths, or respiratory cycles, that occur each minute. Respiratory rate can be an important indicator of disease, as the rate may increase or decrease during an illness or in a disease condition. The respiratory rate is controlled by the respiratory centre located within the medulla oblongata in the brain, which responds primarily to changes in carbon dioxide, oxygen, and pH levels in the blood.

The normal respiratory rate of a child decreases from birth to adolescence. A child under 1 year of age has a normal respiratory rate between 30 and 60 breaths per minute, but by the time a child is about 10 years old, the normal rate is closer to 18 to 30. By adolescence, the normal respiratory rate is similar to that of adults, 12 to 18 breaths per minute.

Ventilation Control Centres

The control of ventilation involves a complex interplay of multiple regions in the brain that signal the muscles used in pulmonary ventilation to contract (Table 21.2). The result is typically a rhythmic, consistent ventilation rate that provides the body with sufficient amounts of oxygen while adequately removing carbon dioxide.

Neurons that innervate the muscles of the respiratory system are responsible for controlling and regulating pulmonary ventilation. The major brain centres involved in pulmonary ventilation are the medullary respiratory centre (which includes the dorsal respiratory group and the ventral respiratory group) and the pontine respiratory group (Figure 21.16).

The medulla oblongata contains the **dorsal respiratory group** (**DRG**) and the **ventral respiratory group** (**VRG**). The DRG is involved in maintaining a constant breathing rhythm by stimulating the diaphragm and intercostal muscles to contract, resulting in inspiration. When activity in the DRG ceases, it no longer stimulates the diaphragm and intercostals to contract, allowing

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Table 21.2 Summary of Ventilation Regulation

System component	Function
Medullary respiratory centre	Sets the basic rhythm of breathing
Ventral respiratory group (VRG)	Generates the breathing rhythm and integrates data coming into the medulla
Dorsal respiratory group (DRG)	Integrates input from the stretch receptors and the chemoreceptors in the periphery
Pontine respiratory group (PRG)	Influences and modifies the medulla oblongata's functions
Aortic body	Monitors blood PCO_2, PO_2, and pH
Carotid body	Monitors blood PCO_2, PO_2, and pH
Hypothalamus	Monitors emotional state and body temperature
Cortical areas of the brain	Control voluntary breathing
Proprioceptors	Send impulses regarding joint and muscle movements
Pulmonary irritant reflexes	Protect the respiratory zones of the system from foreign material
Inflation reflex	Protects the lungs from overinflating

them to relax, resulting in expiration. The VRG is involved in forced breathing, as the neurons in the VRG stimulate the accessory muscles involved in forced breathing to contract, resulting in forced inspiration. The VRG also stimulates the accessory muscles involved in forced expiration to contract.

The second respiratory centre of the brain is located within the pons, called the pontine respiratory group, and consists of the apneustic and pneumotaxic centres. The **apneustic centre** is a double cluster of neuronal cell bodies that stimulates neurons in the DRG, controlling the depth of inspiration, particularly for deep breathing. The **pneumotaxic centre** is a network of neurons that inhibits the activity of neurons in the DRG, allowing relaxation after inspiration, and thus controlling the overall rate.

Factors That Affect the Rate and Depth of Respiration

The respiratory rate and the depth of inspiration are regulated by the medulla oblongata and pons; however, these regions of the brain do so in response to systemic stimuli. It is a dose-response, negative-feedback relationship in which

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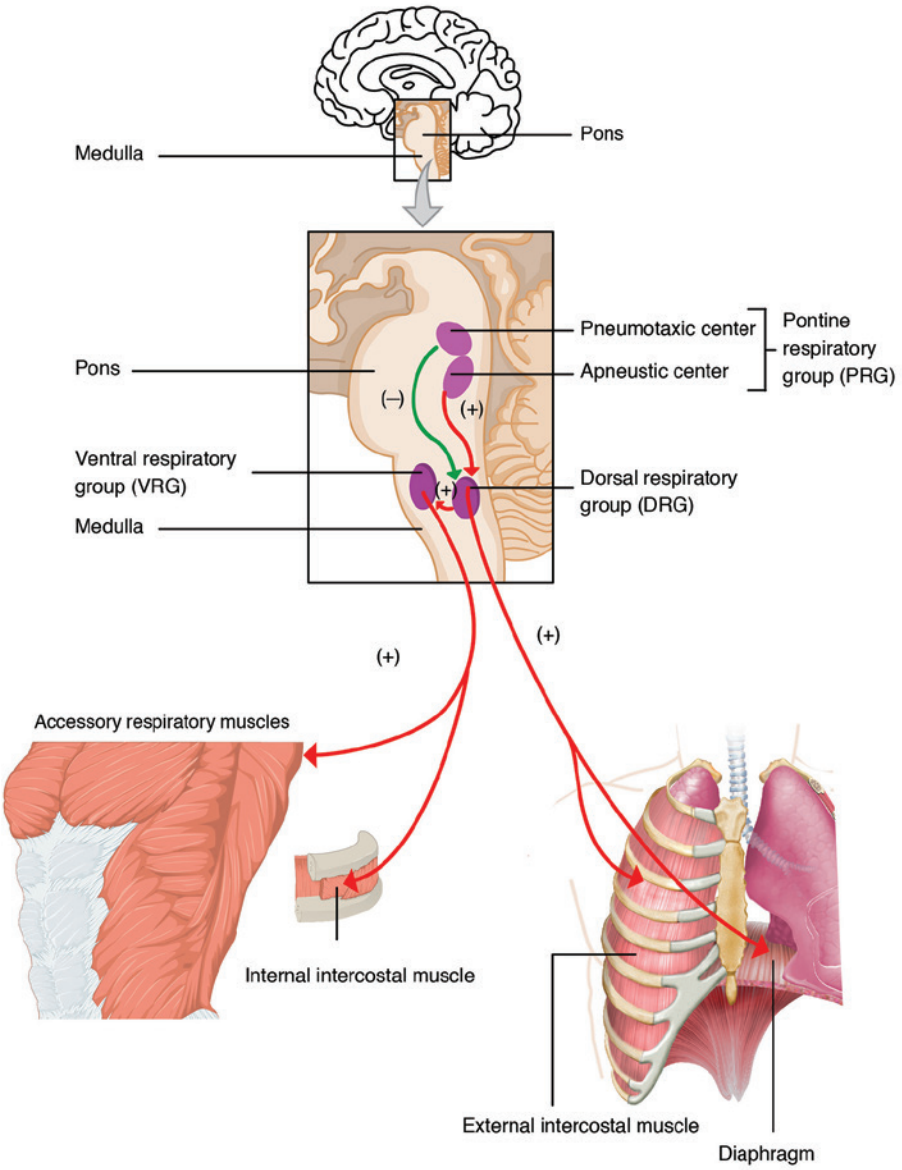


Figure 21.16 Respiratory Centres of the Brain.

the greater the stimulus, the greater the response. Thus, increasing stimuli results in forced breathing.

Multiple systemic factors are involved in stimulating the brain to produce pulmonary ventilation.

The major factor that stimulates the medulla oblongata and pons to produce respiration is surprisingly not oxygen concentration but rather the concentration of carbon dioxide in the blood. As you recall, carbon dioxide is a waste product of cellular respiration and can be toxic. Concentrations of chemicals

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are sensed by chemoreceptors. A **central chemoreceptor** is one of the specialized receptors located in the brain and brain stem, whereas a **peripheral chemoreceptor** is one of the specialized receptors located in the carotid arteries and aortic arch.

Concentration changes in certain substances, such as carbon dioxide or hydrogen ions, stimulate these receptors, which in turn signal the respiration centres of the brain. In the case of carbon dioxide, as the concentration of CO_2 in the blood increases, it readily diffuses across the blood-brain barrier, where it collects in the extracellular fluid. As will be explained in more detail later, increased carbon dioxide levels lead to increased levels of hydrogen ions, decreasing pH. The increase in hydrogen ions in the brain triggers the central chemoreceptors to stimulate the respiratory centres to initiate contraction of the diaphragm and intercostal muscles. As a result, the rate and depth of respiration increase, allowing more carbon dioxide to be expelled, which brings more air into and out of the lungs, promoting a reduction in the blood levels of carbon dioxide, and therefore hydrogen ions, in the blood. In contrast, low levels of carbon dioxide in the blood cause low levels of hydrogen ions in the brain, leading to a decrease in the rate and depth of pulmonary ventilation, producing shallow, slow breathing.

Another factor involved in influencing the respiratory activity of the brain is systemic arterial concentrations of hydrogen ions. Increasing carbon dioxide levels can lead to increased H^+ levels as well as other metabolic activities, such as lactic acid accumulation after strenuous exercise. Peripheral chemoreceptors of the aortic arch and carotid arteries sense arterial levels of hydrogen ions. When peripheral chemoreceptors sense decreasing, or more acidic, pH levels, they stimulate an increase in ventilation to remove carbon dioxide from the blood at a quicker rate. Removal of carbon dioxide from the blood helps reduce hydrogen ions, thus increasing systemic pH.

Blood levels of oxygen are also important in influencing respiratory rate. The peripheral chemoreceptors are responsible for sensing large changes in blood oxygen levels. If blood oxygen levels become quite low—about 60 mm Hg or less—then peripheral chemoreceptors stimulate an increase in respiratory activity. The chemoreceptors are only able to sense dissolved oxygen molecules, not the oxygen that is bound to hemoglobin. As you recall, the majority of oxygen is bound by hemoglobin; when dissolved levels of oxygen drop, hemoglobin releases oxygen.

Therefore, a large drop in oxygen levels is required to stimulate the chemoreceptors of the aortic arch and carotid arteries.

The hypothalamus and other brain regions associated with the limbic system also play roles in influencing the regulation of breathing by interacting with the

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respiratory centres. The hypothalamus and other regions associated with the limbic system are involved in regulating respiration in response to emotions, pain, and temperature.

For example, an increase in body temperature causes an increase in respiratory rate. Feeling excited or the fight-or-flight response will also result in an increase in respiratory rate.

21.4 Gas Exchange

Learning Objectives

By the end of this section, you will be able to:

- Compare the composition of atmospheric air and alveolar air
- Describe the mechanisms that drive gas exchange
- Discuss the importance of sufficient ventilation and perfusion and how the body adapts when they are insufficient
- Discuss the process of external respiration
- Describe the process of internal respiration

The purpose of the respiratory system is to perform gas exchange. Pulmonary ventilation provides air to the alveoli for this gas exchange process. At the respiratory membrane, where the alveolar and capillary walls meet, gases move across the membranes, with oxygen entering the bloodstream and carbon dioxide exiting. It is through this mechanism that blood is oxygenated and carbon dioxide, the waste product of cellular respiration, is removed from the body. In order to understand the mechanisms of gas exchange in the lung, it is important to understand the underlying principles of gases and their behaviour. In addition to Boyle's law, several other gas laws help describe the behaviour of gases.

Gas Laws and Air Composition

Gas molecules exert force on the surfaces with which they are in contact; this force is called pressure. In natural systems, gases are normally present as a mixture of different types of molecules.

For example, the atmosphere consists of oxygen, nitrogen, carbon dioxide, and other gaseous molecules, and this gaseous mixture exerts a certain pressure referred to as atmospheric pressure (Table 21.3).

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Table 21.3 Partial Pressures of Atmospheric Gases

Gas	Percent of total composition	Partial pressure (mm Hg)
Nitrogen (N_2)	78.60	597.4
Oxygen (O_2)	20.90	158.8
Water (H_2O)	0.40	3.0
Carbon dioxide (CO_2)	0.04	0.3
Others	0.06	0.5
Total composition / total atmospheric pressure	100.00	760.0

Partial pressure (P_x) is the pressure of a single type of gas in a mixture of gases.

For example, in the atmosphere, oxygen exerts a partial pressure, and nitrogen exerts another partial pressure independent of the partial pressure of oxygen (Figure 21.17). **Total pressure** is the sum of all the partial pressures of a gaseous mixture. **Dalton's law** describes the behaviour of nonreactive gases in a gaseous mixture and states that a specific gas type in a mixture exerts its own pressure; thus, the total pressure exerted by a mixture of gases is the sum of the partial pressures of the gases in the mixture.

Partial pressure is extremely important in predicting the movement of gases. Recall that gases tend to equalize their pressure in two connected regions. A gas will move from an area where its partial pressure is higher to an area where its partial pressure is lower. In addition, the greater the partial pressure difference between the two areas, the more rapid the movement of gases.

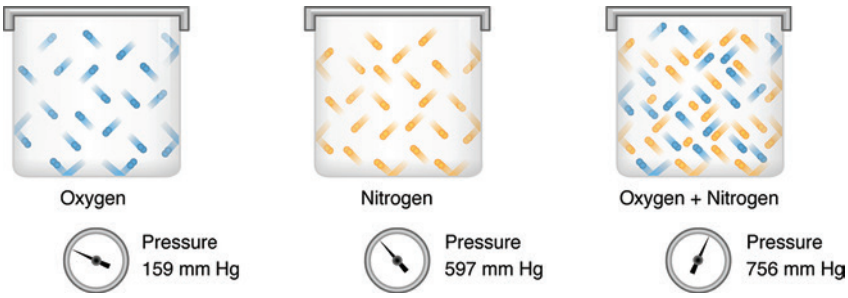


Figure 21.17 Partial and Total Pressures of a Gas. Partial pressure is the force exerted by a gas. The sum of the partial pressures of all the gases in a mixture equals the total pressure.

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Solubility of Gases in Liquids

Henry's law describes the behaviour of gases when they come into contact with a liquid, such as blood. Henry's law states that the concentration of gas in a liquid is directly proportional to the solubility and partial pressure of that gas. The greater the partial pressure of the gas, the greater the number of gas molecules that will dissolve in the liquid. The concentration of the gas in a liquid is also dependent on the solubility of the gas in the liquid.

For example, although nitrogen is present in the atmosphere, very little nitrogen dissolves into the blood, because the solubility of nitrogen in blood is very low. The exception to this occurs in scuba divers; the composition of the compressed air that divers breathe causes nitrogen to have a higher partial pressure than normal, causing it to dissolve in the blood in greater amounts than normal. Too much nitrogen in the bloodstream results in a serious condition that can be fatal if not corrected. Gas molecules establish an equilibrium between those molecules dissolved in liquid and those in air.

The composition of air in the atmosphere and in the alveoli differs. In both cases, the relative concentration of gases is nitrogen > oxygen > water vapor > carbon dioxide. The amount of water vapor present in alveolar air is greater than that in atmospheric air (Table 21.4). Recall that the respiratory system works to humidify incoming air, thereby causing the air present in the alveoli to have a greater amount of water vapor than atmospheric air. In addition, alveolar air contains a greater amount of carbon dioxide and less oxygen than atmospheric air. This is no surprise, as gas exchange removes oxygen from and adds carbon dioxide to alveolar air. Both deep and forced breathing cause the alveolar air composition to be changed more rapidly than during quiet breathing. As a result, the partial pressures of oxygen and carbon dioxide change, affecting the diffusion process that moves these materials across the membrane. This will cause oxygen to enter and carbon dioxide to leave the blood more quickly.

Table 21.4 Composition and Partial Pressures of Alveolar Air

Gas	Percent of total composition	Partial pressure (mm Hg)
Nitrogen (N_2)	74.9	569.0
Oxygen (O_2)	13.7	104.0
Water (H_2O)	6.2	40.0
Carbon dioxide (CO_2)	5.2	47.0
Total composition / total alveolar pressure	100.0	760.0

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Ventilation and Perfusion

Two important aspects of gas exchange in the lung are ventilation and perfusion. **Ventilation** is the movement of air into and out of the lungs, and perfusion is the flow of blood in the pulmonary capillaries. For gas exchange to be efficient, the volumes involved in ventilation and perfusion should be compatible. However, factors such as regional gravity's effects on blood, blocked alveolar ducts, or disease can cause ventilation and perfusion to be imbalanced.

The partial pressure of oxygen in alveolar air is about 104 mm Hg, whereas the partial pressure of oxygenated blood in pulmonary veins is about 100 mm Hg. When ventilation is sufficient, oxygen enters the alveoli at a high rate, and the partial pressure of oxygen in the alveoli remains high. In contrast, when ventilation is insufficient, the partial pressure of oxygen in the alveoli drops. Without the large difference in partial pressure between the alveoli and the blood, oxygen does not diffuse efficiently across the respiratory membrane. The body has mechanisms that counteract this problem. In cases when ventilation is not sufficient for an alveolus, the body redirects blood flow to alveoli that are receiving sufficient ventilation. This is achieved by constricting the pulmonary arterioles that serve the dysfunctional alveolus, which redirects blood to other alveoli that have sufficient ventilation. At the same time, the pulmonary arterioles that serve alveoli receiving sufficient ventilation vasodilate, which brings in greater blood flow. Factors such as carbon dioxide, oxygen, and pH levels can all serve as stimuli for adjusting blood flow in the capillary networks associated with the alveoli.

Ventilation is regulated by the diameter of the airways, whereas perfusion is regulated by the diameter of the blood vessels. The diameter of the bronchioles is sensitive to the partial pressure of carbon dioxide in the alveoli. A greater partial pressure of carbon dioxide in the alveoli causes the bronchioles to increase their diameter, as will a decreased level of oxygen in the blood supply, allowing carbon dioxide to be exhaled from the body at a greater rate. As mentioned, a greater partial pressure of oxygen in the alveoli causes the pulmonary arterioles to dilate, increasing blood flow.

Sites of Gas Exchange

Gas exchange occurs at two sites in the body: in the lungs, where oxygen is picked up and carbon dioxide is released at the respiratory membrane, and at the tissues, where oxygen is released and carbon dioxide is picked up. External respiration is the exchange of gases with the external environment and occurs in the alveoli of the lungs. Internal respiration is the exchange of gases with the internal environment and occurs in the tissues. The actual exchange of

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gases occurs due to simple diffusion. Energy is not required to move oxygen or carbon dioxide across membranes. Instead, these gases follow pressure gradients that allow them to diffuse. The anatomy of the lung maximizes the diffusion of gases: The respiratory membrane is highly permeable to gases, the respiratory and blood capillary membranes are very thin, and there is a large surface area throughout the lungs.

External Respiration

The pulmonary artery carries deoxygenated blood into the lungs from the heart, where it branches and eventually becomes the capillary network composed of pulmonary capillaries. These pulmonary capillaries create the respiratory membrane with the alveoli. As the blood is pumped through this capillary network, gas exchange occurs.

Although a small amount of the oxygen is able to dissolve directly into plasma from the alveoli, most of the oxygen is picked up by erythrocytes (red blood cells) and binds to a protein called hemoglobin, a process described in section 21.5 Transport of Gases. Oxygenated hemoglobin is red, causing the overall appearance of bright-red oxygenated blood, which returns to the heart through the pulmonary veins. Carbon dioxide is released in the opposite direction of oxygen, from the blood to the alveoli. Some of the carbon dioxide is returned on hemoglobin but can also be dissolved in plasma or is present as a converted form, also explained in greater detail in section 21.5.

External respiration occurs as a function of partial pressure differences in oxygen and carbon dioxide between the alveoli and the blood in the pulmonary capillaries.

Although the solubility of oxygen in blood is not high, there is a drastic difference in the partial pressure of oxygen in the alveoli versus in the blood of the pulmonary capillaries. This difference is about 64 mm Hg: The partial pressure of oxygen in the alveoli is about 104 mm Hg, whereas its partial pressure in the blood of the capillary is about 40 mm Hg. This large difference in partial pressure creates a very strong pressure gradient that causes oxygen to rapidly cross the respiratory membrane from the alveoli into the blood.

The partial pressure of carbon dioxide is also different between the alveolar air and the blood of the capillary. However, the partial pressure difference is less than that of oxygen, about 5 mm Hg. The partial pressure of carbon dioxide in the blood of the capillary is about 45 mm Hg, whereas its partial pressure in the alveoli is about 40 mm Hg. However, the solubility of carbon dioxide is much greater than that of oxygen—by a factor of about 20—in both blood and alveolar fluids. As a result, the relative concentrations of oxygen and carbon dioxide that diffuse across the respiratory membrane are similar.

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Internal Respiration

Internal respiration is gas exchange that occurs at the level of body tissues (Figure 21.18). Similar to external respiration, internal respiration also occurs as simple diffusion due to a partial pressure gradient. However, the partial pressure gradients are opposite of those present at the respiratory membrane. The partial pressure of oxygen in tissues is low, about 40 mm Hg, because oxygen is continuously used for cellular respiration. In contrast, the partial pressure of oxygen in the blood is about 100 mm Hg. This creates a pressure gradient that causes oxygen to dissociate from hemoglobin, diffuse out of the blood, cross the interstitial space, and enter the tissue. Hemoglobin that has little oxygen bound to it loses much of its brightness, so blood returning to the heart is more burgundy in colour.

Considering that cellular respiration continuously produces carbon dioxide, the partial pressure of carbon dioxide is lower in the blood than it is in the tissue, causing carbon dioxide to diffuse out of the tissue, cross the interstitial fluid, and enter the blood. It is then carried back to the lungs either bound to hemoglobin, dissolved in plasma, or in a converted form. By the time blood returns to the heart, the partial pressure of oxygen has returned to about 40 mm Hg, and the partial pressure of carbon dioxide has returned to about 45 mm Hg. The blood is then pumped back to the lungs to be oxygenated once again during external respiration.

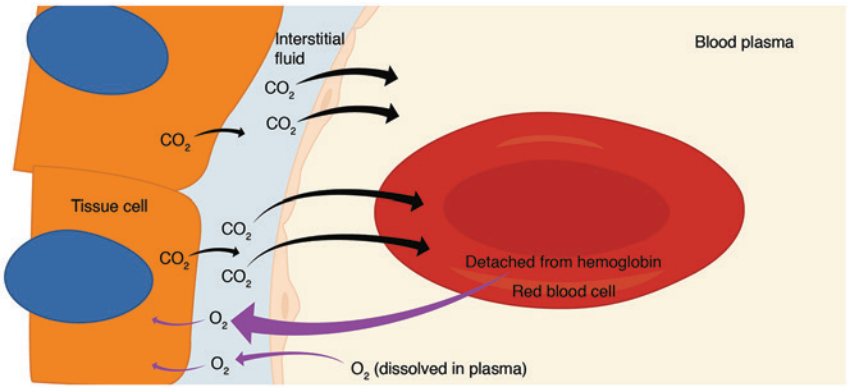


Figure 21.18 Internal Respiration. Oxygen diffuses out of the capillary and into cells, whereas carbon dioxide diffuses out of cells and into the capillary.

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21.5 Transport of Gases

Learning Objectives

By the end of this section, you will be able to:

- Describe the principles of oxygen transport
- Describe the structure of hemoglobin
- Compare and contrast fetal and adult hemoglobin
- Describe the principles of carbon dioxide transport

The other major activity in the lungs is the process of respiration, the process of gas exchange. The function of respiration is to provide oxygen for use by body cells during cellular respiration and to eliminate carbon dioxide, a waste product of cellular respiration, from the body. In order for the exchange of oxygen and carbon dioxide to occur, both gases must be transported between the external and internal respiration sites. Although carbon dioxide is more soluble than oxygen in blood, both gases require a specialized transport system for the majority of the gas molecules to be moved between the lungs and other tissues.

Oxygen Transport in the Blood

Even though oxygen is transported via the blood, you may recall that oxygen is not very soluble in liquids. A small amount of oxygen does dissolve in the blood and is transported in the bloodstream, but it is only about 1.5 percent of the total amount. The majority of oxygen molecules are carried from the lungs to the body's tissues by a specialized transport system, which relies on the erythrocyte—the red blood cell. Erythrocytes contain a metalloprotein, hemoglobin, which serves to bind oxygen molecules to the erythrocyte (Figure 21.19). Heme is the portion of hemoglobin that contains iron, and it is heme that binds oxygen. Each hemoglobin molecule contains four iron-containing heme molecules, and because of this, one hemoglobin molecule is capable of carrying up to four molecules of oxygen. As oxygen diffuses across the respiratory membrane from the alveolus to the capillary, it also diffuses into the red blood cell and is bound by hemoglobin. The following reversible chemical reaction describes the production of the final product, **oxyhemoglobin** (HbO_2), which is formed when oxygen binds to hemoglobin.

Oxyhemoglobin is a bright-red-coloured molecule that contributes to the bright-red colour of oxygenated blood.

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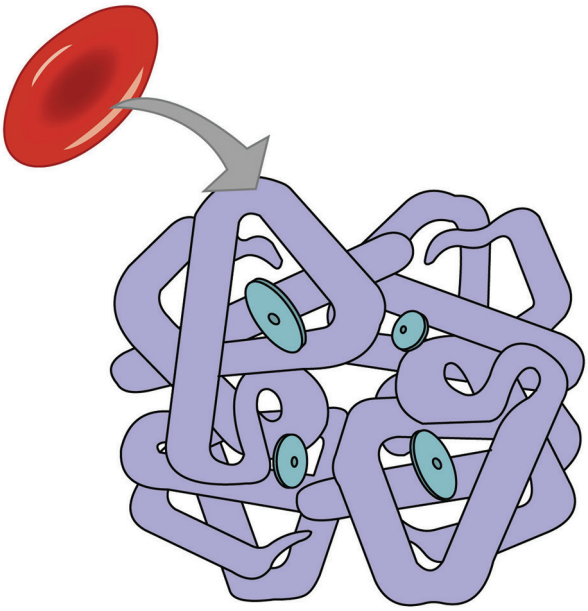


Figure 21.19 Erythrocyte and Hemoglobin. Hemoglobin consists of four subunits, each of which contains one molecule of iron.

$$Hb + O_2 \leftrightarrow HbO_2$$

In this formula, Hb represents reduced hemoglobin—that is, hemoglobin that does not have oxygen bound to it. There are multiple factors involved in how readily heme binds to and dissociates from oxygen, which will be discussed in the subsequent sections.

Function of Hemoglobin

Hemoglobin is composed of subunits, a protein structure that is referred to as a quaternary structure. Each of the four subunits that make up hemoglobin is arranged in a ring-like fashion, with an iron atom covalently bound to the heme in the centre of each subunit. Binding of the first oxygen molecule causes a conformational change in hemoglobin that allows the second molecule of oxygen to bind more readily. As each molecule of oxygen is bound, it further facilitates the binding of the next molecule, until all four heme sites are occupied by oxygen. The opposite occurs as well: After the first oxygen molecule dissociates and is "dropped off" at the tissues, the next oxygen molecule dissociates more readily. When all four heme sites are occupied, the hemoglobin is said to be saturated. When one to three heme sites are occupied, the hemoglobin is said to be partially saturated. Therefore, when considering the blood as a whole, the

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percentage of the available heme units that are bound to oxygen at a given time is called hemoglobin saturation. Hemoglobin saturation of 100 percent means that every heme unit in all of the erythrocytes of the body is bound to oxygen. In a healthy individual with normal hemoglobin levels, hemoglobin saturation generally ranges from 95 percent to 99 percent.

Oxygen Dissociation from Hemoglobin

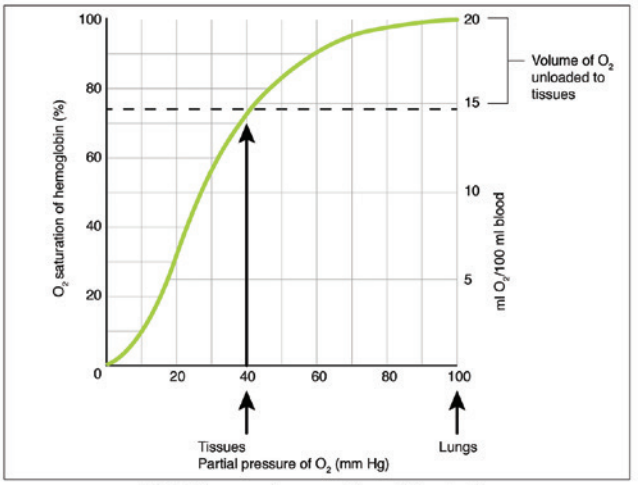
Partial pressure is an important aspect of the binding of oxygen to and dissociation from heme. An **oxygen-hemoglobin dissociation curve** is a graph that describes the relationship of partial pressure of oxygen to the binding of oxygen to heme and its subsequent dissociation from heme (Figure 21.20).

Remember that gases travel from an area of higher partial pressure to an area of lower partial pressure. In addition, the affinity of an oxygen molecule for heme increases as more oxygen molecules are bound. Therefore, in the oxygen-hemoglobin saturation curve, as the partial pressure of oxygen increases, a proportionately greater number of oxygen molecules are bound by heme. Not surprisingly, the oxygen-hemoglobin saturation/dissociation curve also shows that the lower the partial pressure of oxygen, the fewer oxygen molecules are bound to heme. As a result, the partial pressure of oxygen plays a major role in determining the degree of binding of oxygen to heme at the site of the respiratory membrane as well as the degree of dissociation of oxygen from heme at the site of body tissues (see Figure 21.20a).

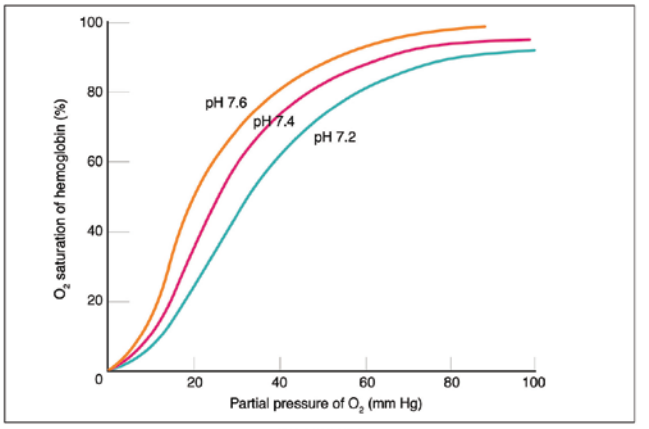
The mechanisms behind the oxygen-hemoglobin saturation/dissociation curve also serve as automatic control mechanisms that regulate how much oxygen is delivered to different tissues throughout the body. This is important because some tissues have a higher metabolic rate than others. Highly active tissues, such as muscle, rapidly use oxygen to produce ATP, lowering the partial pressure of oxygen in the tissue to about 20 mm Hg. The partial pressure of oxygen inside capillaries is about 100 mm Hg, so the difference between the two becomes quite high, about 80 mm Hg. As a result, a greater number of oxygen molecules dissociate from hemoglobin and enter the tissues. The reverse is true of tissues such as adipose (body fat), which have lower metabolic rates. Because less oxygen is used by these cells, the partial pressure of oxygen within such tissues remains relatively high, resulting in fewer oxygen molecules dissociating from hemoglobin and entering the tissue interstitial fluid. Although venous blood is said to be deoxygenated, some oxygen is still bound to hemoglobin in its red blood cells. This provides an oxygen reserve that can be used when tissues suddenly demand more oxygen.

Factors other than partial pressure also affect the oxygen-hemoglobin saturation/dissociation curve. For example, a higher temperature promotes

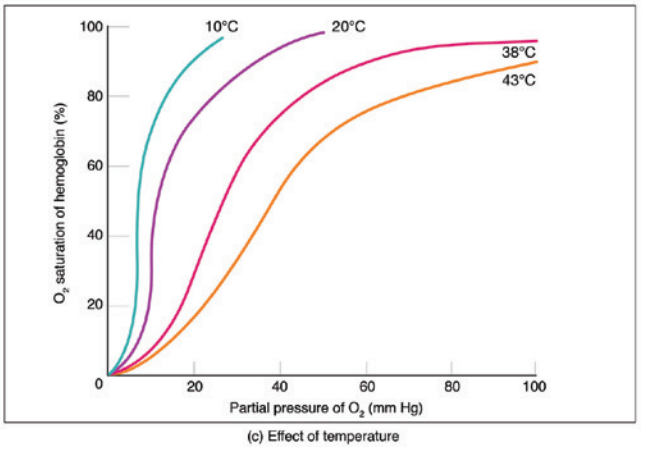
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(a) Partial pressure of oxygen and hemoglobin saturation



(b) Effect of pH



(c) Effect of temperature

Figure 21.20 Oxygen-Hemoglobin Dissociation and Effects of pH and Temperature. These three graphs show (a) the relationship between the partial pressure of oxygen and hemoglobin saturation, (b) the effect of pH on the oxygen-hemoglobin dissociation curve, and (c) the effect of temperature on the oxygen-hemoglobin dissociation curve.

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hemoglobin and oxygen to dissociate faster, whereas a lower temperature inhibits its dissociation (see Figure 21.20c). However, the human body tightly regulates temperature, so this factor may not affect gas exchange throughout the body. The exception to this is in highly active tissues, which may release a larger amount of energy than is given off as heat. As a result, oxygen readily dissociates from hemoglobin, which is a mechanism that helps provide active tissues with more oxygen.

Certain hormones, such as androgens, epinephrine, thyroid hormones, and growth hormone, can affect the oxygen-hemoglobin saturation/disassociation curve by stimulating the production of a compound called 2,3-bisphosphoglycerate (BPG) by erythrocytes. BPG is a by-product of glycolysis. Because erythrocytes do not contain mitochondria, glycolysis is the sole method by which these cells produce ATP. BPG promotes the disassociation of oxygen from hemoglobin. Therefore, the greater the concentration of BPG, the more readily oxygen dissociates from hemoglobin, despite its partial pressure.

The pH of the blood is another factor that influences the oxygen-hemoglobin saturation/dissociation curve (see Figure 21.20b). The **Bohr effect** is a phenomenon that arises from the relationship between pH and oxygen's affinity for hemoglobin: A lower, more acidic pH promotes oxygen dissociation from hemoglobin. In contrast, a higher, or more basic, pH inhibits oxygen dissociation from hemoglobin. The greater the amount of carbon dioxide in the blood, the more molecules that must be converted, which in turn generates hydrogen ions and thus lowers blood pH. Furthermore, blood pH may become more acidic when certain by-products of cell metabolism, such as lactic acid, carbonic acid, and carbon dioxide, are released into the bloodstream.

Hemoglobin of the Fetus

The fetus has its own circulation with its own erythrocytes; however, it is dependent on the pregnant person for oxygen. Blood is supplied to the fetus by way of the umbilical cord, which is connected to the placenta and separated from maternal blood by the chorion. The mechanism of gas exchange at the chorion is similar to gas exchange at the respiratory membrane. However, the partial pressure of oxygen is lower in the maternal blood in the placenta, at about 35 to 50 mm Hg, than it is in maternal arterial blood.

Carbon Dioxide Transport in the Blood

Carbon dioxide is transported by three major mechanisms. The first mechanism of carbon dioxide transport is by blood plasma, as some carbon dioxide molecules dissolve in the blood. The second mechanism is transport in the form of bicarbonate (HCO_3^-), which also dissolves in plasma. The third mechanism of carbon dioxide transport is similar to the transport of oxygen by erythrocytes (Figure 21.21).

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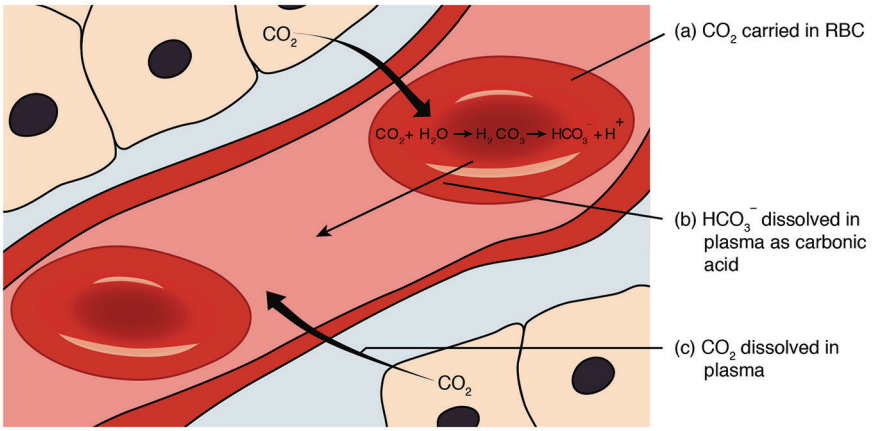


Figure 21.21 Carbon Dioxide Transport. Carbon dioxide is transported by three different methods: (a) in erythrocytes; (b) after forming carbonic acid (H_2CO_3), which is dissolved in plasma; (c) and in plasma.

Dissolved Carbon Dioxide

Although carbon dioxide is not considered to be highly soluble in blood, a small fraction—about 7 to 10 percent—of the carbon dioxide that diffuses into the blood from the tissues dissolves in plasma. The dissolved carbon dioxide then travels in the bloodstream, and when the blood reaches the pulmonary capillaries, the dissolved carbon dioxide diffuses across the respiratory membrane into the alveoli, where it is then exhaled during pulmonary ventilation.

Bicarbonate Buffer

A large fraction—about 70 percent—of the carbon dioxide molecules that diffuse into the blood is transported to the lungs as bicarbonate. Most bicarbonate is produced in erythrocytes after carbon dioxide diffuses into the capillaries and subsequently into red blood cells. **Carbonic anhydrase** (**CA**) causes carbon dioxide and water to form carbonic acid (H_2CO_3), which dissociates into two ions: bicarbonate (HCO_3–) and hydrogen (H^+). The following formula depicts this reaction:

$$CO_2 + H_2O \overset{CA}{\leftrightarrow} H_2CO_3 \leftrightarrow H^+ + HCO_{3-}$$

Bicarbonate tends to build up in the erythrocytes, so there is a greater concentration of bicarbonate in the erythrocytes than in the surrounding blood plasma. As a result, some of the bicarbonate will leave the erythrocytes and move down its concentration gradient into the plasma in exchange for chloride (Cl^-) ions. This phenomenon is referred to as the **chloride shift** and occurs

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because by exchanging one negative ion for another negative ion, neither the electrical charge of the erythrocytes nor that of the blood is altered.

At the pulmonary capillaries, the chemical reaction that produced bicarbonate (shown in the equation above) is reversed, and carbon dioxide and water are the products. Much of the bicarbonate in the plasma reenters the erythrocytes in exchange for chloride ions. Hydrogen ions and bicarbonate ions join to form carbonic acid, which is converted into carbon dioxide and water by carbonic anhydrase. Carbon dioxide diffuses out of the erythrocytes and into the plasma, where it can further diffuse across the respiratory membrane into the alveoli to be exhaled during pulmonary ventilation.

Carbaminohemoglobin

About 20 percent of carbon dioxide is bound by hemoglobin and is transported to the lungs. Carbon dioxide does not bind to iron as oxygen does; instead, carbon dioxide binds amino acid moieties on the globin portions of hemoglobin to form **carbaminohemoglobin**, which forms when hemoglobin and carbon dioxide bind. When hemoglobin is not transporting oxygen, it tends to have a bluish-purple tone to it, creating the darker maroon colour typical of deoxygenated blood. The following formula depicts this reversible reaction:

$$CO_2 + Hb \leftrightarrow HbCO_2$$

Similar to the transport of oxygen by heme, the binding and dissociation of carbon dioxide to and from hemoglobin is dependent on the partial pressure of carbon dioxide. Because carbon dioxide is released from the lungs, blood that leaves the lungs and reaches body tissues has a lower partial pressure of carbon dioxide than is found in the tissues. As a result, carbon dioxide leaves the tissues because of its higher partial pressure, enters the blood, and then moves into red blood cells, binding to hemoglobin. In contrast, in the pulmonary capillaries, the partial pressure of carbon dioxide is high compared to within the alveoli. As a result, carbon dioxide dissociates readily from hemoglobin and diffuses across the respiratory membrane into the air.

In addition to the partial pressure of carbon dioxide, the oxygen saturation of hemoglobin and the partial pressure of oxygen in the blood also influence the affinity of hemoglobin for carbon dioxide. The **Haldane effect** is a phenomenon that arises from the relationship between the partial pressure of oxygen and the affinity of hemoglobin for carbon dioxide. Hemoglobin that is saturated with oxygen does not readily bind to carbon dioxide. However, when oxygen is not bound to heme and the partial pressure of oxygen is low, hemoglobin readily binds to carbon dioxide.

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Interactive Link 21.4

Watch this video (http://oer.aupress.ca/oer-202505/21.4) to see the transport of oxygen from the lungs to the tissues. Why is oxygenated blood bright red, whereas deoxygenated blood tends to be more of a purple colour?

Key Terms

ala (plural = alae): Small, flaring structure of a nostril that forms the lateral side of the nares.

alar cartilage: Cartilage that supports the apex of the nose and helps shape the nares; it is connected to the septal cartilage and connective tissue of the alae.

alveolar dead space: Air space within alveoli that are unable to participate in gas exchange.

alveolar duct: Small tube that leads from the terminal bronchiole to the respiratory bronchiole and is the point of attachment for alveoli.

alveolar macrophage: Immune system cell of the alveolus that removes debris and pathogens.

alveolar pore: Opening that allows airflow between neighbouring alveoli.

alveolar sac: Cluster of alveoli.

alveolus: Small, grape-like sac that performs gas exchange in the lungs.

anatomical dead space: Air space present in the airway that never reaches the alveoli and therefore never participates in gas exchange.

apex: Tip of the external nose.

apneustic centre: Network of neurons within the pons that stimulate the neurons in the dorsal respiratory group; controls the depth of inspiration.

atmospheric pressure: Amount of force exerted by gases in the air surrounding any given surface.

Bohr effect: Relationship between blood pH and oxygen dissociation from hemoglobin.

Boyle's law: Relationship between volume and pressure as described by the formula $P_1V_1 = P_2V_2$.

bridge: Portion of the external nose that lies in the area of the nasal bones.

bronchial tree: Collective name for the multiple branches of the bronchi and bronchioles of the respiratory system.

bronchiole: Branch of bronchi that are 1 mm or less in diameter and terminate at alveolar sacs.

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bronchoconstriction: Decrease in the size of the bronchiole due to relaxation of the muscular wall.

bronchodilation: Increase in the size of the bronchiole due to contraction of the muscular wall.

bronchus: Tube connected to the trachea that branches into many subsidiaries and provides a passageway for air to enter and leave the lungs.

carbaminohemoglobin: Bound form of hemoglobin and carbon dioxide.

carbonic anhydrase (CA): Enzyme that catalyzes the reaction that causes carbon dioxide and water to form carbonic acid.

cardiac notch: Indentation on the surface of the left lung that allows space for the heart.

central chemoreceptor: One of the specialized receptors located in the brain that senses changes in hydrogen ion, oxygen, or carbon dioxide concentrations in the brain.

chloride shift: Facilitated diffusion that exchanges bicarbonate (HCO_3^-) with chloride (Cl^-) ions.

conducting zone: Region of the respiratory system that includes the organs and structures that provide passageways for air and are not directly involved in gas exchange.

cricoid cartilage: Portion of the larynx composed of a ring of cartilage with a wide posterior region and a thinner anterior region; attached to the esophagus.

Dalton's law: Statement of the principle that a specific gas type in a mixture exerts its own pressure as if that specific gas type was not part of a mixture of gases.

dorsal respiratory group (DRG): Region of the medulla oblongata that stimulates the contraction of the diaphragm and intercostal muscles to induce inspiration.

dorsum nasi: Intermediate portion of the external nose that connects the bridge to the apex and is supported by the nasal bone.

epiglottis: Leaf-shaped piece of elastic cartilage that is a portion of the larynx that swings to close the trachea during swallowing.

expiration (also exhalation): Process that causes the air to leave the lungs.

expiratory reserve volume (ERV): Amount of air that can be forcefully exhaled after a normal tidal exhalation.

external nose: Region of the nose that is easily visible to others.

external respiration: Gas exchange that occurs in the alveoli.

fauces: Portion of the posterior oral cavity that connects the oral cavity to the oropharynx.

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fibroelastic membrane: Specialized membrane that connects the ends of the C-shape cartilage in the trachea; contains smooth muscle fibres.

fissures: Separate the lobes of the lungs from each other.

forced breathing (also hyperpnea): Mode of breathing that occurs during exercise or by active thought that requires muscle contraction for both inspiration and expiration.

functional residual capacity (FRC): Sum of ERV and RV, which is the amount of air that remains in the lungs after a tidal expiration.

glottis: Opening between the vocal folds through which air passes when producing speech.

Haldane effect: Relationship between the partial pressure of oxygen and the affinity of hemoglobin for carbon dioxide.

Henry's law: Statement of the principle that the concentration of gas in a liquid is directly proportional to the solubility and partial pressure of that gas.

hilum: Concave structure on the mediastinal surface of the lungs where blood vessels, lymphatic vessels, nerves, and a bronchus enter the lung.

inspiration (also inhalation): Process that causes air to enter the lungs.

inspiratory capacity (IC): Sum of the TV and IRV, which is the amount of air that can maximally be inhaled past a tidal expiration.

inspiratory reserve volume (IRV): Amount of air that enters the lungs due to deep inhalation past the tidal volume.

internal respiration: Gas exchange that occurs at the level of body tissues.

intra-alveolar pressure (intrapulmonary pressure): Pressure of the air within the alveoli.

intrapleural pressure: Pressure of the air within the pleural cavity.

laryngeal prominence: Region where the two lamine of the thyroid cartilage join, forming a protrusion known as the "Adam's apple."

laryngopharynx: Portion of the pharynx bordered by the oropharynx superiorly and esophagus and trachea inferiorly; serves as a route for both air and food.

larynx: Cartilaginous structure that produces the voice, prevents food and beverages from entering the trachea, and regulates the volume of air that enters and leaves the lungs.

lingual tonsil: Lymphoid tissue located at the base of the tongue.

lobes: Smaller units of the lung.

lung: Organ of the respiratory system that performs gas exchange.

meatus: One of three recesses (superior, middle, and inferior) in the nasal cavity attached to the conchae that increases the surface area of the nasal cavity.

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naris (plural = nares): Opening of the nostrils.
nasal bone: Bone of the skull that lies under the root and bridge of the nose and is connected to the frontal and maxillary bones.
nasal cavity: Nares open into this segment of the respiratory system, which is separated into left and right sections by the nasal septum.
nasal septum: Wall composed of bone and cartilage that separates the left and right nasal cavities.
nasopharynx: Portion of the pharynx flanked by the conchae and oropharynx that serves as an airway.
oropharynx: Portion of the pharynx flanked by the nasopharynx, oral cavity, and laryngopharynx that is a passageway for both air and food.
oxygen-hemoglobin dissociation curve: Graph that describes the relationship of partial pressure to the binding and disassociation of oxygen to and from heme.
oxyhemoglobin ($Hb–O_2$): Bound form of hemoglobin and oxygen.
palatine tonsil: One of the paired structures composed of lymphoid tissue located anterior to the uvula at the roof of the isthmus of the fauces.
paranasal sinus: One of the cavities within the skull that is connected to the conchae that serves to warm and humidify incoming air, produce mucus, and lighten the weight of the skull; consists of frontal, maxillary, sphenoidal, and ethmoidal sinuses.
parietal pleura: Outermost layer of the pleura that connects to the thoracic wall, mediastinum, and diaphragm.
partial pressure: Force exerted by each gas in a mixture of gases.
peripheral chemoreceptor: One of the specialized receptors located in the aortic arch and carotid arteries that senses changes in pH, carbon dioxide, or oxygen blood levels.
pharyngeal tonsil: Structure composed of lymphoid tissue located in the nasopharynx.
pharynx: Region of the conducting zone that forms a tube of skeletal muscle lined with respiratory epithelium; located between the nasal conchae and the esophagus and trachea.
philtrum: Concave surface of the face that connects the apex of the nose to the top lip.
pleural cavity: Space between the visceral and parietal pleurae.
pleural fluid: Substance that acts as a lubricant for the visceral and parietal layers of the pleura during the movement of breathing.
pneumotaxic centre: Network of neurons within the pons that inhibits the activity of the neurons in the dorsal respiratory group; controls rate of breathing.

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primary bronchi: Bronchi that enter the lungs at the hilum.
pulmonary artery: Artery that arises from the pulmonary trunk and carries deoxygenated, arterial blood to the alveoli.
pulmonary surfactant: Substance composed of phospholipids and proteins that reduces the surface tension of the alveoli; made by type II alveolar cells.
pulmonary ventilation: Exchange of gases between the lungs and the atmosphere; breathing.
quiet breathing (also eupnea): Mode of breathing that occurs at rest and does not require the cognitive thought of the individual.
residual volume (RV): Amount of air that remains in the lungs after maximum exhalation.
respiratory bronchiole: Specific type of bronchiole that leads to alveolar sacs.
respiratory cycle: One sequence of inspiration and expiration.
respiratory epithelium: Ciliated lining of much of the conducting zone that is specialized to remove debris and pathogens and produce mucus.
respiratory membrane: Alveolar and capillary wall together, which form an air-blood barrier that facilitates the simple diffusion of gases.
respiratory rate: Total number of breaths taken each minute.
respiratory volume: Varying amounts of air within the lung at a given time.
respiratory zone: Includes structures of the respiratory system that are directly involved in gas exchange.
root: Region of the external nose between the eyebrows.
terminal bronchioles: Smallest airways that lead to the structures of gas exchange.
thoracic wall compliance: Ability of the thoracic wall to stretch while under pressure.
thyroid cartilage: Largest piece of cartilage that makes up the larynx and consists of two lamine.
tidal volume (TV): Amount of air that normally enters the lungs during quiet breathing.
total dead space: Sum of the anatomical dead space and alveolar dead space.
total lung capacity (TLC): Total amount of air that can be held in the lungs; sum of TV, ERV, IRV, and RV.
total pressure: Sum of all the partial pressures of a gaseous mixture.
trachea: Tube composed of cartilaginous rings and supporting tissue that connects the lung bronchi and the larynx; provides a route for air to enter and exit the lung.
trachealis muscle: Smooth muscle located in the fibroelastic membrane of the trachea.

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transpulmonary pressure: Pressure difference between the intrapleural and intra-alveolar pressures.
true vocal cord: One of the pair of folded, white membranes that have a free inner edge that oscillates as air passes through to produce sound.
type I alveolar cell: Squamous epithelial cells that are the major cell type in the alveolar wall; highly permeable to gases.
type II alveolar cell: Cuboidal epithelial cells that are the minor cell type in the alveolar wall; secrete pulmonary surfactant.
ventilation: Movement of air into and out of the lungs; consists of inspiration and expiration.
ventral respiratory group (VRG): Region of the medulla oblongata that stimulates the contraction of the accessory muscles involved in respiration to induce forced inspiration and expiration.
vestibular fold: Part of the folded region of the glottis composed of mucous membrane; supports the epiglottis during swallowing.
visceral pleura: Innermost layer of the pleura that is superficial to the lungs and extends into the lung fissures.
vital capacity (VC): Sum of TV, ERV, and IRV, which is all the volumes that participate in gas exchange.

Chapter Review

21.1 Organs and Structures of the Respiratory System

The respiratory system is responsible for obtaining oxygen and getting rid of carbon dioxide and aiding in speech production and in sensing odours. From a functional perspective, the respiratory system can be divided into two major areas: the conducting zone and the respiratory zone. The conducting zone consists of all of the structures that provide passageways for air to travel into and out of the lungs: the nasal cavity, pharynx, trachea, bronchi, and most bronchioles. The nasal passages contain the conchae and meatuses that expand the surface area of the cavity, which helps warm and humidify incoming air while removing debris and pathogens. The pharynx is composed of three major sections: the nasopharynx, which is continuous with the nasal cavity; the oropharynx, which borders the nasopharynx and the oral cavity; and the laryngopharynx, which borders the oropharynx, trachea, and esophagus. The respiratory zone includes the structures of the lung that are directly involved in gas exchange: the terminal bronchioles and alveoli.

The lining of the conducting zone is composed mostly of pseudostratified ciliated columnar epithelium with goblet cells. The mucus traps pathogens and debris, whereas beating cilia move the mucus superiorly toward the throat,

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where it is swallowed. As the bronchioles become smaller and smaller and nearer the alveoli, the epithelium thins and is simple squamous epithelium in the alveoli. The endothelium of the surrounding capillaries, together with the alveolar epithelium, forms the respiratory membrane. This is a blood-air barrier through which gas exchange occurs by simple diffusion.

21.2 The Lungs

The lungs are the major organs of the respiratory system and are responsible for performing gas exchange. The lungs are paired and separated into lobes; the left lung consists of two lobes, whereas the right lung consists of three lobes. Blood circulation is very important, as blood is required to transport oxygen from the lungs to other tissues throughout the body. The function of the pulmonary circulation is to aid in gas exchange. The pulmonary artery provides deoxygenated blood to the capillaries that form respiratory membranes with the alveoli, and the pulmonary veins return newly oxygenated blood to the heart for further transport throughout the body. The lungs are innervated by the parasympathetic and sympathetic nervous systems, which coordinate the bronchodilation and bronchoconstriction of the airways. The lungs are enclosed by the pleura, a membrane that is composed of visceral and parietal pleural layers. The space between these two layers is called the pleural cavity. The mesothelial cells of the pleural membrane create pleural fluid, which serves as both a lubricant (to reduce friction during breathing) and an adhesive to adhere the lungs to the thoracic wall (to facilitate movement of the lungs during ventilation).

21.3 The Process of Breathing

Pulmonary ventilation is the process of breathing, which is driven by pressure differences between the lungs and the atmosphere. Atmospheric pressure is the force exerted by gases present in the atmosphere. The force exerted by gases within the alveoli is called intra-alveolar (intrapulmonary) pressure, whereas the force exerted by gases in the pleural cavity is called intrapleural pressure. Typically, intrapleural pressure is lower, or negative to, intra-alveolar pressure. The difference in pressure between intrapleural and intra-alveolar pressures is called transpulmonary pressure. In addition, intra-alveolar pressure will equalize with the atmospheric pressure. Pressure is determined by the volume of the space occupied by a gas and is influenced by resistance. Air flows when a pressure gradient is created, from a space of higher pressure to a space of lower pressure. Boyle's law describes the relationship between volume and pressure. A gas is at lower pressure in a larger volume because the gas molecules have more space in which to move. The same quantity of gas in a smaller volume results in gas molecules crowding together, producing increased pressure.

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Resistance is created by inelastic surfaces as well as the diameter of the airways. Resistance reduces the flow of gases. The surface tension of the alveoli also influences pressure, as it opposes the expansion of the alveoli. However, pulmonary surfactant helps reduce the surface tension so that the alveoli do not collapse during expiration. The ability of the lungs to stretch, called lung compliance, also plays a role in gas flow.

The more the lungs can stretch, the greater the potential volume of the lungs. The greater the volume of the lungs, the lower the air pressure within the lungs.

Pulmonary ventilation consists of the process of inspiration (or inhalation), where air enters the lungs, and expiration (or exhalation), where air leaves the lungs. During inspiration, the diaphragm and external intercostal muscles contract, causing the rib cage to expand and move outward, and expanding the thoracic cavity and lung volume. This creates a lower pressure within the lung than that of the atmosphere, causing air to be drawn into the lungs. During expiration, the diaphragm and intercostals relax, causing the thorax and lungs to recoil. The air pressure within the lungs increases to above the pressure of the atmosphere, causing air to be forced out of the lungs. However, during forced exhalation, the internal intercostals and abdominal muscles may be involved in forcing air out of the lungs.

Respiratory volume describes the amount of air in a given space within the lungs or that can be moved by the lung and is dependent on a variety of factors. Tidal volume refers to the amount of air that enters the lungs during quiet breathing, whereas inspiratory reserve volume is the amount of air that enters the lungs when a person inhales past the tidal volume. Expiratory reserve volume is the extra amount of air that can leave with forceful expiration following tidal expiration.

Residual volume is the amount of air that is left in the lungs after expelling the expiratory reserve volume. Respiratory capacity is the combination of two or more volumes. Anatomical dead space refers to the air within the respiratory structures that never participates in gas exchange, because it does not reach functional alveoli. Respiratory rate is the number of breaths taken per minute, which may change during certain diseases or conditions.

Both respiratory rate and depth are controlled by the respiratory centres of the brain, which are stimulated by factors such as chemical and pH changes in the blood. These changes are sensed by central chemoreceptors, which are located in the brain, and peripheral chemoreceptors, which are located in the aortic arch and carotid arteries. A rise in carbon dioxide or a decline in oxygen levels in the blood stimulates an increase in respiratory rate and depth.

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21.4 Gas Exchange

The behaviour of gases can be explained by the principles of Dalton's law and Henry's law, both of which describe aspects of gas exchange. Dalton's law states that each specific gas in a mixture of gases exerts force (its partial pressure) independently of the other gases in the mixture. Henry's law states that the amount of a specific gas that dissolves in a liquid is a function of its partial pressure. The greater the partial pressure of a gas, the more of that gas will dissolve in a liquid as the gas moves toward equilibrium. Gas molecules move down a pressure gradient; in other words, gas moves from a region of high pressure to a region of low pressure. The partial pressure of oxygen is high in the alveoli and low in the blood of the pulmonary capillaries. As a result, oxygen diffuses across the respiratory membrane from the alveoli into the blood. In contrast, the partial pressure of carbon dioxide is high in the pulmonary capillaries and low in the alveoli. Therefore, carbon dioxide diffuses across the respiratory membrane from the blood into the alveoli. The amount of oxygen and carbon dioxide that diffuses across the respiratory membrane is similar.

Ventilation is the process that moves air into and out of the alveoli, and perfusion affects the flow of blood in the capillaries. Both are important in gas exchange, as ventilation must be sufficient to create a high partial pressure of oxygen in the alveoli. If ventilation is insufficient and the partial pressure of oxygen drops in the alveolar air, the capillary is constricted, and blood flow is redirected to alveoli with sufficient ventilation. External respiration refers to gas exchange that occurs in the alveoli, whereas internal respiration refers to gas exchange that occurs in the tissue. Both are driven by partial pressure differences.

21.5 Transport of Gases

Oxygen is primarily transported through the blood by erythrocytes. These cells contain a metalloprotein called hemoglobin, which is composed of four subunits with a ring-like structure. Each subunit contains one atom of iron bound to a molecule of heme. Heme binds oxygen so that each hemoglobin molecule can bind up to four oxygen molecules. When all of the heme units in the blood are bound to oxygen, hemoglobin is considered to be saturated. Hemoglobin is partially saturated when only some heme units are bound to oxygen. An oxygen-hemoglobin saturation/dissociation curve is a common way to depict the relationship of how easily oxygen binds to or dissociates from hemoglobin as a function of the partial pressure of oxygen. As the partial pressure of oxygen increases, hemoglobin more readily binds to oxygen. At the same time, once one molecule of oxygen is bound by hemoglobin, additional oxygen molecules more

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readily bind to hemoglobin. Other factors such as temperature, pH, the partial pressure of carbon dioxide, and the concentration of 2,3-bisphosphoglycerate can enhance or inhibit the binding of hemoglobin and oxygen as well. Fetal hemoglobin has a different structure than adult hemoglobin, which results in fetal hemoglobin having a greater affinity for oxygen than adult hemoglobin.

Carbon dioxide is transported in blood by three different mechanisms: as dissolved carbon dioxide, as bicarbonate, or as carbaminohemoglobin. A small portion of carbon dioxide remains. The largest amount of transported carbon dioxide is as bicarbonate, formed in erythrocytes. For this conversion, carbon dioxide is combined with water with the aid of an enzyme called carbonic anhydrase. This combination forms carbonic acid, which spontaneously dissociates into bicarbonate and hydrogen ions. As bicarbonate builds up in erythrocytes, it is moved across the membrane into the plasma in exchange for chloride ions by a mechanism called the chloride shift. At the pulmonary capillaries, bicarbonate reenters erythrocytes in exchange for chloride ions, and the reaction with carbonic anhydrase is reversed, re-creating carbon dioxide and water. Carbon dioxide then diffuses out of the erythrocyte and across the respiratory membrane into the air. An intermediate amount of carbon dioxide binds directly to hemoglobin to form carbaminohemoglobin. The partial pressures of carbon dioxide and oxygen, as well as the oxygen saturation of hemoglobin, influence how readily hemoglobin binds to carbon dioxide. The less saturated hemoglobin is and the lower the partial pressure of oxygen in the blood is, the more readily hemoglobin binds to carbon dioxide. This is an example of the Haldane effect.

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22

The Digestive System

Chapter Objectives

After studying this chapter, you will be able to:

- List and describe the functional anatomy of the organs and accessory organs of the digestive system
- Discuss the processes and control of ingestion, propulsion, mechanical digestion, chemical digestion, absorption, and defecation
- Discuss the roles of the liver, pancreas, and gallbladder in digestion
- Compare and contrast the digestion of the three macronutrients

The digestive system is continually at work, yet people seldom appreciate the complex tasks it performs in a choreographed biologic symphony. Consider what happens when you eat an apple. Of course, you enjoy the apple's taste as you chew it, but in the hours that follow, unless something goes amiss and you get a stomachache, you don't notice that your digestive system is working. You may be taking a walk or studying or sleeping, having forgotten all about the apple, but your stomach and intestines are busy digesting it and absorbing its vitamins and other nutrients. By the time any waste material is excreted, the body has appropriated all it can use from the apple. In short, whether you pay attention or not, the organs of the digestive system perform their specific functions, allowing you to use the food you eat to keep you going. This chapter examines the structure and functions of these organs and explores the mechanics and chemistry of the digestive processes.

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22.1 Overview of the Digestive System

Learning Objectives

By the end of this section, you will be able to:

- Identify the organs of the alimentary canal from proximal to distal, and briefly state their function
- Identify the accessory digestive organs and briefly state their function
- Describe the four fundamental tissue layers of the alimentary canal
- Contrast the contributions of the enteric and autonomic nervous systems to digestive system functioning
- Explain how the peritoneum anchors the digestive organs

The function of the digestive system is to break down the foods you eat, release their nutrients, and absorb those nutrients into the body. Although the small intestine is the workhorse of the system, where the majority of digestion occurs and where most of the released nutrients are absorbed into the blood or lymph, each of the digestive system organs makes a vital contribution to this process (Figure 22.1).

As is the case with all body systems, the digestive system does not work in isolation; it functions cooperatively with the other systems of the body. Consider, for example, the interrelationship between the digestive and cardiovascular systems. Arteries supply the digestive organs with oxygen and processed nutrients, and veins drain the digestive tract. These intestinal veins, constituting the hepatic portal system, are unique; they do not return blood directly to the heart. Rather, this blood is diverted to the liver, where its nutrients are off-loaded for processing before blood completes its circuit back to the heart. At the same time, the digestive system provides nutrients to the heart muscle and vascular tissue to support their functioning. The interrelationship of the digestive and endocrine systems is also critical. Hormones secreted by several endocrine glands, as well as endocrine cells of the pancreas, the stomach, and the small intestine, contribute to the control of digestion and nutrient metabolism. In turn, the digestive system provides the nutrients to fuel endocrine function.

Table 22.1 gives a quick glimpse at how these other systems contribute to the functioning of the digestive system.

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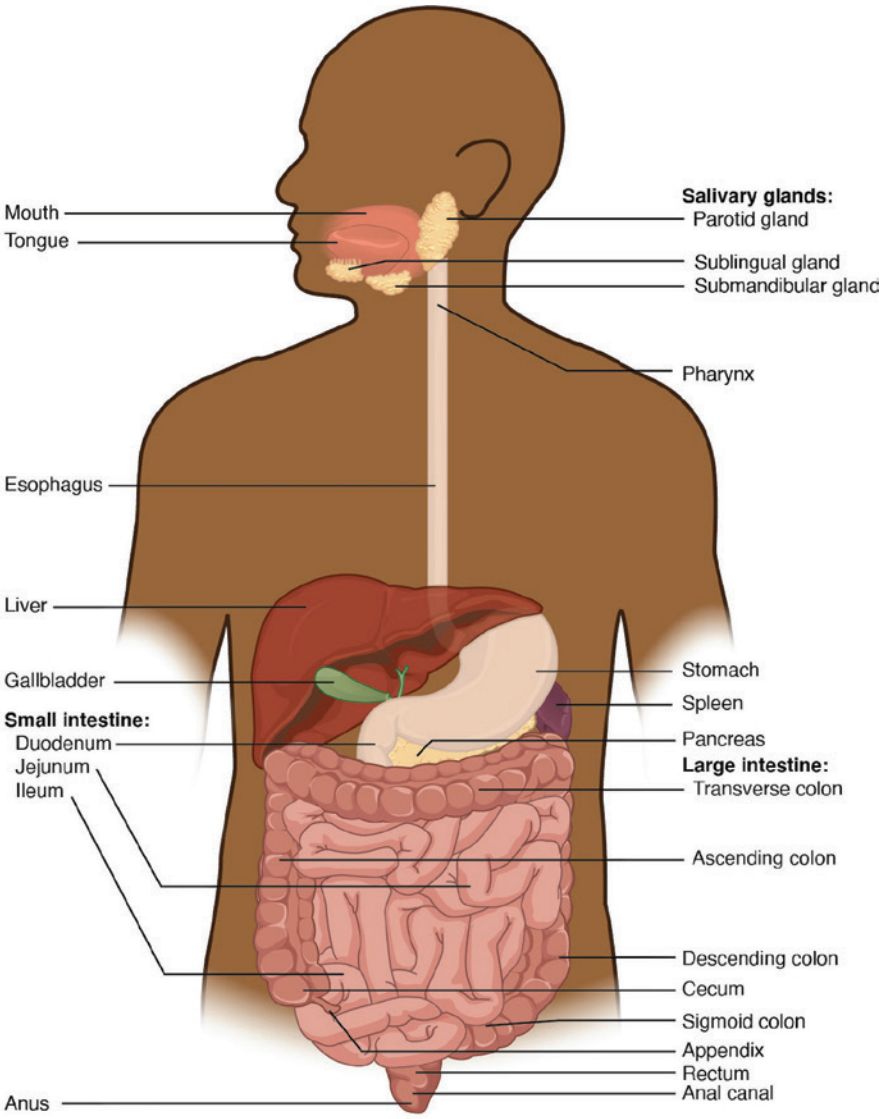


Figure 22.1 Components of the Digestive System. All digestive organs play integral roles in the life-sustaining process of digestion.

Digestive System Organs

The easiest way to understand the digestive system is to divide its organs into two main categories. The first group is the organs that make up the alimentary canal. Accessory digestive organs compose the second group and are critical for orchestrating the breakdown of food and the assimilation of its nutrients into the body. Accessory digestive organs, despite their name, are critical to the function of the digestive system.

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Table 22.1 Contribution of Other Body Systems to the Digestive System

Body system	Benefits received by the digestive system
Cardiovascular	Blood supplies digestive organs with oxygen and processed nutrients
Endocrine	Endocrine hormones help regulate secretion in digestive glands and accessory organs
Integumentary	Skin helps protect digestive organs and synthesizes vitamin D for calcium absorption
Lymphatic	Mucosa-associated lymphoid tissue and other lymphatic tissue defend against entry of pathogens; lacteals absorb lipids; lymphatic vessels transport lipids to bloodstream
Muscular	Skeletal muscles support and protect abdominal organs
Nervous	Sensory and motor neurons help regulate secretions and muscle contractions in the digestive tract
Respiratory	Respiratory organs provide oxygen and remove carbon dioxide
Skeletal	Bones help protect and support digestive organs
Urinary	Kidneys convert vitamin D into its active form, allowing calcium absorption in the small intestine

Alimentary Canal Organs

Also called the gastrointestinal (GI) tract or gut, the **alimentary canal** is a one-way tube about 7.62 m in length during life and closer to 10.67 m in length when measured after death, once smooth muscle tone is lost. The main function of the organs of the alimentary canal is to nourish the body. This tube begins at the mouth and terminates at the anus. Between those two points, the canal is modified as the pharynx, esophagus, stomach, and small and large intestines to fit the functional needs of the body. Both the mouth and the anus are open to the external environment; thus, food and waste within the alimentary canal are technically considered to be outside the body. Only through the process of absorption do the nutrients in food enter into and nourish the body's "inner space."

Accessory Structures

Each **accessory digestive organ** aids in the breakdown of food (Figure 22.2). Within the mouth, the teeth and tongue begin mechanical digestion, whereas the salivary glands begin chemical digestion. Once food products enter the small

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intestine, the gallbladder, liver, and pancreas release secretions—such as bile and enzymes—essential for digestion to continue. Together, these are called accessory organs because they sprout from the lining cells of the developing gut (mucosa) and augment its function; indeed, you could not live without their vital contributions, and many significant diseases result from their malfunction. Even after development is complete, they maintain a connection to the gut by way of ducts.

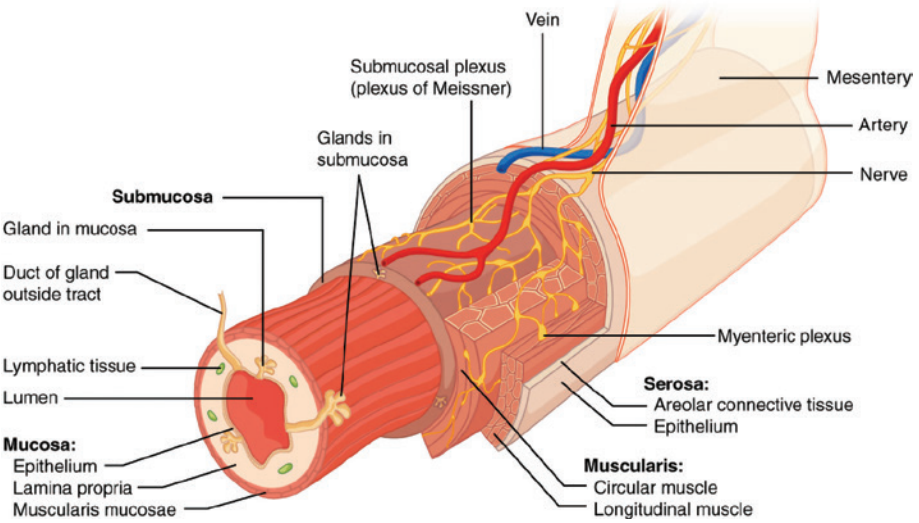


Figure 22.2 Layers of the Alimentary Canal. The wall of the alimentary canal has four basic tissue layers: the mucosa, submucosa, muscularis, and serosa.

Histology of the Alimentary Canal

Throughout its length, the alimentary tract is composed of the same four tissue layers; the details of their structural arrangements vary to fit their specific functions. Starting from the **lumen** (the central space that food travels through) and moving outward, these layers are the mucosa, submucosa, muscularis, and serosa, which is continuous with the mesentery (see Figure 22.2).

The **mucosa** (**mucous membrane**) is so named because **mucus** production is a characteristic feature of gut epithelium. The membrane consists of epithelium, which is in direct contact with ingested food, and the lamina propria, a layer of connective tissue analogous to the dermis. In addition, the mucosa has a thin, smooth muscle layer called the muscularis mucosae (not to be confused with the muscularis layer, described below).

Epithelium—In the mouth, pharynx, esophagus, and anal canal, the epithelium is primarily a nonkeratinized, stratified squamous epithelium. In the stomach and intestines, it is a simple columnar epithelium. Notice that the epithelium

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is in direct contact with the lumen, the space inside the alimentary canal. Interspersed among its epithelial cells are goblet cells, which secrete mucus and fluid into the lumen, and enteroendocrine cells, which secrete hormones into the interstitial spaces between cells. Epithelial cells have a very brief lifespan, averaging from only a couple of days (in the mouth) to about a week (in the gut). This process of rapid renewal helps preserve the health of the alimentary canal, despite the wear and tear resulting from continued contact with foodstuffs.

Lamina propria—In addition to loose connective tissue, the lamina propria contains numerous blood and lymphatic vessels that transport nutrients absorbed through the alimentary canal to other parts of the body. The lamina propria also serves an immune function by housing clusters of lymphocytes, making up the mucosa-associated lymphoid tissue (MALT). These lymphocyte clusters are particularly substantial in the distal ileum, where they are known as Peyer's patches. When you consider that the alimentary canal is exposed to foodborne bacteria and other foreign matter, it is not hard to appreciate why the immune system has evolved a means of defending against the pathogens encountered within it.

Muscularis mucosae—This thin layer of smooth muscle is in a constant state of tension, pulling the mucosa of the stomach and small intestine into undulating folds. These folds dramatically increase the surface area available for digestion and absorption.

As its name implies, the **submucosa** lies immediately beneath the mucosa. A broad layer of dense connective tissue, it connects the overlying mucosa to the underlying muscularis. It includes blood and lymphatic vessels (which transport absorbed nutrients) and a scattering of submucosal glands that release digestive secretions. Additionally, it serves as a conduit for a dense branching network of nerves, the submucosal plexus, which functions as described in the Nerve Supply section.

The third layer of the alimentary canal is the **muscularis** (also called the muscularis externa). The muscularis in the small intestine is made up of a double layer of smooth muscle: an inner circular layer and an outer longitudinal layer. The contractions of these layers promote mechanical digestion, expose more of the food to digestive chemicals, and move the food along the canal. In the most proximal and distal regions of the alimentary canal, including the mouth, pharynx, anterior part of the esophagus, and external anal sphincter, the muscularis is made up of skeletal muscle, which gives you voluntary control over swallowing and defecation. The basic two-layer structure found in the small intestine is modified in the organs proximal and distal to it. The stomach is equipped for its churning function by the addition of a third layer, the oblique

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muscle. While the colon has two layers like the small intestine, its longitudinal layer is segregated into three narrow parallel bands, the teniae coli, that make it look like a series of pouches rather than a simple tube.

The **serosa** is the portion of the alimentary canal superficial to the muscularis. Present only in the region of the alimentary canal within the abdominal cavity, it consists of a layer of visceral peritoneum overlying a layer of loose connective tissue. Instead of serosa, the mouth, pharynx, and esophagus have a dense sheath of collagen fibres called the adventitia. These tissues serve to hold the alimentary canal in place near the ventral surface of the vertebral column.

Nerve Supply

As soon as food enters the mouth, it is detected by receptors that send impulses along the sensory neurons of cranial nerves. Without these nerves, not only would your food be without taste, but you would also be unable to feel either the food or the structures of your mouth, and you would be unable to avoid biting yourself as you chew, an action enabled by the motor branches of cranial nerves.

Intrinsic innervation of much of the alimentary canal is provided by the enteric nervous system, which runs from the esophagus to the anus and contains approximately 100 million motor, sensory, and interneurons (unique to this system compared to all other parts of the peripheral nervous system). These enteric neurons are grouped into two plexuses. The **myenteric plexus** (plexus of Auerbach) lies in the muscularis layer of the alimentary canal and is responsible for **motility**, especially the rhythm and force of the contractions of the muscularis. The **submucosal plexus** (plexus of Meissner) lies in the submucosal layer and is responsible for regulating digestive secretions and reacting to the presence of food (see Figure 22.2).

Extrinsic innervations of the alimentary canal are provided by the autonomic nervous system, which includes both sympathetic and parasympathetic nerves. In general, sympathetic activation (the fight-or-flight response) restricts the activity of enteric neurons, thereby decreasing GI secretion and motility. In contrast, parasympathetic activation (the rest-and-digest response) increases GI secretion and motility by stimulating neurons of the enteric nervous system.

Blood Supply

The blood vessels serving the digestive system have two functions. They transport the protein and carbohydrate nutrients absorbed by mucosal cells after food is digested in the lumen. Lipids are absorbed via lacteals, tiny structures of the lymphatic system. The blood vessels' second function is to supply the organs of the alimentary canal with the nutrients and oxygen needed to drive their cellular processes.

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Specifically, the more anterior parts of the alimentary canal are supplied with blood by arteries branching off the aortic arch and thoracic aorta. Below this point, the alimentary canal is supplied with blood by arteries branching from the abdominal aorta. The celiac trunk services the liver, stomach, and duodenum, whereas the superior and inferior mesenteric arteries supply blood to the remaining small and large intestines.

The veins that collect nutrient-rich blood from the small intestine (where most absorption occurs) empty into the hepatic portal system. This venous network takes the blood into the liver, where the nutrients are either processed or stored for later use. Only then does the blood drained from the alimentary canal viscera circulate back to the heart. To appreciate just how demanding the digestive process is on the cardiovascular system, consider that while you are "resting and digesting," about one-fourth of the blood pumped with each heartbeat enters arteries serving the intestines.

The Peritoneum

The digestive organs within the abdominal cavity are held in place by the **peritoneum**, a broad serous membranous sac made up of squamous epithelial tissue surrounded by connective tissue. It is composed of two different regions: the **parietal peritoneum**, which lines the abdominal wall, and the **visceral peritoneum**, which envelopes the abdominal organs (Figure 22.3).

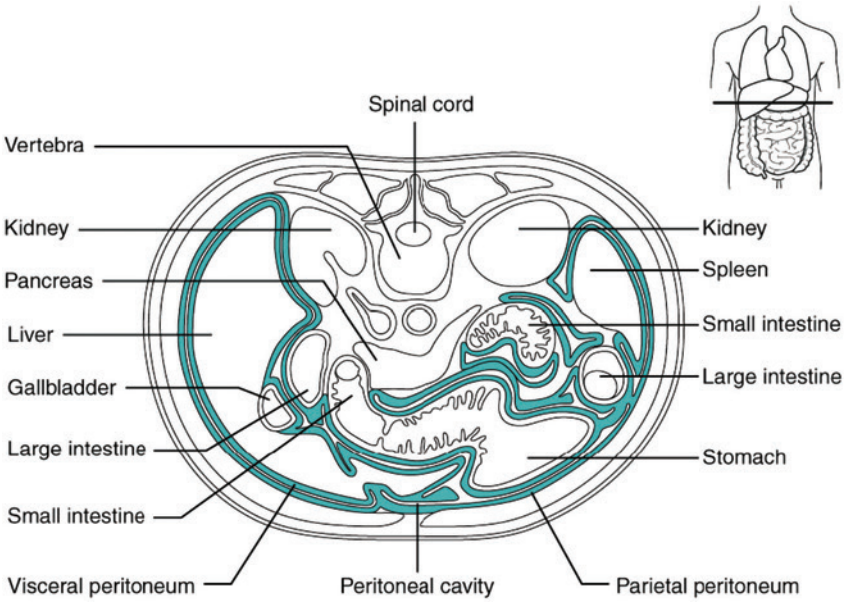


Figure 22.3 The Peritoneum. A cross section of the abdomen shows the relationship between abdominal organs and the peritoneum (darker lines).

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The **peritoneal cavity** is the space bounded by the visceral and parietal peritoneal surfaces. A few millilitres of watery fluid act as a lubricant to minimize friction between the serosal surfaces of the peritoneum.

The visceral peritoneum includes multiple large folds that envelop various abdominal organs, holding them to the dorsal surface of the body wall. Within these folds are blood vessels, lymphatic vessels, and nerves that innervate the organs with which they are in contact, supplying their adjacent organs. The five major **peritoneal folds** are the greater omentum, falciform ligament, lesser omentum, mesentery, and mesocolon. See details in Table 22.2. Note that during fetal development, certain digestive structures, including the first portion of the small intestine (called the duodenum), the pancreas, and portions of the large intestine (the ascending and descending colon and the rectum), remain completely or partially posterior to the peritoneum. Thus, the location of these organs is described as **retroperitoneal**.

Interactive Link 22.1

By clicking on this link (http://oer.aupress.ca/oer-202505/22.1), you can watch a short video of what happens to the food you eat as it passes from your mouth to your intestine. Along the way, note how the food changes consistency and form. How does this change in consistency facilitate your gaining nutrients from food?

Table 22.2 The Five Major Peritoneal Folds

Fold	Description
Greater omentum	Apron-like structure that lies superficial to the small intestine and transverse colon; a site of fat deposition in people who are overweight
Falciform ligament	Anchors the liver to the anterior abdominal wall and inferior border of the diaphragm
Lesser omentum	Suspends the stomach from the inferior border of the liver; provides a pathway for structures connecting to the liver
Mesentery	Vertical band of tissue anterior to the lumbar vertebrae and anchoring all of the small intestine except the initial portion (the duodenum)
Mesocolon	Attaches two portions of the large intestine (the transverse and sigmoid colon) to the posterior abdominal wall

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22.2 Digestive System Processes and Regulation

Learning Objectives

By the end of this section, you will be able to:

- Discuss six fundamental activities of the digestive system, giving an example of each
- Compare and contrast the neural and hormonal controls involved in digestion

The digestive system uses mechanical and chemical activities to break food down into absorbable substances during its journey through the digestive system. Table 22.3 provides an overview of the basic functions of the digestive organs.

Interactive Link 22.2

Visit this site (http://oer.aupress.ca/oer-202505/22.2) for an overview of digestion of food in different regions of the digestive tract. Note the route of nonfat nutrients from the small intestine to their release as nutrients to the body.

Digestive Processes

The processes of digestion include six activities: ingestion, propulsion, mechanical or physical digestion, chemical digestion, absorption, and defecation.

The first of these processes, **ingestion**, refers to the entry of food into the alimentary canal through the mouth. There, the food is chewed and mixed with saliva, which contains enzymes that begin breaking down the carbohydrates in the food plus some lipid digestion via lingual lipase. Chewing increases the surface area of the food and allows an appropriately sized bolus to be produced.

Food leaves the mouth when the tongue and pharyngeal muscles propel it into the esophagus. This act of swallowing, the last voluntary act until defecation, is an example of **propulsion**, which refers to the movement of food through the digestive tract. It includes both the voluntary process of swallowing and the involuntary process of peristalsis. **Peristalsis** consists of sequential, alternating waves of contraction and relaxation of the alimentary wall's smooth muscles, which act to propel food along (Figure 22.4). These waves also play a role in mixing food with digestive juices. Peristalsis is so powerful that foods and liquids you swallow enter your stomach even if you are standing on your head.

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Table 22.3 Functions of the Digestive Organs

Organ	Major functions	Other functions
Mouth	• Ingests food • Chews and mixes food • Begins chemical breakdown of carbohydrates • Moves food into the pharynx • Begins breakdown of lipids via lingual lipase	• Moistens and dissolves food, allowing you to taste it • Cleans and lubricates the teeth and oral cavity • Has some antimicrobial activity
Pharynx	• Propels food from the oral cavity to the esophagus	• Lubricates food and passageways
Esophagus	• Propels food to the stomach	• Lubricates food and passageways
Stomach	• Mixes and churns food with gastric juices to form chyme • Begins chemical breakdown of proteins • Releases food into the duodenum as chyme • Absorbs some fat-soluble substances (e.g., alcohol, aspirin) • Possesses antimicrobial functions	• Stimulates protein-digesting enzymes • Secretes intrinsic factor required for vitamin B_{12} absorption in small intestine
Small intestine	• Mixes chyme with digestive juices • Propels food at a rate slow enough for digestion and absorption • Absorbs breakdown products of carbohydrates, proteins, lipids, and nucleic acids, along with vitamins, minerals, and water • Performs physical digestion via segmentation	• Provides optimal medium for enzymatic activity
Accessory organs	• Liver: Produces bile salts, which emulsify lipids, aiding their digestion and absorption • Gallbladder: Stores, concentrates, and releases bile • Pancreas: Produces digestive enzymes and bicarbonate	• Bicarbonate-rich pancreatic juices help neutralize acidic chyme and provide optimal environment for enzymatic activity
Large intestine	• Further breaks down food residue • Absorbs most residual water, electrolytes, and vitamins produced by enteric bacteria • Propels feces toward rectum • Eliminates feces	• Concentrates and stores food residue temporarily prior to defecation • Mucus eases passage of feces through colon

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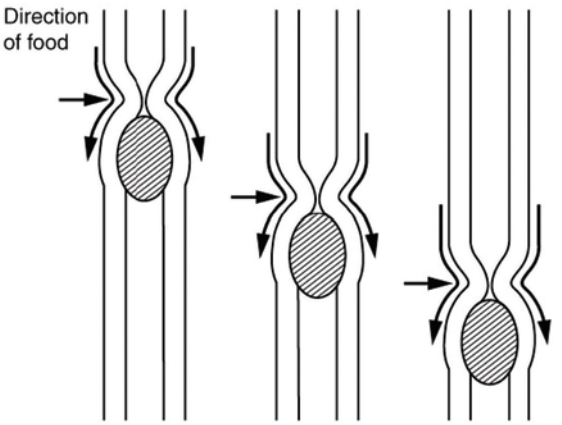


Figure 22.4 Peristalsis. Peristalsis moves food through the digestive tract with alternating waves of muscle contraction and relaxation.

Digestion includes both mechanical and chemical processes. **Mechanical digestion** is a purely physical process that does not change the chemical nature of the food. Instead, it makes the food smaller to increase both surface area and mobility. It includes **mastication**, or chewing, as well as tongue movements that help break food into smaller bits and mix food with saliva. Although there may be a tendency to think that mechanical digestion is limited to the first steps of the digestive process, it occurs after the food leaves the mouth as well. The mechanical churning of food in the stomach serves to further break it apart and expose more of its surface area to digestive juices, creating an acidic "soup" called **chyme**. **Segmentation**, which occurs mainly in the small intestine, consists of localized contractions of circular muscle of the muscularis layer of the alimentary canal. These contractions isolate small sections of the intestine, moving their contents back and forth while continuously subdividing, breaking up, and mixing the contents. By moving food back and forth in the intestinal lumen, segmentation mixes food with digestive juices and facilitates absorption.

In **chemical digestion**, starting in the mouth, digestive secretions break down complex food molecules into their chemical building blocks (for example, proteins into separate amino acids). These secretions vary in composition but typically contain water, various enzymes, acids, and salts. The process is completed in the small intestine.

Food that has been broken down is of no value to the body unless it enters the bloodstream and its nutrients are put to work. This occurs through the process of **absorption**, which takes place primarily within the small intestine.

There, most nutrients are absorbed from the lumen of the alimentary canal into the bloodstream through the epithelial cells that make up the mucosa. Lipids are absorbed into lacteals and are transported via the lymphatic vessels

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to the bloodstream (the subclavian veins near the heart). The details of these processes will be discussed later.

In **defecation**, the final step in digestion, undigested materials are removed from the body as feces.

In some cases, a single organ is in charge of a digestive process. For example, ingestion occurs only in the mouth and defecation only in the anus. However, most digestive processes involve the interaction of several organs and occur gradually as food moves through the alimentary canal (Figure 22.5).

Some chemical digestion occurs in the mouth. Some absorption can occur in the mouth and stomach—for example, alcohol and aspirin.

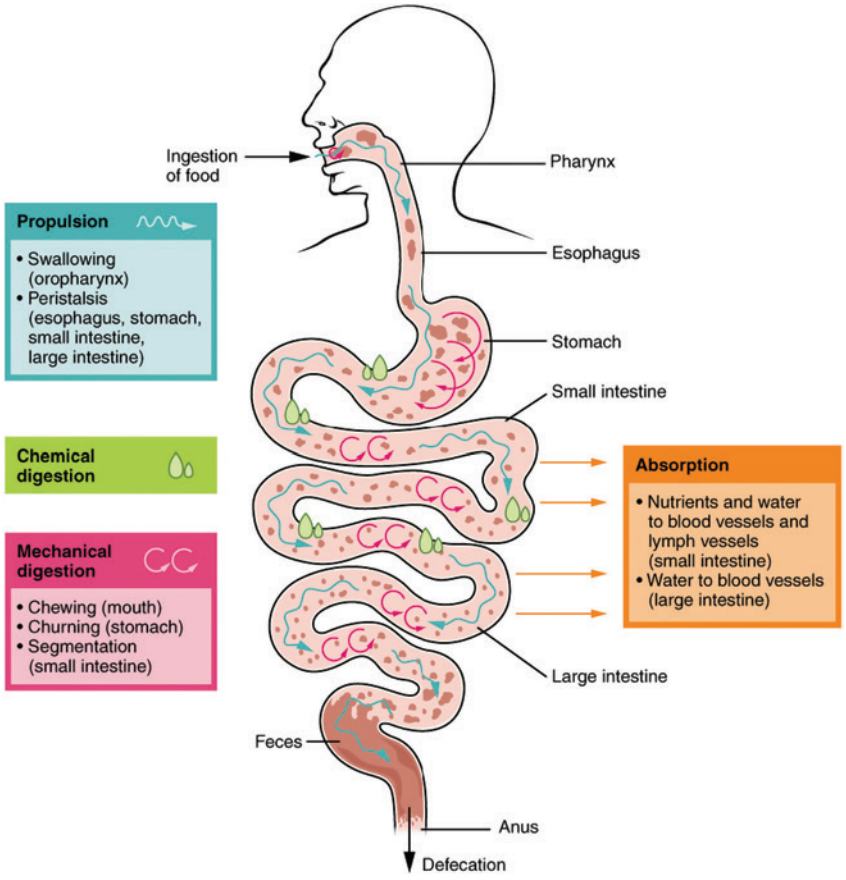


Figure 22.5 Digestive Processes. The digestive processes are ingestion, propulsion, mechanical digestion, chemical digestion, absorption, and defecation.

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Regulatory Mechanisms

Neural and endocrine regulatory mechanisms work to maintain the optimal conditions in the lumen needed for digestion and absorption. These regulatory mechanisms, which stimulate digestive activity through mechanical and chemical activity, are controlled both extrinsically and intrinsically.

Neural Controls

The walls of the alimentary canal contain a variety of sensors that help regulate digestive functions. These include mechanoreceptors, chemoreceptors, and osmoreceptors, which are capable of detecting mechanical, chemical, and osmotic stimuli, respectively. For example, these receptors can sense when the presence of food has caused the stomach to expand, whether food particles have been sufficiently broken down, how much liquid is present, and the type of nutrients in the food (lipids, carbohydrates, and/or proteins). Stimulation of these receptors provokes an appropriate reflex that furthers the process of digestion. This may entail sending a message that activates the glands that secrete digestive juices into the lumen, or it may mean the stimulation of muscles within the alimentary canal, thereby activating peristalsis and segmentation that move food along the intestinal tract.

The walls of the entire alimentary canal are embedded with nerve plexuses that interact with the central nervous system and other nerve plexuses—either within the same digestive organ or in different ones. These interactions prompt several types of reflexes. Extrinsic nerve plexuses orchestrate long reflexes, which involve the central and autonomic nervous systems and work in response to stimuli from outside the digestive system. Short reflexes, on the other hand, are orchestrated by intrinsic nerve plexuses within the alimentary canal wall. These two plexuses and their connections were introduced earlier as the enteric nervous system. Short reflexes regulate activities in one area of the digestive tract and may coordinate local peristaltic movements and stimulate digestive secretions. For example, the sight, smell, and taste of food initiate long reflexes that begin with a sensory neuron delivering a signal to the medulla oblongata. The response to the signal is to stimulate cells in the stomach to begin secreting digestive juices in preparation for incoming food. In contrast, food that distends the stomach initiates short reflexes that cause cells in the stomach wall to increase their secretion of digestive juices.

Hormonal Controls

A variety of hormones are involved in the digestive process. The main digestive hormone of the stomach is **gastrin**, which is secreted in response to the

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presence of food. Gastrin stimulates the secretion of gastric acid by the parietal cells of the stomach mucosa. Other GI hormones are produced and act upon the gut and its accessory organs.

Hormones produced by the duodenum include secretin, which stimulates a watery secretion of bicarbonate by the pancreas; cholecystokinin (CCK), which stimulates the secretion of pancreatic enzymes and bile from the liver and release of bile from the gallbladder; and gastric inhibitory peptide, which inhibits gastric secretion and slows gastric emptying and motility. These GI hormones are secreted by specialized epithelial cells located in the mucosal epithelium of the stomach and small intestine. These hormones then enter the bloodstream, through which they can reach their target organs.

22.3 The Mouth, Pharynx, and Esophagus

Learning Objectives

By the end of this section, you will be able to:

- Describe the structures of the mouth, including its three accessory digestive organs
- Group the 32 adult teeth according to name, location, and function
- Describe the process of swallowing, including the roles of the tongue, upper esophageal sphincter, and epiglottis
- Trace the pathway food follows from ingestion into the mouth through release into the stomach

In this section, you will examine the anatomy and functions of the three main organs of the upper alimentary canal—the mouth, pharynx, and esophagus—as well as three associated accessory organs—the tongue, salivary glands, and teeth.

The Mouth

The cheeks, tongue, and palate frame the mouth, which is also called the **oral cavity** (or buccal cavity). The structures of the mouth are illustrated in Figure 22.6.

At the entrance to the mouth are the lips, or **labia** (singular = labium). Their outer covering is skin, which transitions to a mucous membrane in the mouth proper. Lips are very vascular with a thin layer of keratin—hence the reason they are "red." They have a huge representation on the cerebral cortex, which probably explains the human fascination with kissing! The lips cover the orbicularis oris muscle, which regulates what comes in and goes out of the mouth. The **labial frenulum** is a midline fold of mucous membrane that

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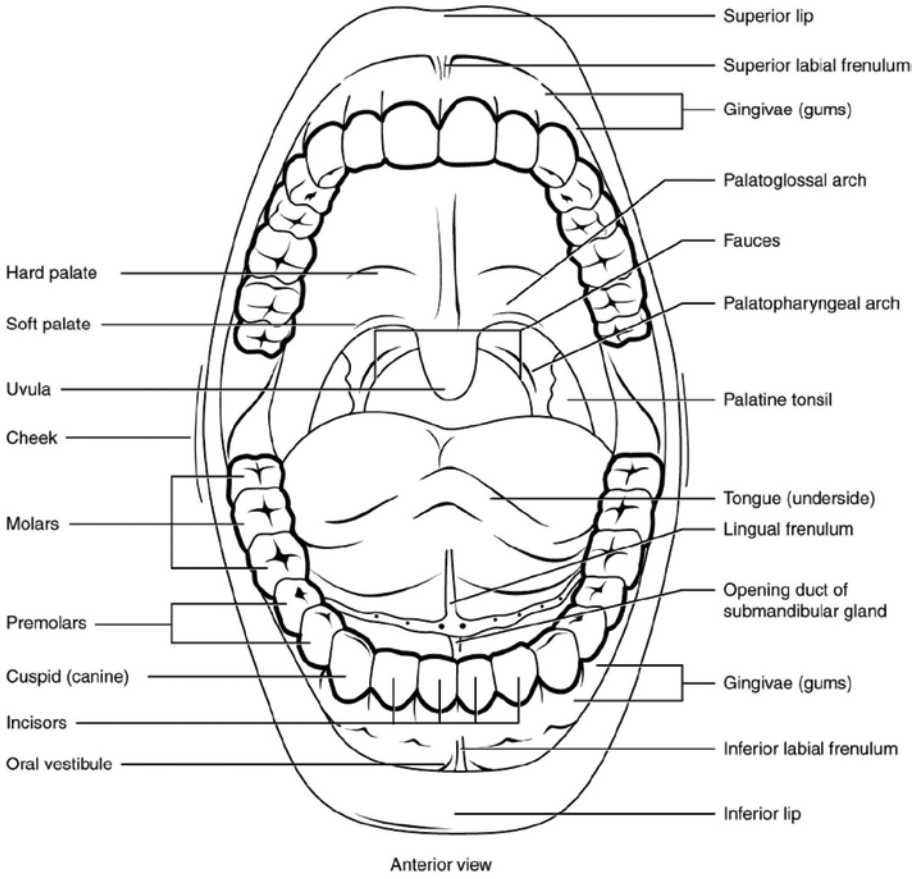


Figure 22.6 Mouth. The mouth includes the lips, tongue, palate, gums, and teeth.

attaches the inner surface of each lip to the gum. The cheeks make up the oral cavity's sidewalls. While their outer covering is skin, their inner covering is mucous membrane. This membrane is made up of nonkeratinized, stratified squamous epithelium. Between the skin and mucous membranes are connective tissue and buccinator muscles. The next time you eat some food, notice how the buccinator muscles in your cheeks and the orbicularis oris muscle in your lips contract, helping you keep the food from falling out of your mouth. Additionally, notice how these muscles work when you are speaking.

The pocket-like part of the mouth that is framed on the inside by the gums and teeth and on the outside by the cheeks and lips is called the **oral vestibule**. Moving farther into the mouth, the opening between the oral cavity and throat (oropharynx) is called the **fauces** (like the kitchen "faucet"). The main open area of the mouth, or oral cavity proper, runs from the gums and teeth to the fauces.

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When you are chewing, you do not find it difficult to breathe simultaneously. The next time you have food in your mouth, notice how the arched shape of the roof of your mouth allows you to handle both digestion and respiration at the same time. This arch is called the palate. The anterior region of the palate serves as a wall (or septum) between the oral and nasal cavities as well as a rigid shelf against which the tongue can push food. It is created by the maxillary and palatine bones of the skull and, given its bony structure, is known as the **hard palate**. If you run your tongue along the roof of your mouth, you'll notice that the hard palate ends in the posterior oral cavity, and the tissue becomes fleshier. This part of the palate, known as the **soft palate**, is composed mainly of skeletal muscle.

You can therefore manipulate, subconsciously, the soft palate—for instance, to yawn, swallow, or sing (see Figure 22.6).

A fleshy bead of tissue called the **uvula** drops down from the centre of the posterior edge of the soft palate. Although some have suggested that the uvula is a vestigial organ, it serves an important purpose. When you swallow, the soft palate and uvula move upward, helping keep foods and liquid from entering the nasal cavity. Unfortunately, it can also contribute to the sound produced by snoring. Two muscular folds extend downward from the soft palate, on either side of the uvula. Toward the front, the **palatoglossal arch** lies next to the base of the tongue; behind it, the **palatopharyngeal arch** forms the superior and lateral margins of the fauces. Between these two arches are the palatine tonsils, clusters of lymphoid tissue that protect the pharynx. The lingual tonsils are located at the base of the tongue.

The Tongue

Perhaps you have heard it said that the **tongue** is the strongest muscle in the body. Those who stake this claim cite its strength proportionate to its size. Although it is difficult to quantify the relative strength of different muscles, it remains indisputable that the tongue is a workhorse, facilitating ingestion, mechanical digestion, chemical digestion (lingual lipase), sensation (of taste, texture, and temperature of food), swallowing, and vocalization.

The tongue is attached to the mandible, the styloid processes of the temporal bones, and the hyoid bone. The hyoid is unique in that it only distantly/indirectly articulates with other bones. The tongue is positioned over the floor of the oral cavity. A medial septum extends the entire length of the tongue, dividing it into symmetrical halves.

Beneath its mucous membrane covering, each half of the tongue is composed of the same number and type of intrinsic and extrinsic skeletal muscles.

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These allow you to change the size and shape of your tongue as well as to stick it out, if you wish. Having such a flexible tongue facilitates both swallowing and speech. Working in concert, these muscles perform three important digestive functions in the mouth: (1) position food for optimal chewing, (2) gather food into a **bolus** (rounded mass), and (3) position food so it can be swallowed.

The top and sides of the tongue are studded with **papillae**, extensions of lamina propria of the mucosa, which are covered in stratified squamous epithelium (Figure 22.7). Fungiform papillae, which are mushroom shaped, cover a large area of the tongue; they tend to be larger toward the rear of the tongue and smaller on the tip and sides. In contrast, filiform papillae are long and thin. Fungiform papillae contain **taste buds**, and filiform papillae have touch receptors that help the tongue move food around in the mouth. The filiform papillae create an abrasive surface that performs mechanically, much like a cat's rough tongue that is used for grooming. **Lingual glands** in the lamina propria of the tongue secrete mucus and a watery serous fluid that contains the enzyme **lingual lipase**, which plays a minor role in breaking down triglycerides but does not begin working until it is activated in the stomach. A fold of mucous membrane on the underside of the tongue, the **lingual frenulum**, tethers the tongue to the floor of the mouth.

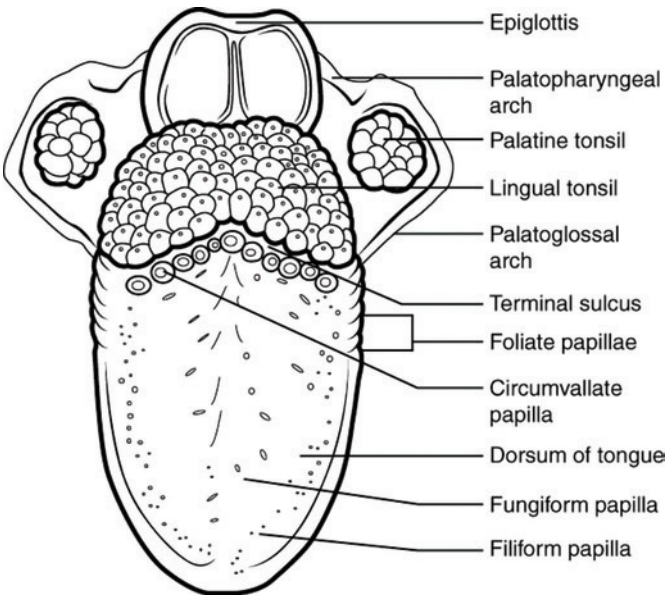


Figure 22.7 Tongue. This superior view of the tongue shows the locations and types of lingual papillae.

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The Salivary Glands

Many small **salivary glands** are housed within the mucous membranes of the mouth and tongue. These minor exocrine glands are constantly secreting saliva, either directly into the oral cavity or indirectly through ducts, even while you sleep. In fact, an average of 1 to 1.5 L of saliva is secreted each day. Usually just enough saliva is present to moisten the mouth and teeth. Secretion increases when you eat, because saliva is essential to moisten food and initiate the chemical breakdown of carbohydrates. Small amounts of saliva are also secreted by the labial glands in the lips. In addition, the buccal glands in the cheeks, palatal glands in the palate, and lingual glands in the tongue help ensure that all areas of the mouth are supplied with adequate saliva.

The Major Salivary Glands

Outside the oral mucosa are three pairs of major salivary glands, which secrete the majority of saliva into ducts that open into the mouth:

- The **submandibular glands**, which are in the floor of the mouth, secrete saliva into the mouth through the submandibular ducts.
- The **sublingual glands**, which lie below the tongue, use the lesser sublingual ducts to secrete saliva into the oral cavity.
- The **parotid glands** lie between the skin and the masseter muscle, near the ears. They secrete saliva into the mouth through the parotid duct, which is located near the second upper molar tooth (Figure 22.8).

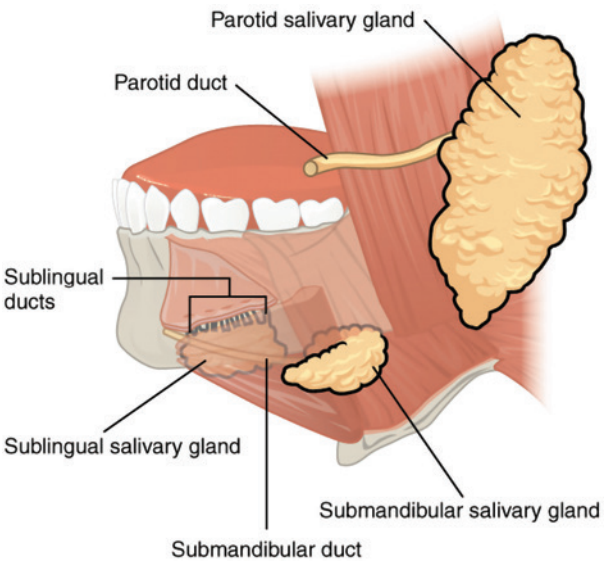


Figure 22.8 Salivary Glands. The major salivary glands are located outside the oral mucosa and deliver saliva into the mouth through ducts.

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Saliva

Saliva is essentially (98 to 99.5 percent) water. The remaining 4.5 percent is a complex mixture of ions, glycoproteins, enzymes, growth factors, and waste products. Perhaps the most important ingredient in saliva from the perspective of digestion is the enzyme **salivary amylase**, which initiates the breakdown of carbohydrates. Food does not spend enough time in the mouth to allow all the carbohydrates to break down, but salivary amylase continues acting until it is inactivated by stomach acids. Bicarbonate and phosphate ions function as chemical buffers, maintaining saliva at a pH between 6.35 and 6.85. Salivary mucus helps lubricate food, facilitating movement in the mouth, bolus formation, and swallowing. Saliva contains immunoglobulin A, which prevents microbes from penetrating the epithelium, and **lysozyme**, which makes saliva antimicrobial. Saliva also contains epidermal growth factor.

Each of the major salivary glands secretes a unique formulation of saliva according to its cellular makeup. For example, the parotid glands secrete a watery solution that contains salivary amylase. The submandibular glands have cells similar to those of the parotid glands as well as mucus-secreting cells. Therefore, saliva secreted by the submandibular glands also contains amylase, but in a liquid thickened with mucus. The sublingual glands contain mostly mucous cells, and they secrete the thickest saliva with the least amount of salivary amylase.

Regulation of Salivation

The autonomic nervous system regulates **salivation** (the secretion of saliva). In the absence of food, parasympathetic stimulation keeps saliva flowing at just the right level for comfort as you speak, swallow, sleep, and generally go about life. Oversalivation can occur, for example, if you are stimulated by the smell of food, but that food is not available for you to eat. Drooling is an extreme instance of the overproduction of saliva. During times of stress, such as before speaking in public, sympathetic stimulation takes over, reducing salivation and producing the symptom of dry mouth often associated with anxiety. When you are dehydrated, salivation is reduced, causing the mouth to feel dry and prompting you to take action to quench your thirst.

Salivation can be stimulated by the sight, smell, and taste of food. It can even be stimulated by thinking about food. You might notice whether reading about food and salivation right now has had any effect on your production of saliva.

How does the salivation process work while you are eating? Food contains chemicals that stimulate taste receptors on the tongue, which send impulses to the superior and inferior salivatory nuclei in the brain stem. These two nuclei then send back parasympathetic impulses through fibres in the glossopharyngeal

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and facial nerves, which stimulate salivation. Even after you swallow food, salivation is increased to cleanse the mouth and to water down and neutralize any irritating chemical remnants, such as that hot sauce in your burrito. Most saliva is swallowed along with food and is reabsorbed, so that fluid is not lost.

The Teeth

The teeth, or **dentes** (singular = dens), are organs similar to bones that you use to tear, grind, and otherwise mechanically break down food.

Types of Teeth

During the course of your lifetime, you have two sets of teeth (one set of teeth is a **dentition**). Your 20 **deciduous teeth**, or baby teeth, first begin to appear at about 6 months of age. Between approximately age 6 and 12, these teeth are replaced by 32 **permanent teeth**. Moving from the centre of the mouth toward the side, these are as follows (Figure 22.9):

- The eight **incisors**, four top and four bottom, are the sharp front teeth you use for biting into food.
- The four **cuspids** (or canines) flank the incisors and have a pointed edge (cusp) to tear up food. These fang-like teeth are superb for piercing tough or fleshy foods.
- Posterior to the cuspids are the eight **premolars** (or bicuspids), which have an overall flatter shape with two rounded cusps useful for mashing foods.
- The most posterior and largest are the 12 **molars**, which have several pointed cusps used to crush food so it is ready for swallowing. The third members of each set of 3 molars, top and bottom, are commonly referred to as the wisdom teeth, because their eruption is commonly delayed until early adulthood. It is not uncommon for wisdom teeth to fail to erupt; that is, they remain impacted. In these cases, the teeth are typically removed by orthodontic surgery.

Anatomy of a Tooth

The teeth are secured in the alveolar processes (sockets) of the maxilla and the mandible. **Gingivae** (commonly called the gums) are soft tissues that line the alveolar processes and surround the necks of the teeth. Teeth are also held in their sockets by a connective tissue called the periodontal ligament.

The two main parts of a tooth are the **crown**, which is the portion projecting above the gum line, and the **root**, which is embedded within the maxilla and mandible. Both parts contain an inner **pulp cavity**, containing loose connective

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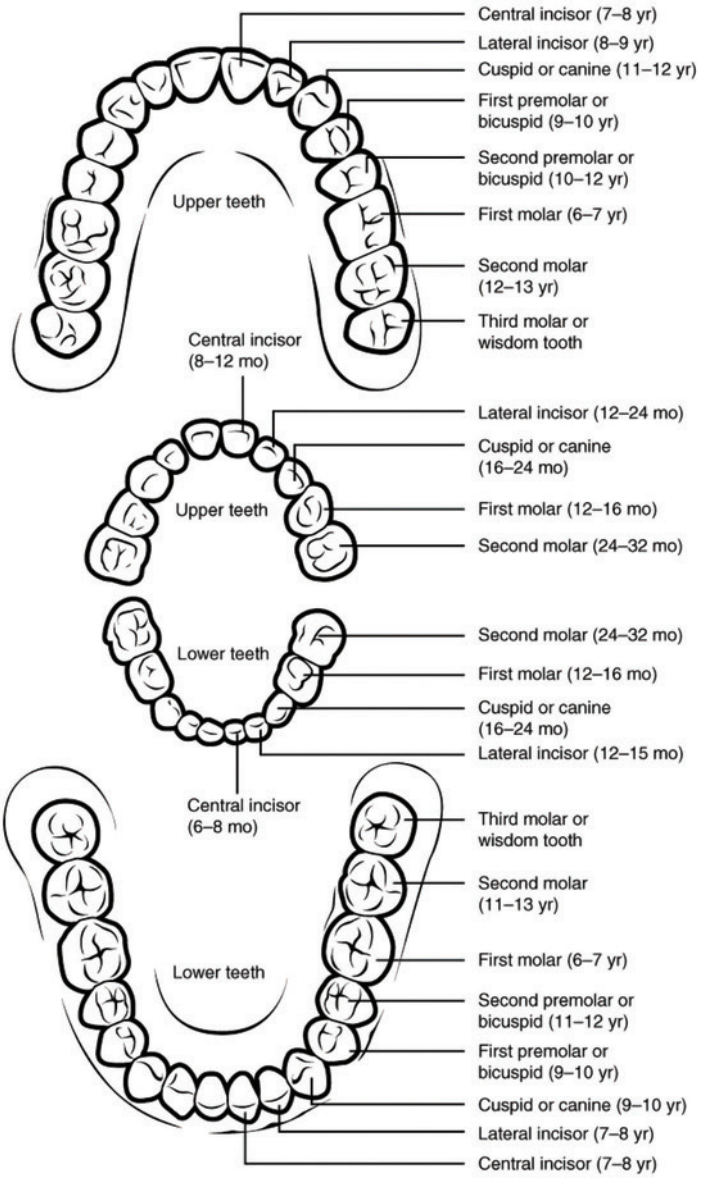


Figure 22.9 Permanent and Deciduous Teeth. This figure of two human dentitions shows the arrangement of teeth in the maxilla and mandible and the relationship between the deciduous and permanent teeth.

tissue through which nerves and blood vessels run. The region of the pulp cavity that runs through the root of the tooth is called the root canal. Surrounding the pulp cavity is **dentin**, a bone-like tissue. In the root of each tooth, the dentin is covered by an even harder bone-like layer called **cementum**. In the crown of each tooth, the dentin is covered by an outer layer of **enamel**, the hardest substance in the body (Figure 22.10).

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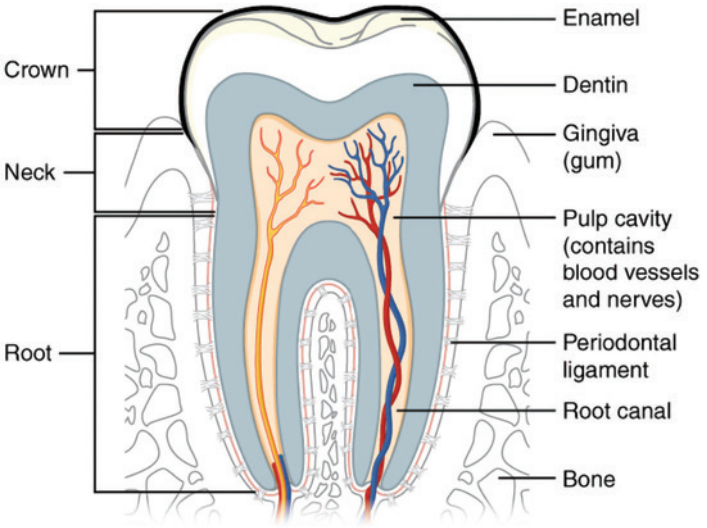


Figure 22.10 The Structure of the Tooth. This longitudinal section through a molar in its alveolar socket shows the relationships between enamel, dentin, and pulp.

Although enamel protects the underlying dentin and pulp cavity, it is still nonetheless susceptible to mechanical and chemical erosion, or what is known as tooth decay. The most common form, dental caries (cavities), develops when colonies of bacteria feeding on sugars in the mouth release acids that cause soft tissue inflammation and degradation of the calcium crystals of the enamel. The digestive functions of the mouth are summarized in Table 22.4.

The Pharynx

The **pharynx** (throat) is involved in both digestion and respiration. It receives food and air from the mouth and air from the nasal cavities. When food enters the pharynx, involuntary muscle contractions close off the air passageways (Figure 22.11).

A short tube of skeletal muscle lined with a mucous membrane, the pharynx runs from the posterior oral and nasal cavities to the opening of the esophagus and larynx. It has three subdivisions. The most superior, the **nasopharynx**, is involved only in breathing and speech. The other two subdivisions, the **oropharynx** and the **laryngopharynx**, are used for both breathing and digestion. The oropharynx begins inferior to the nasopharynx and is continuous below with the laryngopharynx. The inferior border of the laryngopharynx connects to the esophagus, whereas the anterior portion connects to the larynx, allowing air to flow into the bronchial tree.

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Table 22.4 Digestive Functions of the Mouth

Structure	Action	Outcome
Lips and cheeks	Confine food between teeth	• Ensure food is chewed evenly during mastication
Salivary glands	Secrete saliva	• Moisten and lubricate the lining of the mouth and pharynx • Moisten, soften, and dissolve food • Clean the mouth and teeth • Salivary amylase breaks down starch
Tongue's extrinsic muscles	Move tongue sideways and in and out	• Manipulate food for chewing • Shape food into a bolus • Manipulate food for swallowing
Tongue's intrinsic muscles	Change tongue shape	• Manipulate food for swallowing
Taste buds	Sense food in mouth and sense taste	• Conduct nerve impulses to salivary nuclei in the brain stem and then to salivary glands, stimulating saliva secretion
Lingual glands	Secrete lingual lipase	• Activate in the stomach • Break down triglycerides into fatty acids and diglycerides
Teeth	Shred and crush food	• Break down solid food into smaller particles for deglutition

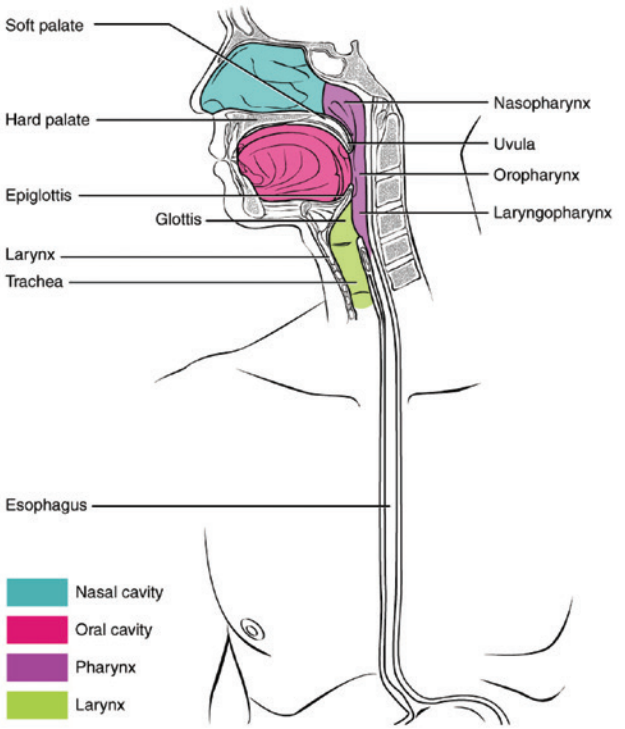


Figure 22.11 Pharynx. The pharynx runs from the nostrils to the esophagus and the larynx.

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The Esophagus

The **esophagus** is a muscular tube that connects the pharynx to the stomach. It is approximately 25.4 cm (10 in) in length, located posterior to the trachea, and remains in a collapsed form when not engaged in swallowing. As you can see in Figure 22.12, the esophagus runs a mainly straight route through the mediastinum of the thorax. To enter the abdomen, the esophagus penetrates the diaphragm through an opening called the esophageal hiatus.

Passage of Food Through the Esophagus

The **upper esophageal sphincter**, which is continuous with the inferior pharyngeal constrictor, controls the movement of food from the pharynx into the esophagus. The upper two-thirds of the esophagus consists of both smooth and skeletal muscle fibres, with the latter fading out in the bottom third of the esophagus. Rhythmic waves of peristalsis, which begin in the upper esophagus, propel the bolus of food toward the stomach. Meanwhile, secretions from the esophageal mucosa lubricate the esophagus and food. Food passes from the esophagus into the stomach at the **lower esophageal**

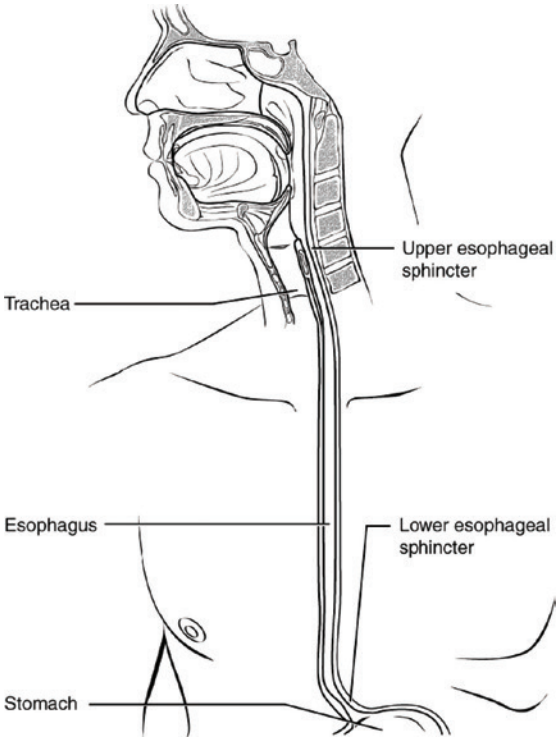


Figure 22.12 Esophagus. The upper esophageal sphincter controls the movement of food from the pharynx to the esophagus. The lower esophageal sphincter controls the movement of food from the esophagus to the stomach.

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sphincter (also called the gastroesophageal or cardiac sphincter). Recall that sphincters are muscles that surround tubes and serve as valves, closing the tube when the sphincters contract and opening it when they relax. The lower esophageal sphincter relaxes to let food pass into the stomach and then contracts to prevent stomach acids from backing up into the esophagus. Surrounding this sphincter is the muscular diaphragm, which helps close off the sphincter when no food is being swallowed. When the lower esophageal sphincter does not completely close, the stomach's contents can reflux (that is, back up into the esophagus), causing heartburn or gastroesophageal reflux disease (GERD).

Histology of the Esophagus

The mucosa of the esophagus is made up of an epithelial lining that contains nonkeratinized, stratified squamous epithelium with a layer of basal and parabasal cells. This epithelium protects against erosion from food particles. The mucosa's lamina propria contains mucus-secreting glands. The muscularis layer changes according to location: In the upper third of the esophagus, the muscularis is skeletal muscle. In the middle third, it is both skeletal and smooth muscle. In the lower third, it is smooth muscle. As mentioned previously, the most superficial layer of the esophagus is called the adventitia, not the serosa. In contrast to the stomach and intestines, the loose connective tissue of the adventitia is not covered by a fold of visceral peritoneum. The digestive functions of the esophagus are identified in Table 22.5.

Table 22.5 Digestive Functions of the Esophagus

Action	Outcome
Upper esophageal sphincter relaxation	Allows the bolus to move from the laryngopharynx to the esophagus
Peristalsis	Propels the bolus through the esophagus
Lower esophageal sphincter relaxation	Allows the bolus to move from the esophagus into the stomach and prevents chyme from entering the esophagus
Mucus secretion	Lubricates the esophagus, allowing easy passage of the bolus

Deglutition

Deglutition is another word for swallowing—the movement of food from the mouth to the stomach. The entire process takes about 4 to 8 seconds for solid or semisolid food and about 1 second for very soft food and liquids. Although

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this sounds quick and effortless, deglutition is, in fact, a complex process that involves both the skeletal muscle of the tongue and the muscles of the pharynx and esophagus. It is aided by the presence of mucus and saliva. There are three stages in deglutition: the voluntary phase, the pharyngeal phase, and the esophageal phase (Figure 22.13). The autonomic nervous system controls the latter two phases.

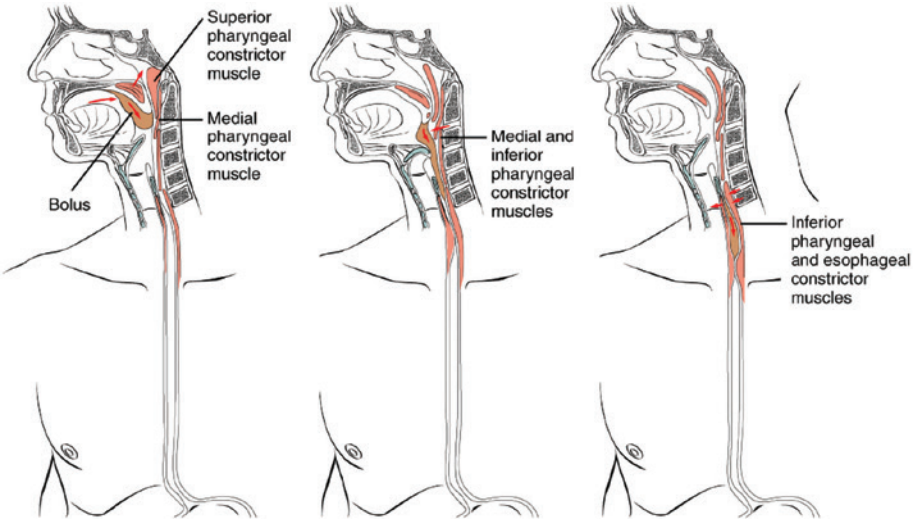


Figure 22.13 Deglutition. Deglutition includes the voluntary phase and two involuntary phases: the pharyngeal phase and the esophageal phase.

The Voluntary Phase

The **voluntary phase** of deglutition (also known as the oral or buccal phase) is so called because you can control when you swallow food. In this phase, chewing has been completed, and swallowing is set in motion. The tongue moves upward and backward against the palate, pushing the bolus to the back of the oral cavity and into the oropharynx. Other muscles keep the mouth closed and prevent food from falling out. At this point, the two involuntary phases of swallowing begin.

The Pharyngeal Phase

In the pharyngeal phase, stimulation of receptors in the oropharynx sends impulses to the deglutition centre (a collection of neurons that controls swallowing) in the medulla oblongata. Impulses are then sent back to the uvula and soft palate, causing them to move upward and close off the nasopharynx. The laryngeal muscles also constrict to prevent aspiration of food into the trachea. At this point, deglutition apnea takes place, which means that breathing ceases for a very brief time. Contractions of the pharyngeal constrictor muscles move

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the bolus through the oropharynx and laryngopharynx. Relaxation of the upper esophageal sphincter then allows food to enter the esophagus.

The Esophageal Phase

The entry of food into the esophagus marks the beginning of the esophageal phase of deglutition and the initiation of peristalsis. As in the previous phase, the complex neuromuscular actions are controlled by the medulla oblongata. Peristalsis propels the bolus through the esophagus and toward the stomach. The circular muscle layer of the muscularis contracts, pinching the esophageal wall and forcing the bolus forward. At the same time, the longitudinal muscle layer of the muscularis also contracts, shortening this area and pushing out its walls to receive the bolus. In this way, a series of contractions keeps moving food toward the stomach. When the bolus nears the stomach, distention of the esophagus initiates a short reflex relaxation of the lower esophageal sphincter that allows the bolus to pass into the stomach. During the esophageal phase, esophageal glands secrete mucus that lubricates the bolus and minimizes friction.

Interactive Link 22.3

Watch this animation (http://oer.aupress.ca/oer-202505/22.3) to see how swallowing is a complex process that involves the nervous system to coordinate the actions of upper respiratory and digestive activities. During which stage of swallowing is there a risk of food entering respiratory pathways, and how is this risk blocked?

22.4 The Stomach

Learning Objectives

By the end of this section, you will be able to:

- Label on a diagram the four main regions of the stomach, its curvatures, and its sphincter
- Identify the four main types of secreting cells in gastric glands and their important products
- Explain why the stomach does not digest itself
- Describe the mechanical and chemical digestion of food entering the stomach

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Although a minimal amount of carbohydrate digestion occurs in the mouth, chemical digestion really gets underway in the stomach. An expansion of the alimentary canal that lies immediately inferior to the esophagus, the stomach links the esophagus to the first part of the small intestine (the duodenum) and is relatively fixed in place at its esophageal and duodenal ends. In between, however, it can be a highly active structure, contracting and continually changing position and size. These contractions provide mechanical assistance to digestion. The empty stomach is only about the size of your fist but can stretch to hold as much as 4 L of food and fluid, or more than 75 times its empty volume, and then return to its resting size when empty. Although you might think that the size of a person's stomach is related to how much food that individual consumes, body weight does not correlate with stomach size. Rather, when you eat greater quantities of food—such as at holiday dinner—you stretch the stomach more than when you eat less.

Popular culture tends to refer to the stomach as the location where all digestion takes place. Of course, this is not true. An important function of the stomach is to serve as a temporary holding chamber. You can ingest a meal far more quickly than it can be digested and absorbed by the small intestine. Thus, the stomach holds food and parses only small amounts into the small intestine at a time. Foods are not processed in the order they are eaten; rather, they are mixed together with digestive juices in the stomach until they are converted into chyme, which is released into the small intestine.

As you will see in the sections that follow, the stomach plays several important roles in chemical digestion, including the continued digestion of carbohydrates and the initial digestion of proteins and triglycerides. Little if any nutrient absorption occurs in the stomach, with the exception of the negligible amount of nutrients in alcohol.

Structure

There are four main regions in the **stomach**: the cardia, fundus, body, and pylorus (Figure 22.14). The **cardia** (or cardiac region) is the point where the esophagus connects to the stomach and through which food passes into the stomach.

Located inferior to the diaphragm, above and to the left of the cardia, is the dome-shaped **fundus**. Below the fundus is the **body**, the main part of the stomach. The funnel-shaped **pylorus** connects the stomach to the duodenum. The wider end of the funnel, the **pyloric antrum**, connects to the body of the stomach. The narrower end is called the **pyloric canal**, which connects to the duodenum (first segment of duodenum). The smooth muscle **pyloric sphincter** is located at this latter point of connection and controls stomach

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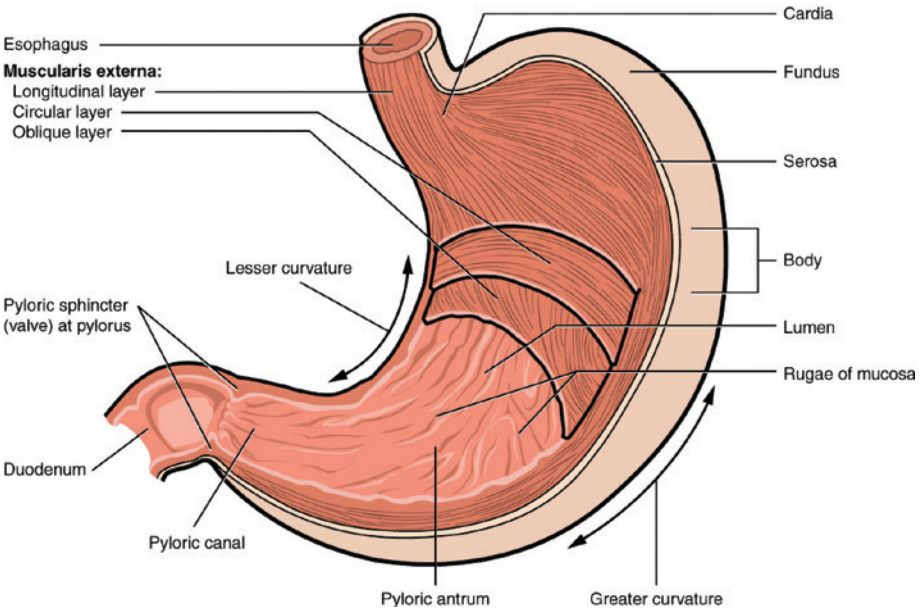


Figure 22.14 Stomach. The stomach has four major regions: the cardia, fundus, body, and pylorus. The addition of an inner oblique smooth muscle layer gives the muscularis the ability to vigorously churn and mix food.

emptying. In the absence of food, the stomach deflates inward, and its mucosa and submucosa fall into numerous large folds called **rugae**.

The convex lateral surface of the stomach is called the **greater curvature**; the concave medial border is the **lesser curvature**. The stomach is held in place by the lesser omentum, which extends from the liver to the lesser curvature, and the greater omentum, which runs from the greater curvature to the posterior abdominal wall.

Histology

The wall of the stomach is made of the same four layers as most of the rest of the alimentary canal but with adaptations to the mucosa and muscularis for the unique functions of this organ. In addition to the typical circular and longitudinal smooth muscle layers, the muscularis has an inner oblique smooth muscle layer (Figure 22.15). As a result, in addition to moving food through the canal, the stomach can vigorously churn food, mechanically breaking it down into smaller particles.

The stomach mucosa's epithelial lining consists only of surface mucus cells, which secrete a protective coat of alkaline mucus. A vast number of **gastric pits** dot the surface of the epithelium, giving it the appearance of a well-used

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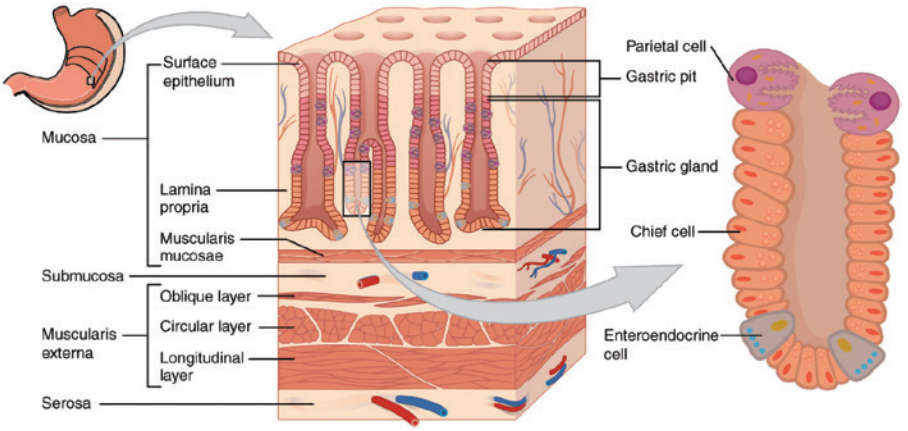


Figure 22.15 Histology of the Stomach. The stomach wall is adapted for the functions of the stomach. In the epithelium, gastric pits lead to gastric glands that secrete gastric juice. The gastric glands (one gland is shown enlarged on the right) contain different types of cells that secrete a variety of enzymes, including hydrochloric acid, which activates the protein-digesting enzyme pepsin.

pincushion, and mark the entry to each **gastric gland**, which secretes a complex digestive fluid referred to as **gastric juice**.

Although the walls of the gastric pits are made up primarily of mucus cells, the gastric glands are made up of different types of cells. The glands of the cardia and pylorus are composed primarily of mucus-secreting cells. Cells that make up the pyloric antrum secrete mucus and a number of hormones, including the majority of the stimulatory hormone **gastrin**. The much larger glands of the fundus and body of the stomach, the site of most chemical digestion, produce most of the gastric secretions. These glands are made up of a variety of secretory cells. These include parietal cells, chief cells, mucous neck cells, and enteroendocrine cells.

Parietal Cells

Located primarily in the middle region of the gastric glands are **parietal cells**, which are among the most highly differentiated of the body's epithelial cells. These relatively large cells produce both **hydrochloric acid** (**HCl**) and **intrinsic factor**. HCl is responsible for the high acidity (pH 1.5 to 3.5) of the stomach contents and is needed to activate the protein-digesting enzyme pepsin. The acidity also kills much of the bacteria you ingest with food and helps denature proteins, making them more available for enzymatic digestion. Intrinsic factor is a glycoprotein necessary for the absorption of vitamin B_{12} in the small intestine.

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Chief Cells

Located primarily in the basal regions of gastric glands are **chief cells**, which secrete **pepsinogen**, the inactive proenzyme form of **pepsin**. HCl is necessary for the conversion of pepsinogen to pepsin. Chief cells also secrete **gastric lipase**, which digests triglycerides.

Mucous Neck Cells

Gastric glands in the upper part of the stomach contain **mucous neck cells** that secrete thin, acidic mucus that is much different from the mucus secreted by the goblet cells of the surface epithelium. The role of this mucus is not currently known.

Enteroendocrine Cells

Finally, **enteroendocrine cells** found in the gastric glands secrete various hormones into the interstitial fluid of the lamina propria. These include **gastrin**, which is released mainly by enteroendocrine **G cells**.

Interactive Link 22.4

Watch this animation (http://oer.aupress.ca/oer-202505/22.4) that depicts the structure of the stomach and how this structure functions in the initiation of protein digestion. This view of the stomach shows the characteristic rugae. What is the function of these rugae?

Gastric Secretion

The secretion of gastric juice is controlled by both nerves and hormones. Stimuli in the brain, stomach, and small intestine activate or inhibit gastric juice production. This is why the three phases of gastric secretion are called the cephalic, gastric, and intestinal phases (Figure 22.16). However, once gastric secretion begins, all three phases can occur simultaneously.

The **cephalic phase** (reflex phase) of gastric secretion, which is relatively brief, takes place before food enters the stomach. The smell, taste, sight, or thought of food triggers this phase. For example, when you bring a piece of sushi to your lips, impulses from receptors in your taste buds or the nose are relayed to your brain, which returns signals that increase gastric secretion to prepare your stomach for digestion. This enhanced secretion is a conditioned reflex, meaning it occurs only if you like or want a particular food. Depression and loss of appetite can suppress the cephalic reflex.

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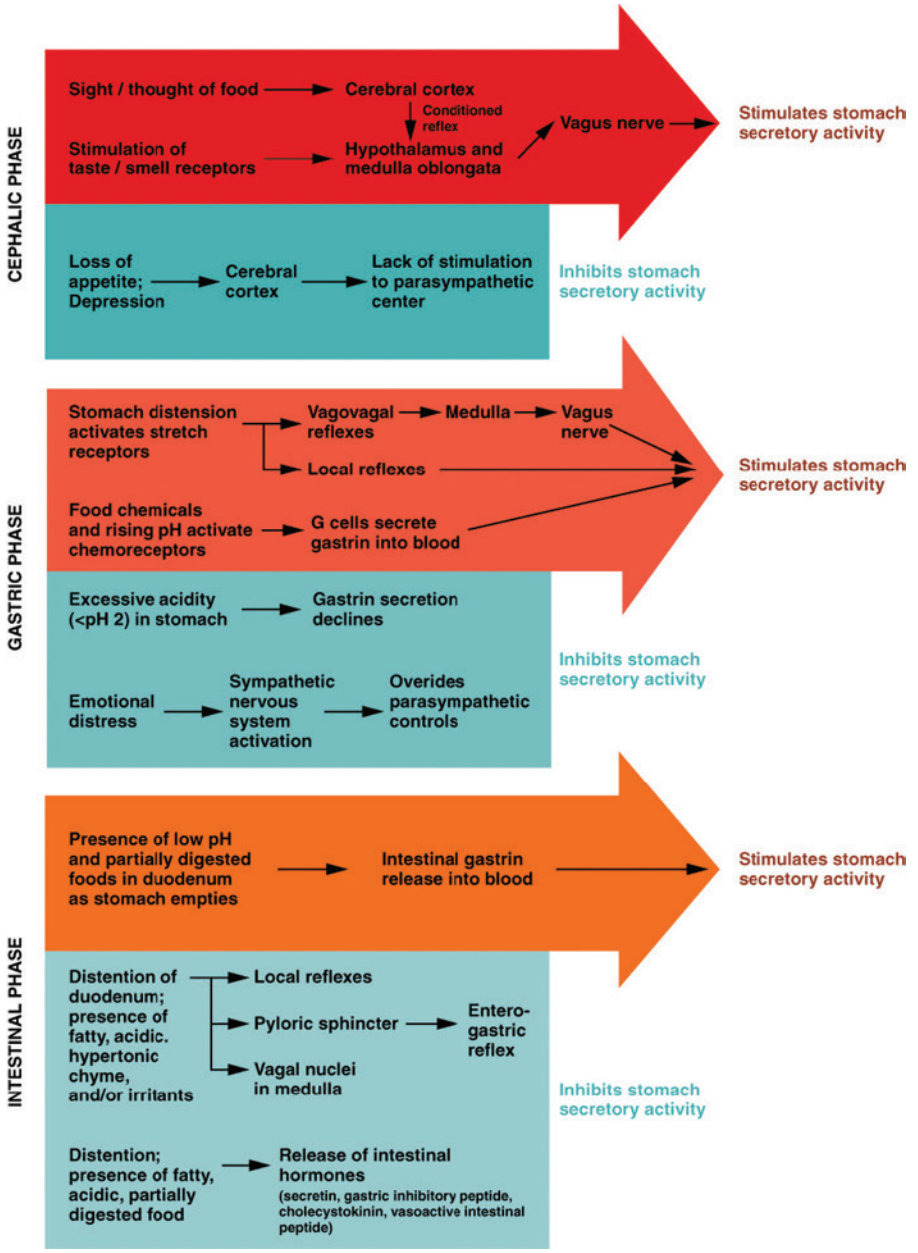


Figure 22.16 The Three Phases of Gastric Secretion. Gastric secretion occurs in three phases: cephalic, gastric, and intestinal. During each phase, the secretion of gastric juice can be stimulated or inhibited.

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The **gastric phase** of secretion lasts 3 to 4 hours and is set in motion by local neural and hormonal mechanisms triggered by the entry of food into the stomach. For example, when your sushi reaches the stomach, it creates distention that activates the stretch receptors. This stimulates parasympathetic neurons to release acetylcholine, which then provokes increased secretion of gastric juice. Partially digested proteins, caffeine, and rising pH stimulate the release of gastrin from enteroendocrine G cells, which in turn induces parietal cells to increase their production of HCl, which is needed to create an acidic environment for the conversion of pepsinogen to pepsin and protein digestion. Additionally, the release of gastrin activates vigorous smooth muscle contractions. However, it should be noted that the stomach does have a natural means of avoiding excessive acid secretion and potential heartburn. Whenever pH levels drop too low, cells in the stomach react by suspending HCl secretion and increasing mucous secretions.

The **intestinal phase** of gastric secretion has both excitatory and inhibitory elements. The duodenum has a major role in regulating the stomach and its emptying. When partially digested food fills the duodenum, intestinal mucosal cells release a hormone called intestinal (enteric) gastrin, which further excites gastric juice secretion. This stimulatory activity is brief, however, because when the intestine distends with chyme, the enterogastric reflex inhibits secretion. One of the effects of this reflex is to close the pyloric sphincter, which blocks additional chyme from entering the duodenum.

The Mucosal Barrier

The mucosa of the stomach is exposed to the highly corrosive acidity of gastric juice. Gastric enzymes that can digest protein can also digest the stomach itself. The stomach is protected from self-digestion by the **mucosal barrier**. This barrier has several components. First, the stomach wall is covered by a thick coating of bicarbonate-rich mucus. This mucus forms a physical barrier, and its bicarbonate ions neutralize acid. Second, the epithelial cells of the stomach's mucosa meet at tight junctions, which block gastric juice from penetrating the underlying tissue layers. Finally, stem cells located where gastric glands join the gastric pits quickly replace damaged epithelial mucosal cells when the epithelial cells are shed. In fact, the surface epithelium of the stomach is completely replaced every 3 to 6 days.

Digestive Functions of the Stomach

The stomach participates in virtually all the digestive activities with the exception of ingestion and defecation. Although almost all absorption takes place in the small intestine, the stomach does absorb some drugs, such as alcohol and aspirin.

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Mechanical Digestion

Within a few moments after food enters your stomach, mixing waves begin to occur at intervals of approximately 20 seconds. A **mixing wave** is a unique type of peristalsis that mixes and softens the food with gastric juices to create chyme. The initial mixing waves are relatively gentle, but these are followed by more intense waves, starting at the body of the stomach and increasing in force as they reach the pylorus. It is fair to say that long before your sushi exits through the pyloric sphincter, it bears little resemblance to the sushi you ate.

The pylorus, which holds around 30 mL of chyme, acts as a filter, permitting only liquids and small food particles to pass through the mostly, but not fully, closed pyloric sphincter. In a process called **gastric emptying**, rhythmic mixing waves force about 3 mL of chyme at a time through the pyloric sphincter and into the duodenum. Release of a greater amount of chyme at one time would overwhelm the capacity of the small intestine to handle it. The rest of the chyme is pushed back into the body of the stomach, where it continues mixing. This process is repeated when the next mixing waves force more chyme into the duodenum.

Gastric emptying is regulated by both the stomach and the duodenum. The presence of chyme in the duodenum activates receptors that inhibit gastric secretion. This prevents additional chyme from being released by the stomach before the duodenum is ready to process it.

Chemical Digestion

The fundus plays an important role, because it stores both undigested food and gases that are released during the process of chemical digestion. Food may sit in the fundus of the stomach for a while before being mixed with the chyme. While the food is in the fundus, the digestive activities of salivary amylase continue until the food begins mixing with the acidic chyme. Ultimately, mixing waves incorporate this food with the chyme, the acidity of which inactivates salivary amylase and activates lingual lipase. Lingual lipase then begins breaking down triglycerides into free fatty acids and mono- and diglycerides.

The breakdown of protein begins in the stomach through the actions of HCl and the enzyme pepsin.

Its numerous digestive functions notwithstanding, there is only one stomach function necessary to life: the production of intrinsic factor. The intestinal absorption of vitamin B_{12}, which is necessary for both the production of mature red blood cells and normal neurological functioning, cannot occur without intrinsic factor. People who undergo total gastrectomy (stomach removal)—for life-threatening stomach cancer, for example—can survive with minimal digestive dysfunction if they receive vitamin B_{12} injections.

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The contents of the stomach are completely emptied into the duodenum within 2 to 4 hours after you eat a meal. Different types of food take different amounts of time to process. Foods heavy in carbohydrates empty fastest, followed by high-protein foods. Meals with a high triglyceride content remain in the stomach the longest. Since enzymes in the small intestine digest fats slowly, food can stay in the stomach for 6 hours or longer when the duodenum is processing fatty chyme. However, note that this is still a fraction of the 24 to 72 hours that full digestion typically takes from start to finish.

22.5 The Small and Large Intestines

Learning Objectives

By the end of this section, you will be able to:

- Compare and contrast the location and gross anatomy of the small and large intestines
- Identify three main adaptations of the small intestine wall that increase its absorptive capacity
- Describe the mechanical and chemical digestion of chyme upon its release into the small intestine
- List three features unique to the wall of the large intestine and identify their contributions to its function
- Identify the beneficial roles of the bacterial flora in digestive system functioning
- Trace the pathway of food waste from its point of entry into the large intestine through its exit from the body as feces

The word *intestine* is derived from a Latin root meaning "internal," and indeed, the two organs together nearly fill the interior of the abdominal cavity. In addition, called the small and large bowel, or colloquially the "guts," they constitute the greatest mass and length of the alimentary canal and, with the exception of ingestion, perform all digestive system functions.

The Small Intestine

Chyme released from the stomach enters the **small intestine**, which is the primary digestive organ in the body. Not only is this where most digestion occurs; it is also where practically all absorption occurs. The longest part of the alimentary canal, the small intestine is about 3.05 m long in a living person (but about twice as long in a cadaver due to the loss of muscle tone). Since this

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makes it about five times longer than the large intestine, you might wonder why it is called "small." In fact, its name derives from its relatively smaller diameter of only about 2.54 cm, compared with 7.62 cm for the large intestine. As we'll see shortly, in addition to its length, the folds and projections of the lining of the small intestine work to give it an enormous surface area, which is approximately 200 m^2, more than 100 times the surface area of your skin. This large surface area is necessary for complex processes of digestion and absorption that occur within it.

Structure

The coiled tube of the small intestine is subdivided into three regions. From proximal (at the stomach) to distal, these are the duodenum, jejunum, and ileum (Figure 22.17).

The shortest region is the 25.4 cm (10 in) **duodenum**, which begins at the pyloric sphincter. Just past the pyloric sphincter, it bends posteriorly behind the peritoneum, becoming retroperitoneal, and then makes a C-shaped curve around the head of the pancreas before ascending anteriorly again to return to the peritoneal cavity and join the jejunum. The duodenum can therefore be subdivided into four segments: the superior, descending, horizontal, and ascending duodenum.

Of particular interest is the **hepatopancreatic ampulla** (ampulla of Vater). Located in the duodenal wall, the ampulla marks the transition from the anterior portion of the alimentary canal to the midregion and is where

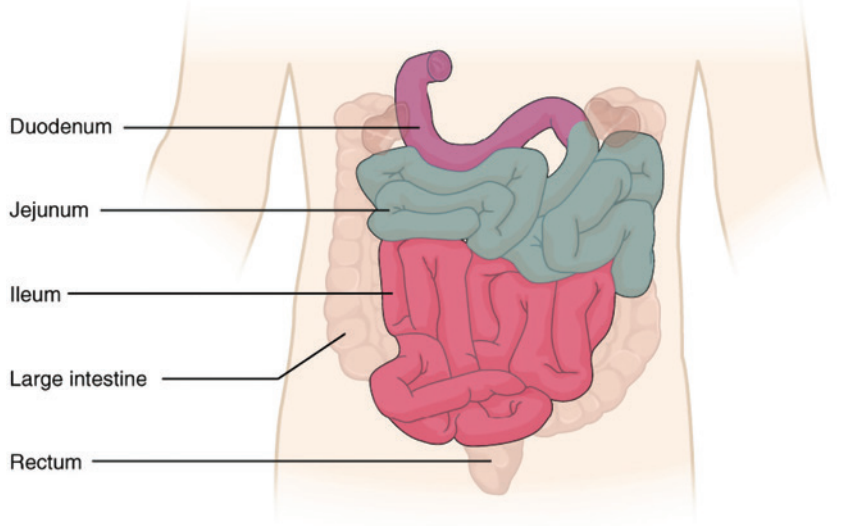


Figure 22.17 Small Intestine. The three regions of the small intestine are the duodenum, jejunum, and ileum.

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the bile duct (through which bile passes from the liver) and the **main pancreatic duct** (through which pancreatic juice passes from the pancreas) join. This ampulla opens into the duodenum at a tiny volcano-shaped structure called the **major duodenal papilla**. The **hepatopancreatic sphincter** (sphincter of Oddi) regulates the flow of both bile and pancreatic juice from the ampulla into the duodenum.

The **jejunum** is about 0.9 m long (in life) and runs from the duodenum to the ileum. No clear demarcation exists between the jejunum and the final segment of the small intestine, the ileum.

The **ileum** is the longest part of the small intestine, measuring about 1.8 m in length. It is thicker and more vascular and has more developed mucosal folds than the jejunum. The ileum joins the cecum, the first portion of the large intestine, at the **ileocecal sphincter** (or valve). The jejunum and ileum are tethered to the posterior abdominal wall by the mesentery. The large intestine frames these three parts of the small intestine.

Parasympathetic nerve fibres from the vagus nerve and sympathetic nerve fibres from the thoracic splanchnic nerve provide extrinsic innervation to the small intestine. The superior mesenteric artery is its main arterial supply. Veins run parallel to the arteries and drain into the superior mesenteric vein. Nutrient-rich blood from the small intestine is then carried to the liver via the hepatic portal vein.

Histology

The wall of the small intestine is composed of the same four layers typically present in the alimentary system. However, three features of the mucosa and submucosa are unique. These features, which increase the absorptive surface area of the small intestine more than 600-fold, include circular folds, villi, and microvilli (Figure 22.18).

These adaptations are most abundant in the proximal two-thirds of the small intestine, where the majority of absorption occurs.

Circular Folds

Also called a plica circulare, a **circular fold** is a deep ridge in the mucosa and submucosa. Beginning near the proximal part of the duodenum and ending near the middle of the ileum, these folds facilitate absorption. Their shape causes the chyme to spiral, rather than move in a straight line, through the small intestine. Spiraling slows the movement of chyme and provides the time needed for nutrients to be fully absorbed.

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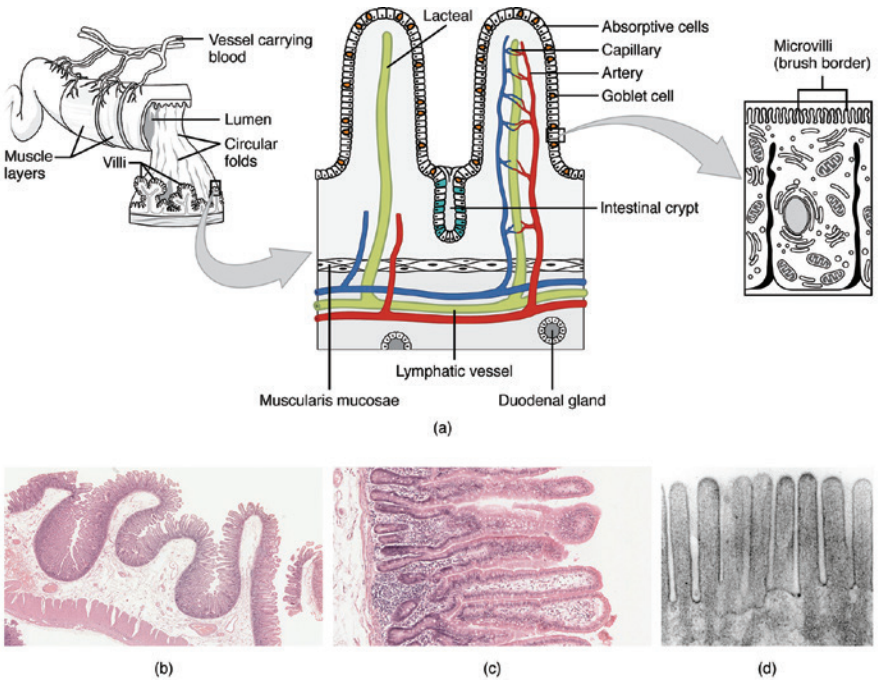


Figure 22.18 Histology of the Small Intestine. (a) The absorptive surface of the small intestine is vastly enlarged by the presence of circular folds, villi, and microvilli. (b) Micrograph of the circular folds. (c) Micrograph of the villi. (d) Electron micrograph of the microvilli. From left to right, LM × 56, LM × 508, EM × 196,000. (credit b-d: Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Villi

Within the circular folds are small (0.5–1 mm long) hairlike vascularized projections called **villi** (singular = villus) that give the mucosa a furry texture. There are about 20 to 40 villi per square millimetre, increasing the surface area of the epithelium tremendously. The mucosal epithelium, primarily composed of absorptive cells, covers the villi. In addition to muscle and connective tissue to support its structure, each villus contains a capillary bed composed of one arteriole and one venule, as well as a lymphatic capillary called a **lacteal**. The breakdown products of carbohydrates and proteins (sugars and amino acids) can enter the bloodstream directly, but lipid breakdown products are absorbed by the lacteals and transported to the bloodstream via the lymphatic system.

Microvilli

As their name suggests, **microvilli** (singular = microvillus) are much smaller (1 μm) than villi. They are cylindrical apical surface extensions of the plasma membrane of the mucosa's epithelial cells and are supported by microfilaments

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within those cells. Although their small size makes it difficult to see each microvillus, their combined microscopic appearance suggests a mass of bristles, which is termed the **brush border**. Fixed to the surface of the microvilli membranes are enzymes that finish digesting carbohydrates and proteins. There are an estimated 200 million microvilli per square millimetre of small intestine, greatly expanding the surface area of the plasma membrane and thus greatly enhancing absorption.

Intestinal Glands

In addition to the three specialized absorptive features just discussed, the mucosa between the villi is dotted with deep crevices that each lead into a tubular **intestinal gland** (crypt of Lieberkühn), which is formed by cells that line the crevices (see Figure 22.18). These produce **intestinal juice**, a slightly alkaline (pH 7.4 to 7.8) mixture of water and mucus. Each day, about 0.95 to 1.9 L are secreted in response to the distention of the small intestine or the irritating effects of chyme on the intestinal mucosa.

The submucosa of the duodenum is the only site of the complex mucus-secreting **duodenal glands** (Brunner's glands), which produce a bicarbonate-rich alkaline mucus that buffers the acidic chyme as it enters from the stomach.

The roles of the cells in the small intestinal mucosa are detailed in Table 22.6.

Intestinal MALT

The lamina propria of the small intestine mucosa is studded with quite a bit of MALT. In addition to solitary lymphatic nodules, aggregations of intestinal MALT, which are typically referred to as Peyer's patches, are concentrated in the distal ileum and serve to keep bacteria from entering the bloodstream. Peyer's patches are most prominent in young people and become less distinct as you age, which coincides with the general activity of our immune system.

Interactive Link 22.5

Watch this animation (http://oer.aupress.ca/oer-202505/22.5) that depicts the structure of the small intestine and, in particular, the villi. Epithelial cells continue the digestion and absorption of nutrients and transport these nutrients to the lymphatic and circulatory systems. In the small intestine, the products of food digestion are absorbed by different structures in the villi. Which structure absorbs and transports fats?

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Table 22.6 Cells of the Small Intestinal Mucosa

Cell type	Location in the mucosa	Function
Absorptive	Epithelium / intestinal glands	Digestion and absorption of nutrients in chyme
Goblet	Epithelium / intestinal glands	Secretion of mucus
Paneth	Intestinal glands	Secretion of the bactericidal enzyme lysozyme; phagocytosis
G cells	Intestinal glands of duodenum	Secretion of the hormone intestinal gastrin
I cells	Intestinal glands of duodenum	Secretion of the hormone cholecystokinin, which stimulates release of pancreatic juices and bile
K cells	Intestinal glands	Secretion of the hormone glucose-dependent insulinotropic peptide, which stimulates the release of insulin
M cells	Intestinal glands of duodenum and jejunum	Secretion of the hormone motilin, which accelerates gastric emptying, stimulates intestinal peristalsis, and stimulates production of pepsin
S cells	Intestinal glands	Secretion of the hormone secretin

Mechanical Digestion in the Small Intestine

The movement of intestinal smooth muscles includes both segmentation and a form of peristalsis called migrating motility complexes. The kind of peristaltic mixing waves seen in the stomach are not observed here.

If you could see into the small intestine when it was going through segmentation, it would look as if the contents were being shoved incrementally back and forth, as the rings of smooth muscle repeatedly contract and then relax. Segmentation in the small intestine does not force chyme through the tract. Instead, it combines the chyme with digestive juices and pushes food particles against the mucosa to be absorbed. The duodenum is where the most rapid segmentation occurs, at a rate of about 12 times per minute. In the ileum, segmentations are only about 8 times per minute (Figure 22.19).

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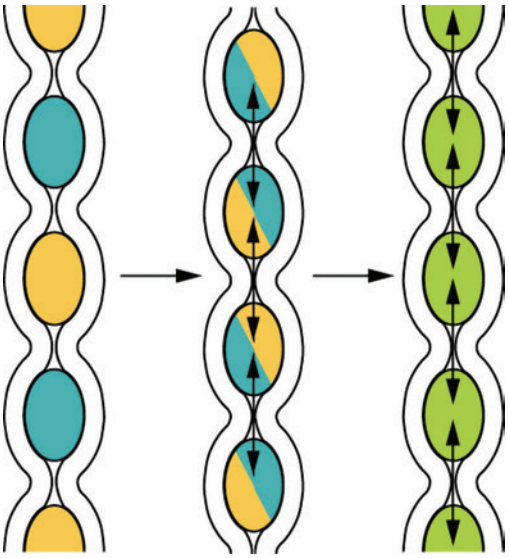


Figure 22.19 Segmentation. Segmentation separates chyme and then pushes it back together, mixing it and providing time for digestion and absorption.

When most of the chyme has been absorbed, the small intestinal wall becomes less distended. At this point, the localized segmentation process is replaced by transport movements. The duodenal mucosa secretes the hormone **motilin**, which initiates peristalsis in the form of a **migrating motility complex**. These complexes, which begin in the duodenum, force chyme through a short section of the small intestine and then stop. The next contraction begins a little bit farther down than the first, forces chyme a bit farther through the small intestine, then stops. These complexes move slowly down the small intestine, forcing chyme on the way, taking around 90 to 120 minutes to finally reach the end of the ileum. At this point, the process is repeated, starting in the duodenum.

The ileocecal valve, a sphincter, is usually in a constricted state, but when motility in the ileum increases, this sphincter relaxes, allowing food residue to enter the first portion of the large intestine, the cecum. Relaxation of the ileocecal sphincter is controlled by both nerves and hormones. First, digestive activity in the stomach provokes the **gastroileal reflex**, which increases the force of ileal segmentation. Second, the stomach releases the hormone gastrin, which enhances ileal motility, thus relaxing the ileocecal sphincter. After chyme passes through, backward pressure helps close the sphincter, preventing backflow into the ileum. Because of this reflex, your lunch is completely emptied from your stomach and small intestine by the time you eat your dinner. It takes about 3 to 5 hours for all chyme to leave the small intestine.

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Chemical Digestion in the Small Intestine

The digestion of proteins and carbohydrates, which partially occurs in the stomach, is completed in the small intestine with the aid of intestinal and pancreatic juices. Lipids arrive in the intestine largely undigested, so much of the focus here is on lipid digestion, which is facilitated by bile and the enzyme pancreatic lipase.

Moreover, intestinal juice combines with pancreatic juice to provide a liquid medium that facilitates absorption. The intestine is also where most water is absorbed, via osmosis. The small intestine's absorptive cells also synthesize digestive enzymes and then place them in the plasma membranes of the microvilli. This distinguishes the small intestine from the stomach; that is, enzymatic digestion occurs not only in the lumen but also on the luminal surfaces of the mucosal cells.

For optimal chemical digestion, chyme must be delivered from the stomach slowly and in small amounts. This is because chyme from the stomach is typically hypertonic, and if large quantities were forced all at once into the small intestine, the resulting osmotic water loss from the blood into the intestinal lumen would result in potentially life-threatening low blood volume. In addition, continued digestion requires an upward adjustment of the low pH of stomach chyme, along with rigorous mixing of the chyme with bile and pancreatic juices. Both processes take time, so the pumping action of the pylorus must be carefully controlled to prevent the duodenum from being overwhelmed with chyme.

The Large Intestine

The **large intestine** is the terminal part of the alimentary canal. The primary function of this organ is to finish absorption of nutrients and water, synthesize certain vitamins, form feces, and eliminate feces from the body.

Structure

The large intestine runs from the appendix to the anus. It frames the small intestine on three sides. Despite its being about one-half as long as the small intestine, it is called large because it is more than twice the diameter of the small intestine, about 7.5 cm.

Subdivisions

The large intestine is subdivided into four main regions: the cecum, the colon, the rectum, and the anus. The ileocecal valve, located at the opening between the ileum and the large intestine, controls the flow of chyme from the small intestine to the large intestine.

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Cecum

The first part of the large intestine is the **cecum**, a sac-like structure that is suspended inferior to the ileocecal valve. It is about 6 cm (2.4 in) long, receives the contents of the ileum, and continues the absorption of water and salts.

The **appendix** (or vermiform appendix) is a winding tube that attaches to the cecum. Although the 7.6 cm (3 in) long appendix contains lymphoid tissue, suggesting an immunologic function, this organ is generally considered vestigial. However, at least one recent report postulates a survival advantage conferred by the appendix: In diarrheal illness, the appendix may serve as a bacterial reservoir to repopulate the enteric bacteria for those surviving the initial phases of the illness. Moreover, its twisted anatomy provides a haven for the accumulation and multiplication of enteric bacteria. The **mesoappendix**, the mesentery of the appendix, tethers it to the mesentery of the ileum.

Colon

The cecum blends seamlessly with the **colon**. Upon entering the colon, the food residue first travels up the **ascending colon** on the right side of the abdomen. At the inferior surface of the liver, the colon bends to form the **right colic flexure** (hepatic flexure) and becomes the **transverse colon**. The region defined as the hindgut begins with the last third of the transverse colon and continues on. Food residue passing through the transverse colon travels across to the left side of the abdomen, where the colon angles sharply immediately inferior to the spleen, at the **left colic flexure** (splenic flexure). From there, food residue passes through the **descending colon**, which runs down the left side of the posterior abdominal wall. After entering the pelvis inferiorly, it becomes the s-shaped **sigmoid colon**, which extends medially to the midline (Figure 22.20). The ascending and descending colon and the rectum (discussed next) are located in the retroperitoneum. The transverse and sigmoid colon are tethered to the posterior abdominal wall by the mesocolon.

Rectum

Food residue leaving the sigmoid colon enters the **rectum** in the pelvic cavity, near the third sacral vertebra. The final 20.3 cm (8 in) of the alimentary canal, the rectum extends anterior to the sacrum and coccyx. This structure follows the curved contour of the sacrum and has three lateral bends that create a trio of internal transverse folds called the **rectal valves**. These valves help separate the feces from gas to prevent the simultaneous passage of feces and gas.

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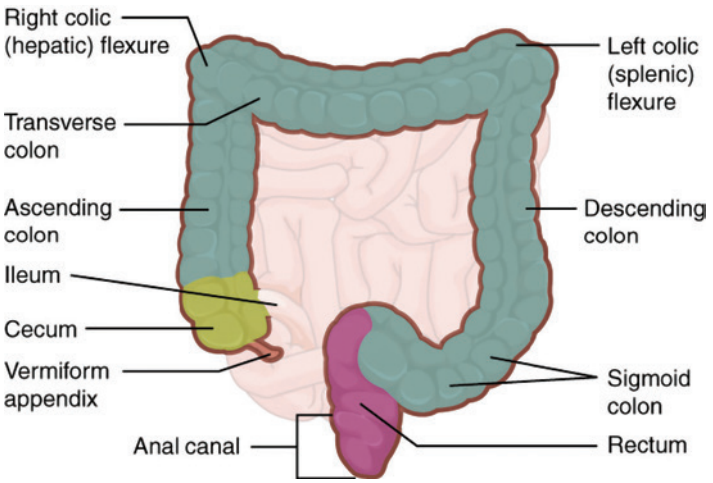


Figure 22.20 Large Intestine. The large intestine includes the cecum, colon, and rectum.

Anal Canal

Finally, food residue reaches the last part of the large intestine, the **anal canal**, which is located in the perineum, completely outside of the abdominopelvic cavity. This 3.8–5 cm (1.5–2 in) long structure opens to the exterior of the body at the anus. The anal canal includes two sphincters. The **internal anal sphincter** is made of smooth muscle, and its contractions are involuntary. The **external anal sphincter** is made of skeletal muscle, which is under voluntary control. Except when defecating, both usually remain closed.

Histology

There are several notable differences between the walls of the large and small intestines (Figure 22.21). For example, few enzyme-secreting cells are found in the wall of the large intestine, and there are no circular folds or villi. Other than in the anal canal, the mucosa of the colon is simple columnar epithelium made mostly of enterocytes (absorptive cells) and goblet cells. In addition, the wall of the large intestine has far more intestinal glands, which contain a vast population of enterocytes and goblet cells. These goblet cells secrete mucus that eases the movement of feces and protects the intestine from the effects of the acids and gases produced by enteric bacteria. The enterocytes absorb water and salts as well as vitamins produced by your intestinal bacteria.

Anatomy

Three features are unique to the large intestine: teniae coli, haustra, and epiploic appendages (Figure 22.22). The **teniae coli** are three bands of smooth muscle that make up the longitudinal muscle layer of the muscularis of the

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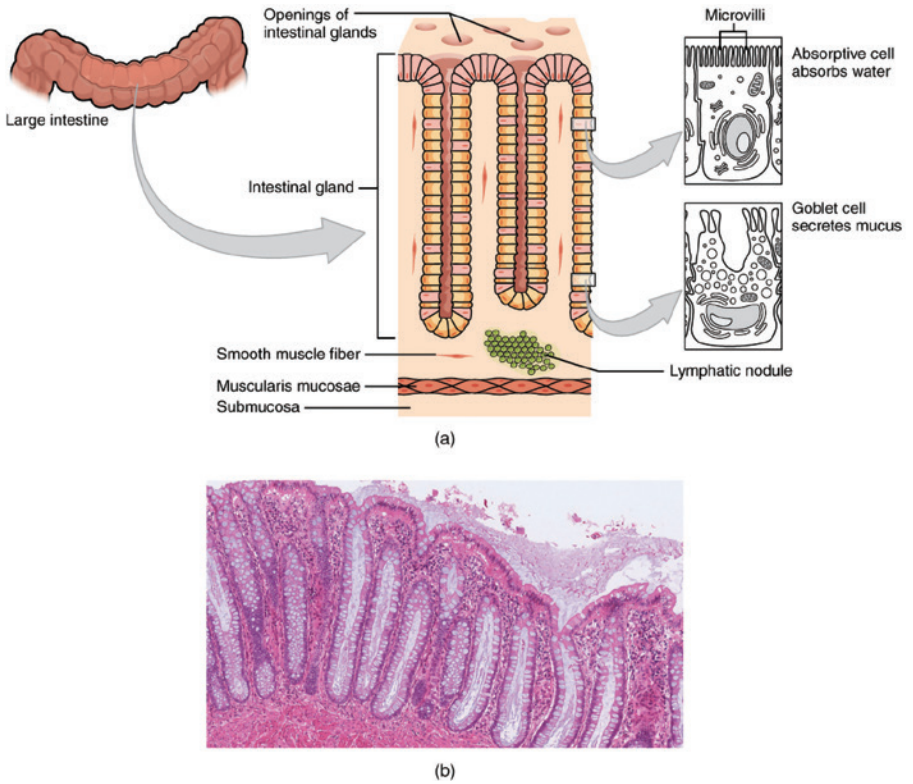


Figure 22.21 Histology of the Large Intestine. (a) The histologies of the large intestine and small intestine (not shown) are adapted for the digestive functions of each organ. (b) This micrograph shows the colon's simple columnar epithelium and goblet cells. LM × 464. (credit b: Micrograph provided by the Regents of University of Michigan Medical School © 2012)

large intestine, except at its terminal end. Tonic contractions of the teniae coli bunch up the colon into a succession of pouches called **haustra** (singular = haustrum), which are responsible for the wrinkled appearance of the colon. Attached to the teniae coli are small, fat-filled sacs of visceral peritoneum called **epiploic appendages**. The purpose of these is unknown. Although the rectum and anal canal have neither teniae coli nor haustra, they do have well-developed layers of muscularis that create the strong contractions needed for defecation.

The stratified squamous epithelial mucosa of the anal canal connects to the skin on the outside of the anus. This mucosa varies considerably from that of the rest of the colon to accommodate the high level of abrasion as feces pass through. The anal canal's mucous membrane is organized into longitudinal folds, each called an **anal column**, which house a grid of arteries and veins. Two superficial venous plexuses are found in the anal canal: one within the anal columns and one at the anus.

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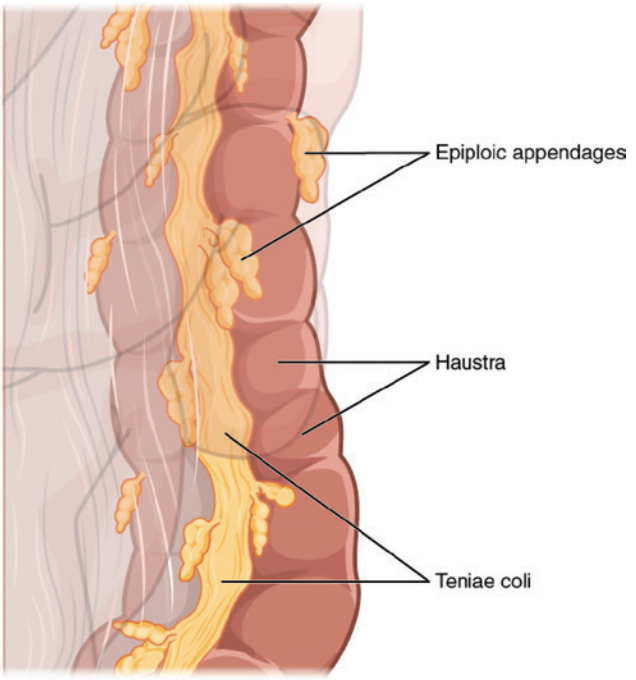


Figure 22.22 Teniae Coli, Haustra, and Epiploic Appendages.

Depressions between the anal columns, each called an **anal sinus**, secrete mucus that facilitates defecation. The pectinate line (or dentate line) is a horizontal, jagged band that runs circumferentially just below the level of the anal sinuses and represents the junction between the hindgut and external skin. The mucosa above this line is fairly insensitive, whereas the area below is very sensitive. The resulting difference in pain threshold is due to the fact that the upper region is innervated by visceral sensory fibres, and the lower region is innervated by somatic sensory fibres.

Bacterial Flora

Most bacteria that enter the alimentary canal are killed by lysozyme, defensins, HCl, or protein-digesting enzymes. However, trillions of bacteria live within the large intestine and are referred to as the **bacterial flora**. Most of the more than 700 species of these bacteria are nonpathogenic commensal organisms that cause no harm as long as they stay in the gut lumen. In fact, many facilitate chemical digestion and absorption, and some synthesize certain vitamins, mainly biotin, pantothenic acid, and vitamin K. Some are linked to increased immune response. A refined system prevents these bacteria from crossing the mucosal barrier. First, peptidoglycan, a component of bacterial cell walls, activates the release of chemicals by the mucosa's epithelial cells, which draft

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immune cells, especially dendritic cells, into the mucosa. Dendritic cells open the tight junctions between epithelial cells and extend probes into the lumen to evaluate the microbial antigens. The dendritic cells with antigens then travel to neighbouring lymphoid follicles in the mucosa where T cells inspect for antigens. This process triggers an IgA-mediated response, if warranted, in the lumen that blocks the commensal organisms from infiltrating the mucosa and setting off a far greater, widespread systematic reaction.

Digestive Functions of the Large Intestine

The residue of chyme that enters the large intestine contains few nutrients except water, which is reabsorbed as the residue lingers in the large intestine, typically for 12 to 24 hours. Thus, it may not surprise you that the large intestine can be completely removed without significantly affecting digestive functioning. For example, in severe cases of inflammatory bowel disease, the large intestine can be removed by a procedure known as a colectomy.

Often, a new fecal pouch can be crafted from the small intestine and sutured to the anus, but if not, an ileostomy can be created by bringing the distal ileum through the abdominal wall, allowing the watery chyme to be collected in a bag-like adhesive appliance.

Mechanical Digestion

In the large intestine, mechanical digestion begins when chyme moves from the ileum into the cecum, an activity regulated by the ileocecal sphincter. Right after you eat, peristalsis in the ileum forces chyme into the cecum. When the cecum is distended with chyme, contractions of the ileocecal sphincter strengthen. Once chyme enters the cecum, colon movements begin.

Mechanical digestion in the large intestine includes a combination of three types of movements. The presence of food residues in the colon stimulates a slow-moving **haustral contraction**. This type of movement involves sluggish segmentation, primarily in the transverse and descending colons. When a haustrum is distended with chyme, its muscle contracts, pushing the residue into the next haustrum. These contractions occur about every 30 minutes, and each last about 1 minute. These movements also mix the food residue, which helps the large intestine absorb water. The second type of movement is peristalsis, which, in the large intestine, is slower than in the more proximal portions of the alimentary canal. The third type is a **mass movement**. These strong waves start midway through the transverse colon and quickly force the contents toward the rectum. Mass movements usually occur three or four times per day, either while you eat or immediately afterward. Distention in the stomach and the breakdown products of digestion in the small intestine provoke

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the **gastrocolic reflex**, which increases motility, including mass movements, in the colon. Fibre in the diet both softens the stool and increases the power of colonic contractions, optimizing the activities of the colon.

Chemical Digestion

Although the glands of the large intestine secrete mucus, they do not secrete digestive enzymes. Therefore, chemical digestion in the large intestine occurs exclusively because of bacteria in the lumen of the colon. Through the process of saccharolytic fermentation, bacteria break down some of the remaining carbohydrates. This results in the discharge of hydrogen, carbon dioxide, and methane gases that create **flatus** (gas) in the colon; flatulence is excessive flatus. Each day, up to 1,500 mL of flatus is produced in the colon. More is produced when you eat foods such as beans, which are rich in otherwise indigestible sugars and complex carbohydrates like soluble dietary fibre.

Absorption, Feces Formation, and Defecation

The small intestine absorbs about 90 percent of the water you ingest (either as liquid or within solid food). The large intestine absorbs most of the remaining water, a process that converts the liquid chyme residue into semisolid **feces** ("stool"). Feces are composed of undigested food residues, unabsorbed digested substances, millions of bacteria, old epithelial cells from the GI mucosa, inorganic salts, and enough water to let it pass smoothly out of the body. Of every 500 mL of food residue that enters the cecum each day, about 150 mL become feces.

Feces are eliminated through contractions of the rectal muscles. You help this process by a voluntary procedure called **Valsalva's maneuver**, in which you increase intra-abdominal pressure by contracting your diaphragm and abdominal wall muscles and closing your glottis.

The process of defecation begins when mass movements force feces from the colon into the rectum, stretching the rectal wall and provoking the defecation reflex, which eliminates feces from the rectum. This parasympathetic reflex is mediated by the spinal cord. It contracts the sigmoid colon and rectum, relaxes the internal anal sphincter, and initially contracts the external anal sphincter. The presence of feces in the anal canal sends a signal to the brain, which gives you the choice of voluntarily opening the external anal sphincter (defecating) or keeping it temporarily closed. If you decide to delay defecation, it takes a few seconds for the reflex contractions to stop and the rectal walls to relax. The next mass movement will trigger additional defecation reflexes until you defecate.

If defecation is delayed for an extended time, additional water is absorbed, making the feces firmer and potentially leading to constipation. On the other

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hand, if the waste matter moves too quickly through the intestines, not enough water is absorbed, and diarrhea can result. This can be caused by the ingestion of foodborne pathogens. In general, diet, health, and stress determine the frequency of bowel movements. The number of bowel movements varies greatly between individuals, ranging from two or three per day to three or four per week.

Interactive Link 22.6

By watching this animation (http://oer.aupress.ca/oer-202505/22.6) you will see that for the various food groups—proteins, fats, and carbohydrates—digestion begins in different parts of the digestion system, though all end in the same place. Of the three major food classes (carbohydrates, fats, and proteins), which is digested in the mouth, the stomach, and the small intestine?

22.6 Accessory Organs in Digestion: The Liver, Pancreas, and Gallbladder

Learning Objectives

By the end of this section, you will be able to:

- State the main digestive roles of the liver, pancreas, and gallbladder
- Identify three main features of liver histology that are critical to its function
- Discuss the composition and function of bile
- Identify the major types of enzymes and buffers present in pancreatic juice

Chemical digestion in the small intestine relies on the activities of three accessory digestive organs: the liver, pancreas, and gallbladder (Figure 22.23). The digestive role of the liver is to produce bile and export it to the duodenum. The gallbladder primarily stores, concentrates, and releases bile. The pancreas produces pancreatic juice, which contains digestive enzymes and bicarbonate ions, and delivers it to the duodenum.

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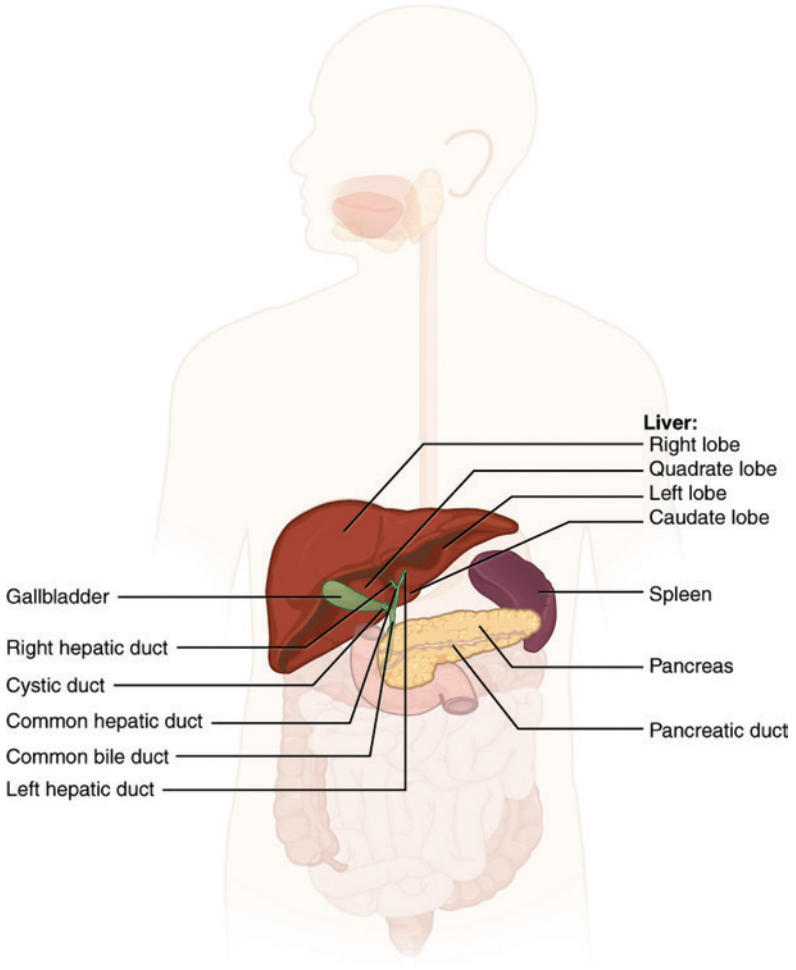


Figure 22.23 Accessory Organs. The liver, pancreas, and gallbladder are considered accessory digestive organs, but their roles in the digestive system are vital.

The Liver

The **liver** is the largest gland in the body, weighing about three pounds in an adult. It is also one of the most important organs. In addition to being an accessory digestive organ, it plays a number of roles in metabolism and regulation. The liver lies inferior to the diaphragm in the right upper quadrant of the abdominal cavity and receives protection from the surrounding ribs.

The liver is divided into two primary lobes: a large right lobe and a much smaller left lobe. In the right lobe, some anatomists also identify an inferior quadrate lobe and a posterior caudate lobe, which are defined by internal features. The liver is connected to the abdominal wall and diaphragm by five peritoneal folds referred to as ligaments. These are the falciform ligament, the

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coronary ligament, two lateral ligaments, and the ligamentum teres hepatis. The falciform ligament and ligamentum teres hepatis are actually remnants of the umbilical vein and separate the right and left lobes anteriorly. The lesser omentum tethers the liver to the lesser curvature of the stomach.

The **porta hepatis** ("gate to the liver") is where the **hepatic artery** and **hepatic portal vein** enter the liver. These two vessels, along with the common hepatic duct, run behind the lateral border of the lesser omentum on the way to their destinations. The hepatic artery delivers oxygenated blood from the heart to the liver. The hepatic portal vein delivers partially deoxygenated blood containing nutrients absorbed from the small intestine and actually supplies more oxygen to the liver than do the much smaller hepatic arteries (Figure 22.24). In addition to nutrients, drugs and toxins are also absorbed. After processing the blood-borne nutrients and toxins, the liver releases nutrients needed by other cells back into the blood, which drains into the central vein and then through the hepatic vein to the inferior vena cava. With this hepatic portal circulation, all blood from the alimentary canal passes through the liver. This largely explains why the liver is the most common site for the metastasis of cancers that originate in the alimentary canal.

Histology

The liver has three main components: hepatocytes, bile canaliculi, and hepatic sinusoids. A **hepatocyte** is the liver's main cell type, accounting for around 80 percent of the liver's volume, as shown in Figure 22.24. These cells play a role in a wide variety of secretory, metabolic, and endocrine functions. Plates of hepatocytes called hepatic laminae radiate outward from the portal vein in each **hepatic lobule**.

Between adjacent hepatocytes, grooves in the cell membranes provide room for each **bile canaliculus** (plural = canaliculi). These small ducts accumulate the bile produced by hepatocytes. From here, bile flows first into bile ductules and then into bile ducts. The bile ducts unite to form the larger right and left hepatic ducts, which themselves merge and exit the liver as the **common hepatic duct**. This duct then joins with the cystic duct from the gallbladder, forming the **common bile duct** through which bile flows into the small intestine, as shown in Figure 22.26.

A **hepatic sinusoid** is an open, porous blood space formed by fenestrated capillaries from nutrient-rich hepatic portal veins and oxygen-rich hepatic arteries. Hepatocytes are tightly packed around the fenestrated endothelium of these spaces, giving them easy access to the blood. From their central position, hepatocytes process the nutrients, toxins, and waste materials carried

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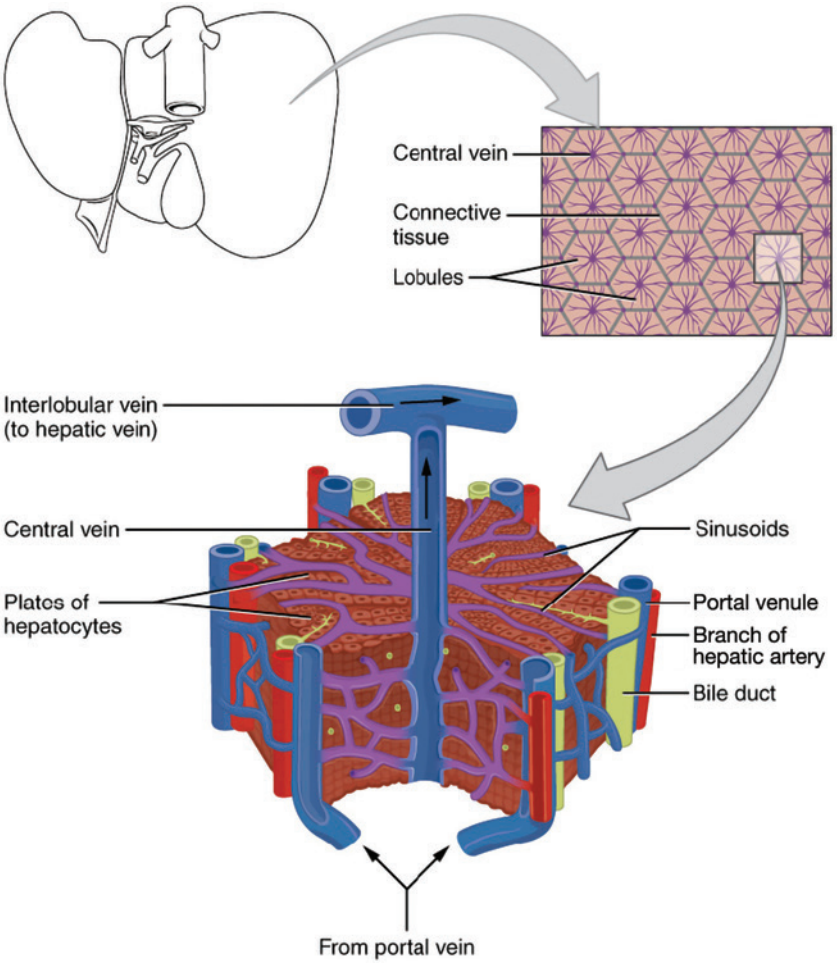


Figure 22.24 Microscopic Anatomy of the Liver. The liver receives oxygenated blood from the hepatic artery and nutrient-rich deoxygenated blood from the hepatic portal vein.

by the blood. Materials such as bilirubin are processed and excreted into the bile canaliculi. Other materials, including proteins, lipids, and carbohydrates, are processed and secreted into the sinusoids or just stored in the cells until called upon. The hepatic sinusoids combine and send blood to a **central vein**. Blood then flows through a **hepatic vein** into the inferior vena cava. The hepatic sinusoids also contain star-shaped **reticuloendothelial cells** (Kupffer cells), phagocytes that remove dead red and white blood cells, bacteria, and other foreign material that enter the sinusoids. The **portal triad** is a distinctive arrangement around the perimeter of hepatic lobules, consisting of three basic structures: a bile duct, a hepatic artery branch, and a hepatic portal vein branch.

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Bile

Recall that lipids are hydrophobic—that is, they do not dissolve in water. Thus, before they can be digested in the watery environment of the small intestine, large lipid globules must be broken down into smaller lipid globules, a process called emulsification. **Bile** is a mixture secreted by the liver to accomplish the emulsification of lipids in the small intestine.

Hepatocytes secrete about 1 L of bile each day. A yellow-brown or yellow-green alkaline solution (pH 7.6 to 8.6), bile is a mixture of water, bile salts, bile pigments, phospholipids (such as lecithin), electrolytes, cholesterol, and triglycerides. The components most critical to emulsification are bile salts and phospholipids, which have a nonpolar (hydrophobic) region as well as a polar (hydrophilic) region. The hydrophobic region interacts with the large lipid molecules, whereas the hydrophilic region interacts with the watery chyme in the intestine. This results in the large lipid globules being pulled apart into many tiny lipid fragments of about 1 μm in diameter. This change dramatically increases the surface area available for lipid-digesting enzyme activity. This is the same way dish soap works on fats mixed with water.

Bile salts act as emulsifying agents, so they are also important for the absorption of digested lipids. While most constituents of bile are eliminated in feces, bile salts are reclaimed by the **enterohepatic circulation**. Once bile salts reach the ileum, they are absorbed and returned to the liver in the hepatic portal blood. The hepatocytes then excrete the bile salts into newly formed bile. Thus, this precious resource is recycled.

Bilirubin, the main bile pigment, is a waste product produced when the spleen removes old or damaged red blood cells from the circulation. These breakdown products, including proteins, iron, and toxic bilirubin, are transported to the liver via the splenic vein of the hepatic portal system. In the liver, proteins and iron are recycled, whereas bilirubin is excreted in the bile. It accounts for the green colour of bile. Bilirubin is eventually transformed by intestinal bacteria into stercobilin, a brown pigment that gives your stool its characteristic colour! In some disease states, bile does not enter the intestine, resulting in white (“acholic”) stool with a high fat content, since virtually no fats are broken down or absorbed.

Hepatocytes work nonstop, but bile production increases when fatty chyme enters the duodenum and stimulates the secretion of the gut hormone secretin. Between meals, bile is produced but conserved. The valve-like hepatopancreatic ampulla closes, allowing bile to divert to the gallbladder, where it is concentrated and stored until the next meal.

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Interactive Link 22.7

Watch this video (http://oer.aupress.ca/oer-202505/22.7) to see the structure of the liver and how this structure supports the functions of the liver, including the processing of nutrients, toxins, and wastes. At rest, about 1,500 mL of blood per minute flow through the liver. What percentage of this blood flow comes from the hepatic portal system?

The Pancreas

The soft, oblong, glandular **pancreas** lies transversely in the retroperitoneum behind the stomach. Its head is nestled into the "c-shaped" curvature of the duodenum with the body extending to the left about 15.2 cm (6 in) and ending as a tapering tail in the hilum of the spleen. It is a curious mix of exocrine (secreting digestive enzymes) and endocrine (releasing hormones into the blood) functions (Figure 22.25).

The exocrine part of the pancreas arises as little grape-like cell clusters, each called an **acinus** (plural = acini), located at the terminal ends of pancreatic ducts. These acinar cells secrete enzyme-rich **pancreatic juice** into tiny merging ducts that form two dominant ducts. The larger **pancreatic duct** fuses with the common bile duct (carrying bile from the liver and gallbladder) just before entering the duodenum via a common opening (the hepatopancreatic ampulla). The smooth muscle sphincter of the hepatopancreatic ampulla controls the release of pancreatic juice and bile into the small intestine. The second and smaller pancreatic duct, the **accessory duct** (duct of Santorini), runs from the pancreas directly into the duodenum, approximately 2.5 cm above the hepatopancreatic ampulla. When present, it is a persistent remnant of pancreatic development.

Scattered through the sea of exocrine acini are small islands of endocrine cells, the islets of Langerhans. These vital cells produce the hormones pancreatic polypeptide, insulin, glucagon, and somatostatin.

Pancreatic Juice

The pancreas produces over a litre of pancreatic juice each day. Unlike bile, it is clear and composed mostly of water along with some salts, sodium bicarbonate, and several digestive enzymes. Sodium bicarbonate is responsible for the slight alkalinity of pancreatic juice (pH 7.1 to 8.2), which serves to buffer the acidic gastric juice in chyme, inactivate pepsin from the stomach, and create an optimal environment for the activity of pH-sensitive digestive enzymes in the small intestine. Pancreatic enzymes are active in the digestion of sugars, proteins, and fats.

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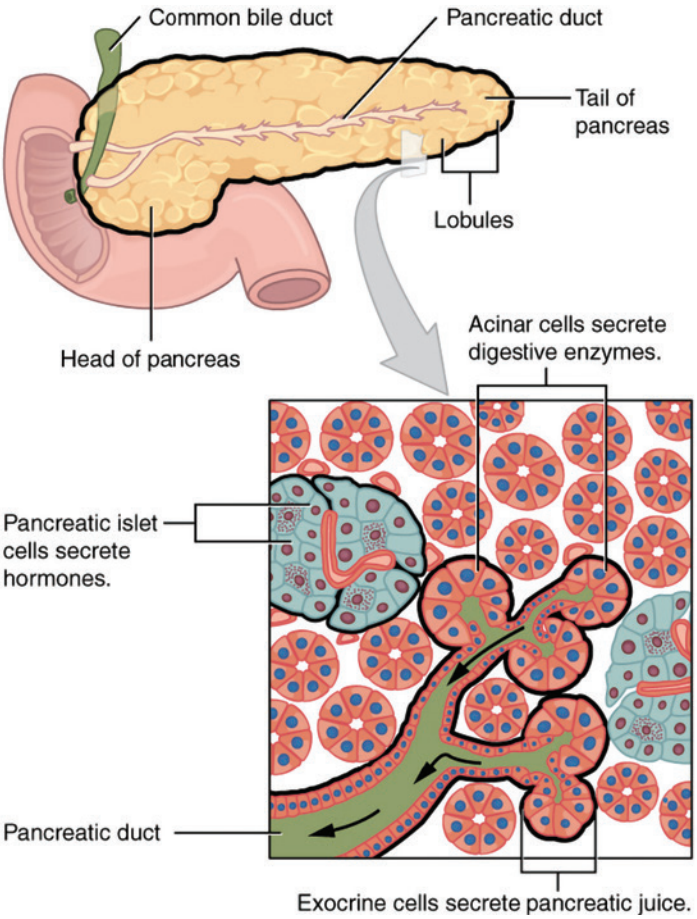


Figure 22.25 Exocrine and Endocrine Pancreas. The pancreas has a head, a body, and a tail. It delivers pancreatic juice to the duodenum through the pancreatic duct.

The pancreas produces protein-digesting enzymes in their inactive forms. These enzymes are activated in the duodenum. If produced in an active form, they would digest the pancreas (which is exactly what occurs in the disease pancreatitis). The intestinal brush border enzyme **enteropeptidase** (**enterokinase**) stimulates the activation of trypsin from trypsinogen of the pancreas, which in turn changes the pancreatic enzymes procarboxypeptidase and chymotrypsinogen into their active forms, carboxypeptidase and chymotrypsin.

The enzymes that digest starch (amylase), fat (lipase), and nucleic acids (nuclease) are secreted in their active forms, since they do not attack the pancreas as do the protein-digesting enzymes.

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Pancreatic Secretion

Regulation of pancreatic secretion is the job of hormones and the parasympathetic nervous system. The entry of acidic chyme into the duodenum stimulates the release of secretin, which in turn causes the duct cells to release bicarbonate-rich pancreatic juice. The presence of proteins and fats in the duodenum stimulates the secretion of CCK, which then stimulates the acini to secrete enzyme-rich pancreatic juice and enhances the activity of secretin. Parasympathetic regulation occurs mainly during the cephalic and gastric phases of gastric secretion, when vagal stimulation prompts the secretion of pancreatic juice.

Usually, the pancreas secretes just enough bicarbonate to counterbalance the amount of HCl produced in the stomach. Hydrogen ions enter the blood when bicarbonate is secreted by the pancreas. Thus, the acidic blood draining from the pancreas neutralizes the alkaline blood draining from the stomach, maintaining the pH of the venous blood that flows to the liver.

The Gallbladder

The **gallbladder** is 8–10 cm (~3–4 in) long and is nested in a shallow area on the posterior aspect of the right lobe of the liver. This muscular sac stores, concentrates, and when stimulated, propels the bile into the duodenum via the common bile duct. It is divided into three regions. The fundus is the widest portion and tapers medially into the body, which in turn narrows to become the neck. The neck angles slightly superiorly as it approaches the hepatic duct. The cystic duct is 1–2 cm (less than 1 in) long and turns inferiorly as it bridges the neck and hepatic duct.

The simple columnar epithelium of the gallbladder mucosa is organized in rugae, similar to those of the stomach. There is no submucosa in the gallbladder wall. The wall's middle muscular coat is made of smooth muscle fibres. When these fibres contract, the gallbladder's contents are ejected through the **cystic duct** and into the bile duct (Figure 22.26). Visceral peritoneum reflected from the liver capsule holds the gallbladder against the liver and forms the outer coat of the gallbladder. The gallbladder's mucosa absorbs water and ions from bile, concentrating it up to 10-fold.

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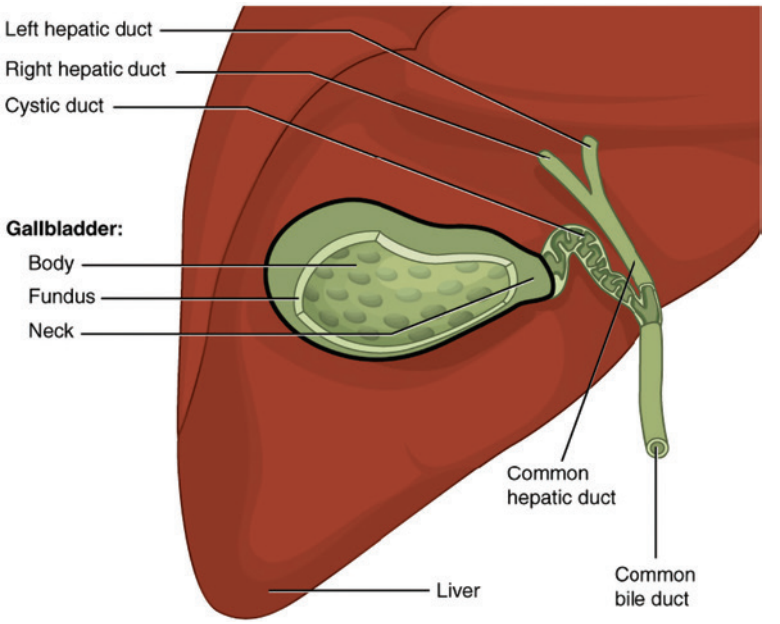


Figure 22.26 Gallbladder. The gallbladder stores and concentrates bile and releases it into the two-way cystic duct when it is needed by the small intestine.

22.7 Chemical Digestion and Absorption: A Closer Look

Learning Objectives

By the end of this section, you will be able to:

- Identify the locations and primary secretions involved in the chemical digestion of carbohydrates, proteins, lipids, and nucleic acids
- Compare and contrast absorption of the hydrophilic and hydrophobic nutrients

As you have learned, the process of mechanical digestion is relatively simple. It involves the physical breakdown of food but does not alter its chemical makeup. Chemical digestion, on the other hand, is a complex process that reduces food into its chemical building blocks, which are then absorbed to nourish the cells of the body (Figure 22.27). In this section, you will look more closely at the processes of chemical digestion and absorption.

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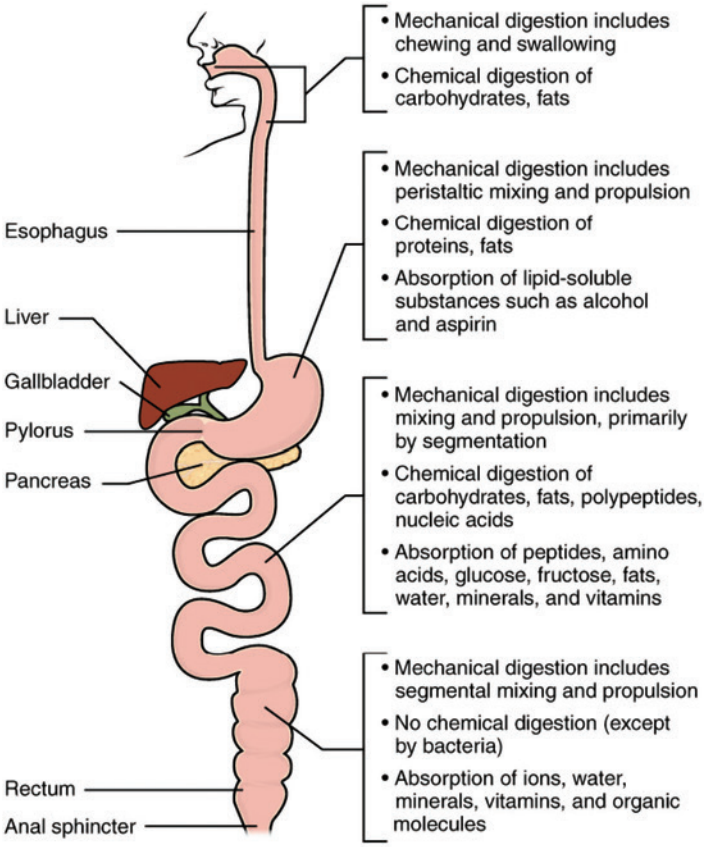


Figure 22.27 Digestion and Absorption. Digestion begins in the mouth and continues as food travels through the small intestine. Most absorption occurs in the small intestine.

Chemical Digestion

Large food molecules (for example, proteins, lipids, nucleic acids, and starches) must be broken down into subunits that are small enough to be absorbed by the lining of the alimentary canal. This is accomplished by enzymes through hydrolysis.

Carbohydrate Digestion

The average American diet is about 50 percent carbohydrates, which may be classified according to the number of monomers they contain of simple sugars (monosaccharides and disaccharides) and/or complex sugars (polysaccharides). Glucose, galactose, and fructose are the three monosaccharides that are commonly consumed and are readily absorbed. Your digestive system is also able to break down the disaccharide sucrose (regular table sugar: glucose + fructose), lactose (milk sugar: glucose + galactose), and maltose (grain sugar: glucose + glucose) and the polysaccharides glycogen and starch (chains of

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monosaccharides). Your bodies do not produce enzymes that can break down most fibrous polysaccharides, such as cellulose. While indigestible polysaccharides do not provide any nutritional value, they do provide dietary fibre, which helps propel food through the alimentary canal.

The chemical digestion of starches begins in the mouth. In the small intestine, **pancreatic amylase** does the "heavy lifting" for starch and carbohydrate digestion (Figure 22.28). After amylases break down starch into smaller fragments, the brush border enzyme **α-dextrinase** starts working on **α-dextrin**, breaking off one glucose unit at a time. Three brush border enzymes hydrolyze sucrose, lactose, and maltose into monosaccharides. **Sucrase** splits sucrose into one molecule of fructose and one molecule of glucose; **maltase** breaks down maltose and maltotriose into two and three glucose molecules, respectively; and **lactase** breaks down lactose into one molecule of glucose and one molecule of galactose. Insufficient lactase can lead to lactose intolerance.

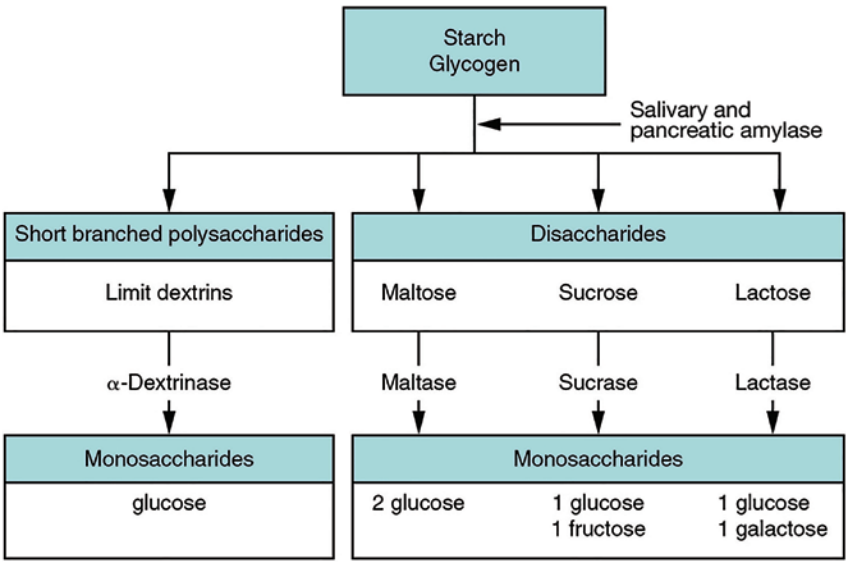


Figure 22.28 Carbohydrate Digestion Flowchart. Carbohydrates are broken down into their monomers in a series of steps.

Protein Digestion

Proteins are polymers composed of amino acids linked by peptide bonds to form long chains. Digestion reduces them to their constituent amino acids. You usually consume about 15 to 20 percent of your total calorie intake as protein. The digestion of protein starts in the stomach, where HCl and pepsin break proteins into smaller polypeptides, which then travel to the small intestine (Figure 22.29).

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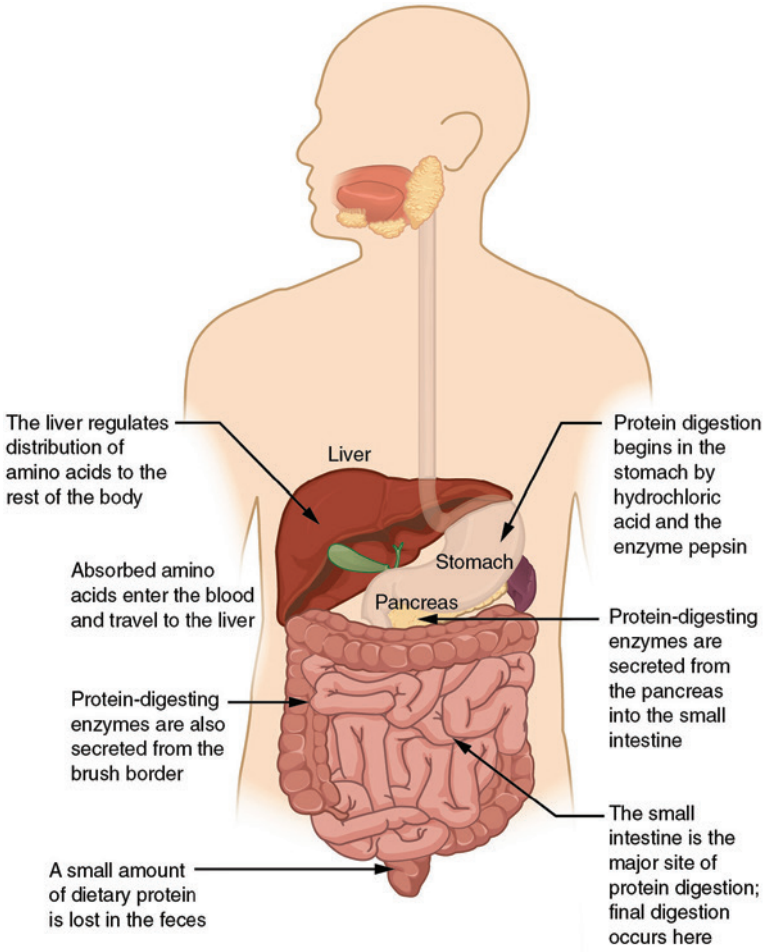


Figure 22.29 Digestion of Protein. The digestion of protein begins in the stomach and is completed in the small intestine.

Chemical digestion in the small intestine is continued by pancreatic enzymes, including chymotrypsin and trypsin, each of which act on specific bonds in amino acid sequences. At the same time, the cells of the brush border secrete enzymes such as **aminopeptidase** and **dipeptidase**, which further break down peptide chains. This results in molecules small enough to enter the bloodstream.

Lipid Digestion

A healthy diet limits lipid intake to 35 percent of total calorie intake. The most common dietary lipids are triglycerides, which are made up of a glycerol molecule bound to three fatty acid chains. Small amounts of dietary cholesterol and phospholipids are also consumed.

The three lipases responsible for lipid digestion are lingual lipase, gastric lipase, and **pancreatic lipase**. However, because the pancreas is the only

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consequential source of lipase, virtually all lipid digestion occurs in the small intestine. Pancreatic lipase breaks down each triglyceride into two free fatty acids and a monoglyceride. The fatty acids include both short-chain (less than 10 to 12 carbons) and long-chain fatty acids.

Nucleic Acid Digestion

The nucleic acids DNA and RNA are found in most of the foods you eat. Two types of **pancreatic nuclease** are responsible for their digestion: **deoxyribonuclease**, which digests DNA, and **ribonuclease**, which digests RNA. The nucleotides produced by this digestion are further broken down by two intestinal brush border enzymes (nucleosidase and phosphatase) into pentoses, phosphates, and nitrogenous bases, which can be absorbed through the alimentary canal wall. The large food molecules that must be broken down into subunits are summarized in Table 22.7.

Table 22.7 Absorbable Food Substances

Source	Substance
Carbohydrates	Monosaccharides: glucose, galactose, and fructose
Proteins	Single amino acids, dipeptides, and tripeptides
Triglycerides	Monoacylglycerides, glycerol, and free fatty acids
Nucleic acids	Pentose sugars, phosphates, and nitrogenous bases

Absorption

The mechanical and digestive processes have one goal: to convert food into molecules small enough to be absorbed by the epithelial cells of the intestinal villi. The absorptive capacity of the alimentary canal is almost endless. Each day, the alimentary canal processes up to 10 L of food, liquids, and GI secretions, yet less than 1 L enters the large intestine. Almost all ingested food, 80 percent of electrolytes, and 90 percent of water are absorbed in the small intestine. Although the entire small intestine is involved in the absorption of water and lipids, most absorption of carbohydrates and proteins occurs in the jejunum. Notably, bile salts and vitamin B_{12} are absorbed in the terminal ileum. By the time chyme passes from the ileum into the large intestine, it is essentially indigestible food residue (mainly plant fibres like cellulose), some water, and millions of bacteria (Figure 22.30).

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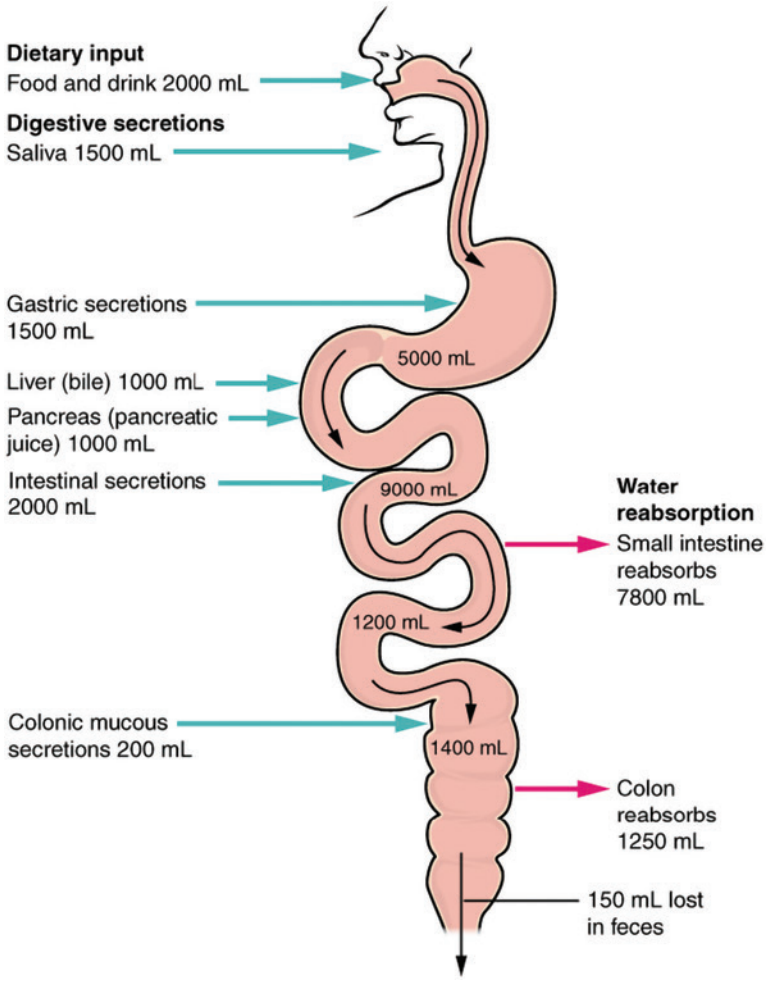


Figure 22.30 Digestive Secretions and Absorption of Water per Day. Absorption is a complex process in which nutrients from digested food are harvested.

Absorption can occur through five mechanisms: (1) active transport, (2) passive diffusion, (3) facilitated diffusion, (4) cotransport (or secondary active transport), and (5) endocytosis. As you will recall from Chapter 3, active transport refers to the movement of a substance across a cell membrane going from an area of lower concentration to an area of higher concentration (up the concentration gradient). In this type of transport, proteins within the cell membrane act as "pumps," using cellular energy (ATP) to move the substance. Passive diffusion refers to the movement of substances from an area of higher concentration to an area of lower concentration, while facilitated diffusion refers to the movement of substances from an area of higher to an area of lower concentration using a carrier protein in the cell membrane. Cotransport uses

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the movement of one molecule through the membrane from higher to lower concentration to power the movement of another from lower to higher. Finally, endocytosis is a transportation process in which the cell membrane engulfs material. It requires energy, generally in the form of ATP.

Because the cell's plasma membrane is made up of hydrophobic phospholipids, water-soluble nutrients must use transport molecules embedded in the membrane to enter cells. Moreover, substances cannot pass between the epithelial cells of the intestinal mucosa because these cells are bound together by tight junctions. Thus, substances can only enter blood capillaries by passing through the apical surfaces of epithelial cells and into the interstitial fluid. Water-soluble nutrients enter the capillary blood in the villi and travel to the liver via the hepatic portal vein.

In contrast to the water-soluble nutrients, lipid-soluble nutrients can diffuse through the plasma membrane. Once inside the cell, they are packaged for transport via the base of the cell and then enter the lacteals of the villi to be transported by lymphatic vessels to the systemic circulation via the thoracic duct. The absorption of most nutrients through the mucosa of the intestinal villi requires active transport fueled by ATP.

Carbohydrate Absorption

All carbohydrates are absorbed in the form of monosaccharides. The small intestine is highly efficient at this, absorbing monosaccharides at an estimated rate of 120 g per hour. All normally digested dietary carbohydrates are absorbed; indigestible fibres are eliminated in the feces. The monosaccharides glucose and galactose are transported into the epithelial cells by common protein carriers via secondary active transport (that is, cotransport with sodium ions). The monosaccharides leave these cells via facilitated diffusion and enter the capillaries through intercellular clefts. The monosaccharide fructose (which is in fruit) is absorbed and transported by facilitated diffusion alone. The monosaccharides combine with the transport proteins immediately after the disaccharides are broken down.

Protein Absorption

Active transport mechanisms, primarily in the duodenum and jejunum, absorb most proteins as their breakdown products, amino acids. Almost all (95 to 98 percent) protein is digested and absorbed in the small intestine. The type of carrier that transports an amino acid varies. Most carriers are linked to the active transport of sodium. Short chains of two amino acids (dipeptides) or three amino acids (tripeptides) are also transported actively. However, after

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they enter the absorptive epithelial cells, they are broken down into their amino acids before leaving the cell and entering the capillary blood via diffusion.

Lipid Absorption

About 95 percent of lipids are absorbed in the small intestine. Bile salts not only speed up lipid digestion; they are also essential to the absorption of the end products of lipid digestion. Short-chain fatty acids are relatively water soluble and can enter the absorptive cells (enterocytes) directly. The small size of short-chain fatty acids enables them to be absorbed by enterocytes via simple diffusion and then take the same path as monosaccharides and amino acids into the blood capillary of a villus.

The large and hydrophobic long-chain fatty acids and monoacylglycerides are not so easily suspended in the watery intestinal chyme. However, bile salts and lecithin resolve this issue by enclosing them in a **micelle**, which is a tiny sphere with polar (hydrophilic) ends facing the watery environment and hydrophobic tails turned to the interior, creating a receptive environment for the long-chain fatty acids. The core also includes cholesterol and fat-soluble vitamins. Without micelles, lipids would sit on the surface of chyme and never come in contact with the absorptive surfaces of the epithelial cells. Micelles can easily squeeze between microvilli and get very near the luminal cell surface. At this point, lipid substances exit the micelle and are absorbed via simple diffusion.

The free fatty acids and monoacylglycerides that enter the epithelial cells are reincorporated into triglycerides. The triglycerides are mixed with phospholipids and cholesterol and surrounded with a protein coat. This new complex, called a **chylomicron**, is a water-soluble lipoprotein. After being processed by the Golgi apparatus, chylomicrons are released from the cell (Figure 22.31). Too big to pass through the basement membranes of blood capillaries, chylomicrons instead enter the large pores of lacteals. The lacteals come together to form the lymphatic vessels.

The chylomicrons are transported in the lymphatic vessels and empty through the thoracic duct into the subclavian vein of the circulatory system. Once in the bloodstream, the enzyme **lipoprotein lipase** breaks down the triglycerides of the chylomicrons into free fatty acids and glycerol. These breakdown products then pass through capillary walls to be used for energy by cells or stored in adipose tissue as fat. Liver cells combine the remaining chylomicron remnants with proteins, forming lipoproteins that transport cholesterol in the blood.

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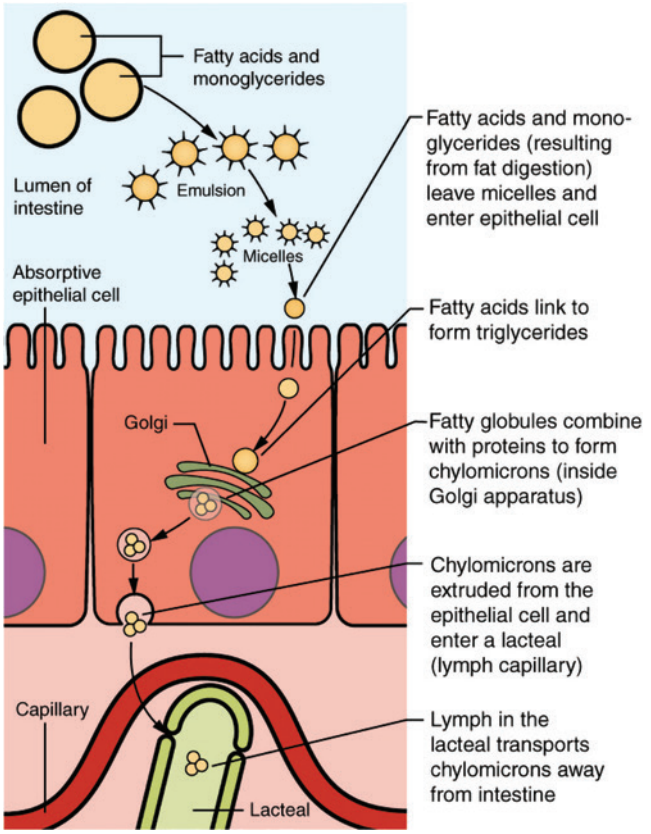


Figure 22.31 Lipid Absorption. Unlike amino acids and simple sugars, lipids are transformed as they are absorbed through epithelial cells.

Nucleic Acid Absorption

The products of nucleic acid digestion—pentose sugars, nitrogenous bases, and phosphate ions—are transported by carriers across the villus epithelium via active transport. These products then enter the bloodstream.

Mineral Absorption

The electrolytes absorbed by the small intestine are from both GI secretions and ingested foods. Since electrolytes dissociate into ions in water, most are absorbed via active transport throughout the entire small intestine. During absorption, cotransport mechanisms result in the accumulation of sodium ions inside the cells, whereas antiport mechanisms reduce the potassium ion concentration inside the cells. To restore the sodium-potassium gradient across the cell membrane, a sodium-potassium pump requiring ATP pumps sodium out and potassium in.

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In general, all minerals that enter the intestine are absorbed, whether you need them or not. Iron and calcium are exceptions; they are absorbed in the duodenum in amounts that meet the body's current requirements, as follows:

Iron

The ionic iron needed for the production of hemoglobin is absorbed into mucosal cells via active transport. Once inside mucosal cells, ionic iron binds to the protein ferritin, creating iron-ferritin complexes that store iron until needed. When the body has enough iron, most of the stored iron is lost when worn-out epithelial cells slough off.

When the body needs iron because, for example, it is lost during acute or chronic bleeding, there is increased uptake of iron from the intestine and accelerated release of iron into the bloodstream. Since females experience significant iron loss during menstruation, they have around four times as many iron transport proteins in their intestinal epithelial cells as do males.

Calcium

Blood levels of ionic calcium determine the absorption of dietary calcium. When blood levels of ionic calcium drop, parathyroid hormone (PTH) secreted by the parathyroid glands stimulates the release of calcium ions from bone matrices and increases the reabsorption of calcium by the kidneys. PTH also upregulates the activation of vitamin D in the kidney, which then facilitates intestinal calcium ion absorption.

Vitamin Absorption

The small intestine absorbs the vitamins that occur naturally in food and supplements. Fat-soluble vitamins (A, D, E, and K) are absorbed along with dietary lipids in micelles via simple diffusion. This is why you are advised to eat some fatty foods when you take fat-soluble vitamin supplements. Most water-soluble vitamins (including most B vitamins and vitamin C) also are absorbed by simple diffusion. An exception is vitamin B_{12}, which is a very large molecule. Intrinsic factor secreted in the stomach binds to vitamin B_{12}, preventing its digestion and creating a complex that binds to mucosal receptors in the terminal ileum, where it is taken up by endocytosis.

Water Absorption

Each day, about 9 L of fluid enter the small intestine. About 2.3 L are ingested in foods and beverages, and the rest is from GI secretions. About 90 percent of this water is absorbed in the small intestine. Water absorption is driven by the

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concentration gradient of the water: The concentration of water is higher in chyme than it is in epithelial cells. Thus, water moves down its concentration gradient from the chyme into cells. As noted earlier, much of the remaining water is then absorbed in the colon.

Key Terms

α-dextrin: Breakdown product of starch.
α-dextrinase: Brush border enzyme that acts on α-dextrins.
absorption: Passage of digested products from the intestinal lumen through mucosal cells and into the bloodstream or lacteals.
accessory digestive organ: Includes teeth, tongue, salivary glands, gallbladder, liver, and pancreas.
accessory duct (also duct of Santorini): Duct that runs from the pancreas into the duodenum.
acinus: Cluster of glandular epithelial cells in the pancreas that secretes pancreatic juice in the pancreas.
alimentary canal: Continuous muscular digestive tube that extends from the mouth to the anus.
aminopeptidase: Brush border enzyme that acts on proteins.
anal canal: Final segment of the large intestine.
anal column: Long fold of mucosa in the anal canal.
anal sinus: Recess between anal columns.
appendix (vermiform appendix): Coiled tube attached to the cecum.
ascending colon: First region of the colon.
bacterial flora: Bacteria in the large intestine.
bile: Alkaline solution produced by the liver and important for the emulsification of lipids.
bile canaliculus: Small duct between hepatocytes that collects bile.
bilirubin: Main bile pigment, which is responsible for the brown colour of feces.
body: Midportion of the stomach.
bolus: Mass of chewed food.
brush border: Fuzzy appearance of the small intestinal mucosa created by microvilli.
cardia (also cardiac region): Part of the stomach surrounding the cardiac orifice (esophageal hiatus).
cecum: Pouch forming the beginning of the large intestine.
cementum: Bone-like tissue covering the root of a tooth.
central vein: Vein that receives blood from hepatic sinusoids.

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cephalic phase (also reflex phase): Initial phase of gastric secretion that occurs before food enters the stomach.
chemical digestion: Enzymatic breakdown of food.
chief cell: Gastric gland cell that secretes pepsinogen.
chylomicron: Large lipid-transport compound made up of triglycerides, phospholipids, cholesterol, and proteins.
chyme: Soupy liquid created when food is mixed with digestive juices.
circular fold (also plica circulare): Deep fold in the mucosa and submucosa of the small intestine.
colon: Part of the large intestine between the cecum and the rectum.
common bile duct: Structure formed by the union of the common hepatic duct and the gallbladder's cystic duct.
common hepatic duct: Duct formed by the merger of the two hepatic ducts.
crown: Portion of tooth visible superior to the gum line.
cuspid (also canine): Pointed tooth used for tearing and shredding food.
cystic duct: Duct through which bile drains and enters the gallbladder.
deciduous tooth: One of 20 "baby teeth."
defecation: Elimination of undigested substances from the body in the form of feces.
deglutition: Three-stage process of swallowing.
dentes: Teeth.
dentin: Bone-like tissue immediately deep to the enamel of the crown or cementum of the root of a tooth.
dentition: Set of teeth.
deoxyribonuclease: Pancreatic enzyme that digests DNA.
descending colon: Part of the colon between the transverse colon and the sigmoid colon.
dipeptidase: Brush border enzyme that acts on proteins.
duodenal gland (also Brunner's gland): Mucous-secreting gland in the duodenal submucosa.
duodenum: First part of the small intestine, which starts at the pyloric sphincter and ends at the jejunum.
enamel: Covering of the dentin of the crown of a tooth.
enteroendocrine cell: Gastric gland cell that releases hormones.
enterohepatic circulation: Recycling mechanism that conserves bile salts.
enteropeptidase (enterokinase): Intestinal brush border enzyme that activates trypsinogen to trypsin.
epiploic appendage: Small sac of fat-filled visceral peritoneum attached to teniae coli.
esophagus: Muscular tube that runs from the pharynx to the stomach.

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external anal sphincter: Voluntary skeletal muscle sphincter in the anal canal.
fauces: Opening between the oral cavity and the oropharynx.
feces: Semisolid waste product of digestion.
flatus: Gas in the intestine.
fundus: Dome-shaped region of the stomach above and to the left of the cardia.
gallbladder: Accessory digestive organ that stores and concentrates bile.
gastric emptying: Process by which mixing waves gradually cause the release of chyme into the duodenum.
gastric gland: Gland in the stomach mucosal epithelium that produces gastric juice.
gastric juice: Complex digestive fluid.
gastric lipase: Secreted by the chief cells in the stomach and responsible for lipid digestion.
gastric phase: Phase of gastric secretion that begins when food enters the stomach.
gastric pit: Narrow channel formed by the epithelial lining of the stomach mucosa.
gastrin: Peptide hormone that stimulates secretion of hydrochloric acid and gut motility.
gastrocolic reflex: Propulsive movement in the colon activated by the presence of food in the stomach.
gastroileal reflex: Long reflex that increases the strength of segmentation in the ileum.
G cell: Gastrin-secreting enteroendocrine cell.
gingiva: Gum.
greater curvature: The convex lateral surface of the stomach.
hard palate: Bony structure in the mouth created by the maxillary and palatine bones of the skull.
haustral contraction: Slow segmentation in the large intestine.
haustrum: Small pouch in the colon created by tonic contractions of teniae coli.
hepatic artery: Artery that supplies oxygenated blood to the liver.
hepatic lobule: Hexagonal-shaped structure composed of hepatocytes that radiate outward from a central vein.
hepatic portal vein: Vein that supplies deoxygenated nutrient-rich blood to the liver.
hepatic sinusoid: Blood capillaries between rows of hepatocytes that receive blood from the hepatic portal vein and the branches of the hepatic artery.

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hepatic vein: Vein that drains into the inferior vena cava.
hepatocytes: Major functional cells of the liver.
hepatopancreatic ampulla (also ampulla of Vater): Bulb-like point in the wall of the duodenum where the bile duct and main pancreatic duct unite.
hepatopancreatic sphincter (also sphincter of Oddi): Sphincter regulating the flow of bile and pancreatic juice into the duodenum.
hydrochloric acid (HCl): Digestive acid secreted by parietal cells in the stomach.
ileocecal sphincter: Sphincter located where the small intestine joins with the large intestine.
ileum: End of the small intestine between the jejunum and the large intestine.
incisor: Midline, chisel-shaped tooth used for cutting into food.
ingestion: Taking food into the GI tract through the mouth.
internal anal sphincter: Involuntary smooth muscle sphincter in the anal canal.
intestinal gland (also crypt of Lieberkühn): Gland in the small intestinal mucosa that secretes intestinal juice.
intestinal juice: Mixture of water and mucus that helps absorb nutrients from chyme.
intestinal phase: Phase of gastric secretion that begins when chyme enters the intestine.
intrinsic factor: Glycoprotein required for vitamin B_{12} absorption in the small intestine.
jejunum: Middle part of the small intestine between the duodenum and the ileum.
labial frenulum: Midline mucous membrane fold that attaches the inner surface of the lips to the gums.
labium: Lip.
lactase: Brush border enzyme that breaks down lactose into glucose and galactose.
lacteal: Lymphatic capillary in the villi.
large intestine: Terminal portion of the alimentary canal.
laryngopharynx: Part of the pharynx that functions in respiration and digestion.
left colic flexure (also splenic flexure): Point where the transverse colon curves below the inferior end of the spleen.
lesser curvature: The concave medial border.
lingual frenulum: Mucous membrane fold that attaches the bottom of the tongue to the floor of the mouth.

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lingual glands: In the lamina propria of the tongue, secrete mucus and a watery serous fluid that contains the enzyme.
lingual lipase: Digestive enzyme from glands in the tongue that acts on triglycerides.
lipoprotein lipase: Enzyme that breaks down triglycerides in chylomicrons into fatty acids and monoglycerides.
liver: Largest gland in the body whose main digestive function is the production of bile.
lower esophageal sphincter: Smooth muscle sphincter that regulates food movement from the esophagus to the stomach.
lumen: The central space that food travels through.
lysozyme: Component of saliva that makes it antimicrobial.
main pancreatic duct (also duct of Wirsung): Duct through which pancreatic juice drains from the pancreas.
major duodenal papilla: Point at which the hepatopancreatic ampulla opens into the duodenum.
maltase: Brush border enzyme that breaks down maltose and maltotriose into two and three molecules of glucose, respectively.
mass movement: Long, slow, peristaltic wave in the large intestine.
mastication: Chewing.
mechanical digestion: Chewing, mixing, and segmentation that prepares food for chemical digestion.
mesoappendix: Mesentery of the appendix.
micelle: Tiny lipid-transport compound composed of bile salts and phospholipids with a fatty acid and monoacylglyceride core.
microvillus: Small projection of the plasma membrane of the absorptive cells of the small intestinal mucosa.
migrating motility complex: Form of peristalsis in the small intestine.
mixing wave: Unique type of peristalsis that occurs in the stomach.
molar: Tooth used for crushing and grinding food.
motilin: Hormone that initiates migrating motility complexes.
motility: Movement of food through the GI tract.
mucosa (mucous membrane): Innermost lining of the alimentary canal.
mucosal barrier: Protective barrier that prevents gastric juice from destroying the stomach itself.
mucous neck cell: Gastric gland cell that secretes a uniquely acidic mucus.
mucus: Alkaline protective coat secreted by the mucus cells in the epithelium.
muscularis: Muscle (skeletal or smooth) layer of the alimentary canal wall.
myenteric plexus (plexus of Auerbach): Major nerve supply to alimentary canal wall; controls motility.

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nasopharynx: The most superior part of the pharynx, which is involved only in breathing and speech.
oral cavity (also buccal cavity): Mouth.
oral vestibule: Part of the mouth bounded externally by the cheeks and lips and internally by the gums and teeth.
oropharynx: Part of the pharynx continuous with the oral cavity that functions in respiration and digestion.
palatoglossal arch: Muscular fold that extends from the lateral side of the soft palate to the base of the tongue.
palatopharyngeal arch: Muscular fold that extends from the lateral side of the soft palate to the side of the pharynx.
pancreas: Accessory digestive organ that secretes pancreatic juice.
pancreatic amylase: Enzyme secreted by the pancreas that completes the chemical digestion of carbohydrates in the small intestine.
pancreatic duct: Duct that fuses with the common bile duct just before entering the duodenum via a common opening.
pancreatic juice: Secretion of the pancreas containing digestive enzymes and bicarbonate.
pancreatic lipase: Enzyme secreted by the pancreas that participates in lipid digestion.
pancreatic nuclease: Enzyme secreted by the pancreas that participates in nucleic acid digestion.
papillae: Extensions of lamina propria of the top and sides of the tongue mucosa.
parietal cell: Gastric gland cell that secretes hydrochloric acid and intrinsic factor.
parietal peritoneum: Lines the abdominal wall.
parotid gland: One of a pair of major salivary glands located inferior and anterior to the ears.
pepsin: Proteolytic enzyme in the stomach.
pepsinogen: Inactive form of pepsin.
peristalsis: Muscular contractions and relaxations that propel food through the GI tract.
peritoneal cavity: The space bounded by the visceral and parietal peritoneal surfaces.
peritoneal fold: Large folds that envelop various abdominal organs, holding them to the dorsal surface of the body wall.
peritoneum: Broad serous membranous sac made up of squamous epithelial tissue surrounded by connective tissue that holds in place the digestive organs within the abdominal cavity.

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permanent tooth: One of 32 adult teeth.
pharynx: Throat.
porta hepatis: "gateway to the liver" where the hepatic artery and hepatic portal vein enter the liver.
portal triad: Bile duct, hepatic artery branch, and hepatic portal vein branch.
premolar (also bicuspid): Transitional tooth used for mastication, crushing, and grinding food.
propulsion: Voluntary process of swallowing and the involuntary process of peristalsis that moves food through the digestive tract.
pulp cavity: Deepest portion of a tooth, containing nerve endings and blood vessels.
pyloric antrum: Wider, more superior part of the pylorus.
pyloric canal: Narrow, more inferior part of the pylorus.
pyloric sphincter: Sphincter that controls stomach emptying.
pylorus: Lower, funnel-shaped part of the stomach that is continuous with the duodenum.
rectal valve: One of three transverse folds in the rectum where feces are separated from flatus.
rectum: Part of the large intestine between the sigmoid colon and anal canal.
reticuloendothelial cell (also Kupffer cell): Phagocyte in hepatic sinusoids that filters out material from venous blood from the alimentary canal.
retroperitoneal: Located posterior to the peritoneum.
ribonuclease: Pancreatic enzyme that digests RNA.
right colic flexure (also hepatic flexure): Point at the inferior surface of the liver where the ascending colon turns abruptly to the left.
root: Portion of a tooth embedded in the alveolar processes beneath the gum line.
rugae: Folds of alimentary canal mucosa and submucosa in the empty stomach and other organs.
saliva: Aqueous solution of proteins and ions secreted into the mouth by the salivary glands.
salivary amylase: Digestive enzyme in saliva that acts on starch.
salivary gland: Exocrine gland that secretes a digestive fluid called saliva.
salivation: Secretion of saliva.
segmentation: Alternating contractions and relaxations of nonadjacent segments of the intestine that move food forward and backward, breaking it apart and mixing it with digestive juices.

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serosa: Outermost layer of the alimentary canal wall present in regions within the abdominal cavity.

sigmoid colon: End portion of the colon, which terminates at the rectum.

small intestine: Section of the alimentary canal where most digestion and absorption occurs.

soft palate: Posterior region of the bottom portion of the nasal cavity that consists of skeletal muscle.

stomach: Alimentary canal organ that contributes to chemical and mechanical digestion of food from the esophagus before releasing it, as chyme, to the small intestine.

sublingual gland: One of a pair of major salivary glands located beneath the tongue.

submandibular gland: One of a pair of major salivary glands located in the floor of the mouth.

submucosa: Layer of dense connective tissue in the alimentary canal wall that binds the overlying mucosa to the underlying muscularis.

submucosal plexus (plexus of Meissner): Nerve supply that regulates activity of glands and smooth muscle.

sucrase: Brush border enzyme that breaks down sucrose into glucose and fructose.

taste buds: Fungiform papillae.

tenia coli: One of three smooth muscle bands that make up the longitudinal muscle layer of the muscularis in all of the large intestine except the terminal end.

tongue: Accessory digestive organ of the mouth, the bulk of which is composed of skeletal muscle.

transverse colon: Part of the colon between the ascending colon and the descending colon.

upper esophageal sphincter: Skeletal muscle sphincter that regulates food movement from the pharynx to the esophagus.

uvula: Fleshy bead of tissue that drops down from the centre of the posterior edge of the soft palate.

Valsalva's maneuver: Voluntary contraction of the diaphragm and abdominal wall muscles and closing of the glottis, which increases intra-abdominal pressure and facilitates defecation.

villus: Projection of the mucosa of the small intestine.

visceral peritoneum: Envelopes the abdominal organs.

voluntary phase: Initial phase of deglutition, in which the bolus moves from the mouth to the oropharynx.

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Chapter Review

22.1 Overview of the Digestive System

The digestive system includes the organs of the alimentary canal and accessory structures. The alimentary canal forms a continuous tube that is open to the outside environment at both ends. The organs of the alimentary canal are the mouth, pharynx, esophagus, stomach, small intestine, and large intestine. The accessory digestive structures include the teeth, tongue, salivary glands, liver, pancreas, and gallbladder. The wall of the alimentary canal is composed of four basic tissue layers: mucosa, submucosa, muscularis, and serosa. The enteric nervous system provides intrinsic innervation, and the autonomic nervous system provides extrinsic innervation.

22.2 Digestive System Processes and Regulation

The digestive system ingests and digests food, absorbs released nutrients, and excretes food components that are indigestible. The six activities involved in this process are ingestion, motility, mechanical digestion, chemical digestion, absorption, and defecation. These processes are regulated by neural and hormonal mechanisms.

22.3 The Mouth, Pharynx, and Esophagus

In the mouth, the tongue and the teeth begin mechanical digestion, and saliva begins chemical digestion. The pharynx, which plays roles in breathing and vocalization as well as digestion, runs from the nasal and oral cavities superiorly to the esophagus inferiorly (for digestion) and to the larynx anteriorly (for respiration). During deglutition (swallowing), the soft palate rises to close off the nasopharynx, the larynx elevates, and the epiglottis folds over the glottis. The esophagus includes an upper esophageal sphincter made of skeletal muscle, which regulates the movement of food from the pharynx to the esophagus. It also has a lower esophageal sphincter, made of smooth muscle, which controls the passage of food from the esophagus to the stomach. Cells in the esophageal wall secrete mucus that eases the passage of the food bolus.

22.4 The Stomach

The stomach participates in all digestive activities except ingestion and defecation. It vigorously churns food. It secretes gastric juices that break down food and absorbs certain drugs, including aspirin and some alcohol. The stomach begins the digestion of protein and continues the digestion of carbohydrates and fats. It stores food as an acidic liquid called chyme and releases it gradually into the small intestine through the pyloric sphincter.

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22.5 The Small and Large Intestines

The three main regions of the small intestine are the duodenum, the jejunum, and the ileum. The small intestine is where digestion is completed and virtually all absorption occurs. These two activities are facilitated by structural adaptations that increase the mucosal surface area by 600-fold, including circular folds, villi, and microvilli. There are around 200 million microvilli per square millimetre of small intestine, which contain brush border enzymes that complete the digestion of carbohydrates and proteins. Combined with pancreatic juice, intestinal juice provides the liquid medium needed to further digest and absorb substances from chyme. The small intestine is also the site of unique mechanical digestive movements.

Segmentation moves the chyme back and forth, increasing mixing and opportunities for absorption. Migrating motility complexes propel the residual chyme toward the large intestine.

The main regions of the large intestine are the cecum, the colon, and the rectum. The large intestine absorbs water and forms feces and is responsible for defecation. Bacterial flora break down additional carbohydrate residue and synthesize certain vitamins. The mucosa of the large intestinal wall is generously endowed with goblet cells, which secrete mucus that eases the passage of feces. The entry of feces into the rectum activates the defecation reflex.

22.6 Accessory Organs in Digestion: The Liver, Pancreas, and Gallbladder

Chemical digestion in the small intestine cannot occur without the help of the liver and pancreas. The liver produces bile and delivers it to the common hepatic duct. Bile contains bile salts and phospholipids, which emulsify large lipid globules into tiny lipid droplets, a necessary step in lipid digestion and absorption. The gallbladder stores and concentrates bile, releasing it when it is needed by the small intestine.

The pancreas produces the enzyme- and bicarbonate-rich pancreatic juice and delivers it to the small intestine through ducts. Pancreatic juice buffers the acidic gastric juice in chyme, inactivates pepsin from the stomach, and enables the optimal functioning of digestive enzymes in the small intestine.

22.7 Chemical Digestion and Absorption: A Closer Look

The small intestine is the site of most chemical digestion and almost all absorption. Chemical digestion breaks large food molecules down into their chemical building blocks, which can then be absorbed through the intestinal wall and into the general circulation.

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Intestinal brush border enzymes and pancreatic enzymes are responsible for the majority of chemical digestion. The breakdown of fat also requires bile.

Most nutrients are absorbed by transport mechanisms at the apical surface of enterocytes. Exceptions include lipids, fat-soluble vitamins, and most water-soluble vitamins. With the help of bile salts and lecithin, the dietary fats are emulsified to form micelles, which can carry the fat particles to the surface of the enterocytes. There, the micelles release their fats to diffuse across the cell membrane. The fats are then reassembled into triglycerides and mixed with other lipids and proteins into chylomicrons that can pass into lacteals. Other absorbed monomers travel from blood capillaries in the villus to the hepatic portal vein and then to the liver.

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23

Metabolism and Nutrition

Chapter Objectives

After studying this chapter, you will be able to:

- Describe the processes involved in anabolic and catabolic reactions
- List and describe the steps necessary for carbohydrate, lipid, and protein metabolism
- Explain the processes that regulate glucose levels during the absorptive and postabsorptive states
- Explain how metabolism is essential to maintaining body temperature (thermoregulation)
- Summarize the importance of vitamins and minerals in the diet

This chapter will take you through some of the chemical reactions essential to life, the sum of which is referred to as metabolism. The focus of these discussions will be anabolic reactions and catabolic reactions. You will examine the various chemical reactions that are important to sustain life, including why you must have oxygen, how mitochondria transfer energy, and the importance of certain "metabolic" hormones and vitamins.

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23.1 Overview of Metabolic Reactions

Learning Objectives

By the end of this section, you will be able to:

- Describe the process by which polymers are broken down into monomers
- Describe the process by which monomers are combined into polymers
- Discuss the role of ATP in metabolism
- Explain oxidation-reduction reactions
- Describe the hormones that regulate anabolic and catabolic reactions

Metabolic processes are constantly taking place in the body. **Metabolism** is the sum of all of the chemical reactions that are involved in catabolism and anabolism. The reactions governing the breakdown of food to obtain energy are called catabolic reactions. Conversely, anabolic reactions use the energy produced by catabolic reactions to synthesize larger molecules from smaller ones, such as when the body forms proteins by stringing together amino acids. Both sets of reactions are critical to maintaining life.

Because catabolic reactions produce energy and anabolic reactions use energy, ideally, energy usage would balance the energy produced. If the net energy change is positive (catabolic reactions release more energy than the anabolic reactions use), then the body stores the excess energy by building fat molecules for long-term storage. On the other hand, if the net energy change is negative (catabolic reactions release less energy than anabolic reactions use), the body uses stored energy to compensate for the deficiency of energy released by catabolism.

Catabolic Reactions

Catabolic reactions break down large organic molecules into smaller molecules, releasing the energy contained in the chemical bonds. These energy releases (conversions) are not 100 percent efficient. The amount of energy released is less than the total amount contained in the molecule. Approximately 40 percent of energy yielded from catabolic reactions is directly transferred to the high-energy molecule **adenosine triphosphate** (**ATP**). ATP, the energy currency of cells, can be used immediately to power molecular machines that support cell, tissue, and organ function. This includes building new tissue and repairing damaged tissue. ATP can also be stored to fulfill future energy demands. The

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remaining 60 percent of the energy released from catabolic reactions is given off as heat, which tissues and body fluids absorb.

The energy from ATP drives all bodily functions, such as contracting muscles, maintaining the electrical potential of nerve cells, and absorbing food in the gastrointestinal tract. The metabolic reactions that produce ATP come from various sources.

Of the four major macromolecular groups (carbohydrates, lipids, proteins, and nucleic acids) that are processed by digestion, carbohydrates are considered the most common source of energy to fuel the body. They take the form of either complex carbohydrates, polysaccharides like starch and glycogen, or simple sugars (monosaccharides) like glucose and fructose. Sugar catabolism breaks polysaccharides down into their individual monosaccharides. Among the monosaccharides, glucose is the most common fuel for ATP production in cells, and as such, there are a number of endocrine control mechanisms to regulate glucose concentration in the bloodstream. Excess glucose is either stored as an energy reserve in the liver and skeletal muscles as the complex polymer glycogen or converted into fat (triglyceride) in adipose cells (adipocytes).

Among the lipids (fats), triglycerides are most often used for energy via a metabolic process called β-oxidation. About one-half of excess fat is stored in adipocytes that accumulate in the subcutaneous tissue under the skin, whereas the rest is stored in adipocytes in other tissues and organs.

Proteins, which are polymers, can be broken down into their monomers, individual amino acids. Amino acids can be used as building blocks of new proteins or broken down further for the production of ATP. When one is chronically starving, this use of amino acids for energy production can lead to a wasting away of the body as more and more proteins are broken down.

Nucleic acids are present in most of the foods you eat. During digestion, nucleic acids including DNA and various RNAs are broken down into their constituent nucleotides. These nucleotides are readily absorbed and transported throughout the body to be used by individual cells during nucleic acid metabolism.

Anabolic Reactions

In contrast to catabolic reactions, **anabolic reactions** involve the joining of smaller molecules into larger ones. Anabolic reactions combine monosaccharides to form polysaccharides, fatty acids to form triglycerides, amino acids to form proteins, and nucleotides to form nucleic acids. These processes require energy in the form of ATP molecules generated by catabolic reactions. Anabolic reactions, also called **biosynthesis reactions**, create new molecules that form new cells and tissues and revitalize organs.

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Hormonal Regulation of Metabolism

Catabolic and anabolic hormones in the body help regulate metabolic processes. **Catabolic hormones** stimulate the breakdown of molecules and the production of energy. These include cortisol, glucagon, adrenaline/epinephrine, and cytokines. All of these hormones are mobilized at specific times to meet the needs of the body. **Anabolic hormones** are required for the synthesis of molecules and include growth hormone, insulin-like growth factor, insulin, testosterone, and estrogen. Table 23.1 summarizes the function of each of the catabolic hormones, and Table 23.2 summarizes the functions of the anabolic hormones.

Table 23.1 Catabolic Hormones

Hormone	Function
Cortisol	Released from the adrenal gland in response to stress; main role to increase blood glucose levels by gluconeogenesis (breaking down fats and proteins)
Glucagon	Released from alpha cells in the pancreas either when starving or when the body needs to generate additional energy; stimulates the breakdown of glycogen in the liver to increase blood glucose levels; effect is the opposite of insulin; glucagon and insulin are part of a negative-feedback system that stabilizes blood glucose levels
Adrenaline/ epinephrine	Released in response to the activation of the sympathetic nervous system; increases heart rate and heart contractility, constricts blood vessels, is a bronchodilator that opens (dilates) the bronchi of the lungs to increase air volume in the lungs, and stimulates gluconeogenesis

Oxidation-Reduction Reactions

The chemical reactions underlying metabolism involve the transfer of electrons from one compound to another by processes catalyzed by enzymes. The electrons in these reactions commonly come from hydrogen atoms, which consist of an electron and a proton. A molecule gives up a hydrogen atom in the form of a hydrogen ion (H^+) and an electron, breaking the molecule into smaller parts. The loss of an electron, or **oxidation**, releases a small amount of energy; both the electron and the energy are then passed to another molecule in the process of **reduction**, or the gaining of an electron. These two reactions always happen together in an **oxidation-reduction reaction** (also called a redox reaction)—when an electron is passed between molecules, the donor is oxidized and the recipient is reduced. Oxidation-reduction reactions often happen in a series so that a molecule that is reduced is subsequently

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Table 23.2 Anabolic Hormones

Hormone	Function
Growth hormone (GH)	Synthesized and released from the pituitary gland; stimulates the growth of cells, tissues, and bones
Insulin-like growth factor (IGF)	Stimulates the growth of muscle and bone while also inhibiting cell death (apoptosis)
Insulin	Produced by the beta cells of the pancreas; plays an essential role in carbohydrate and fat metabolism, controls blood glucose levels, and promotes uptake of glucose into body cells; causes cells in muscle, adipose tissue, and liver to take up glucose from the blood and store it in the liver and muscle as glycogen; effect is the opposite of glucagon; glucagon and insulin are a part of a negative-feedback system that stabilizes blood glucose levels
Testosterone	Produced by the testes in males and the ovaries in females; stimulates an increase in muscle mass and strength as well as the growth and strengthening of bone
Estrogen	Produced primarily by the ovaries, also produced by the liver and adrenal glands; anabolic functions include increasing metabolism and fat deposition

oxidized, passing on not only the electron it just received but also the energy it received. As the series of reactions progresses, energy accumulates that is used to combine P_i and ADP to form ATP, the high-energy molecule that the body uses for fuel. Oxidation-reduction reactions are catalyzed by enzymes that trigger the removal of hydrogen atoms. Coenzymes work with enzymes and accept hydrogen atoms.

23.2 Carbohydrate Metabolism

Learning Objectives

By the end of this section, you will be able to:

- Explain the processes of glycolysis
- Describe the pathway of a pyruvate molecule through the Krebs cycle
- Explain the transport of electrons through the electron transport chain
- Describe the process of ATP production through oxidative phosphorylation
- Summarize the process of gluconeogenesis

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Carbohydrates are organic molecules composed of carbon, hydrogen, and oxygen atoms. The family of carbohydrates includes both simple and complex sugars. Glucose and fructose are examples of simple sugars, and starch, glycogen, and cellulose are all examples of complex sugars. The complex sugars are also called **polysaccharides** and are made of multiple **monosaccharide** molecules. Polysaccharides serve as energy storage (e.g., starch and glycogen) and as structural components (e.g., chitin in insects and cellulose in plants).

During digestion, carbohydrates are broken down into simple, soluble sugars that can be transported across the intestinal wall into the circulatory system to be transported throughout the body. Carbohydrate digestion begins in the mouth with the action of **salivary amylase** on starches and ends with monosaccharides being absorbed across the epithelium of the small intestine. Once the absorbed monosaccharides are transported to the tissues, the process of **cellular respiration** begins. This section will focus first on glycolysis, a process where the monosaccharide glucose is oxidized, releasing the energy stored in its bonds to produce ATP.

Glycolysis

Glucose is the body's most readily available source of energy. After digestive processes break polysaccharides down into monosaccharides, including glucose, the monosaccharides are transported across the wall of the small intestine and into the circulatory system, which transports them to the liver. In the liver, hepatocytes either pass the glucose on through the circulatory system or store excess glucose as glycogen. Cells in the body take up the circulating glucose in response to insulin and, through a series of reactions called **glycolysis**, transfer some of the energy in glucose to ADP to form ATP. The last step in glycolysis produces the product **pyruvate**. Glycolysis uses two ATPs but generates four ATPs, yielding a net gain of two ATPs and two molecules of pyruvate. In the presence of oxygen, pyruvate continues on to the Krebs cycle (also called the **citric acid cycle** or **tricarboxylic acid cycle [TCA]**), where additional energy is extracted and passed on.

Interactive Link 23.1

Watch this video (http://oer.aupress.ca/oer-202505/23.1) to learn about glycolysis.

Glycolysis can be divided into two phases: energy consuming (also called chemical priming) and energy yielding. The first phase is the **energy-consuming**

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phase, so it requires two ATP molecules to start the reaction for each molecule of glucose. However, the end of the reaction produces four ATPs, resulting in a net gain of two ATP energy molecules.

Glycolysis can be expressed as glucose in combination with ATP (the energy source), NAD^+ (a coenzyme that serves as an electron acceptor), and inorganic phosphate breaking down into two pyruvate molecules, generating four ATP molecules—for a net yield of two ATP—and two energy-containing NADH coenzymes. The NADH that is produced in this process will be used later to produce ATP in the mitochondria. Importantly, by the end of this process, one glucose molecule generates two pyruvate molecules, two high-energy ATP molecules, and two electron-carrying NADH molecules. In the next step of the first phase of glycolysis, one glucose molecule is broken down into two glyceraldehyde-3-phosphate molecules.

The second phase of glycolysis, the **energy-yielding phase**, creates the energy that is the product of glycolysis. Each phosphate released in this reaction can convert one molecule of ADP into one high-energy ATP molecule, resulting in a gain of two ATP molecules.

In summary, one glucose molecule breaks down into two pyruvate molecules and creates two net ATP molecules and two NADH molecules by glycolysis. Therefore, glycolysis generates energy for the cell and creates pyruvate molecules that can be processed further through the aerobic Krebs cycle (also called the citric acid cycle or tricarboxylic acid cycle), converted into lactic acid or alcohol (in yeast) by fermentation, or used later for the synthesis of glucose through gluconeogenesis.

Anaerobic Respiration

When oxygen is limited or absent, pyruvate enters an anaerobic pathway called fermentation. In these reactions, pyruvate can be converted into lactic acid. In addition to generating an additional ATP, this pathway serves to keep the pyruvate concentration low so glycolysis continues, and it oxidizes NADH into the NAD^+ needed by glycolysis. In this reaction, lactic acid replaces oxygen as the final electron acceptor. Anaerobic respiration occurs in most cells of the body when oxygen is limited or mitochondria are absent or nonfunctional. For example, because erythrocytes (red blood cells) lack mitochondria, they must produce their ATP from anaerobic respiration. This is an effective pathway of ATP production for short periods of time, ranging from seconds to a few minutes. The lactic acid produced diffuses into the plasma and is carried to the liver, where it is converted back into pyruvate or glucose via the Cori cycle. Similarly, when a person exercises, muscles use ATP faster than oxygen can be delivered to them. They depend on glycolysis and lactic acid production for rapid ATP production.

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Aerobic Respiration

In the presence of oxygen, pyruvate can enter the Krebs cycle, where additional energy is extracted as electrons are transferred from the pyruvate to the receptors NAD^+, GDP, and FAD, with carbon dioxide being a "waste product." The NADH and $FADH_2$ pass electrons on to the electron transport chain, which uses the transferred energy to produce ATP.

Krebs Cycle / Citric Acid Cycle / Tricarboxylic Acid Cycle

The pyruvate molecules generated during glycolysis are transported across the mitochondrial membrane into the inner mitochondrial matrix, where they are metabolized by enzymes in a pathway called the **Krebs cycle**. The Krebs cycle is also commonly called the citric acid cycle or the tricarboxylic acid (TCA) cycle. During the Krebs cycle, high-energy molecules, including ATP, NADH, and $FADH_2$, are created. NADH and $FADH_2$ then pass electrons through the electron transport chain in the mitochondria to generate more ATP molecules.

Interactive Link 23.2

Watch this animation (http://oer.aupress.ca/oer-202505/23.2) to observe the Krebs cycle.

The three-carbon pyruvate molecule generated during glycolysis moves from the cytoplasm into the mitochondrial matrix, where it is converted by the enzyme pyruvate dehydrogenase into a two-carbon **acetyl coenzyme A** (**acetyl CoA**) molecule. This reaction is an oxidative decarboxylation reaction. It converts the three-carbon pyruvate into a two-carbon acetyl CoA molecule, releasing carbon dioxide and transferring two electrons that combine with NAD^+ to form NADH. Acetyl CoA enters the Krebs cycle by combining with a four-carbon molecule, oxaloacetate, to form the six-carbon molecule citrate, or citric acid, at the same time releasing the coenzyme A molecule.

The six-carbon citrate molecule is systematically converted to a five-carbon molecule and then a four-carbon molecule, ending with oxaloacetate, the beginning of the cycle. Along the way, each citrate molecule will produce one ATP, one $FADH_2$, and three NADH. The $FADH_2$ and NADH will enter the oxidative phosphorylation system located in the inner mitochondrial membrane. In addition, the Krebs cycle supplies the starting materials to process and break down proteins and fats.

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Oxidative Phosphorylation and the Electron Transport Chain

The **electron transport chain** (**ETC**) uses the NADH and $FADH_2$ produced by the Krebs cycle to generate ATP. Electrons from NADH and $FADH_2$ are transferred through protein complexes embedded in the inner mitochondrial membrane by a series of enzymatic reactions. The electron transport chain consists of a series of four enzyme complexes (Complex I–Complex IV) and two coenzymes (ubiquinone and Cytochrome c), which act as electron carriers and proton pumps used to transfer H^+ ions into the space between the inner and outer mitochondrial membranes (Figure 23.1). The ETC couples the transfer of electrons between a donor (like NADH) and an electron acceptor (like O_2) with the transfer of protons (H^+ ions) across the inner mitochondrial membrane, enabling the process of **oxidative phosphorylation**. In the presence of oxygen, energy is passed, stepwise, through the electron carriers to collect gradually the energy needed to attach a phosphate to ADP and produce ATP. The role of molecular oxygen, O_2, is as the terminal electron acceptor for the ETC. This means that once the electrons have passed through the entire ETC, they must be passed to another separate molecule. These electrons, O_2, and H^+ ions from the matrix combine to form new water molecules. This is the basis for your need to breathe in oxygen. Without oxygen, electron flow through the ETC ceases.

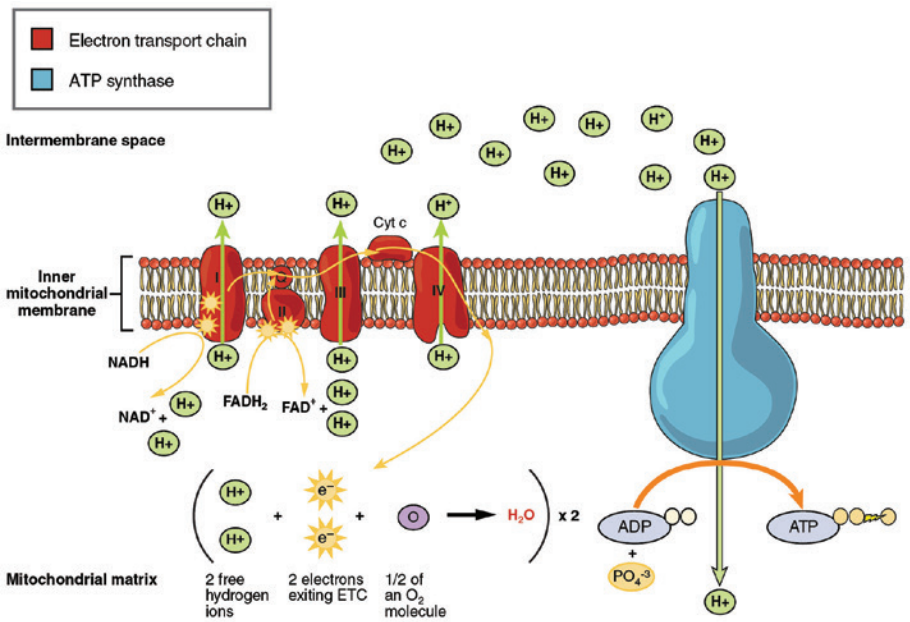


Figure 23.1 Electron Transport Chain. The electron transport chain is a series of electron carriers and ion pumps that are used to pump H^+ ions out of the inner mitochondrial matrix.

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Interactive Link 23.3

Watch this video (http://oer.aupress.ca/oer-202505/23.3) to learn about the electron transport chain.

The electrons released from NADH and $FADH_2$ are passed along the chain by each of the carriers, which are reduced when they receive the electron and oxidized when passing it on to the next carrier. Each of these reactions releases a small amount of energy, which is used to pump H^+ ions across the inner membrane. The accumulation of these protons in the space between the membranes creates a proton gradient with respect to the mitochondrial matrix.

Also embedded in the inner mitochondrial membrane is an amazing protein pore complex called **ATP synthase**. Effectively, it is a turbine that is powered by the flow of H^+ ions across the inner membrane down a gradient and into the mitochondrial matrix. As the H^+ ions traverse the complex, the shaft of the complex rotates. This rotation enables other portions of ATP synthase to encourage ADP and P_i to create ATP. In accounting for the total number of ATP produced per glucose molecule through aerobic respiration, it is important to remember the following points:

- A net of two ATP is produced through glycolysis (four produced and two consumed during the energy-consuming stage). However, these two ATPs are used for transporting the NADH produced during glycolysis from the cytoplasm into the mitochondria. Therefore, the net production of ATP during glycolysis is zero.
- In all phases after glycolysis, the number of ATP, NADH, and $FADH_2$ produced must be multiplied by two to reflect how each glucose molecule produces two pyruvate molecules.
- In the ETC, about three ATPs are produced for every oxidized NADH. However, only about two ATPs are produced for every oxidized $FADH_2$. The electrons from $FADH_2$ produce less ATP, because they start at a lower point in the ETC (Complex II) compared to the electrons from NADH (Complex I; see Figure 23.1).

Therefore, for every glucose molecule that enters aerobic respiration, a net total of 36 ATPs is produced (Figure 23.2).

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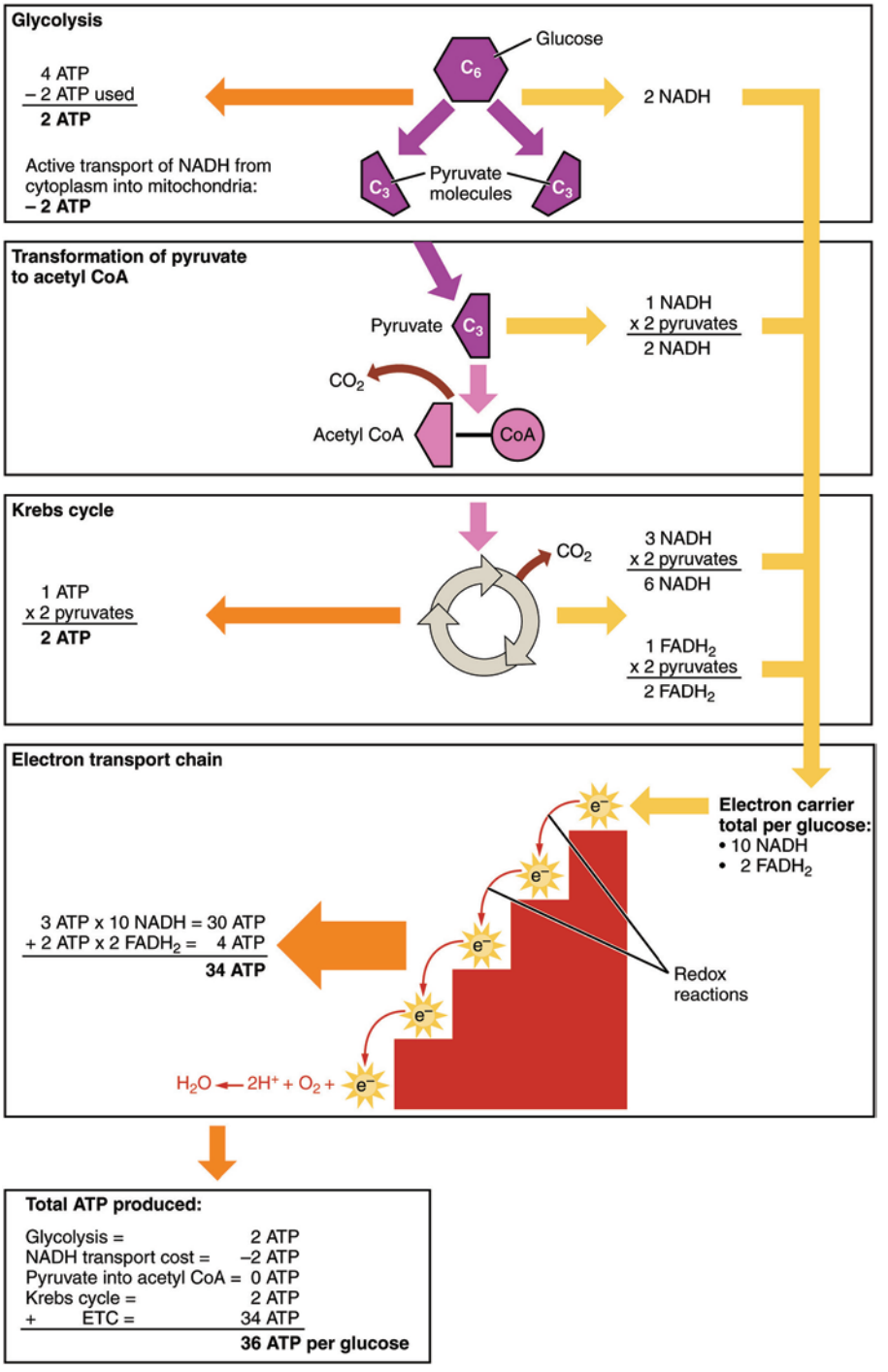


Figure 23.2 Carbohydrate Metabolism. Carbohydrate metabolism involves glycolysis, the Krebs cycle, and the electron transport chain.

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Gluconeogenesis

Gluconeogenesis is the synthesis of new glucose molecules from pyruvate, lactate, glycerol, or the amino acids alanine or glutamine. This process takes place primarily in the liver during periods of low glucose—that is, under conditions of fasting, starvation, and low-carbohydrate diets. So the question can be raised as to why the body would create something it has just spent a fair amount of effort to break down. Certain key organs, including the brain, can use only glucose as an energy source; therefore, it is essential that the body maintains a minimum blood glucose concentration. When the blood glucose concentration falls below that certain point, new glucose is synthesized by the liver to raise the blood concentration to normal.

Gluconeogenesis is not simply the reverse of glycolysis. There are some important differences. Pyruvate is a common starting material for gluconeogenesis.

23.3 Lipid Metabolism

Learning Objectives

By the end of this section, you will be able to:

- Explain how energy can be derived from fat
- Explain the purpose and process of ketogenesis
- Describe the process of ketone body oxidation
- Explain the purpose and the process of lipogenesis

Fats (or triglycerides) within the body are ingested as food or synthesized by adipocytes or hepatocytes from carbohydrate precursors. Lipid metabolism entails the oxidation of fatty acids to either generate energy or synthesize new lipids from smaller constituent molecules. Lipid metabolism is associated with carbohydrate metabolism, as products of glucose (such as acetyl CoA) can be converted into lipids.

Lipid metabolism begins in the intestine, where ingested **triglycerides** are broken down into smaller-chain fatty acids and subsequently into **monoglyceride molecules** by **pancreatic lipases**, enzymes that break down fats after they are emulsified by **bile salts**. When food reaches the small intestine in the form of chyme, a digestive system hormone called **cholecystokinin** (**CCK**) is released by intestinal cells in the intestinal mucosa. CCK stimulates the release of pancreatic lipase from the pancreas and stimulates the contraction of the

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gallbladder to release stored bile salts into the intestine. CCK also travels to the brain, where it can act as a hunger suppressant.

Together, the pancreatic lipases and bile salts break down triglycerides into free fatty acids. These fatty acids can be transported across the intestinal membrane. However, once they cross the membrane, they are recombined to again form triglyceride molecules. Within the intestinal cells, these triglycerides are packaged along with cholesterol molecules in phospholipid vesicles called **chylomicrons** (Figure 23.3). The chylomicrons enable fats and cholesterol to move within the aqueous environment of your lymphatic and circulatory systems. Chylomicrons leave the enterocytes by exocytosis and enter the lymphatic system via lacteals in the villi of the intestine. From the lymphatic system, the chylomicrons are transported to the circulatory system. Once in the circulation, they can either go to the liver or be stored in fat cells (adipocytes) that compose adipose (fat) tissue found throughout the body.

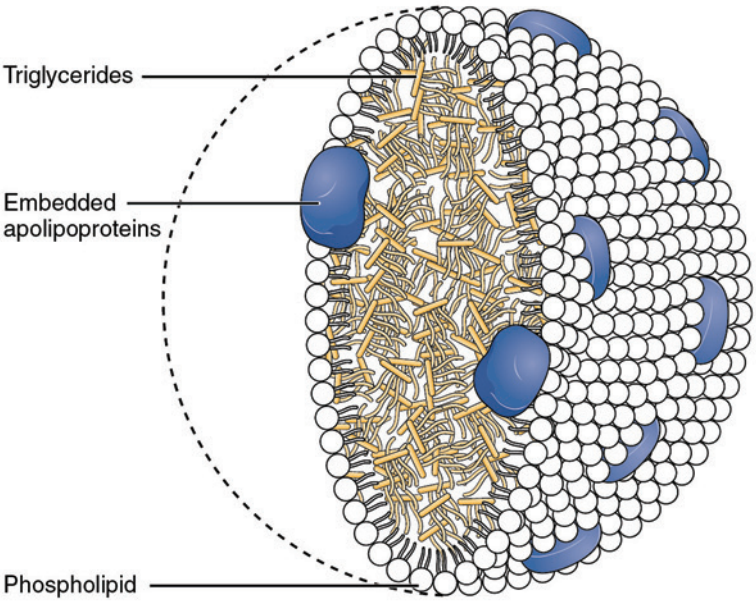


Figure 23.3 Chylomicrons. Chylomicrons contain triglycerides, cholesterol molecules, and other apolipoproteins (protein molecules). They function to carry these water-insoluble molecules from the intestine, through the lymphatic system, and into the bloodstream, which carries the lipids to adipose tissue for storage.

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Lipolysis

To obtain energy from fat, triglycerides must first be broken down by hydrolysis into their two principal components, fatty acids and glycerol. This process, called **lipolysis**, takes place in the cytoplasm. The resulting fatty acids are oxidized by β-oxidation into acetyl CoA, which is used by the Krebs cycle. The glycerol that is released from triglycerides after lipolysis directly enters the glycolysis pathway as DHAP. Because one triglyceride molecule yields three fatty acid molecules with as many as 16 or more carbons in each one, fat molecules yield more energy than carbohydrates and are an important source of energy for the human body. Triglycerides yield more than twice the energy per unit mass when compared to carbohydrates and proteins. Therefore, when glucose levels are low, triglycerides can be converted into acetyl CoA molecules and used to generate ATP through aerobic respiration.

The breakdown of fatty acids, called **fatty acid oxidation** or **beta (β)-oxidation**, begins in the cytoplasm, where fatty acids are converted into fatty acyl CoA molecules, then at the end into acetyl CoA. The newly formed acetyl CoA enters the Krebs cycle and is used to produce ATP in the same way as acetyl CoA derived from pyruvate.

Ketogenesis

If excessive acetyl CoA is created from the oxidation of fatty acids and the Krebs cycle is overloaded and cannot handle it, the acetyl CoA is diverted to create **ketone bodies**. These ketone bodies can serve as a fuel source if glucose levels are too low in the body. Ketones serve as fuel in times of prolonged starvation or when patients suffer from uncontrolled diabetes and cannot utilize most of the circulating glucose. In both cases, fat stores are liberated to generate energy through the Krebs cycle and will generate ketone bodies when too much acetyl CoA accumulates.

Ketone Body Oxidation

Organs that have classically been thought to be dependent solely on glucose, such as the brain, can actually use ketones as an alternative energy source. This keeps the brain functioning when glucose is limited. When ketones are produced faster than they can be used, they can be broken down into CO_2 and acetone. The acetone is removed by exhalation. The carbon dioxide produced can acidify the blood, leading to diabetic ketoacidosis, a dangerous condition in people with diabetes.

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Lipogenesis

When glucose levels are plentiful, the excess acetyl CoA generated by glycolysis can be converted into fatty acids, triglycerides, cholesterol, steroids, and bile salts. This process, called **lipogenesis**, creates lipids (fat) from the acetyl CoA and takes place in the cytoplasm of adipocytes (fat cells) and hepatocytes (liver cells). When you eat more glucose or carbohydrates than your body needs, your system uses acetyl CoA to turn the excess into fat.

Although there are several metabolic sources of acetyl CoA, it is most commonly derived from glycolysis. Acetyl CoA availability is significant because it initiates lipogenesis. Lipogenesis begins with acetyl CoA and advances by the subsequent addition of two carbon atoms from another acetyl CoA; this process is repeated until fatty acids are the appropriate length. Because this is a bond-creating anabolic process, ATP is consumed. However, the creation of triglycerides and lipids is an efficient way of storing the energy available in carbohydrates. Triglycerides and lipids, high-energy molecules, are stored in adipose tissue until they are needed.

Although lipogenesis occurs in the cytoplasm, the necessary acetyl CoA is created in the mitochondria and cannot be transported across the mitochondrial membrane. To solve this problem, pyruvate is converted into both oxaloacetate and acetyl CoA. The acetyl CoA is converted into malonyl CoA, which is used to synthesize fatty acids.

23.4 Protein Metabolism

Learning Objectives

By the end of this section, you will be able to:

- Describe how the body digests proteins
- Explain how the urea cycle prevents toxic concentrations of nitrogen
- Differentiate between glucogenic and ketogenic amino acids
- Explain how protein can be used for energy

Much of the body is made of protein, and these proteins take on a myriad of forms. They represent cell-signalling receptors, signalling molecules, structural members, enzymes, intracellular trafficking components, extracellular matrix scaffolds, ion pumps, ion channels, and oxygen and CO_2 transporters (hemoglobin). That is not even the complete list! There is protein in bones (collagen), muscles, and tendons; the hemoglobin that transports oxygen;

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and enzymes that catalyze all biochemical reactions. Protein is also used for growth and repair. Amid all these necessary functions, proteins also hold the potential to serve as a metabolic fuel source. Proteins are not stored for later use, so excess proteins must be converted into glucose or triglycerides and used to supply energy or build energy reserves. Although the body can synthesize proteins from amino acids, food is an important source of those amino acids, especially because humans cannot synthesize all of the 20 amino acids used to build proteins.

Protein Digestion

The digestion of proteins begins in the stomach. When protein-rich foods enter the stomach, they are greeted by a mixture of the enzyme **pepsin** and hydrochloric acid (HCl; 0.5 percent). The latter produces an environmental pH of 1.5–3.5 that denatures proteins within food. Pepsin cuts proteins into smaller polypeptides and their constituent amino acids. When the food–gastric juice mixture (chyme) enters the small intestine, the pancreas releases **sodium bicarbonate** to neutralize the HCl. This helps protect the lining of the intestine. The small intestine also releases digestive system hormones, including **secretin** and CCK, which stimulate digestive processes to break down the proteins further. Secretin also stimulates the pancreas to release sodium bicarbonate. The pancreas releases most of the digestive enzymes, including the proteases trypsin, chymotrypsin, and elastase, which aid protein digestion.

Together, all of these enzymes break complex proteins into smaller individual amino acids (Figure 23.4), which are then transported across the intestinal mucosa to be used to create new proteins or to be converted into fats or acetyl CoA and used in the Krebs cycle.

In order to avoid breaking down the proteins that make up the pancreas and small intestine, pancreatic enzymes are released as **inactive proenzymes** that are only activated in the small intestine. In the pancreas, vesicles store **trypsin** and **chymotrypsin** as **trypsinogen** and **chymotrypsinogen**. Once released into the small intestine, an enzyme found in the wall of the small intestine, called **enterokinase**, binds to trypsinogen and converts it into its active form, trypsin. Trypsin then binds to chymotrypsinogen to convert it into the active chymotrypsin. Trypsin and chymotrypsin break down large proteins into smaller peptides, a process called **proteolysis**. These smaller peptides are catabolized into their constituent amino acids, which are transported across the apical surface of the intestinal mucosa in a process that is mediated by sodium-amino acid transporters. These transporters bind sodium and then bind the amino acid to transport it across the membrane. At the basal surface

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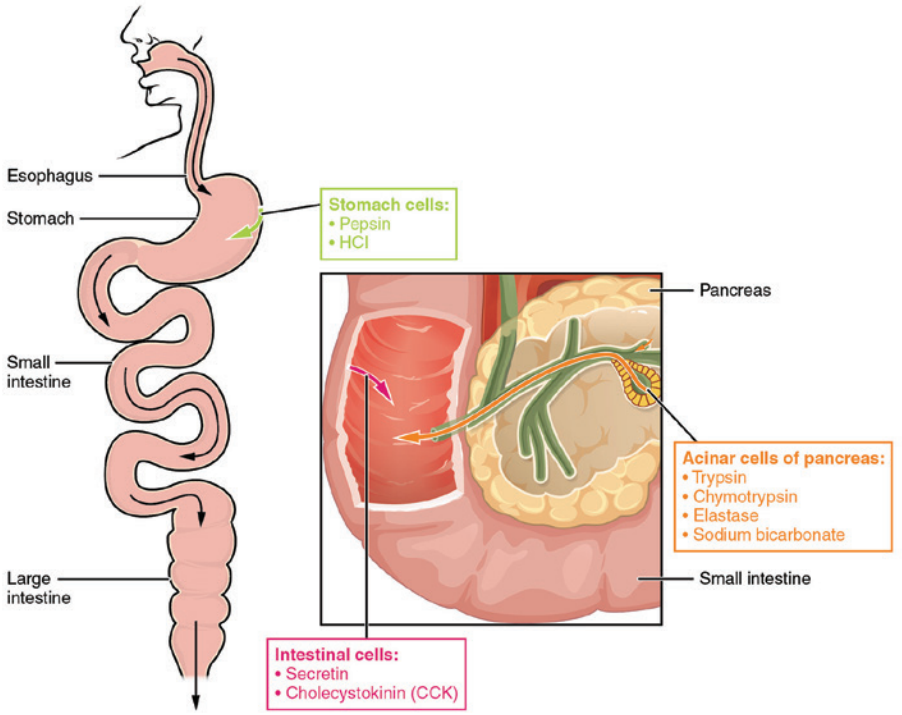


Figure 23.4 Digestive Enzymes and Hormones. Enzymes in the stomach and small intestine break down proteins into amino acids. HCl in the stomach aids in proteolysis, and hormones secreted by intestinal cells direct the digestive processes.

of the mucosal cells, the sodium and amino acids are released. The sodium can be reused in the transporter, whereas the amino acids are transferred into the bloodstream to be transported to the liver and cells throughout the body for protein synthesis.

Freely available amino acids are used to create proteins. If amino acids exist in excess, the body has no capacity or mechanism for their storage; thus, they are converted into glucose or ketones, or they are decomposed. Amino acid decomposition results in hydrocarbons and nitrogenous waste. However, high concentrations of nitrogenous by-products are toxic. The urea cycle processes nitrogen and facilitates its excretion from the body.

Urea Cycle

The **urea cycle** is a set of biochemical reactions that produces urea from ammonium ions in order to prevent a toxic level of ammonium in the body. It occurs primarily in the liver and, to a lesser extent, in the kidney. Prior to the urea cycle, ammonium ions are produced from the breakdown of amino acids. In

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these reactions, an amine group, or ammonium ion, from the amino acid is exchanged with a keto group on another molecule. This transamination event creates a molecule that is necessary for the Krebs cycle and an ammonium ion that enters into the urea cycle to be eliminated.

In the urea cycle, ammonium is combined with CO_2, resulting in urea and water. The urea is eliminated through the kidneys in the urine.

Amino acids can also be used as a source of energy, especially in times of starvation. Because the processing of amino acids results in the creation of metabolic intermediates, amino acids can serve as a source of energy production through the Krebs cycle.

23.5 Metabolic States of the Body

Learning Objectives

By the end of this section, you will be able to:

- Describe what defines each of the three metabolic states
- Describe the processes that occur during the absorptive state of metabolism
- Describe the processes that occur during the postabsorptive state of metabolism
- Explain how the body processes glucose when the body is starved of fuel

You eat periodically throughout the day; however, your organs, especially the brain, need a continuous supply of glucose. How does the body meet this constant demand for energy? Your body processes the food you eat both to use immediately and, importantly, to store as energy for later demands. If there were no method in place to store excess energy, you would need to eat constantly in order to meet energy demands. Distinct mechanisms are in place to facilitate energy storage and to make stored energy available during times of fasting and starvation.

The Absorptive State

The **absorptive state**, or the fed state, occurs after a meal when your body is digesting the food and absorbing the nutrients (anabolism exceeds catabolism). Digestion begins the moment you put food into your mouth, as the food is broken down into its constituent parts to be absorbed through the intestine.

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The digestion of carbohydrates begins in the mouth, whereas the digestion of proteins and fats begins in the stomach and small intestine. The constituent parts of these carbohydrates, fats, and proteins are transported across the intestinal wall and enter the bloodstream (sugars and amino acids) or the lymphatic system (fats). From the intestines, these systems transport them to the liver, adipose tissue, or muscle cells that will process and use, or store, the energy.

Depending on the amounts and types of nutrients ingested, the absorptive state can linger for up to 4 hours. The ingestion of food and the rise of glucose concentrations in the bloodstream stimulate pancreatic beta cells to release **insulin** into the bloodstream, where it initiates the absorption of blood glucose by liver hepatocytes and by adipose and muscle cells. Once inside these cells, glucose is immediately converted into glucose-6-phosphate. By doing this, a concentration gradient is established where glucose levels are higher in the blood than in the cells. This allows glucose to continue moving from the blood to the cells where it is needed. Insulin also stimulates the storage of glucose as glycogen in the liver and muscle cells, where it can be used for later energy needs of the body. Insulin also promotes the synthesis of protein in muscle. As you will see, muscle protein can be catabolized and used as fuel in times of starvation.

If energy is exerted shortly after eating, the dietary fats and sugars that were just ingested will be processed and used immediately for energy. If not, the excess glucose is stored as glycogen in the liver and muscle cells or as fat in adipose tissue; excess dietary fat is also stored as triglycerides in adipose tissues. Figure 23.5 summarizes the metabolic processes occurring in the body during the absorptive state.

The Postabsorptive State

The **postabsorptive state**, or the fasting state, occurs when the food has been digested, absorbed, and stored. You commonly fast overnight, but skipping meals during the day puts your body in the postabsorptive state as well.

During this state, the body must rely initially on stored **glycogen**. Glucose levels in the blood begin to drop as it is absorbed and used by the cells. In response to the decrease in glucose, insulin levels also drop. Glycogen and triglyceride storage slows. However, due to the demands of the tissues and organs, blood glucose levels must be maintained in the normal range of 80–120 mg/dL. In response to a drop in blood glucose concentration, the hormone glucagon is released from the alpha cells of the pancreas. Glucagon acts on the liver cells, where it inhibits the synthesis of glycogen and stimulates the breakdown of stored glycogen back into glucose. This glucose is released from the liver to be

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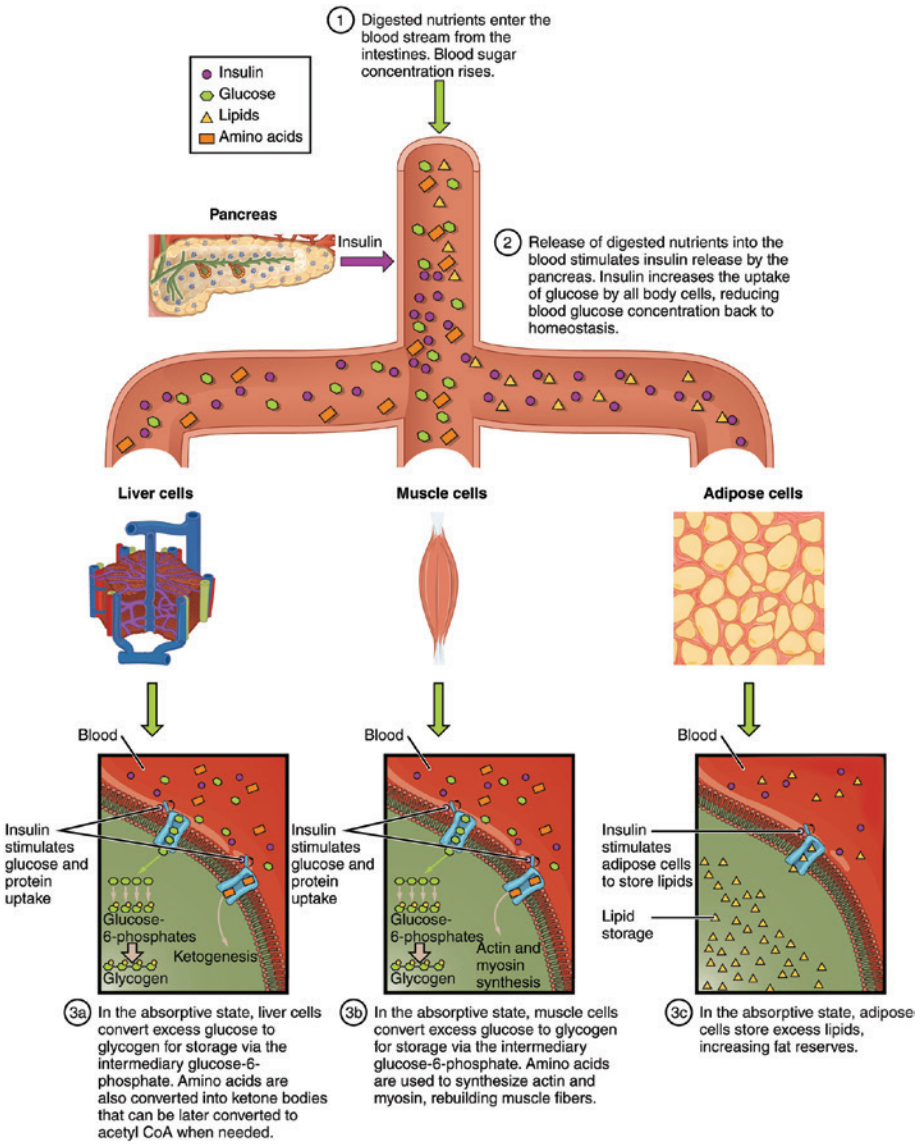


Figure 23.5 Absorptive State. During the absorptive state, the body digests food and absorbs the nutrients.

used by the peripheral tissues and the brain. As a result, blood glucose levels begin to rise. Gluconeogenesis will also begin in the liver to replace the glucose that has been used by the peripheral tissues.

After ingestion of food, fats and proteins are processed as described previously; however, the glucose processing changes a bit. The peripheral tissues preferentially absorb glucose. The liver, which normally absorbs and processes glucose, will not do so after a prolonged fast. The gluconeogenesis that has been

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ongoing in the liver will continue after fasting to replace the glycogen stores that were depleted in the liver. After these stores have been replenished, excess glucose that is absorbed by the liver will be converted into triglycerides and fatty acids for long-term storage. Figure 23.6 summarizes the metabolic processes occurring in the body during the postabsorptive state.

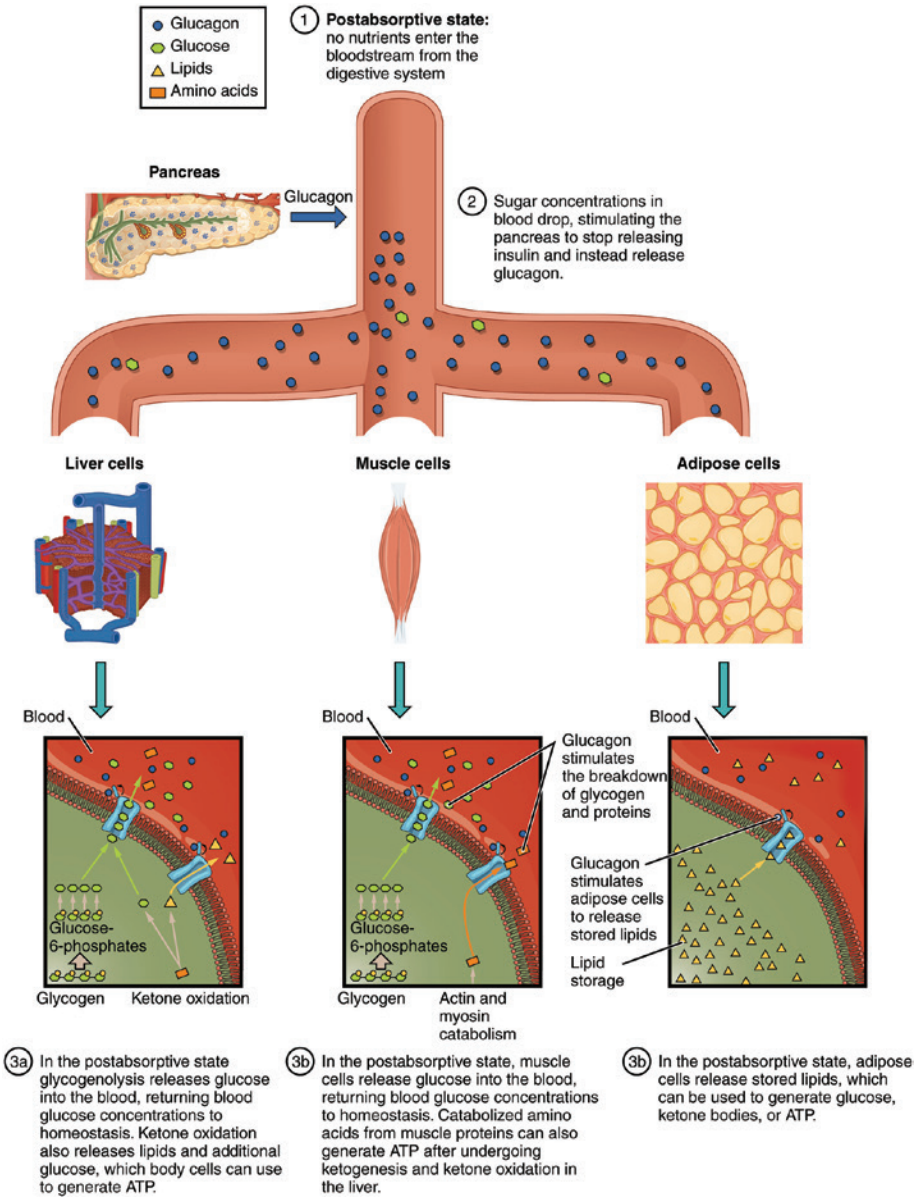


Figure 23.6 Postabsorptive State. During the postabsorptive state, the body must rely on stored glycogen for energy.

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Starvation

When the body is deprived of nourishment for an extended period of time, it goes into "survival mode." The first priority for survival is to provide enough glucose or fuel for the brain. The second priority is the conservation of amino acids for proteins. Therefore, the body uses ketones to satisfy the energy needs of the brain and other glucose-dependent organs and to maintain proteins in the cells. Because glucose levels are very low during starvation, glycolysis will shut off in cells that can use alternative fuels. For example, muscles will switch from using glucose to fatty acids as fuel. As previously explained, fatty acids can be converted into acetyl CoA and processed through the Krebs cycle to make ATP. Pyruvate, lactate, and alanine from muscle cells are not converted into acetyl CoA and used in the Krebs cycle but are exported to the liver to be used in the synthesis of glucose. As starvation continues and more glucose is needed, glycerol from fatty acids can be liberated and used as a source for gluconeogenesis.

After several days of starvation, ketone bodies become the major source of fuel for the heart and other organs. As starvation continues, fatty acids and triglyceride stores are used to create ketones for the body. This prevents the continued breakdown of proteins that serve as carbon sources for gluconeogenesis. Once these stores are fully depleted, proteins from muscles are released and broken down for glucose synthesis. Overall survival is dependent on the amount of fat and protein stored in the body.

23.6 Energy and Heat Balance

Learning Objectives

By the end of this section, you will be able to:

- Describe how the body regulates temperature
- Explain the significance of the metabolic rate

The body tightly regulates its temperature through a process called **thermoregulation**, in which the body can maintain its temperature within certain boundaries, even when the surrounding temperature is very different. The core temperature of the body remains steady at around 36.5–37.5°C. In the process of ATP production by cells throughout the body, approximately 60 percent of the energy produced is in the form of heat used to maintain body temperature. Thermoregulation is an example of negative feedback.

The hypothalamus in the brain is the master switch that works as a thermostat to regulate the body's core temperature (Figure 23.7). If the temperature

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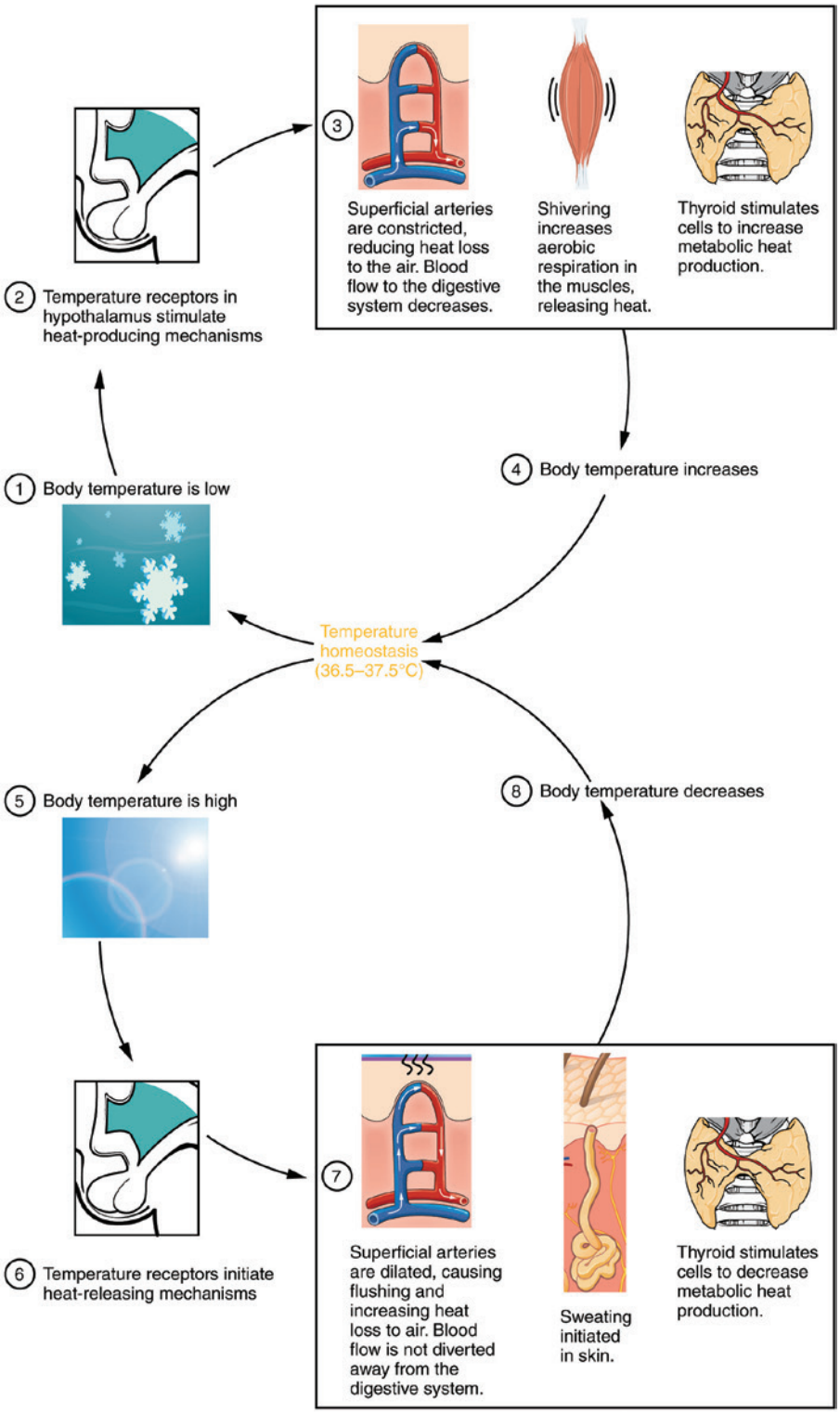


Figure 23.7 Hypothalamus Controls Thermoregulation. The hypothalamus controls thermoregulation.

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is too high, the hypothalamus can initiate several processes to lower it. These include increasing the circulation of the blood to the surface of the body to allow for the dissipation of heat through the skin and initiation of sweating to allow evaporation of water on the skin to cool its surface. Conversely, if the temperature falls below the set core temperature, the hypothalamus can initiate shivering to generate heat. The body uses more energy and generates more heat. In addition, thyroid hormone will stimulate more energy use and heat production by cells throughout the body. An environment is said to be **thermoneutral** when the body does not expend or release energy to maintain its core temperature. For a naked human, this is an ambient air temperature of around 29°C. If the temperature is higher—for example, when wearing clothes—the body compensates with cooling mechanisms. The body loses heat through the mechanisms of heat exchange.

Mechanisms of Heat Exchange

When the environment is not thermoneutral, the body uses four mechanisms of heat exchange to maintain homeostasis: conduction, convection, radiation, and evaporation. Each of these mechanisms relies on the property of heat to flow from a higher concentration to a lower concentration; therefore, each of the mechanisms of heat exchange varies in rate according to the temperature and conditions of the environment.

Conduction is the transfer of heat between two objects that are in direct contact with one another. It occurs when the skin comes in contact with a cold or warm object. For example, when you are holding a glass of ice water, the heat from your skin will warm the glass and in turn melt the ice. Alternatively, on a cold day, you might warm up by wrapping your cold hands around a hot mug of coffee. Only about 3 percent of the body's heat is lost through conduction.

Convection is the transfer of heat to the air surrounding the skin. The warmed air rises away from the body and is replaced by cooler air that is subsequently heated. Convection can also occur in water. When the water temperature is lower than the body's temperature, the body loses heat by warming the water closest to the skin, which moves away to be replaced by cooler water. The convection currents created by the temperature changes continue to draw heat away from the body more quickly than the body can replace it, resulting in hyperthermia. About 15 percent of the body's heat is lost through convection.

Radiation is the transfer of heat via infrared waves. This occurs between any two objects when their temperatures differ. A radiator can warm a room via radiant heat. On a sunny day, the radiation from the sun warms the skin. The same principle works from the body to the environment. About 60 percent of the heat lost by the body is lost through radiation.

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Evaporation is the transfer of heat by the evaporation of water. Because it takes a great deal of energy for a water molecule to change from a liquid to a gas, evaporating water (in the form of sweat) takes with it a great deal of energy from the skin. However, the rate at which evaporation occurs depends on relative humidity—more sweat evaporates in lower-humidity environments. Sweating is the primary means of cooling the body during exercise, whereas at rest, about 20 percent of the heat lost by the body occurs through evaporation.

Metabolic Rate

The **metabolic rate** is the amount of energy consumed minus the amount of energy expended by the body. The **basal metabolic rate** (**BMR**) describes the amount of daily energy expended by humans at rest, in a neutrally temperate environment, while in the postabsorptive state. It measures how much energy the body needs for normal, basic, daily activity. About 70 percent of all daily energy expenditure comes from the basic functions of the organs in the body. Another 20 percent comes from physical activity, and the remaining 10 percent is necessary for body thermoregulation or temperature control. This rate will be higher if a person is more active or has more lean body mass. As you age, the BMR generally decreases as the percentage of lean muscle mass decreases.

23.7 Nutrition and Diet

Learning Objectives

By the end of this section, you will be able to:

- Explain how different foods can affect metabolism
- Describe a healthy diet
- List reasons why vitamins and minerals are critical to a healthy diet

The carbohydrates, lipids, and proteins in the foods you eat are used for energy to power molecular, cellular, and organ system activities. Importantly, the energy is stored primarily as fats. The quantity and quality of food that is ingested, digested, and absorbed affects the amount of fat that is stored as excess calories. Diet—both what you eat and how much you eat—has a dramatic impact on your health. Eating too much or too little food can lead to serious medical issues, including cardiovascular disease, cancer, anorexia, and diabetes, among others. Combine an unhealthy diet with unhealthy environmental conditions, such as smoking, and the potential medical complications increase significantly.

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Food and Metabolism

The amount of energy that is needed or ingested per day is measured in calories. The nutritional **Calorie** (C) is the amount of heat it takes to raise 1 kg (1,000 g) of water by 1°C. This is different from the calorie (c) used in the physical sciences, which is the amount of heat it takes to raise 1 g of water by 1°C. When we refer to "calorie," we are referring to the nutritional Calorie.

On average, a person needs 1,500 to 2,000 calories per day to sustain (or carry out) daily activities. The total number of calories needed by one person is dependent on their body mass, age, height, gender, activity level, and amount of exercise per day. If exercise is a regular part of one's day, more calories are required. As a rule, people underestimate the number of calories ingested and overestimate the amount they burn through exercise. This can lead to ingestion of too many calories per day. The accumulation of an extra 3,500 calories adds one pound of weight. If an excess of 200 calories per day is ingested, one extra pound of body weight will be gained every 18 days. At that rate, an extra 20 pounds can be gained over the course of a year. Of course, this increase in calories could be offset by increased exercise. Running or jogging one mile burns almost 100 calories.

The type of food ingested also affects the body's metabolic rate. Processing of carbohydrates requires less energy than processing of proteins. In fact, the breakdown of carbohydrates requires the least amount of energy, whereas the processing of proteins demands the most energy. In general, the amount of calories ingested and the amount of calories burned determine the overall weight. To lose weight, the number of calories burned per day must exceed the number ingested. Calories are in almost everything you ingest, so when considering calorie intake, beverages must also be considered.

Vitamins

Vitamins are organic compounds found in foods and are a necessary part of the biochemical reactions in the body. They are involved in a number of processes, including mineral and bone metabolism and cell and tissue growth, and they act as cofactors for energy metabolism. The B vitamins play the largest role of any vitamins in metabolism.

You get most of your vitamins through your diet, although some can be formed from the precursors absorbed during digestion. For example, the body synthesizes vitamin A from the β-carotene in orange vegetables like carrots and sweet potatoes. Vitamins are either fat soluble or water soluble. Fat-soluble vitamins A, D, E, and K are absorbed through the intestinal tract with lipids in chylomicrons. Vitamin D is also synthesized in the skin through exposure to

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sunlight. Because they are carried in lipids, fat-soluble vitamins can accumulate in the lipids stored in the body. If excess vitamins are retained in the lipid stores in the body, hypervitaminosis can result.

Water-soluble vitamins, including the eight B vitamins and vitamin C, are absorbed with water in the gastrointestinal tract. These vitamins move easily through bodily fluids, which are water based, so they are not stored in the body.

Excess water-soluble vitamins are excreted in the urine. Therefore, hypervitaminosis of water-soluble vitamins rarely occurs, except with an excess of vitamin supplements.

Minerals

Minerals in food are inorganic compounds that work with other nutrients to ensure the body functions properly. Minerals cannot be made in the body; they come from the diet. The amount of minerals in the body is small—only 4 percent of the total body mass—and most of that consists of the minerals that the body requires in moderate quantities: potassium, sodium, calcium, phosphorus, magnesium, and chloride.

The most common minerals in the body are calcium and phosphorous, both of which are stored in the skeleton and necessary for the hardening of bones. Most minerals are ionized, and their ionic forms are used in physiological processes throughout the body. Sodium and chloride ions are electrolytes in the blood and extracellular tissues, and iron ions are critical to the formation of hemoglobin. There are additional trace minerals that are still important to the body's functions, but their required quantities are much lower.

Like vitamins, minerals can be consumed in toxic quantities (although it is rare). A healthy diet includes most of the minerals your body requires, so supplements and processed foods can add potentially toxic levels of minerals.

Key Terms

absorptive state: Also called the fed state; the metabolic state occurring during the first few hours after ingesting food in which the body is digesting food and absorbing the nutrients.

acetyl coenzyme A (acetyl CoA): Starting molecule of the Krebs cycle.

adenosine triphosphate (ATP): The energy currency of cells.

anabolic hormones: Hormones that stimulate the synthesis of new, larger molecules.

anabolic reactions: Reactions that build smaller molecules into larger molecules.

ATP synthase: Protein pore complex that creates ATP.

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basal metabolic rate (BMR): Amount of energy expended by the body at rest.
beta (β)-oxidation: Fatty acid oxidation.
bile salts: Salts that are released from the liver in response to lipid ingestion and surround the insoluble triglycerides to aid in their conversion to monoglycerides and free fatty acids.
biosynthesis reactions: Reactions that create new molecules, also called anabolic reactions.
calorie: Amount of heat it takes to raise 1 kg (1,000 g) of water by 1°C.
catabolic hormones: Hormones that stimulate the breakdown of larger molecules.
catabolic reactions: Reactions that break down larger molecules into their constituent parts.
cellular respiration: Production of ATP from glucose oxidation via glycolysis, the Krebs cycle, and oxidative phosphorylation.
cholecystokinin (CCK): Hormone that stimulates the release of pancreatic lipase and the contraction of the gallbladder to release bile salts.
chylomicrons: Vesicles containing cholesterol and triglycerides that transport lipids out of the intestinal cells and into the lymphatic and circulatory systems.
chymotrypsin: Pancreatic enzyme that digests protein.
chymotrypsinogen: Proenzyme that is activated by trypsin into chymotrypsin.
citric acid cycle: Also called the Krebs cycle or the tricarboxylic acid cycle; converts pyruvate into CO_2 and high-energy $FADH_2$, NADH, and ATP molecules.
conduction: Transfer of heat through physical contact.
convection: Transfer of heat between the skin and air or water.
electron transport chain (ETC): ATP production pathway in which electrons are passed through a series of oxidation-reduction reactions that forms water and produces a proton gradient.
energy-consuming phase: First phase of glycolysis, in which two molecules of ATP are necessary to start the reaction.
energy-yielding phase: Second phase of glycolysis, during which energy is produced.
enterokinase: Enzyme located in the wall of the small intestine that activates trypsin.
evaporation: Transfer of heat that occurs when water changes from a liquid to a gas.
fatty acid oxidation: Breakdown of fatty acids into smaller-chain fatty acids and acetyl CoA.

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gluconeogenesis: Process of glucose synthesis from pyruvate or other molecules.

glycogen: Form that glucose assumes when it is stored.

glycolysis: Series of metabolic reactions that breaks down glucose into pyruvate and produces ATP.

inactive proenzymes: Forms in which proteases are stored and released to prevent the inappropriate digestion of the native proteins of the stomach, pancreas, and small intestine.

insulin: Hormone secreted by the pancreas that stimulates the uptake of glucose into the cells.

ketone bodies: Alternative source of energy when glucose is limited, created when too much acetyl CoA is created during fatty acid oxidation.

Krebs cycle: Also called the citric acid cycle or the tricarboxylic acid cycle, converts pyruvate into CO_2 and high-energy $FADH_2$, NADH, and ATP molecules.

lipogenesis: Synthesis of lipids that occurs in the liver or adipose tissues.

lipolysis: Breakdown of triglycerides into glycerol and fatty acids.

metabolic rate: Amount of energy consumed minus the amount of energy expended by the body.

metabolism: Sum of all catabolic and anabolic reactions that take place in the body.

minerals: Inorganic compounds required by the body to ensure proper function of the body.

monoglyceride molecules: Lipid consisting of a single fatty acid chain attached to a glycerol backbone.

monosaccharide: Smallest, monomeric sugar molecule.

oxidation: Loss of an electron.

oxidation-reduction reaction (also redox reaction): Pair of reactions in which an electron is passed from one molecule to another, oxidizing one and reducing the other.

oxidative phosphorylation: Process that converts high-energy NADH and $FADH_2$ into ATP.

pancreatic lipases: Enzymes released from the pancreas that digest lipids in the diet.

pepsin: Enzyme that begins to break down proteins in the stomach.

polysaccharides: Complex carbohydrates made up of many monosaccharides.

postabsorptive state: Also called the fasting state; the metabolic state occurring after digestion, when food is no longer the body's source of energy and it must rely on stored glycogen.

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proteolysis: Process of breaking proteins into smaller peptides.
pyruvate: Three-carbon end product of glycolysis and starting material that is converted into acetyl CoA that enters the Krebs cycle.
radiation: Transfer of heat via infrared waves.
reduction: Gaining of an electron.
salivary amylase: Digestive enzyme that is found in the saliva and begins the digestion of carbohydrates in the mouth.
secretin: Hormone released in the small intestine to aid in digestion.
sodium bicarbonate: Anion released into the small intestine to neutralize the pH of the food from the stomach.
thermoneutral: External temperature at which the body does not expend any energy for thermoregulation, about 29°C.
thermoregulation: Process of regulating the temperature of the body.
tricarboxylic acid cycle (TCA): Also called the Krebs cycle or the citric acid cycle; converts pyruvate into CO_2 and high-energy $FADH_2$, NADH, and ATP molecules.
triglycerides: Lipids, or fats, consisting of three fatty acid chains attached to a glycerol backbone.
trypsin: Pancreatic enzyme that activates chymotrypsin and digests protein.
trypsinogen: Proenzyme form of trypsin.
urea cycle: Process that converts potentially toxic nitrogen waste into urea that can be eliminated through the kidneys.
vitamins: Organic compounds required by the body to perform biochemical reactions like metabolism and bone, cell, and tissue growth.

Chapter Review

23.1 Overview of Metabolic Reactions

Metabolism is the sum of all catabolic (breakdown) and anabolic (synthesis) reactions in the body. The metabolic rate measures the amount of energy used to maintain life. An organism must ingest a sufficient amount of food to maintain its metabolic rate if the organism is to stay alive for very long.

Catabolic reactions break down larger molecules, such as carbohydrates, lipids, and proteins from ingested food, into their constituent smaller parts. They also include the breakdown of ATP, which releases the energy needed for metabolic processes in all cells throughout the body.

Anabolic reactions, or biosynthetic reactions, synthesize larger molecules from smaller constituent parts, using ATP as the energy source for these reactions. Anabolic reactions build bone, muscle mass, and new proteins, fats,

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and nucleic acids. Oxidation-reduction reactions transfer electrons across molecules by oxidizing one molecule and reducing another and collecting the released energy to convert P_i and ADP into ATP. Errors in metabolism alter the processing of carbohydrates, lipids, proteins, and nucleic acids and can result in a number of disease states.

23.2 Carbohydrate Metabolism

Metabolic enzymes catalyze catabolic reactions that break down carbohydrates contained in food. The energy released is used to power the cells and systems that make up your body. Excess or unutilized energy is stored as fat or glycogen for later use. Carbohydrate metabolism begins in the mouth, where the enzyme salivary amylase begins to break down complex sugars into monosaccharides. These can then be transported across the intestinal membrane into the bloodstream and then to body tissues. In the cells, glucose, a six-carbon sugar, is processed through a sequence of reactions into smaller sugars, and the energy stored inside the molecule is released. The first step of carbohydrate catabolism is glycolysis, which produces pyruvate, NADH, and ATP. Under anaerobic conditions, the pyruvate can be converted into lactate to keep glycolysis working. Under aerobic conditions, pyruvate enters the Krebs cycle, also called the citric acid cycle or tricarboxylic acid cycle. In addition to ATP, the Krebs cycle produces high-energy $FADH_2$ and NADH molecules, which provide electrons to the oxidative phosphorylation process that generates more high-energy ATP molecules. For each molecule of glucose that is processed in glycolysis, a net of 36 ATPs can be created by aerobic respiration.

Under anaerobic conditions, ATP production is limited to those generated by glycolysis. While a total of four ATPs are produced by glycolysis, two are needed to begin glycolysis, so there is a net yield of two ATP molecules.

In conditions of low glucose, such as fasting, starvation, or low-carbohydrate diets, glucose can be synthesized from lactate, pyruvate, glycerol, alanine, or glutamate. This process, called gluconeogenesis, is almost the reverse of glycolysis and serves to create glucose molecules for glucose-dependent organs, such as the brain, when glucose levels fall below normal.

23.3 Lipid Metabolism

Lipids are available to the body from three sources. They can be ingested in the diet, stored in the adipose tissue of the body, or synthesized in the liver. Fats ingested in the diet are digested in the small intestine. The triglycerides are broken down into monoglycerides and free fatty acids, then imported across the intestinal mucosa. Once across, the triglycerides are resynthesized and transported to the liver or adipose tissue. Fatty acids are oxidized through fatty

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acid or β-oxidation into two-carbon acetyl CoA molecules, which can then enter the Krebs cycle to generate ATP. If excess acetyl CoA is created and overloads the capacity of the Krebs cycle, the acetyl CoA can be used to synthesize ketone bodies. When glucose is limited, ketone bodies can be oxidized and used for fuel.

Excess acetyl CoA generated from excess glucose or carbohydrate ingestion can be used for fatty acid synthesis or lipogenesis. Acetyl CoA is used to create lipids, triglycerides, steroid hormones, cholesterol, and bile salts. Lipolysis is the breakdown of triglycerides into glycerol and fatty acids, making them easier for the body to process.

23.4 Protein Metabolism

Digestion of proteins begins in the stomach, where HCl and pepsin begin the process of breaking down proteins into their constituent amino acids. As the chyme enters the small intestine, it mixes with bicarbonate and digestive enzymes. The bicarbonate neutralizes the acidic HCl, and the digestive enzymes break down the proteins into smaller peptides and amino acids. Digestive hormones secretin and CCK are released from the small intestine to aid in digestive processes, and digestive proenzymes are released from the pancreas (trypsinogen and chymotrypsinogen). Enterokinase, an enzyme located in the wall of the small intestine, activates trypsin, which in turn activates chymotrypsin. These enzymes liberate the individual amino acids that are then transported via sodium-amino acid transporters across the intestinal wall into the cell. The amino acids are then transported into the bloodstream for dispersal to the liver and cells throughout the body to be used to create new proteins. When in excess, the amino acids are processed and stored as glucose or ketones. The nitrogen waste that is liberated in this process is converted to urea in the urea acid cycle and eliminated in the urine. In times of starvation, amino acids can be used as an energy source and processed through the Krebs cycle.

23.5 Metabolic States of the Body

There are three main metabolic states of the body: absorptive (fed), postabsorptive (fasting), and starvation. During any given day, your metabolism switches between absorptive and postabsorptive states. Starvation states happen very rarely in generally well-nourished individuals. When the body is fed, glucose, fats, and proteins are absorbed across the intestinal membrane and enter the bloodstream and lymphatic system to be used immediately for fuel. Any excess is stored for later fasting stages. As blood glucose levels rise, the pancreas releases insulin to stimulate the uptake of glucose by hepatocytes in the liver, muscle cells/fibres, and adipocytes (fat cells) and to promote its conversion to glycogen. As the postabsorptive state begins, glucose levels drop, and there is a

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corresponding drop in insulin levels. Falling glucose levels trigger the pancreas to release glucagon to turn off glycogen synthesis in the liver and stimulate its breakdown into glucose. The glucose is released into the bloodstream to serve as a fuel source for cells throughout the body. If glycogen stores are depleted during fasting, alternative sources, including fatty acids and proteins, can be metabolized and used as fuel.

When the body once again enters the absorptive state after fasting, fats and proteins are digested and used to replenish fat and protein stores, whereas glucose is processed and used first to replenish the glycogen stores in the peripheral tissues, then in the liver. If the fast is not broken and starvation begins to set in, during the initial days, glucose produced from gluconeogenesis is still used by the brain and organs. After a few days, however, ketone bodies are created from fats and serve as the preferential fuel source for the heart and other organs so that the brain can still use glucose. Once these stores are depleted, proteins will be catabolized first from the organs with fast turnover, such as the intestinal lining. Muscle will be spared to prevent the wasting of muscle tissue; however, these proteins will be used if alternative stores are not available.

23.6 Energy and Heat Balance

Some of the energy from the food that is ingested is used to maintain the core temperature of the body. Most of the energy derived from the food is released as heat. The core temperature is kept around 36.5–37.5°C. This is tightly regulated by the hypothalamus in the brain, which senses changes in the core temperature and operates like a thermostat to increase sweating or shivering or induce other mechanisms to return the temperature to its normal range. The body can also gain or lose heat through mechanisms of heat exchange. Conduction transfers heat from one object to another through physical contact. Convection transfers heat to air or water. Radiation transfers heat via infrared radiation. Evaporation transfers heat as water changes state from a liquid to a gas.

23.7 Nutrition and Diet

Nutrition and diet affect your metabolism. More energy is required to break down fats and proteins than carbohydrates; however, all excess calories that are ingested will be stored as fat in the body. On average, a person requires 1,500 to 2,000 calories for normal daily activity, although routine exercise will increase that amount. If you ingest more than that, the remainder is stored for later use. Conversely, if you ingest less than that, the energy stores in your body will be depleted. Both the quantity and quality of the food you eat affect your metabolism and can affect your overall health. Eating too much or too

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little can result in serious medical conditions, including cardiovascular disease, cancer, and diabetes.

Vitamins and minerals are essential parts of the diet. They are needed for the proper function of metabolic pathways in the body. Vitamins are not stored in the body, so they must be obtained from the diet or synthesized from precursors available in the diet.

Minerals are also obtained from the diet, but they are also stored, primarily in skeletal tissues.

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24

The Urinary System

Chapter Objectives

After studying this chapter, you will be able to:

- Describe the composition of urine
- Label structures of the urinary system
- Characterize the roles of each of the parts of the urinary system
- Illustrate the macroscopic and microscopic structures of the kidney
- Trace the flow of blood through the kidney
- Outline how blood is filtered in the kidney nephron
- Provide symptoms of kidney failure
- List some of the solutes filtered, secreted, and reabsorbed in different parts of the nephron
- Describe the role of a portal system in the kidney
- Explain how urine osmolarity is hormonally regulated
- Describe the regulation of major ions by the kidney
- Summarize the role of the kidneys in maintaining acid-base balance

This chapter will help you understand the anatomy of the urinary system and how it enables the physiologic functions critical to homeostasis. It is best to think of the kidney as a regulator of plasma makeup rather than simply a urine producer. As you read each section, ask yourself this question: "What happens if this does not work?" This question will help you understand how the urinary system maintains homeostasis and affects all the other systems of the body and the quality of one's life.

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Interactive Link 24.1

Watch this video (http://oer.aupress.ca/oer-202505/24.1) from the Howard Hughes Medical Institute for an introduction to the urinary system.

24.1 Physical Characteristics of Urine

Learning Objectives

By the end of this section, you will be able to:

- Compare and contrast blood plasma, glomerular filtrate, and urine characteristics
- Describe the characteristics of a normal urine sample, including normal range of pH, osmolarity, and volume

The urinary system's ability to filter the blood resides in about two to three million tufts of specialized capillaries—the glomeruli—distributed more or less equally between the two kidneys. Because the glomeruli filter the blood based mostly on particle size, large elements like blood cells, platelets, antibodies, and albumen are excluded. The glomerulus is the first part of the nephron, which then continues as a highly specialized tubular structure responsible for creating the final urine composition. All other solutes, such as ions, amino acids, vitamins, and wastes, are filtered to create a filtrate composition very similar to plasma. The glomeruli create about 200 L of this filtrate every day, yet you excrete less than 2 L of waste you call urine.

Characteristics of the urine change depending on influences such as water intake, exercise, environmental temperature, nutrient intake, and other factors. Some of the characteristics, such as colour and odour, are rough descriptors of your state of hydration.

For example, if you exercise or work outside and sweat a great deal, your urine will turn darker and produce a slight odour, even if you drink plenty of water. Athletes are often advised to consume water until their urine is clear. This is good advice; however, it takes time for the kidneys to process body fluids and store them in the bladder.

Another way of looking at this is that the quality of the urine produced is an average over the time it takes to make that urine. Producing clear urine may take only a few minutes if you are drinking a lot of water or several hours if you are working outside and not drinking much.

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Urinalysis (urine analysis) often provides clues to renal disease. Normally, only traces of protein are found in urine, and when higher amounts are found, damage to the glomeruli is the likely basis. Unusually large quantities of urine may point to diseases like diabetes mellitus or hypothalamic tumors that cause diabetes insipidus. The colour of urine is determined mostly by the breakdown products of red blood cell destruction. Dehydration produces darker, concentrated urine that may also possess the slight odour of ammonia.

Urine volume varies considerably. The normal range is one to 2 L per day. The kidneys must produce a minimum urine volume of about 500 mL/day to rid the body of wastes. Output below this level may be caused by severe dehydration or renal disease and is termed **oliguria**. The virtual absence of urine production is termed **anuria**. Excessive urine production is **polyuria**, which may be due to diabetes mellitus or diabetes insipidus.

The pH (hydrogen ion concentration) of the urine can vary more than 1000-fold, from a normal low of 4.5 to a maximum of 8.0. Diet can influence pH; meats lower the pH, whereas citrus fruits, vegetables, and dairy products raise the pH.

Specific gravity is a measure of the quantity of solutes per unit volume of a solution and is traditionally easier to measure than osmolarity. Urine will always have a specific gravity greater than pure water (water = 1.0) due to the presence of solutes. Laboratories can now measure urine osmolarity directly, which is a more accurate indicator of urinary solutes than specific gravity. Remember that osmolarity is the number of osmoles or milliosmoles per litre of fluid (mOsmol/L). Urine osmolarity ranges from a low of 50–100 mOsmol/L to as high as 1,200 mOsmol/L of H_2O.

Cells are not normally found in the urine. The presence of leukocytes may indicate a urinary tract infection.

Protein does not normally leave the glomerular capillaries, so only trace amounts of protein should be found in the urine, approximately 10 mg/100 mL in a random sample. If excessive protein is detected in the urine, it usually means that the glomerulus is damaged and is allowing protein to "leak" into the filtrate.

Ketones are by-products of fat metabolism. Finding ketones in the urine suggests that the body is using fat as an energy source in preference to glucose. In diabetes mellitus, whether due to insufficient insulin production (type I diabetes mellitus) or insulin resistance (type II diabetes mellitus), glucose is abundant in the blood, but without effective insulin action, cells cannot absorb it, causing blood glucose levels to remain elevated. Instead, the cells are forced to use fat as their energy source, and fat consumed at such a level produces excessive ketones as by-products. These excess ketones will appear in the

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urine. Ketones may also appear if there is a severe deficiency of proteins or carbohydrates in the diet.

Nitrates (NO_3–) occur normally in the urine. Gram-negative bacteria metabolize nitrate into nitrite (NO_2–), and its presence in the urine is indirect evidence of infection.

There should be no blood found in the urine. It may sometimes appear in urine samples as a result of menstrual contamination, but this is not an abnormal condition. Now that you understand what the normal characteristics of urine are, the next section will introduce you to how you store and dispose of this waste product and how you make it.

24.2 Gross Anatomy of Urine Transport

Learning Objectives

By the end of this section, you will be able to:

- Identify the ureters, urinary bladder, and urethra, as well as their location, structure, histology, and function
- Compare and contrast male and female urethras
- Describe the micturition reflex
- Describe voluntary and involuntary neural control of micturition

Rather than start with urine formation, this section will start with urine excretion. Urine is a fluid of variable composition that requires specialized structures to remove it from the body safely and efficiently. Blood is filtered, and the filtrate is transformed into urine at a relatively constant rate throughout the day. This processed liquid is stored until a convenient time for excretion. All structures involved in the transport and storage of the urine are large enough to be visible to the naked eye. This transport and storage system not only stores the waste, but it protects the tissues from damage due to the wide range of pH and osmolarity of the urine, prevents infection by foreign organisms, and for the male, provides reproductive functions.

Urethra

The **urethra** transports urine from the bladder to the outside of the body for disposal. The urethra is the only urologic organ that shows any significant anatomic difference between males and females; all other urine transport structures are identical (Figure 24.1).

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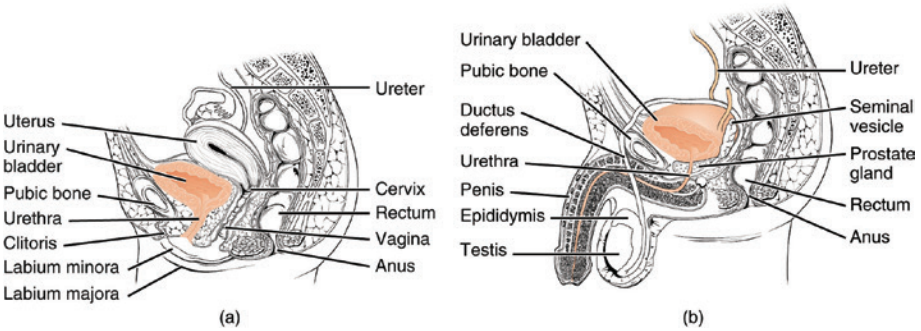


Figure 24.1 Female and Male Urethras. The urethra transports urine from the bladder to the outside of the body. This image shows (a) a female urethra and (b) a male urethra.

The urethra in both males and females begins inferior and central to the two ureteral openings forming the three points of a triangular-shaped area at the base of the bladder called the **trigone**. The urethra tracks posterior and inferior to the pubic symphysis (see Figure 24.1a). In both males and females, the proximal urethra is lined by transitional epithelium, whereas the terminal portion is a nonkeratinized, stratified squamous epithelium. In the male, pseudostratified columnar epithelium lines the urethra between these two cell types. Voiding is regulated by an involuntary autonomic nervous system–controlled **internal urinary** (**urethral**) **sphincter**, consisting of smooth muscle and voluntary skeletal muscle that forms the **external urinary** (**urethral**) **sphincter** below it.

Female Urethra

The external urethral orifice is embedded in the anterior vaginal wall inferior to the clitoris, superior to the vaginal opening (introitus), and medial to the labia minora. Its short length, about 4 cm, is less of a barrier to fecal bacteria than the longer male urethra and the best explanation for the greater incidence of UTI in females. Voluntary control of the external urethral sphincter is a function of the pudendal nerve. It arises in the sacral region of the spinal cord, travelling via the S2–S4 nerves of the sacral plexus.

Male Urethra

The male urethra passes through the prostate gland immediately inferior to the bladder before passing below the pubic symphysis (see Figure 24.1b). The length of the male urethra varies between people but averages 20 cm in length. It is divided into four regions: the preprostatic urethra, the prostatic urethra, the membranous urethra, and the spongy or penile urethra. The preprostatic urethra is very short and incorporated into the bladder wall. The prostatic urethra passes through the prostate gland. During sexual intercourse, it receives sperm

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via the ejaculatory ducts and secretions from the seminal vesicles. Paired Cowper's glands (bulbourethral glands) produce and secrete mucus into the urethra to buffer urethral pH during sexual stimulation. The mucus neutralizes the usually acidic environment and lubricates the urethra, decreasing the resistance to ejaculation. The membranous urethra passes through the deep muscles of the perineum, where it is invested by the overlying urethral sphincters. The spongy urethra exits at the tip (external urethral orifice) of the penis after passing through the corpus spongiosum. Mucous glands are found along much of the length of the urethra and protect the urethra from extremes of urine pH. Innervation is the same in both males and females.

Bladder

The urinary bladder collects urine from both ureters (Figure 24.2). The bladder lies anterior to the uterus in females, posterior to the pubic bone and anterior to the rectum. During late pregnancy, its capacity is reduced due to compression by the enlarging uterus, resulting in increased frequency of urination. In males, the anatomy is similar, minus the uterus and with the addition of the prostate inferior to the bladder. The bladder is a **retroperitoneal** organ whose "dome" distends superiorly when the bladder is filling with urine.

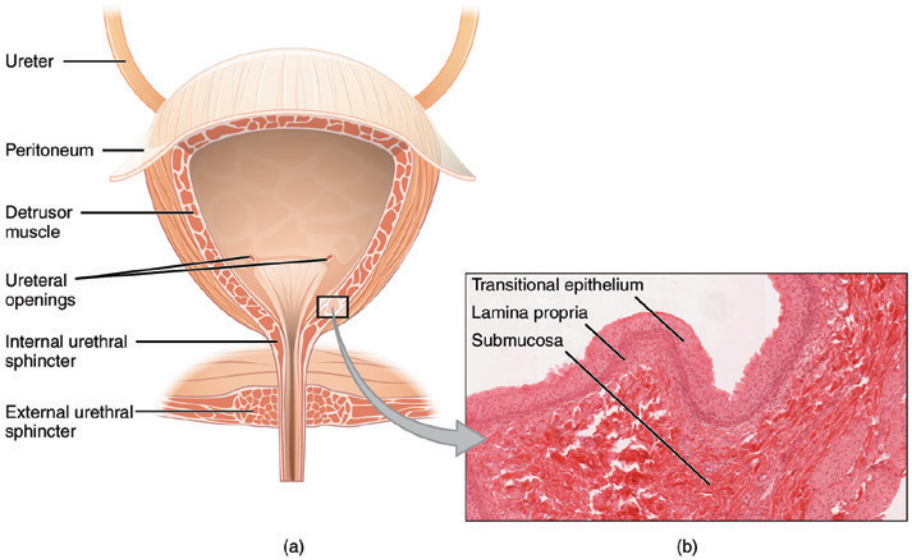


Figure 24.2 Bladder. (a) Anterior cross section of the bladder. (b) The detrusor muscle of the bladder (source: monkey tissue). LM × 448. (Micrograph provided by the Regents of the University of Michigan Medical School © 2012)

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Interactive Link 24.2

View the University of Michigan WebScope (http://oer.aupress.ca/oer-202505/24.2) to explore the tissue sample in greater detail.

The bladder is a highly distensible organ comprising irregular crisscrossing bands of smooth muscle collectively called the **detrusor muscle**. The interior surface is made of transitional cellular epithelium that is structurally suited for the large volume fluctuations of the bladder. When empty, it resembles columnar epithelia, but when stretched, it "transitions" (hence the name) to a squamous appearance (see Figure 24.2). Volumes in adults can range from nearly 0 to 500–600 ml.

The detrusor muscle contracts with significant force in the young. The bladder's strength diminishes with age, but voluntary contractions of abdominal skeletal muscles can increase intra-abdominal pressure to promote more forceful bladder emptying. Such voluntary contraction is also used in forceful defecation and childbirth.

Micturition is a less-often used but proper term for urination or voiding. It results from an interplay of involuntary and voluntary actions by the internal and external urethral sphincters. When bladder volume reaches about 150 mL, an urge to void is sensed but is easily overridden. Voluntary control of urination relies on consciously preventing relaxation of the external urethral sphincter to maintain urinary continence. As the bladder fills, subsequent urges become harder to ignore. Ultimately, voluntary constraint fails with resulting **incontinence**, which will occur as bladder volume approaches 300 to 400 mL.

Normal micturition is a result of stretch receptors in the bladder wall that transmit nerve impulses to the sacral region of the spinal cord to generate a spinal reflex. The resulting parasympathetic neural outflow causes contraction of the detrusor muscle and relaxation of the involuntary internal urethral sphincter. At the same time, the spinal cord inhibits somatic motor neurons, resulting in the relaxation of the skeletal muscle of the external urethral sphincter. The micturition reflex is active in infants, but with maturity, children learn to override the reflex by asserting external sphincter control, thereby delaying voiding (potty training).

Ureters

The kidneys and ureters are completely retroperitoneal, and the bladder has a peritoneal covering only over the dome. As urine is formed, it drains into the calyces of the kidney, which merge to form the funnel-shaped renal pelvis in the hilum of each kidney. The renal pelvis narrows to become the ureter

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of each kidney. As urine passes through the ureter, it does not passively drain into the bladder but rather is propelled by waves of peristalsis. As the ureters enter the pelvis, they sweep laterally, hugging the pelvic walls. As they approach the bladder, they turn medially and pierce the bladder wall obliquely. This is important because it creates a one-way valve (a **physiological sphincter** rather than an **anatomical sphincter**) that allows urine into the bladder but prevents reflux of urine from the bladder back into the ureter. Children born lacking this oblique course of the ureter through the bladder wall are susceptible to "vesicoureteral reflux," which dramatically increases their risk of serious UTI. Pregnancy also increases the likelihood of reflux and UTI.

The ureters are approximately 30 cm long. The inner mucosa is lined with transitional epithelium (Figure 24.3) and scattered goblet cells that secrete protective mucus. The muscular layer of the ureter consists of longitudinal and circular smooth muscles that create the peristaltic contractions to move the urine into the bladder without the aid of gravity. Finally, a loose adventitial layer composed of collagen and fat anchors the ureters between the parietal peritoneum and the posterior abdominal wall.

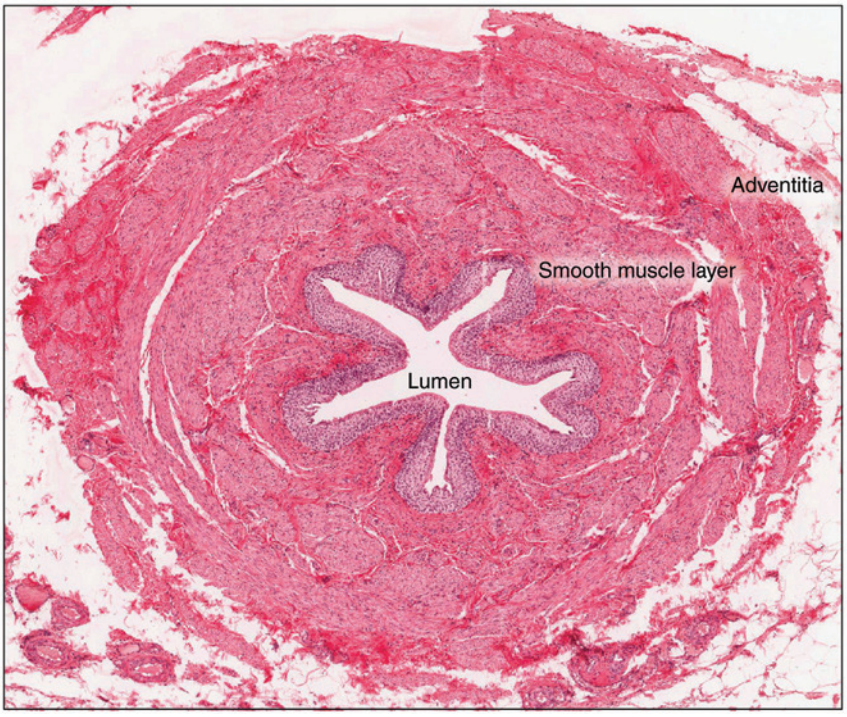


Figure 24.3 Ureter. Peristaltic contractions help move urine through the lumen with contributions from fluid pressure and gravity. LM × 128. (Micrograph provided by the Regents of the University of Michigan Medical School © 2012)

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24.3 Gross Anatomy of the Kidney

Learning Objectives

By the end of this section, you will be able to:

- Describe the external structure of the kidney, including its location, support structures, and covering
- Identify the major internal divisions and structures of the kidney
- Identify the major blood vessels associated with the kidney, and trace the path of blood through the kidney
- Compare and contrast the cortical and juxtamedullary nephrons
- Name structures found in the cortex and medulla
- Describe the physiological characteristics of the cortex and medulla

The kidneys lie on either side of the spine in the retroperitoneal space between the parietal peritoneum and the posterior abdominal wall, well protected by muscle, fat, and ribs. They are roughly the size of your fist, and the male kidney is typically a bit larger than the female kidney. The kidneys are well vascularized, receiving about 25 percent of the cardiac output at rest.

Interactive Link 24.3

There have never been sufficient kidney donations to provide a kidney to each person needing one. Watch this video (http://oer.aupress.ca/oer-202505/24.3) to learn about the TED (Technology, Entertainment, Design) Conference held in March 2011. In this video, Dr. Anthony Atala discusses a cutting-edge technique in which a new kidney is "printed." The successful utilization of this technology is still several years in the future, but imagine a time when you can print a replacement organ or tissue on demand.

External Anatomy

The left kidney is located at about the T12 to L3 vertebrae, whereas the right is lower due to slight displacement by the liver. Upper portions of the kidneys are somewhat protected by the eleventh and twelfth ribs (Figure 24.4). Each kidney weighs about 125–175 g in males and 115–155 g in females. They are about 11–14 cm in length, 6 cm wide, and 4 cm thick and are directly covered by a fibrous capsule composed of dense, irregular connective tissue that helps

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hold their shape and protect them. This capsule is covered by a shock-absorbing layer of adipose tissue called the renal fat pad, which in turn is encompassed by a tough renal fascia. The fascia and, to a lesser extent, the overlying peritoneum serve to firmly anchor the kidneys to the posterior abdominal wall in a retroperitoneal position.

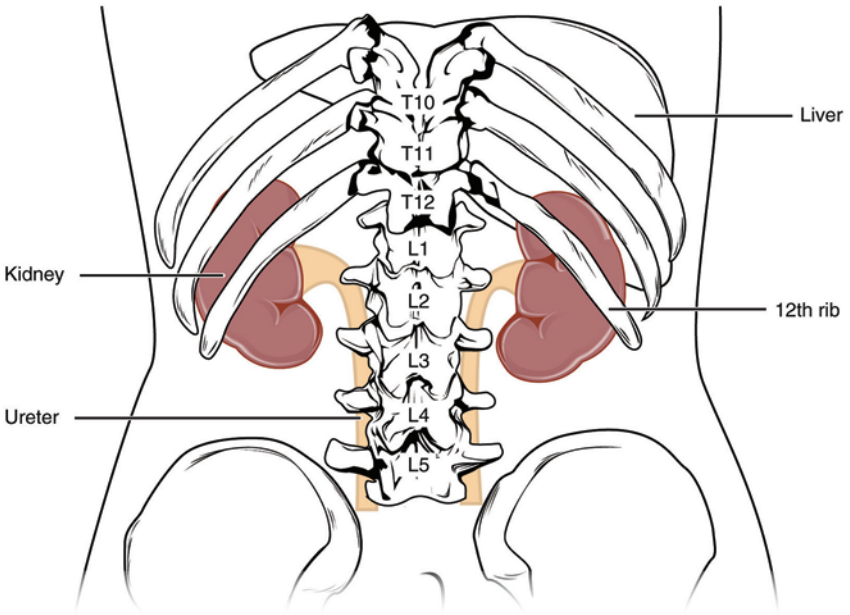


Figure 24.4 Kidneys. The kidneys are slightly protected by the ribs and are surrounded by fat for protection (not shown).

On the superior aspect of each kidney is the adrenal gland. The adrenal cortex directly influences renal function through the production of the hormone aldosterone to stimulate sodium reabsorption.

Internal Anatomy

A frontal section through the kidney reveals an outer region called the **renal cortex** and an inner region called the **medulla** (Figure 24.5). The **renal columns** are connective tissue extensions that radiate downward from the cortex through the medulla to separate the most characteristic features of the medulla, the **renal pyramids** and **renal papillae**. The papillae are bundles of collecting ducts that transport urine made by nephrons to the **calyces** of the kidney for excretion. The renal columns also serve to divide the kidney into 6–8 lobes and provide a supportive framework for vessels that enter and exit the cortex. The pyramids and renal columns taken together constitute the kidney lobes.

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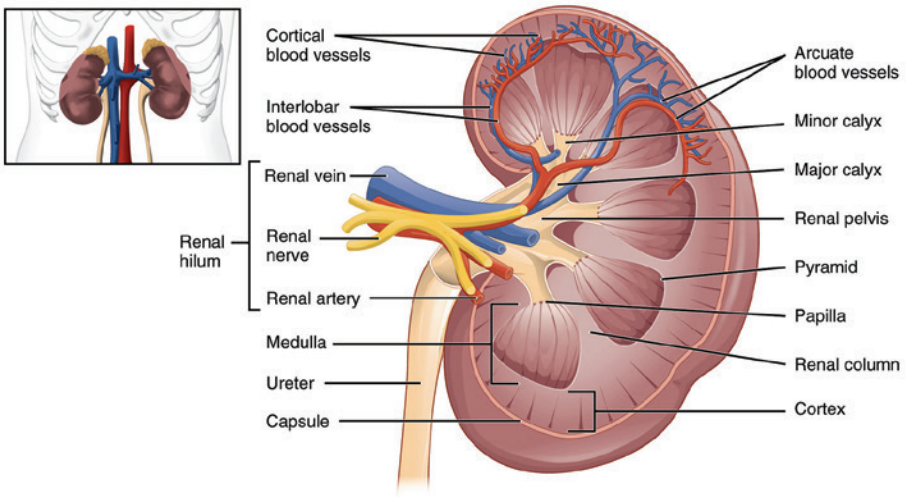


Figure 24.5 **Left Kidney.**

Renal Hilum

The **renal hilum** is the entry and exit site for structures servicing the kidneys: vessels, nerves, lymphatics, and ureters. The medial-facing hila are tucked into the sweeping convex outline of the cortex. Emerging from the hilum is the renal pelvis, which is formed from the major and minor calyxes in the kidney. The smooth muscle in the renal pelvis funnels urine via peristalsis into the ureter. The renal arteries form directly from the descending aorta, whereas the renal veins return cleansed blood directly to the inferior vena cava. The artery, vein, and renal pelvis are arranged in an anterior-to-posterior order.

Nephrons and Vessels

The renal artery first divides into segmental arteries, followed by further branching to form interlobar arteries that pass through the renal columns to reach the cortex (Figure 24.6). The interlobar arteries, in turn, branch into arcuate arteries, cortical radiate arteries, and then **afferent arterioles**. The afferent arterioles service about 1.3 million nephrons in each kidney.

Nephrons are the "functional units" of the kidney; they cleanse the blood and balance the constituents of the circulation. The afferent arterioles form a tuft of high-pressure capillaries about 200 μm in diameter, the **glomerulus**. The rest of the nephron consists of a continuous sophisticated tubule whose proximal end surrounds the glomerulus in an intimate embrace—this is **Bowman's** (**glomerular**) **capsule**. The glomerulus and Bowman's capsule together form the **renal corpuscle**. As mentioned earlier, these glomerular capillaries filter the blood based on particle size. After passing through the renal corpuscle,

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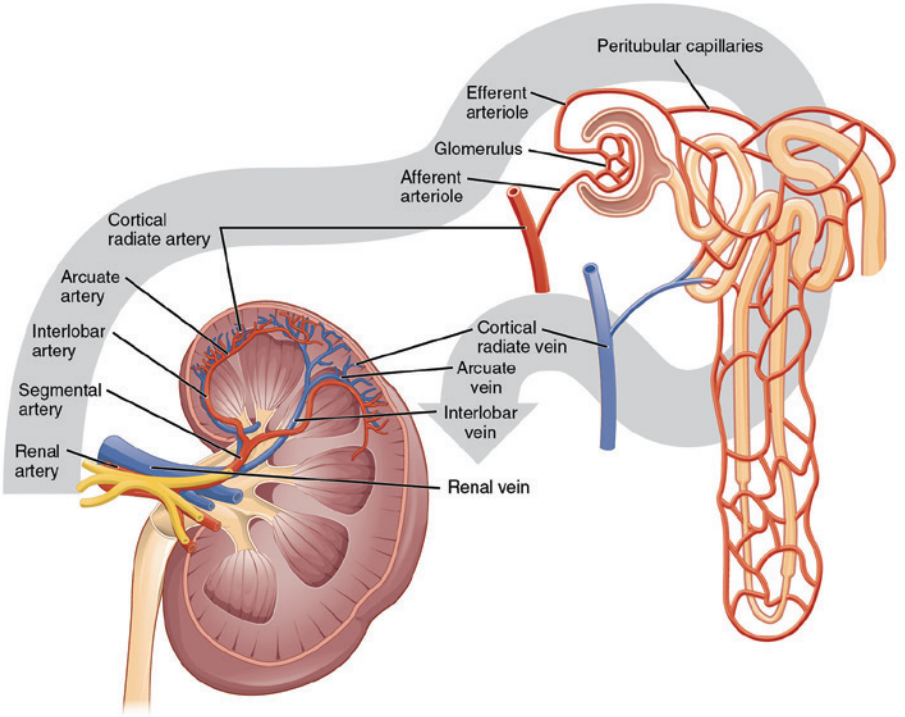


Figure 24.6 **Blood Flow in the Kidney.**

the capillaries form a second arteriole, the **efferent arteriole** (Figure 24.7). These will next form a capillary network around the more distal portions of the nephron tubule, the **peritubular capillaries** and **vasa recta**, before returning to the venous system. As the glomerular filtrate progresses through the nephron, these capillary networks recover most of the solutes and water and return them to the circulation. Since a capillary bed (the glomerulus) drains into a vessel that in turn forms a second capillary bed, the definition of a portal system is met. This is the only portal system in which an arteriole is found between the first and second capillary beds. (Portal systems also link the hypothalamus to the anterior pituitary and the blood vessels of the digestive viscera to the liver.)

Interactive Link 24.4

Visit this link (http://oer.aupress.ca/oer-202505/24.4) to view an interactive tutorial of the flow of blood through the kidney.

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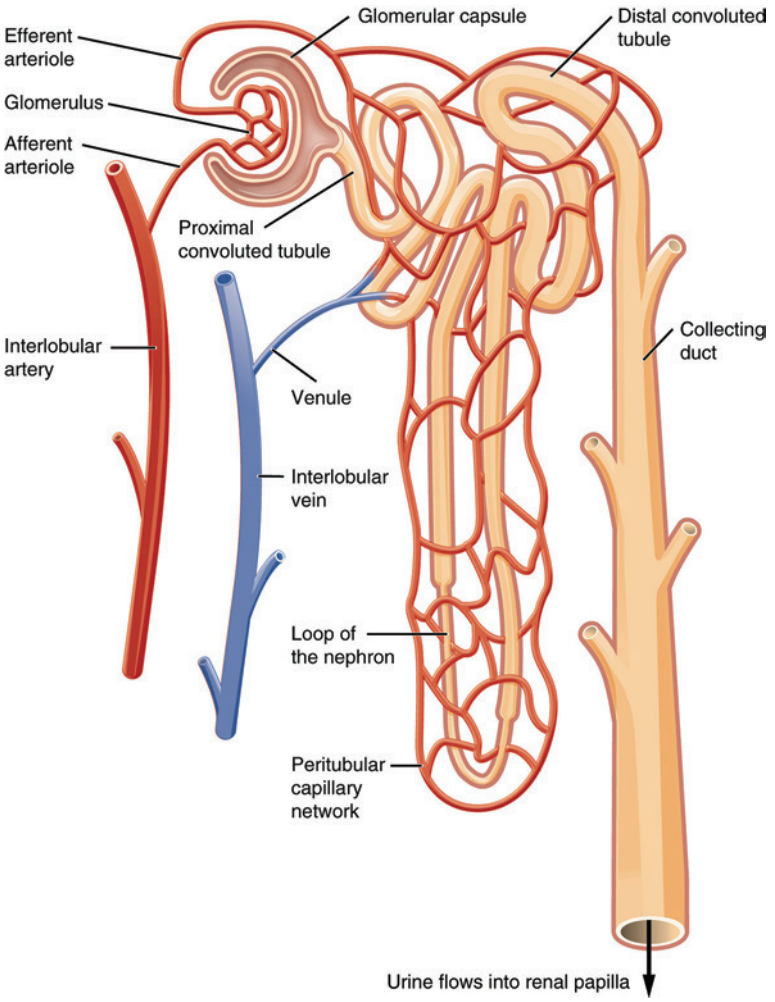


Figure 24.7 Blood Flow in the Nephron. The two capillary beds are clearly shown in this figure. The efferent arteriole is the connecting vessel between the glomerulus and the peritubular capillaries and vasa recta.

Cortex

In a dissected kidney, it is easy to identify the cortex; it appears lighter in colour compared to the rest of the kidney. All of the renal corpuscles as well as both the **proximal convoluted tubules** (**PCTs**) and the **distal convoluted tubules** (**DCTs**) are found here. Some nephrons have a short **loop of Henle** that does not dip beyond the cortex. These nephrons are called **cortical nephrons**. About 15 percent of nephrons have long loops of Henle that extend deep into the medulla and are called **juxtamedullary nephrons**.

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24.4 Microscopic Anatomy of the Kidney

Learning Objectives

By the end of this section, you will be able to:

- Distinguish the histological differences between the renal cortex and medulla
- Describe the structure of the filtration membrane
- Identify the major structures and subdivisions of the renal corpuscles, renal tubules, and renal capillaries
- Discuss the function of the peritubular capillaries and vasa recta
- Identify the location of the juxtaglomerular apparatus and describe the cells that line it
- Describe the histology of the proximal convoluted tubule, loop of Henle, distal convoluted tubule, and collecting ducts

The renal structures that conduct the essential work of the kidney cannot be seen by the naked eye. Only a light or electron microscope can reveal these structures. Even then, serial sections and computer reconstruction are necessary to give us a comprehensive view of the functional anatomy of the nephron and its associated blood vessels.

Nephrons take a simple filtrate of the blood and modify it into urine. Many changes take place in the different parts of the nephron before urine is created for disposal. The term **forming urine** will be used hereafter to describe the filtrate as it is modified into true urine. The principle task of the nephron population is to balance the plasma to homeostatic set points and excrete potential toxins in the urine. They do this by accomplishing three principle functions—filtration, reabsorption, and secretion. They also have additional secondary functions that exert control in three areas: blood pressure (via production of **renin**), red blood cell production (via the hormone EPO), and calcium absorption (via conversion of calcidiol into calcitriol, the active form of vitamin D).

Renal Corpuscle

The renal corpuscle consists of a tuft of capillaries called the glomerulus that is largely surrounded by Bowman's (glomerular) capsule. The glomerulus is a high-pressure capillary bed between afferent and efferent arterioles. Bowman's capsule surrounds the glomerulus to form a lumen and captures and directs this filtrate to the PCT. The outermost part of Bowman's capsule, the parietal layer, is a

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simple squamous epithelium. It transitions onto the glomerular capillaries in an intimate embrace to form the visceral layer of the capsule. Here, the cells are not squamous, but uniquely shaped cells (**podocytes**) extending fingerlike arms (**pedicels**) to cover the glomerular capillaries (Figure 24.8). These projections interdigitate to form **filtration slits**, leaving small gaps between the digits to form a sieve. As blood passes through the glomerulus, 10 to 20 percent of the plasma filters between these sieve-like fingers to be captured by Bowman's capsule and funneled to the PCT. Where the fenestrae (windows) in the glomerular capillaries match the spaces between the podocyte "fingers," the only thing separating the capillary lumen and the lumen of Bowman's capsule is their shared basement membrane (Figure 24.9). These three features compose what is known as the filtration membrane. This membrane permits very rapid movement of filtrate from capillary to capsule through pores that are only 70 nm in diameter.

The **fenestrations** prevent filtration of blood cells or large proteins but allow most other constituents through. These substances cross readily if they are less than 4 nm in size, and most pass freely up to 8 nm in size. An additional factor affecting the ability of substances to cross this barrier is their electric charge. The proteins associated with these pores are negatively charged, so they tend to repel negatively charged substances and allow positively charged substances to pass more readily. The basement membrane prevents filtration of medium-to-large proteins such as globulins. There are also **mesangial** cells in the filtration membrane that can contract to help regulate the rate of filtration of the glomerulus. Overall, filtration is regulated by fenestrations in capillary

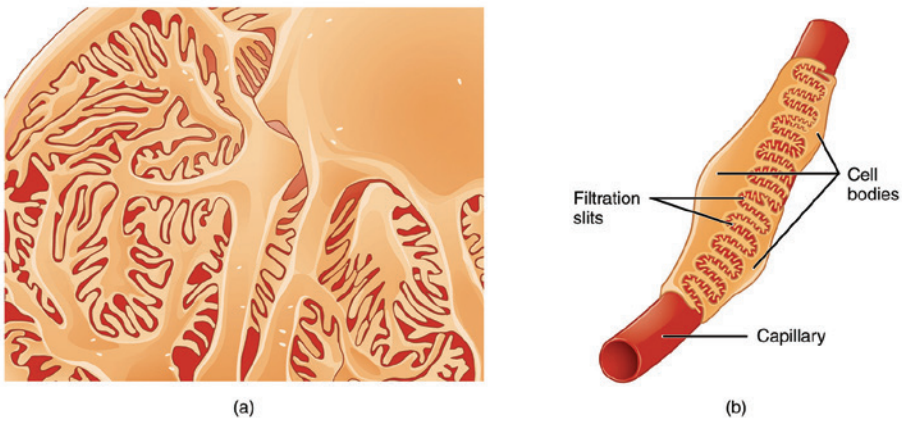


Figure 24.8 Podocytes. Podocytes interdigitate with structures called pedicels and filter substances in a way similar to fenestrations. In (a), the large cell body can be seen at the top right corner, with branches extending from the cell body. The smallest fingerlike extensions are the pedicels. Pedicels on one podocyte always interdigitate with the pedicels of another podocyte. (b) This capillary has two podocytes wrapped around it.

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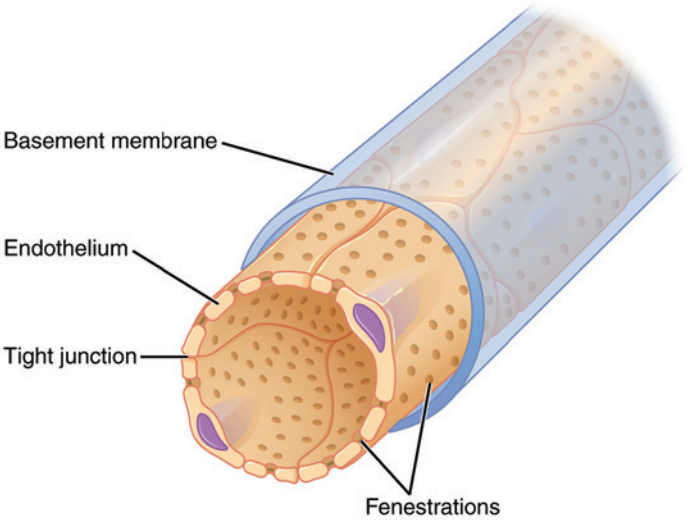


Figure 24.9 Fenestrated Capillary. Fenestrations allow many substances to diffuse from the blood based primarily on size.

endothelial cells, podocytes with filtration slits, membrane charge, and the basement membrane between capillary cells. The result is the creation of a filtrate that does not contain cells or large proteins and has a slight predominance of positively charged substances.

Lying just outside Bowman's capsule and the glomerulus is the **juxtaglomerular apparatus** (**JGA**; Figure 24.10). At the juncture where the afferent and efferent arterioles enter and leave Bowman's capsule, the initial part of the distal convoluted tubule (DCT) comes into direct contact with the arterioles. The wall of the DCT at that point forms a part of the JGA known as the **macula densa**. This cluster of cuboidal epithelial cells monitors the composition of fluid flowing through the DCT. In response to the concentration of Na^+ in the fluid flowing past them, these cells release paracrine signals. They also have a single, nonmotile cilium that responds to the rate of fluid movement in the tubule. The paracrine signals released in response to changes in flow rate and Na^+ concentration are adenosine triphosphate (ATP) and adenosine.

A second cell type in this apparatus is the **juxtaglomerular cell**. This is a modified, smooth muscle cell lining the afferent arteriole that can contract or relax in response to ATP or adenosine released by the macula densa. Such contraction and relaxation regulate blood flow to the glomerulus. If the osmolarity of the filtrate is too high (hyperosmotic), the juxtaglomerular cells will contract, decreasing the **glomerular filtration rate** (**GFR**) so less plasma is filtered, leading to less urine formation and greater retention of fluid. This will ultimately decrease blood osmolarity toward the physiologic norm. If the osmolarity of

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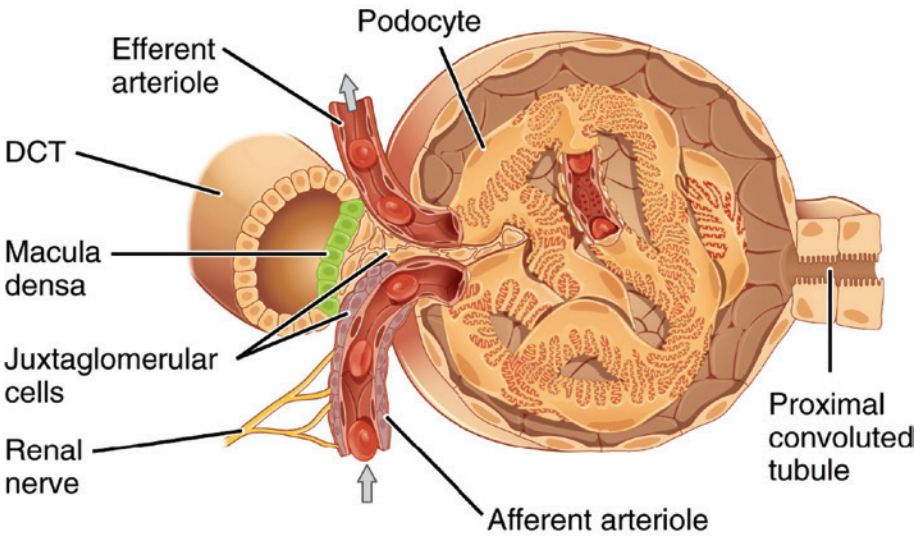


Figure 24.10 Juxtaglomerular Apparatus and Glomerulus. The JGA allows specialized cells to monitor the composition of the fluid in the DCT and adjust the glomerular filtration rate.

the filtrate is too low, the juxtaglomerular cells will relax, increasing the GFR and enhancing the loss of water to the urine, causing blood osmolarity to rise. In other words, when blood osmolarity goes up, filtration and urine formation decrease and water is retained. When blood osmolarity goes down, filtration and urine formation increase and water is lost by way of the urine. The net result of these opposing actions is to keep the rate of filtration relatively constant. A second function of the macula densa cells is to regulate **renin** release from the juxtaglomerular cells of the afferent arteriole (Figure 24.11). Active renin is a protein composed of 304 amino acids that cleaves several amino acids from **angiotensinogen** (a plasma protein) to produce **angiotensin I**. Angiotensin I is not biologically active until converted to angiotensin II by **angiotensin-converting enzyme** (**ACE**) from the lungs. **Angiotensin II** is a systemic vasoconstrictor that helps regulate blood pressure by increasing it. Angiotensin II also stimulates the release of the steroid hormone aldosterone from the adrenal cortex. Aldosterone stimulates Na^+ reabsorption by the kidney, which also results in water retention and increased blood pressure.

Proximal Convoluted Tubule (PCT)

Filtered fluid collected by Bowman's capsule enters into the PCT. It is called *convoluted* due to its tortuous path. Simple cuboidal cells form this tubule with prominent microvilli on the luminal surface, forming a **brush border**. These microvilli create a large surface area to maximize the absorption and secretion

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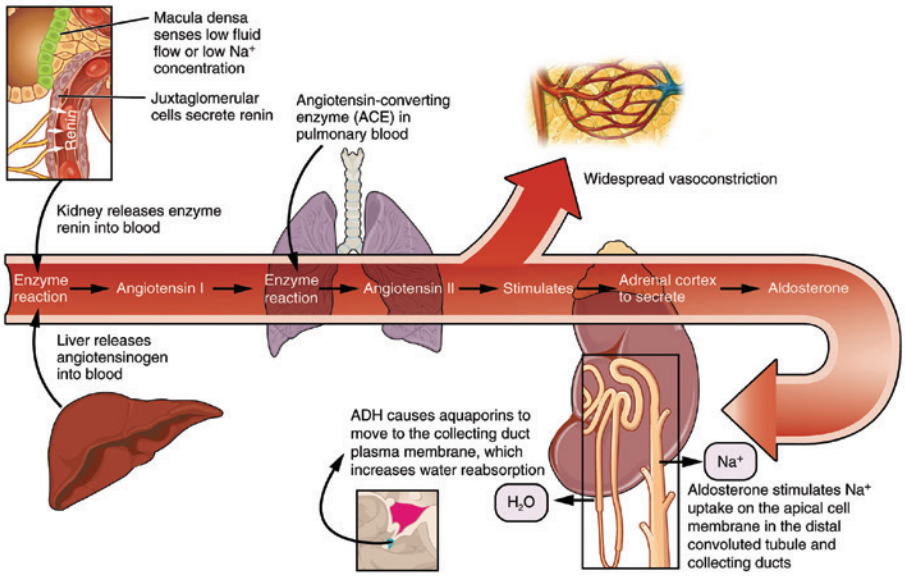


Figure 24.11 Conversion of Angiotensin I to Angiotensin II. The enzyme renin converts angiotensinogen into the proenzyme angiotensin I; the lung-derived enzyme ACE converts angiotensin I into active angiotensin II.

of solutes (Na^+, Cl^-, glucose, etc.), the most essential function of this portion of the nephron. These cells actively transport ions across their membranes, so they possess a high concentration of mitochondria in order to produce sufficient ATP.

Loop of Henle

The descending and ascending portions of the loop of Henle (sometimes referred to as the nephron loop) are, of course, just continuations of the same tubule. They run adjacent and parallel to each other after having made a hairpin turn at the deepest point of their descent. The descending loop of Henle consists of an initial short, thick portion and long, thin portion, whereas the ascending loop consists of an initial short, thin portion followed by a long, thick portion. The descending thick portion consists of simple cuboidal epithelium similar to that of the PCT. The descending and ascending thin portions consist of simple squamous epithelium. As you will see later, these are important differences, since different portions of the loop have different permeabilities for solutes and water. The ascending thick portion consists of simple cuboidal epithelium similar to the DCT.

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Distal Convoluted Tubule (DCT)

The DCT, like the PCT, is very tortuous and formed by simple cuboidal epithelium, but it is shorter than the PCT. These cells are not as active as those in the PCT; thus, there are fewer microvilli on the apical surface. However, these cells must also pump ions against their concentration gradient, so you will find large numbers of mitochondria, although fewer than in the PCT.

Collecting Ducts

The collecting ducts are continuous with the nephron but not technically part of it. In fact, each duct collects filtrate from several nephrons for final modification. Collecting ducts merge as they descend deeper in the medulla to form about 30 terminal ducts, which empty at a papilla. They are lined with simple squamous epithelium with receptors for ADH. When stimulated by ADH, these cells will insert **aquaporin** channel proteins into their membranes, which as their name suggests, allow water to pass from the duct lumen through the cells and into the interstitial spaces to be recovered by the vasa recta. This process allows for the recovery of large amounts of water from the filtrate back into the blood. In the absence of ADH, these channels are not inserted, resulting in the excretion of water in the form of dilute urine. Most, if not all, cells of the body contain aquaporin molecules, whose channels are so small that only water can pass. At least 10 types of aquaporins are known in humans, and 6 of those are found in the kidney. The function of all aquaporins is to allow the movement of water across the lipid-rich, hydrophobic cell membrane (Figure 24.12).

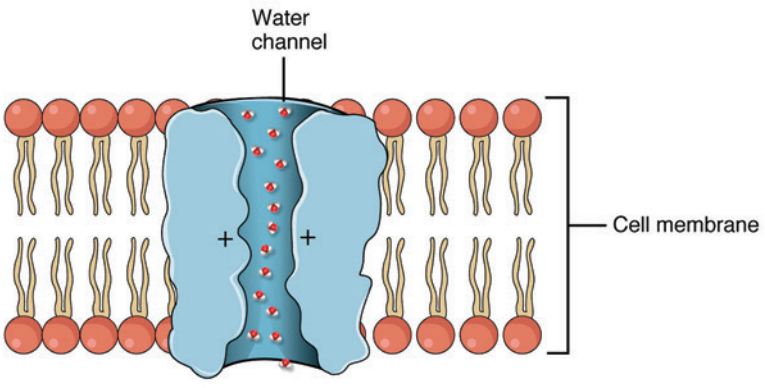


Figure 24.12 Aquaporin Water Channel. Positive charges inside the channel prevent the leakage of electrolytes across the cell membrane while allowing water to move due to osmosis.

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24.5 Physiology of Urine Formation

Learning Objectives

By the end of this section, you will be able to:

- Describe the hydrostatic and colloid osmotic forces that favor and oppose filtration
- Describe glomerular filtration rate (GFR), state the average value of GFR, and explain how clearance rate can be used to measure GFR
- Predict specific factors that will increase or decrease GFR
- State the percent of the filtrate that is normally reabsorbed, and explain why the process of reabsorption is so important

Having reviewed the anatomy and microanatomy of the urinary system, now is the time to focus on the physiology. You will discover that different parts of the nephron utilize specific processes to produce urine: filtration, reabsorption, and secretion. You will learn how each of these processes works and where they occur along the nephron and collecting ducts. The physiologic goal is to modify the composition of the plasma and, in doing so, produce the waste product urine.

Glomerular Filtration Rate (GFR)

The volume of filtrate formed by both kidneys per minute is termed the **glomerular filtration rate** (**GFR**). The heart pumps about 5 L blood per minute under resting conditions. Approximately 20 percent or 1 L enters the kidneys to be filtered. On average, this litre results in the production of about 125 mL/min filtrate produced in males (range of 90 to 140 mL/min) and 105 mL/min filtrate produced in females (range of 80 to 125 mL/min). This amount equates to a volume of about 180 L/day in males and 150 L/day in females. Ninety-nine percent of this filtrate is returned to the circulation by reabsorption so that only about 1–2 L of urine are produced per day.

GFR is influenced by the hydrostatic pressure and colloid osmotic pressure on either side of the capillary membrane of the glomerulus. Recall that filtration occurs as pressure forces fluid and solutes through a semipermeable barrier with the solute movement constrained by particle size. Hydrostatic pressure is the pressure produced by a fluid against a surface. If you have a fluid on both sides of a barrier, both fluids exert a pressure in opposing directions.

Net fluid movement will be in the direction of the lower pressure. Osmosis is the movement of solvent (water) across a membrane that is impermeable to

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a solute in the solution. This creates a pressure, osmotic pressure, which will exist until the solute concentration is the same on both sides of a semipermeable membrane. As long as the concentration differs, water will move. Glomerular filtration occurs when glomerular hydrostatic pressure exceeds the luminal hydrostatic pressure of Bowman's capsule. There is also an opposing force, the osmotic pressure, which is typically higher in the glomerular capillary.

To understand why this is so, look more closely at the microenvironment on either side of the filtration membrane. You will find osmotic pressure exerted by the solutes inside the lumen of the capillary as well as inside of Bowman's capsule. Since the filtration membrane limits the size of particles crossing the membrane, the osmotic pressure inside the glomerular capillary is higher than the osmotic pressure in Bowman's capsule. Recall that cells and the medium-to-large proteins cannot pass between the podocyte processes or through the fenestrations of the capillary endothelial cells. This means that red and white blood cells, platelets, albumins, and other proteins too large to pass through the filter remain in the capillary, creating an average colloid osmotic pressure of 30 mm Hg within the capillary. The absence of proteins in Bowman's space (the lumen within Bowman's capsule) results in an osmotic pressure near zero. Thus, the only pressure moving fluid across the capillary wall into the lumen of Bowman's space is hydrostatic pressure. Hydrostatic (fluid) pressure is sufficient to push water through the membrane despite the osmotic pressure working against it. The sum of all of the influences, both osmotic and hydrostatic, results in a **net filtration pressure** (**NFP**) of about 10 mm Hg (Figure 24.13).

A proper concentration of solutes in the blood is important in maintaining osmotic pressure both in the glomerulus and systemically. There are disorders in which too much protein passes through the filtration slits into the kidney filtrate. This excess protein in the filtrate leads to a deficiency of circulating plasma proteins. In turn, the presence of protein in the urine increases its osmolarity; this holds more water in the filtrate and results in an increase in urine volume. Because there is less circulating protein, principally albumin, the osmotic pressure of the blood falls. Less osmotic pressure pulling water into the capillaries tips the balance toward hydrostatic pressure, which tends to push it out of the capillaries. The net effect is that water is lost from the circulation to interstitial tissues and cells. This "plumps up" the tissues and cells, a condition termed **systemic edema**.

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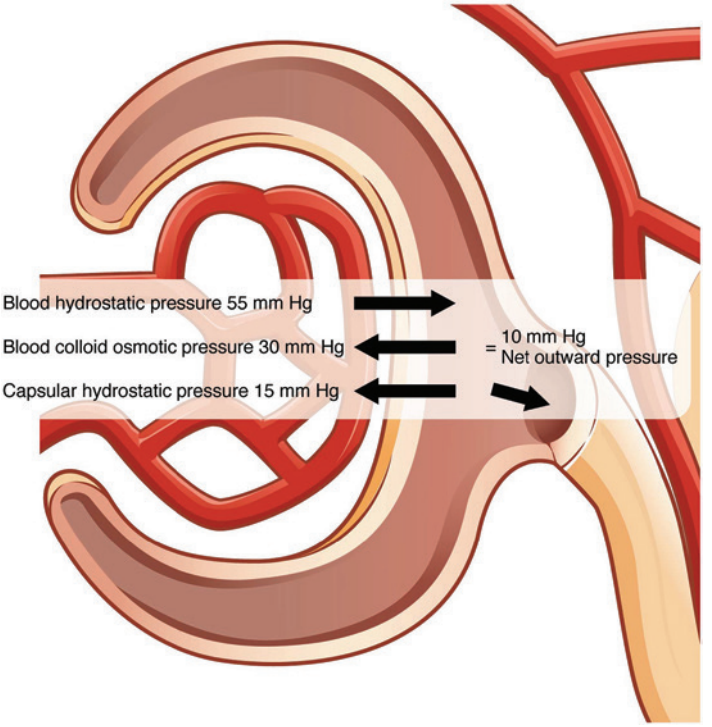


Figure 24.13 Net Filtration Pressure. The NFP is the sum of osmotic and hydrostatic pressures.

Net Filtration Pressure (NFP)

NFP determines filtration rates through the kidney. It is determined as follows:

NFP = Glomerular blood hydrostatic pressure (GBHP) − [capsular hydrostatic pressure (CHP) + blood colloid osmotic pressure (BCOP)] = 10 mm Hg

That is,

$$NFP = GBHP - [CHP + BCOP] = 10 \text{ mm Hg}$$

or

$$NFP = 55 - [15 + 30] = 10 \text{ mm Hg}$$

As you can see, there is a low net pressure across the filtration membrane. Intuitively, you should realize that minor changes in osmolarity of the blood or changes in capillary blood pressure result in major changes in the amount of filtrate formed at any given point in time. The kidney is able to cope with a

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wide range of blood pressures. In large part, this is due to the autoregulatory nature of smooth muscle. When you stretch it, it contracts. Thus, when blood pressure goes up, smooth muscle in the afferent capillaries contracts to limit any increase in blood flow and filtration rate. When blood pressure drops, the same capillaries relax to maintain blood flow and filtration rate. The net result is a relatively steady flow of blood into the glomerulus and a relatively steady filtration rate in spite of significant systemic blood pressure changes. Mean arterial blood pressure is calculated by adding one-third of the difference between the systolic and diastolic pressures to the diastolic pressure. Therefore, if the blood pressure is 110/80, the difference between systolic and diastolic pressure is 30. One-third of this is 10, and when you add this to the diastolic pressure of 80, you arrive at a calculated mean arterial pressure of 90 mm Hg. Therefore, if you use mean arterial pressure for the GBHP in the formula for calculating NFP, you can determine that as long as mean arterial pressure is above approximately 60 mm Hg, the pressure will be adequate to maintain glomerular filtration. Blood pressures below this level will impair renal function and cause systemic disorders that are severe enough to threaten survival. This condition is called shock.

24.6 Tubular Reabsorption

Learning Objectives

By the end of this section, you will be able to:

- List specific transport mechanisms occurring in different parts of the nephron, including active transport, osmosis, facilitated diffusion, and passive electrochemical gradients
- List the different membrane proteins of the nephron, including channels, transporters, and ATPase pumps
- Compare and contrast passive and active tubular reabsorption
- Explain why the differential permeability or impermeability of specific sections of the nephron tubules is necessary for urine formation
- Describe how and where water, organic compounds, and ions are reabsorbed in the nephron
- Explain the role of the loop of Henle, the vasa recta, and the countercurrent multiplication mechanisms in the concentration of urine
- List the locations in the nephron where tubular secretion occurs

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With up to 180 L per day passing through the nephrons of the kidney, it is quite obvious that most of that fluid and its contents must be reabsorbed. That recovery occurs in the PCT, loop of Henle, DCT, and the collecting ducts (Figure 24.14).

Various portions of the nephron differ in their capacity to reabsorb water and specific solutes. While much of the reabsorption and secretion occur passively based on concentration gradients, the amount of water that is reabsorbed or lost is tightly regulated. This control is exerted directly by ADH and aldosterone and indirectly by renin. Most water is recovered in the PCT, loop of Henle, and DCT. About 10 percent (about 18 L) reaches the collecting ducts. The collecting

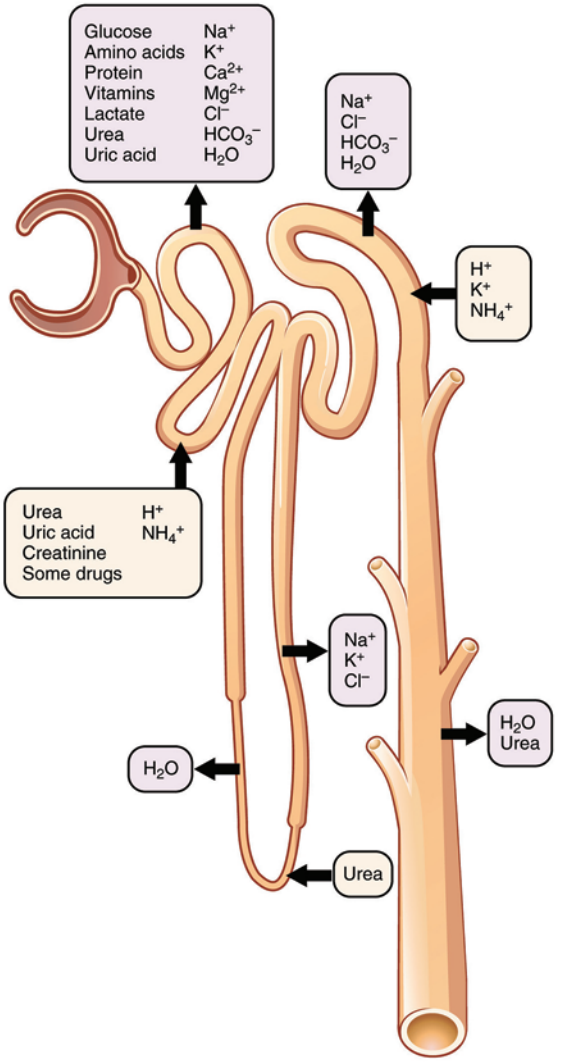


Figure 24.14 Locations of Secretion and Reabsorption in the Nephron.

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ducts, under the influence of ADH, can recover almost all of the water passing through them, in cases of dehydration, or almost none of the water, in cases of overhydration.

Mechanisms of Recovery

Mechanisms by which substances move across membranes for reabsorption or secretion include active transport, diffusion, facilitated diffusion, secondary active transport, and osmosis. These were discussed in chapter 3, and you may wish to review them.

Active transport utilizes energy, usually the energy found in a phosphate bond of ATP, to move a substance across a membrane from a low to a high concentration. It is very specific and must have an appropriately shaped receptor for the substance to be transported.

An example would be the active transport of Na^+ out of a cell and K^+ into a cell by the Na^+/K^+ pump. Both ions are moved in opposite directions from a lower to a higher concentration.

Simple diffusion moves a substance from a higher to a lower concentration down its concentration gradient. It requires no energy and only needs to be soluble.

Facilitated diffusion is similar to diffusion in that it moves a substance down its concentration gradient. The difference is that it requires specific membrane receptors or channel proteins for movement. The movement of glucose and, in certain situations, Na^+ ions is an example of facilitated diffusion. In some cases of mediated transport, two different substances share the same channel protein port; these mechanisms are described by the terms *symport* and *antiport*.

Symport mechanisms move two or more substances in the same direction at the same time, whereas antiport mechanisms move two or more substances in opposite directions across the cell membrane. Both mechanisms may utilize concentration gradients maintained by ATP pumps. As described previously, when active transport powers the transport of another substance in this way, it is called "secondary active transport." Glucose reabsorption in the kidneys is by secondary active transport. Na^+/K^+ ATPases on the basal membrane of a tubular cell constantly pump Na^+ out of the cell, maintaining a strong electrochemical gradient for Na^+ to move into the cell from the tubular lumen. On the luminal (apical) surface, a Na^+/glucose symport protein assists both Na^+ and glucose movement into the cell. The cotransporter moves glucose into the cell against its concentration gradient as Na^+ moves down the electrochemical gradient created by the basal membranes Na^+/K^+ ATPases. The glucose molecule then diffuses across the basal membrane by facilitated diffusion into the interstitial space and from there into peritubular capillaries.

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Most of the Ca^{++}, Na^{+}, glucose, and amino acids must be reabsorbed by the nephron to maintain homeostatic plasma concentrations. Other substances, such as urea, K^{+}, ammonia (NH_3), creatinine, and some drugs, are secreted into the filtrate as waste products. Acid-base balance is maintained through actions of the lungs and kidneys: The lungs rid the body of H^{+}, whereas the kidneys secrete or reabsorb H^{+} and HCO_3–. In the case of urea, about 50 percent is passively reabsorbed by the PCT. More is recovered by the collecting ducts as needed. ADH induces the insertion of urea transporters and aquaporin channel proteins.

Reabsorption and Secretion in the PCT

The renal corpuscle filters the blood to create a filtrate that differs from blood mainly in the absence of cells and large proteins. From this point to the ends of the collecting ducts, the filtrate or forming urine is undergoing modification through secretion and reabsorption before true urine is produced. The first point at which the forming urine is modified is in the PCT. Here, some substances are reabsorbed, whereas others are secreted. Note the use of the term *reabsorbed*. All of these substances were "absorbed" in the digestive tract—99 percent of the water and most of the solutes filtered by the nephron must be reabsorbed. Water and substances that are reabsorbed are returned to the circulation by the peritubular and vasa recta capillaries. It is important to understand the difference between the glomerulus and the peritubular and vasa recta capillaries. The glomerulus has a relatively high pressure inside its capillaries and can sustain this by dilating the afferent arteriole while constricting the efferent arteriole. This ensures adequate filtration pressure even as the systemic blood pressure varies. Movement of water into the peritubular capillaries and vasa recta will be influenced primarily by osmolarity and concentration gradients. Sodium is actively pumped out of the PCT into the interstitial spaces between cells and diffuses down its concentration gradient into the peritubular capillary. As it does so, water will follow passively to maintain an isotonic fluid environment inside the capillary. This is called obligatory water reabsorption because water is "obliged" to follow the Na^{+} (Figure 24.15).

More substances move across the membranes of the PCT than any other portion of the nephron. Many of these substances (amino acids and glucose) use symport mechanisms for transport along with Na^{+}. Antiport, active transport, diffusion, and facilitated diffusion are additional mechanisms by which substances are moved from one side of a membrane to the other. Recall that cells have two surfaces: apical and basal. The apical surface is the one facing the lumen or open space of a cavity or tube—in this case, the inside of the PCT. The basal surface of the cell faces the connective tissue base to which the cell attaches (basement membrane) or the cell membrane closer to the basement

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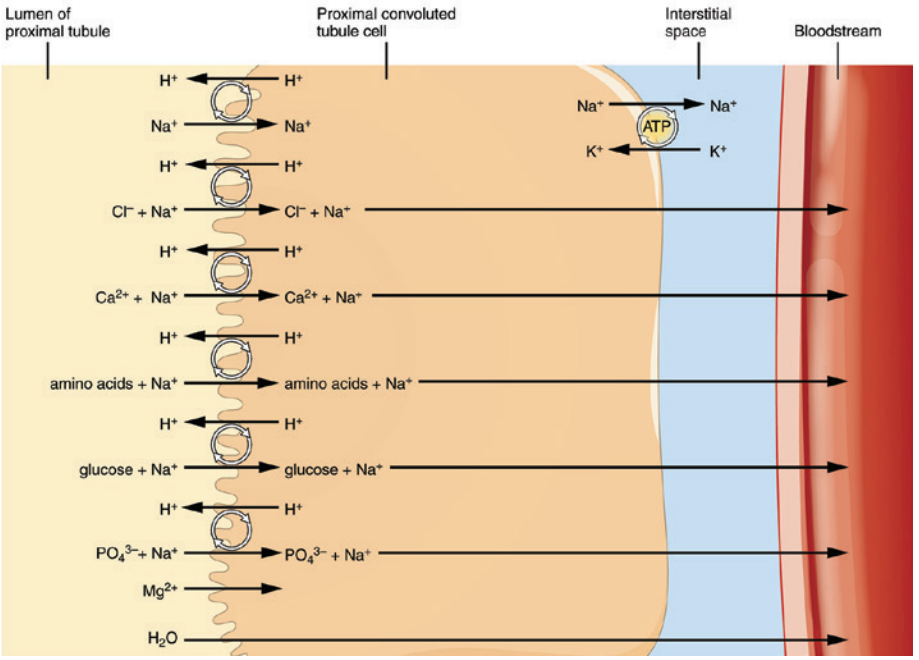


Figure 24.15 **Substances Reabsorbed and Secreted by the PCT.**

membrane if there is a stratified layer of cells. In the PCT, there is a single layer of simple cuboidal endothelial cells against the basement membrane. The numbers and particular types of pumps and channels vary between the apical and basilar surfaces. A few of the substances that are transported with Na^+ (symport mechanism) on the apical membrane include Cl^-, Ca^{++}, amino acids, glucose, and PO_4^{3-}. Sodium is actively exchanged for K^+ using ATP on the basal membrane. Most of the substances transported by a symport mechanism on the apical membrane are transported by facilitated diffusion on the basal membrane. At least three ions, K^+, Ca^{++}, and Mg^{++}, diffuse laterally between adjacent cell membranes (transcellular).

About 67 percent of the water, Na^+, and K^+ entering the nephron is reabsorbed in the PCT and returned to the circulation. Almost 100 percent of glucose, amino acids, and other organic substances such as vitamins are normally recovered here. Some glucose may appear in the urine if circulating glucose levels are high enough that all the glucose transporters in the PCT are saturated so that their capacity to move glucose is exceeded (transport maximum, or T_m). In males, the maximum amount of glucose that can be recovered is about 375 mg/min, whereas in females, it is about 300 mg/min. This recovery rate translates to an arterial concentration of about 200 mg/dL. Though an exceptionally high sugar intake might cause sugar to appear briefly in the urine, the appearance of **glycosuria** usually points to type I or II diabetes mellitus. The transport of

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glucose from the lumen of the PCT to the interstitial space is similar to the way it is absorbed by the small intestine. Both glucose and Na^+ bind simultaneously to the same symport proteins on the apical surface of the cell to be transported in the same direction, toward the interstitial space. Sodium moves down its electrochemical and concentration gradient into the cell and takes glucose with it. Na^+ is then actively pumped out of the cell at the basal surface of the cell into the interstitial space. Glucose leaves the cell to enter the interstitial space by facilitated diffusion. The energy to move glucose comes from the Na^+/K^+ ATPase that pumps Na^+ out of the cell on the basal surface. Fifty percent of Cl^- and variable quantities of Ca^{++}, Mg^{++}, and HPO_4^{2-} are also recovered in the PCT.

Recovery of bicarbonate (HCO_3–) is vital to the maintenance of acid-base balance, since it is a very powerful and fast-acting buffer. An important enzyme is used to catalyze this mechanism: carbonic anhydrase (CA). The same enzyme and reaction are used in red blood cells in the transportation of CO_2, in the stomach to produce hydrochloric acid, and in the pancreas to produce HCO_3– to buffer acidic chyme from the stomach. In the kidney, most of the CA is located within the cell, but a small amount is bound to the brush border of the membrane on the apical surface of the cell. In the lumen of the PCT, HCO_3– combines with hydrogen ions to form carbonic acid (H_2CO_3). This is enzymatically catalyzed into CO_2 and water, which diffuse across the apical membrane into the cell. Water can move osmotically across the lipid bilayer membrane due to the presence of aquaporin water channels. Inside the cell, the reverse reaction occurs to produce bicarbonate ions (HCO_3–). These bicarbonate ions are cotransported with Na^+ across the basal membrane to the interstitial space around the PCT (Figure 24.16). At the same time this is occurring, a Na^+/H^+ antiporter excretes H^+ into the lumen while it recovers Na^+. Note how the hydrogen ion is recycled so that bicarbonate can be recovered. Also note that a Na^+ gradient is created by the Na^+/K^+ pump:

$$HCO_3^- + H^+ \leftrightarrow H_2CO_3 \leftrightarrow CO_2 + H_2O$$

The significant recovery of solutes from the PCT lumen to the interstitial space creates an osmotic gradient that promotes water recovery. As noted before, water moves through channels created by the aquaporin proteins. These proteins are found in all cells in varying amounts and help regulate water movement across membranes and through cells by creating a passageway across the hydrophobic lipid bilayer membrane. Changing the number of aquaporin proteins in membranes of the collecting ducts also helps regulate the osmolarity of the blood. The movement of many positively charged ions also creates an electrochemical gradient. This charge promotes the movement of negative ions toward the interstitial spaces and the movement of positive ions toward the lumen.

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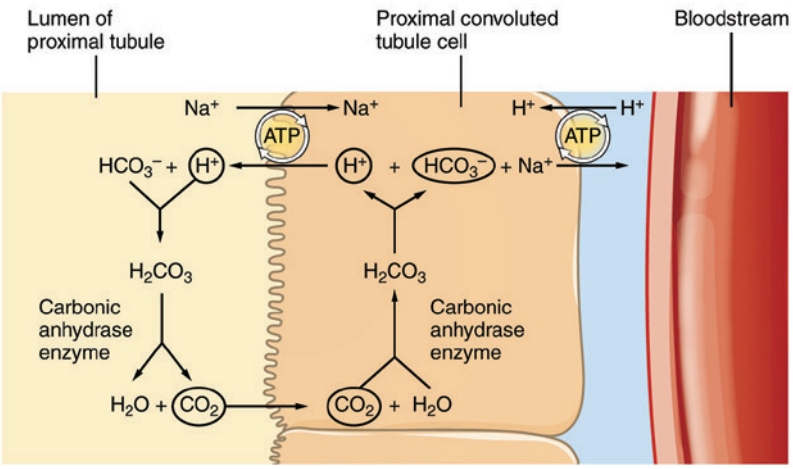


Figure 24.16 **Reabsorption of Bicarbonate from the PCT.**

Reabsorption and Secretion in the Loop of Henle

The loop of Henle consists of two sections: thick and thin descending and thin and thick ascending sections. The loops of cortical nephrons do not extend into the renal medulla very far, if at all. Juxtamedullary nephrons have loops that extend variable distances, some very deep into the medulla. The descending and ascending portions of the loop are highly specialized to enable recovery of much of the Na^+ and water that were filtered by the glomerulus. As the forming urine moves through the loop, the osmolarity will change from isosmotic with blood (about 278–300 mOsmol/kg) to both a very hypertonic solution of about 1,200 mOsmol/kg and a very hypotonic solution of about 100 mOsmol/kg. These changes are accomplished by osmosis in the descending limb and active transport in the ascending limb. Solutes and water recovered from these loops are returned to the circulation by way of the vasa recta.

Descending Loop

The majority of the descending loop is composed of simple squamous epithelial cells; to simplify the function of the loop, this discussion focuses on these cells. These membranes have permanent aquaporin channel proteins that allow unrestricted movement of water from the descending loop into the surrounding interstitium as osmolarity increases from about 300 mOsmol/kg to about 1,200 mOsmol/kg in the filtrate. This increase results in reabsorption of up to 15 percent of the water entering the nephron. Modest amounts of urea, Na^+, and other ions are also recovered here.

Most of the solutes that were filtered in the glomerulus have now been recovered along with a majority of water, about 82 percent. As the forming

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urine enters the ascending loop, major adjustments will be made to the concentration of solutes to create what you perceive as urine.

Ascending Loop

The ascending loop is made of very short thin and longer thick portions. Once again, to simplify the function, this section only considers the thick portion. The thick portion is lined with simple cuboidal epithelium without a brush border. It is completely impermeable to water due to the absence of aquaporin proteins, but ions, mainly Na^+ and Cl^-, are actively reabsorbed by a cotransport system. This has two significant effects: Removal of NaCl while retaining water leads to a hypoosomotic filtrate by the time it reaches the DCT; pumping NaCl into the interstitial space contributes to the hyperosmotic environment in the kidney medulla.

The Na^+/K^+ ATPase pumps in the basal membrane create an electrochemical gradient, allowing reabsorption of Cl^- by Na^+/Cl^- symporters in the apical membrane. At the same time that Na^+ is actively pumped from the basal side of the cell into the interstitial fluid, Cl^- follows the Na^+ from the lumen into the interstitial fluid by a paracellular route between cells through **leaky tight junctions**. These are found between cells of the ascending loop, where they allow certain solutes to move according to their concentration gradient. Most of the K^+ that enters the cell via symporters returns to the lumen (down its concentration gradient) through leaky channels in the apical membrane. Note the environment now created in the interstitial space: With the "back door exiting" K^+, there is one Na^+ and two Cl^- ions left in the interstitium surrounding the ascending loop. Therefore, in comparison to the lumen of the loop, the interstitial space is now a negatively charged environment. This negative charge attracts cations (Na^+, K^+, Ca^{++}, and Mg^{++}) from the lumen via a paracellular route to the interstitial space and vasa recta.

Countercurrent Multiplier System

The structure of the loop of Henle and associated vasa recta create a **countercurrent multiplier system** (Figure 24.17). The countercurrent term comes from the fact that the descending and ascending loops are next to each other, and their fluid flows in opposite directions (countercurrent). The multiplier term is due to the action of solute pumps that increase (multiply) the concentrations of urea and Na^+ deep in the medulla.

As discussed in the previous section, the ascending loop actively reabsorbs NaCl out of the forming urine into the interstitial spaces. In addition, collecting ducts have urea pumps that actively pump urea into the interstitial spaces. This results in the recovery of NaCl to the circulation via the vasa recta and creates a high osmolar environment in the depths of the medulla.

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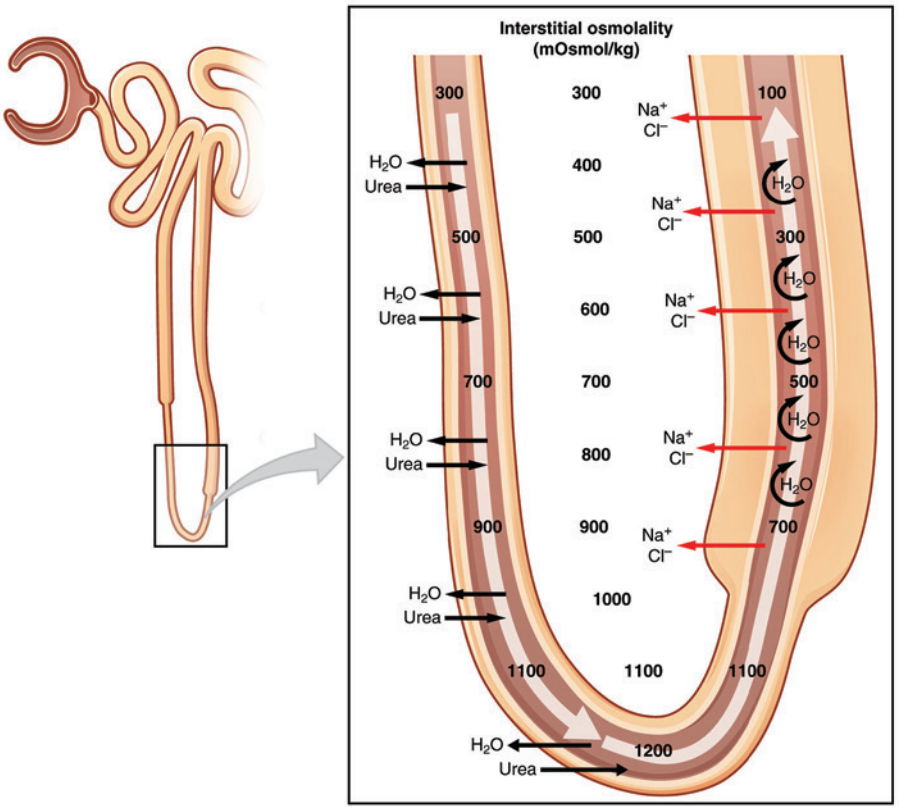


Figure 24.17 **Countercurrent Multiplier System.**

Ammonia (NH_3) is a toxic by-product of protein metabolism. It is formed as amino acids are deaminated by liver hepatocytes. That means that the amine group, NH_2, is removed from amino acids as they are broken down. Most of the resulting ammonia is converted into urea by liver hepatocytes. Urea is not only less toxic but utilized to aid in the recovery of water by the loop of Henle and collecting ducts. At the same time that water is freely diffusing out of the descending loop through aquaporin channels into the interstitial spaces of the medulla, urea freely diffuses into the lumen of the descending loop as it descends deeper into the medulla, much of it to be reabsorbed from the forming urine when it reaches the collecting duct. Thus, the movement of Na^+ and urea into the interstitial spaces by these mechanisms creates the hyperosmotic environment of the medulla. The net result of this countercurrent multiplier system is to recover both water and Na^+ in the circulation.

The amino acid glutamine can be deaminated by the kidney. As NH_2 from the amino acid is converted into NH_3 and pumped into the lumen of the PCT, Na^+ and HCO_3– are excreted into the interstitial fluid of the renal pyramid via a symport mechanism. When this process occurs in the cells of the PCT, the added benefit

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is a net loss of a hydrogen ion (complexed to ammonia to form the weak acid NH_4) in the urine and a gain of a bicarbonate ion (HCO_3–) in the blood. Ammonia and bicarbonate are exchanged in a one-to-one ratio. This exchange is yet another means by which the body can buffer and excrete acid. The presence of aquaporin channels in the descending loop allows prodigious quantities of water to leave the loop and enter the hyperosmolar interstitium of the pyramid, where it is returned to the circulation by the vasa recta. As the loop turns to become the ascending loop, there is an absence of aquaporin channels, so water cannot leave the loop. However, in the basal membrane of cells of the thick ascending loop, ATPase pumps actively remove Na^+ from the cell. A $Na^+/K^+/2Cl^-$ symporter in the apical membrane passively allows these ions to enter the cell cytoplasm from the lumen of the loop down a concentration gradient created by the pump. This mechanism works to dilute the fluid of the ascending loop ultimately to approximately 50–100 mOsmol/L.

At the transition from the DCT to the collecting duct, about 20 percent of the original water is still present and about 10 percent of the sodium. If no other mechanism for water reabsorption existed, about 20–25 L of urine would be produced. Now consider what is happening in the adjacent capillaries, the vasa recta. They are recovering both solutes and water at a rate that preserves the countercurrent multiplier system. In general, blood flows slowly in capillaries to allow time for exchange of nutrients and wastes. In the vasa recta particularly, this rate of flow is important for two additional reasons. The flow must be slow to allow blood cells to lose and regain water without either crenating or bursting. Second, a rapid flow would remove too much Na^+ and urea, destroying the osmolar gradient that is necessary for the recovery of solutes and water. Thus, by flowing slowly to preserve the countercurrent mechanism, as the vasa recta descend, Na^+ and urea are freely able to enter the capillary, while water freely leaves; as they ascend, Na^+ and urea are secreted into the surrounding medulla, while water reenters and is removed.

Interactive Link 24.5

Watch this video (http://oer.aupress.ca/oer-202505/24.5) to learn about the countercurrent multiplier system.

Reabsorption and Secretion in the Distal Convoluted Tubule

Approximately 80 percent of filtered water has been recovered by the time the dilute forming urine enters the DCT. The DCT will recover another 10–15 percent

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before the forming urine enters the collecting ducts. Aldosterone increases the amount of Na^+/K^+ ATPase in the basal membrane of the DCT and collecting duct. The movement of Na^+ out of the lumen of the collecting duct creates a negative charge that promotes the movement of Cl^- out of the lumen into the interstitial space by a paracellular route across tight junctions. Peritubular capillaries receive the solutes and water, returning them to the circulation.

Cells of the DCT also recover Ca^{++} from the filtrate. Receptors for parathyroid hormone (PTH) are found in DCT cells and, when bound to PTH, induce the insertion of calcium channels on their luminal surface. The channels enhance Ca^{++} recovery from the forming urine. In addition, as Na^+ is pumped out of the cell, the resulting electrochemical gradient attracts Ca^{++} into the cell. Finally, calcitriol (1,25-dihydroxyvitamin D, the active form of vitamin D) is very important for calcium recovery. It induces the production of calcium-binding proteins that transport Ca^{++} into the cell. These binding proteins are also important for the movement of calcium inside the cell and aid in exocytosis of calcium across the basolateral membrane. Any Ca^{++} not reabsorbed at this point is lost in the urine.

Collecting Ducts and Recovery of Water

Solutes move across the membranes of the collecting ducts, which contain two distinct cell types: principal cells and intercalated cells. A **principal cell** possesses channels for the recovery or loss of sodium and potassium. An **intercalated cell** secretes or absorbs acid or bicarbonate. As in other portions of the nephron, there is an array of micromachines (pumps and channels) on display in the membranes of these cells.

Regulation of urine volume and osmolarity are major functions of the collecting ducts. By varying the amount of water that is recovered, the collecting ducts play a major role in maintaining the body's normal osmolarity. If the blood becomes hyperosmotic, the collecting ducts recover more water to dilute the blood and restore normal osmolarity; if the blood becomes hypoosmotic, the collecting ducts recover less water, allowing more water to be excreted in the urine and helping return the blood's osmolarity to normal. Another way of saying this is if plasma osmolarity rises, more water is recovered and urine volume decreases; if plasma osmolarity falls, less water is recovered and urine volume increases. This function is regulated by the posterior pituitary hormone ADH (vasopressin). With mild dehydration, plasma osmolarity rises slightly. This increase is detected by osmoreceptors in the hypothalamus, which stimulates the release of ADH from the posterior pituitary. If plasma osmolarity decreases slightly, the opposite occurs.

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When stimulated by ADH, aquaporin channels are inserted into the apical membrane of principal cells, which line the collecting ducts. As the ducts descend through the medulla, the osmolarity surrounding them increases (due to the countercurrent mechanisms described above). If aquaporin water channels are present, water will be osmotically pulled from the collecting duct into the surrounding interstitial space and into the peritubular capillaries. Therefore, the final urine will be more concentrated. If less ADH is secreted, fewer aquaporin channels are inserted and less water is recovered, resulting in dilute urine. By altering the number of aquaporin channels, the volume of water recovered or lost is altered. This, in turn, regulates the blood osmolarity, blood pressure, and osmolarity of the urine.

As Na^+ is pumped from the forming urine, water is passively recaptured for the circulation; this preservation of vascular volume is critically important for the maintenance of a normal blood pressure. Aldosterone is secreted by the adrenal cortex in response to angiotensin II stimulation. As an extremely potent vasoconstrictor, angiotensin II functions immediately to increase blood pressure. By also stimulating aldosterone production, it provides a longer-lasting mechanism to support blood pressure by maintaining vascular volume (water recovery).

In addition to receptors for ADH, principal cells have receptors for the steroid hormone aldosterone. While ADH is primarily involved in the regulation of water recovery, aldosterone regulates Na^+ recovery. Aldosterone stimulates principal cells to manufacture luminal Na^+ and K^+ channels as well as Na^+/K^+ ATPase pumps on the basal membrane of the cells. When aldosterone output increases, more Na^+ is recovered from the forming urine, and water follows the Na^+ passively. As the pump recovers Na^+ for the body, it is also pumping K^+ into the forming urine, since the pump moves K^+ in the opposite direction. When aldosterone decreases, more Na^+ remains in the forming urine, and more K^+ is recovered in the circulation. Symport channels move Na^+ and Cl^- together. Still other channels in the principal cells secrete K^+ into the collecting duct in direct proportion to the recovery of Na^+.

Intercalated cells play significant roles in regulating blood pH. Intercalated cells reabsorb K^+ and HCO_3- while secreting H^+. This function lowers the acidity of the plasma while increasing the acidity of the urine.

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24.7 Regulation of Renal Blood Flow

Learning Objectives

By the end of this section, you will be able to:

- Describe the myogenic and tubuloglomerular feedback mechanisms and explain how they affect urine volume and composition
- Describe the function of the juxtaglomerular apparatus

It is vital that the flow of blood through the kidney be at a suitable rate to allow filtration. This rate determines how much solute is retained or discarded, how much water is retained or discarded, and ultimately, the osmolarity of blood and the blood pressure of the body.

Sympathetic Nerves

The kidneys are innervated by the sympathetic neurons of the autonomic nervous system via the celiac plexus and splanchnic nerves. Reduction of sympathetic stimulation results in vasodilation and increased blood flow through the kidneys during resting conditions. When the frequency of action potentials increases, the arteriolar smooth muscle constricts (vasoconstriction), resulting in diminished glomerular flow, so less filtration occurs. Under conditions of stress, sympathetic nervous activity increases, resulting in the direct vasoconstriction of afferent arterioles (norepinephrine effect) as well as stimulation of the adrenal medulla. The adrenal medulla, in turn, produces a generalized vasoconstriction through the release of epinephrine. This includes vasoconstriction of the afferent arterioles, further reducing the volume of blood flowing through the kidneys. This process redirects blood to other organs with more immediate needs. If blood pressure falls, the sympathetic nerves will also stimulate the release of renin. Additional renin increases production of the powerful vasoconstrictor angiotensin II. Angiotensin II, as discussed in section 24.6 Tubular Reabsorption, will also stimulate aldosterone production to augment blood volume through retention of more Na^+ and water. Only a 10 mm Hg pressure differential across the glomerulus is required for normal GFR, so very small changes in afferent arterial pressure significantly increase or decrease GFR.

Autoregulation

The kidneys are very effective at regulating the rate of blood flow over a wide range of blood pressures. Your blood pressure will decrease when you are

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relaxed or sleeping. It will increase when exercising. Yet despite these changes, the filtration rate through the kidney will change very little. This is due to two internal autoregulatory mechanisms that operate without outside influence: the myogenic mechanism and the tubuloglomerular feedback mechanism.

Arteriole Myogenic Mechanism

The **myogenic mechanism** regulating blood flow within the kidney depends on a characteristic shared by most smooth muscle cells of the body. When you stretch a smooth muscle cell, it contracts; when you stop, it relaxes, restoring its resting length. This mechanism works in the afferent arteriole that supplies the glomerulus. When blood pressure increases, smooth muscle cells in the wall of the arteriole are stretched and respond by contracting to resist the pressure, resulting in little change in flow. When blood pressure drops, the same smooth muscle cells relax to lower resistance, allowing a continued even flow of blood.

Tubuloglomerular Feedback

The **tubuloglomerular feedback** mechanism involves the JGA and a paracrine signalling mechanism utilizing ATP, adenosine, and nitric oxide (NO). This mechanism stimulates either contraction or relaxation of afferent arteriolar smooth muscle cells (Table 24.1). Recall that the DCT is in intimate contact with the afferent and efferent arterioles of the glomerulus. Specialized macula densa cells in this segment of the tubule respond to changes in the fluid flow rate and Na^+ concentration. As GFR increases, there is less time for NaCl to be reabsorbed in the PCT, resulting in higher osmolarity in the filtrate. The increased fluid movement more strongly deflects single nonmotile cilia on macula densa cells. This increased osmolarity of the forming urine, and the greater flow rate within the DCT, activates macula densa cells to respond by releasing ATP and adenosine (a metabolite of ATP). ATP and adenosine act locally as paracrine factors to stimulate the myogenic juxtaglomerular cells of the afferent arteriole to constrict, slowing blood flow and reducing GFR. Conversely, when GFR decreases, less Na^+ is in the forming urine, and most will be reabsorbed before reaching the macula densa, which will result in decreased ATP and adenosine, allowing the afferent arteriole to dilate and increase GFR. NO has the opposite effect, relaxing the afferent arteriole at the same time ATP and adenosine are stimulating it to contract. Thus, NO fine-tunes the effects of adenosine and ATP on GFR.

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Table 24.1 Paracrine Mechanisms Controlling Glomerular Filtration Rate

Change in GFR	NaCl absorption	Role of ATP and adenosine / role of NO	Effect on GFR
Increased GFR	Tubular NaCl increases	ATP and adenosine increase, causing vasoconstriction	Vasoconstriction slows GFR
Decreased GFR	Tubular NaCl decreases	ATP and adenosine decrease, causing vasodilation	Vasodilation increases GFR
Increased GFR	Tubular NaCl increases	NO increases, causing vasodilation	Vasodilation increases GFR
Decreased GFR	Tubular NaCl decreases	NO decreases, causing vasoconstriction	Vasoconstriction decreases GFR

24.8 Endocrine Regulation of Kidney Function

Learning Objectives

By the end of this section, you will be able to:

- Describe how each of the following functions in the extrinsic control of GFR: renin-angiotensin mechanism, natriuretic peptides, and sympathetic adrenergic activity
- Describe how each of the following works to regulate reabsorption and secretion so as to affect urine volume and composition: renin-angiotensin system, aldosterone, antidiuretic hormone, and natriuretic peptides
- Name and define the roles of other hormones that regulate kidney control

Several hormones have specific, important roles in regulating kidney function. They act to stimulate or inhibit blood flow. Some of these are endocrine, acting from a distance, whereas others are paracrine, acting locally.

Renin-Angiotensin-Aldosterone

Renin is an enzyme that is produced by the juxtaglomerular (JG) cells of the afferent arteriole at the JGA. It enzymatically converts angiotensinogen (made by the liver, freely circulating) into angiotensin I. Its release is stimulated by

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prostaglandins and NO from the JGA in response to decreased extracellular fluid volume.

ACE is not a hormone, but it is functionally important in regulating systemic blood pressure and kidney function. It is produced in the lungs but binds to the surfaces of endothelial cells in the afferent arterioles and glomerulus. It enzymatically converts inactive angiotensin I into active angiotensin II. ACE is important in raising blood pressure. People with high blood pressure are sometimes prescribed ACE inhibitors to lower their blood pressure.

Angiotensin II is a potent vasoconstrictor that plays an immediate role in the regulation of blood pressure. It acts systemically to cause vasoconstriction as well as constriction of both the afferent and efferent arterioles of the glomerulus. In instances of blood loss or dehydration, it reduces both GFR and renal blood flow, thereby limiting fluid loss and preserving blood volume. Its release is usually stimulated by decreases in blood pressure, and so the preservation of adequate blood pressure is its primary role.

Aldosterone, often called the "salt-retaining hormone," is released from the adrenal cortex in response to angiotensin II or directly in response to increased plasma K^+. It promotes Na^+ reabsorption by the nephron, promoting the retention of water. It is also important in regulating K^+, promoting its excretion. (This dual effect on two minerals and its origin in the adrenal cortex explains its designation as a mineralocorticoid.) As a result, renin has an immediate effect on blood pressure due to angiotensin II–stimulated vasoconstriction and a prolonged effect through Na^+ recovery due to aldosterone. At the same time that aldosterone causes increased recovery of Na^+, it also causes greater loss of K^+. Progesterone is a steroid that is structurally similar to aldosterone. It binds to the aldosterone receptor and weakly stimulates Na^+ reabsorption and increased water recovery. This process is unimportant in males due to low levels of circulating progesterone. It may cause increased retention of water during some periods of the menstrual cycle in females when progesterone levels increase.

Antidiuretic Hormone (ADH)

Diuretics are drugs that can increase water loss by interfering with the recapture of solutes and water from the forming urine. They are often prescribed to lower blood pressure. Coffee, tea, and alcoholic beverages are familiar diuretics. ADH, a nine-amino acid peptide released by the posterior pituitary, works to do the exact opposite. It promotes the recovery of water, decreases urine volume, and maintains plasma osmolarity and blood pressure. It does so by stimulating the movement of aquaporin proteins into the apical cell membrane of principal cells of the collecting ducts to form water channels, allowing the transcellular

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movement of water from the lumen of the collecting duct into the interstitial space in the medulla of the kidney by osmosis. From there, it enters the vasa recta capillaries to return to the circulation. Water is attracted by the high osmotic environment of the deep kidney medulla.

Endothelin

Endothelins, 21-amino acid peptides, are extremely powerful vasoconstrictors. They are produced by endothelial cells of the renal blood vessels, mesangial cells, and cells of the DCT. Hormones stimulating endothelin release include angiotensin II, bradykinin, and epinephrine. They do not typically influence blood pressure in healthy people. On the other hand, in people with diabetic kidney disease, endothelin is chronically elevated, resulting in sodium retention. They also diminish GFR by damaging the podocytes and by potently vasoconstricting both the afferent and efferent arterioles.

Natriuretic Hormones

Natriuretic hormones are peptides that stimulate the kidneys to excrete sodium—an effect opposite that of aldosterone. Natriuretic hormones act by inhibiting aldosterone release and therefore inhibiting Na^+ recovery in the collecting ducts. If Na^+ remains in the forming urine, its osmotic force will cause a concurrent loss of water. Natriuretic hormones also inhibit ADH release, which of course will result in less water recovery. Therefore, natriuretic peptides inhibit both Na^+ and water recovery, thus reducing blood volume and blood pressure.

One example from this family of hormones is atrial natriuretic hormone (ANH), a 28-amino acid peptide produced by heart atria in response to overstretching of the atrial wall. The overstretching occurs in persons with elevated blood pressure or heart failure. It increases GFR through concurrent vasodilation of the afferent arteriole and vasoconstriction of the efferent arteriole. These events lead to an increased loss of water and sodium in the forming urine. It also decreases sodium reabsorption in the DCT.

Parathyroid Hormone

Parathyroid hormone (PTH) is an 84-amino acid peptide produced by the parathyroid glands in response to decreased circulating Ca^{++} levels. Among its targets is the PCT, where it stimulates the hydroxylation of calcidiol to calcitriol (1,25-hydroxycholecalciferol, the active form of vitamin D). It also blocks reabsorption of phosphate (PO_3^-), causing its loss in the urine. The retention of phosphate would result in the formation of calcium phosphate in the plasma, reducing circulating Ca^{++} levels. By ridding the blood of phosphate, higher circulating Ca^{++} levels are permitted.

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24.9 The Urinary System and Homeostasis

Learning Objectives

By the end of this section, you will be able to:

- Describe the role of the kidneys in vitamin D activation
- Describe the role of the kidneys in regulating erythropoiesis
- Demonstrate how the urinary system responds to maintain homeostasis in the body
- Explain how the urinary system relates to other body systems in maintaining homeostasis
- Predict factors or situations affecting the urinary system that could disrupt homeostasis
- Predict the types of problems that would occur in the body if the urinary system could not maintain homeostasis

All systems of the body are interrelated. A change in one system may affect all other systems in the body, with mild to devastating effects. A failure of urinary continence can be embarrassing and inconvenient but is not life threatening. The loss of other urinary functions may prove fatal. A failure to synthesize vitamin D is one such example.

Vitamin D Synthesis

In order for vitamin D to become active, it must undergo a hydroxylation reaction in the kidney—that is, an –OH group must be added to calcidiol to make calcitriol (1,25-dihydroxycholecalciferol). Activated vitamin D is important for absorption of Ca^{++} in the digestive tract, its reabsorption in the kidney, and the maintenance of normal serum concentrations of Ca^{++} and phosphate. Calcium is vitally important in bone health, muscle contraction, hormone secretion, and neurotransmitter release.

Erythropoiesis

EPO is a 193-amino acid protein that stimulates the formation of red blood cells in the bone marrow. The kidney produces 85 percent of circulating EPO; the liver, the remainder. If you move to a higher altitude, the partial pressure of oxygen is lower, meaning there is less pressure to push oxygen across the alveolar membrane and into the red blood cell. One way the body compensates is to manufacture more red blood cells by increasing EPO production. If you start an aerobic exercise program, your tissues will need more oxygen to cope, and

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the kidney will respond with more EPO. If erythrocytes are lost due to severe or prolonged bleeding or underproduced due to disease or severe malnutrition, the kidneys come to the rescue by producing more EPO. Renal failure (loss of EPO production) is associated with anemia, which makes it difficult for the body to cope with increased oxygen demands or to supply oxygen adequately even under normal conditions. Anemia diminishes performance and can be life threatening.

Blood Pressure Regulation

Due to osmosis, water follows where Na^+ leads. Much of the water the kidneys recover from the forming urine follows the reabsorption of Na^+. ADH stimulation of aquaporin channels allows for regulation of water recovery in the collecting ducts. Normally, all of the glucose is recovered, but loss of glucose control (diabetes mellitus) may result in an osmotic diuresis severe enough to produce severe dehydration and death. A loss of renal function means a loss of effective vascular volume control, leading to hypotension (low blood pressure) or hypertension (high blood pressure), which can lead to stroke, heart attack, and aneurysm formation.

The kidneys cooperate with the lungs, liver, and adrenal cortex through the renin-angiotensin-aldosterone system (see Figure 24.11). The liver synthesizes and secretes the inactive precursor angiotensinogen. When the blood pressure is low, the kidney synthesizes and releases renin. Renin converts angiotensinogen into angiotensin I, and ACE produced in the lung converts angiotensin I into biologically active angiotensin II (Figure 24.18). The immediate and short-term effect of angiotensin II is to raise blood pressure by causing widespread vasoconstriction. Angiotensin II also stimulates the adrenal cortex to release the steroid hormone aldosterone, which results in renal reabsorption of Na^+ and its associated osmotic recovery of water. The reabsorption of Na^+ helps raise and maintain blood pressure over a longer term.

Regulation of Osmolarity

Blood pressure and osmolarity are regulated in a similar fashion. Severe hypo-osmolarity can cause problems like lysis (rupture) of blood cells or widespread edema, which is due to a solute imbalance. Inadequate solute concentration (such as protein) in the plasma results in water moving toward an area of greater solute concentration—in this case, the interstitial space and cell cytoplasm. If the kidney glomeruli are damaged by an autoimmune illness, large quantities of protein may be lost in the urine. The resultant drop in serum osmolarity leads to widespread edema that, if severe, may lead to damaging or fatal brain swelling. Severe hypertonic conditions may arise with severe dehydration from lack of

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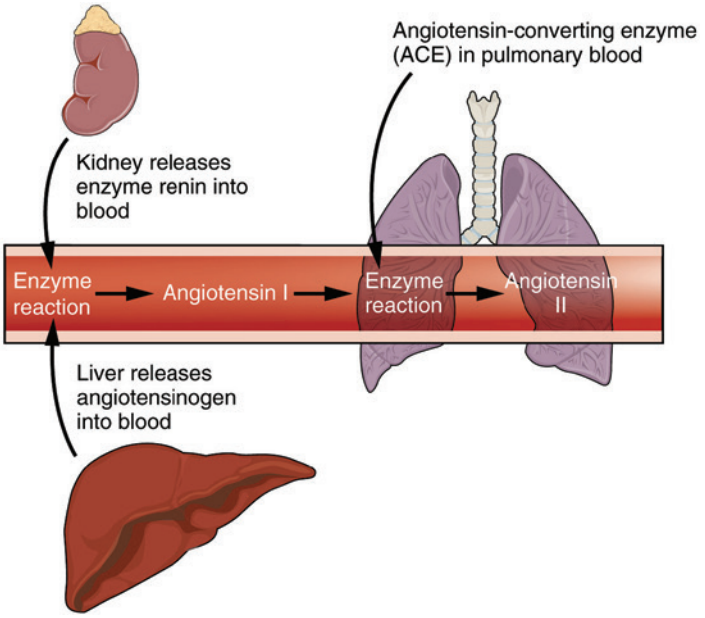


Figure 24.18 **The Enzyme Renin Converts Angiotensinogen into the Proenzyme Angiotensin I.**

water intake, severe vomiting, or uncontrolled diarrhea. When the kidney is unable to recover sufficient water from the forming urine, the consequences may be severe (lethargy, confusion, muscle cramps, and finally, death).

Recovery of Electrolytes

Sodium, calcium, and potassium must be closely regulated. The role of Na^+ and Ca^{++} homeostasis has been discussed at length. Failure of K^+ regulation can have serious consequences on nerve conduction, skeletal muscle function, and most significantly, cardiac muscle contraction and rhythm.

pH Regulation

Recall that enzymes lose their three-dimensional conformation and, therefore, their function if the pH is too acidic or basic. This loss of conformation may be a consequence of the breaking of hydrogen bonds. Move the pH away from the optimum for a specific enzyme and you may severely hamper its function throughout the body, including hormone binding, central nervous system signalling, or myocardial contraction. Proper kidney function is essential for pH homeostasis.

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Key Terms

afferent arterioles: Branches of high-pressure capillaries bringing blood to the glomerulus.

anatomical sphincter: Smooth or skeletal muscle surrounding the lumen of a vessel or hollow organ that can restrict flow when contracted.

angiotensin-converting enzyme (ACE): Enzyme produced by the lungs that catalyzes the reaction of inactive angiotensin I into active angiotensin II.

angiotensin I: Protein produced by the enzymatic action of renin on angiotensinogen; inactive precursor of angiotensin II.

angiotensin II: Protein produced by the enzymatic action of ACE on inactive angiotensin I; actively causes vasoconstriction and stimulates aldosterone release by the adrenal cortex.

angiotensinogen: Inactive protein in the circulation produced by the liver; precursor of angiotensin I; must be modified by the enzymes renin and ACE to be activated.

anuria: Absence of urine produced; production of 50 mL or less per day.

aquaporin: Protein-forming water channels through the lipid bilayer of the cell; allows water to cross; activation in the collecting ducts is under the control of ADH.

Bowman's (glomerular) capsule: Cup-shaped sack lined by a simple squamous epithelium (parietal surface) and specialized cells called podocytes (visceral surface) that participate in the filtration process; receives the filtrate, which then passes on to the PCTs.

brush border: Formed by microvilli on the surface of certain cuboidal cells; in the kidney, it is found in the PCT; increases surface area for absorption in the kidney.

calyces: Cup-like structures receiving urine from the collecting ducts, where it passes on to the renal pelvis and ureter.

cortical nephrons: Nephrons with loops of Henle that do not extend into the renal medulla.

countercurrent multiplier system: Involves the descending and ascending loops of Henle directing forming urine in opposing directions to create a concentration gradient when combined with variable permeability and sodium pumping.

detrusor muscle: Smooth muscle in the bladder wall; fibres run in all directions to reduce the size of the organ when emptying it of urine.

distal convoluted tubules (DCT): Portions of the nephron distal to the loop of Henle that receive hyposmotic filtrate from the loop of Henle and empty into collecting ducts.

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diuretic: Compound that increases urine output, leading to decreased water conservation.

efferent arteriole: Arteriole carrying blood from the glomerulus to the capillary beds around the convoluted tubules and loop of Henle; portion of the portal system.

endothelins: Group of vasoconstrictive, 21-amino acid peptides; produced by endothelial cells of the renal blood vessels, mesangial cells, and cells of the DCT.

external urinary (urethral) sphincter: Skeletal muscle; must be relaxed consciously to void urine.

fenestrations: Small windows through a cell allowing rapid filtration based on size; formed in such a way as to allow substances to cross through a cell without mixing with cell contents.

filtration slits: Formed by pedicels of podocytes; substances filter between the pedicels based on size.

forming urine: Filtrate undergoing modifications through secretion and reabsorption before true urine is produced.

glomerular filtration rate (GFR): Rate of renal filtration.

glomerulus: Tuft of capillaries surrounded by Bowman's capsule; filters the blood based on size.

glycosuria: Presence of glucose in the urine; caused by high blood glucose levels that exceed the ability of the kidneys to reabsorb the glucose; usually the result of untreated or poorly controlled diabetes mellitus.

incontinence: Loss of ability to control micturition.

intercalated cell: Specialized cell of the collecting ducts that secrete or absorb acid or bicarbonate; important in acid-base balance.

internal urinary (urethral) sphincter: Smooth muscle at the juncture of the bladder and urethra; relaxes as the bladder fills to allow urine into the urethra.

juxtaglomerular apparatus (JGA): Located at the juncture of the DCT and the afferent and efferent arterioles of the glomerulus; plays a role in the regulation of renal blood flow and GFR.

juxtaglomerular cell: Modified smooth muscle cells of the afferent arteriole; secretes renin in response to a drop in blood pressure.

juxtamedullary nephrons: Nephrons adjacent to the border of the cortex and medulla with loops of Henle that extend into the renal medulla.

leaky tight junctions: Tight junctions in which the sealing strands of proteins between the membranes of adjacent cells are fewer in number and incomplete; allows limited intercellular movement of solvent and solutes.

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loop of Henle: Descending and ascending portions between the proximal and distal convoluted tubules; those of cortical nephrons do not extend into the medulla, whereas those of juxtamedullary nephrons do extend into the medulla.

macula densa: Cells found in the part of the DCT forming the JGA; sense Na^+ concentration in the forming urine.

medulla: Inner region of the kidney containing the renal pyramids.

mesangial: Contractile cells found in the glomerulus; can contract or relax to regulate filtration rate.

micturition: Also called urination or voiding.

myogenic mechanism: Mechanism by which smooth muscle responds to stretch by contracting; an increase in blood pressure causes vasoconstriction and a decrease in blood pressure causes vasodilation so that blood flow downstream remains steady.

nephrons: Functional units of the kidney that carry out all filtration and modification to produce urine; consist of renal corpuscles, proximal and distal convoluted tubules, and descending and ascending loops of Henle; drain into collecting ducts.

net filtration pressure (NFP): Pressure of fluid across the glomerulus; calculated by taking the hydrostatic pressure of the capillary and subtracting the colloid osmotic pressure of the blood and the hydrostatic pressure of Bowman's capsule.

oliguria: Below-normal urine production of 400–500 mL/day.

pedicels: Fingerlike projections of podocytes surrounding glomerular capillaries; interdigitate to form a filtration membrane.

peritubular capillaries: Second capillary bed of the renal portal system; surround the proximal and distal convoluted tubules; associated with the vasa recta.

physiological sphincter: Sphincter consisting of circular smooth muscle indistinguishable from adjacent muscle but possessing differential innervations, permitting its function as a sphincter; structurally weak.

podocytes: Cells forming fingerlike processes; form the visceral layer of Bowman's capsule; pedicels of the podocytes interdigitate to form a filtration membrane.

polyuria: Urine production in excess of 2.5 L/day; may be caused by diabetes insipidus, diabetes mellitus, or excessive use of diuretics.

principal cells: Found in collecting ducts and possess channels for the recovery or loss of sodium and potassium; under the control of aldosterone; also have aquaporin channels under ADH control to regulate recovery of water.

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proximal convoluted tubules (PCTs): Tortuous tubules receiving filtrate from Bowman's capsule; most active part of the nephron in reabsorption and secretion.

renal columns: Extensions of the renal cortex into the renal medulla; separate the renal pyramids; contain blood vessels and connective tissues.

renal corpuscle: Consists of the glomerulus and Bowman's capsule.

renal cortex: Outer part of the kidney containing all of the nephrons; some nephrons have loops of Henle extending into the medulla.

renal hilum: Recessed medial area of the kidney through which the renal artery, renal vein, ureters, lymphatics, and nerves pass.

renal papillae: Medullary area of the renal pyramids where collecting ducts empty urine into the minor calyces.

renal pyramids: Six to eight cone-shaped tissues in the medulla of the kidney containing collecting ducts and the loops of Henle of juxtamedullary nephrons.

renin: Enzyme produced by juxtaglomerular cells in response to decreased blood pressure or sympathetic nervous activity; catalyzes the conversion of angiotensinogen into angiotensin I.

retroperitoneal: Behind the peritoneum; in the case of the kidney and ureters, between the parietal peritoneum and the abdominal wall.

systemic edema: Increased fluid retention in the interstitial spaces and cells of the body; can be seen as swelling over large areas of the body, particularly the lower extremities.

trigone: Area at the base of the bladder marked by the two ureters in the posterior-lateral aspect and the urethral orifice in the anterior aspect oriented like points on a triangle.

tubuloglomerular feedback: Feedback mechanism involving the JGA; macula densa cells monitor Na^+ concentration in the terminal portion of the ascending loop of Henle and act to cause vasoconstriction or vasodilation of afferent and efferent arterioles to alter GFR.

urethra: Transports urine from the bladder to the outside environment.

urinalysis: Analysis of urine to diagnose disease.

vasa recta: Branches of the efferent arterioles that parallel the course of the loops of Henle and are continuous with the peritubular capillaries; with the glomerulus, form a portal system.

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Chapter Review

24.1 Physical Characteristics of Urine

The kidney glomerulus filters blood mainly based on particle size to produce a filtrate lacking cells or large proteins. Most of the ions and molecules in the filtrate are needed by the body and must be reabsorbed farther down the nephron tubules, resulting in the formation of urine. Urine characteristics change depending on water intake, exercise, environmental temperature, and nutrient intake. Urinalysis analyzes characteristics of the urine and is used to diagnose diseases. A minimum of 400 to 500 mL of urine must be produced daily to rid the body of wastes. Excessive quantities of urine may indicate diabetes insipidus or diabetes mellitus. The pH range of urine is 4.5 to 8.0 and is affected by diet. Osmolarity ranges from 50 to 1,200 milliosmoles and is a reflection of the amount of water being recovered or lost by renal nephrons.

24.2 Gross Anatomy of Urine Transport

The urethra is the only urinary structure that differs significantly between males and females. This is due to the dual role of the male urethra in transporting both urine and semen. The urethra arises from the trigone area at the base of the bladder. Urination is controlled by an involuntary internal sphincter of smooth muscle and a voluntary external sphincter of skeletal muscle. The shorter female urethra contributes to the higher incidence of bladder infections in females. The male urethra receives secretions from the prostate gland, Cowper's gland, and seminal vesicles as well as sperm. The bladder is largely retroperitoneal and can hold up to 500–600 mL of urine. Micturition is the process of voiding the urine and involves both involuntary and voluntary actions. Voluntary control of micturition requires a mature and intact sacral micturition centre. It also requires an intact spinal cord. Loss of control of micturition is called incontinence and results in voiding when the bladder contains about 250 mL of urine. The ureters are retroperitoneal and lead from the renal pelvis of the kidney to the trigone area at the base of the bladder. A thick muscular wall consisting of longitudinal and circular smooth muscle helps move urine toward the bladder by way of peristaltic contractions.

24.3 Gross Anatomy of the Kidney

As noted previously, the structure of the kidney is divided into two principal regions—the peripheral rim of the cortex and the central medulla. The two kidneys receive about 25 percent of cardiac output. They are protected in the retroperitoneal space by the renal fat pad and overlying ribs and muscle. Ureters, blood vessels, lymph vessels, and nerves enter and leave at the renal

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hilum. The renal arteries arise directly from the aorta, and the renal veins drain directly into the inferior vena cava. Kidney function is derived from the actions of about 1.3 million nephrons per kidney; these are the "functional units." A capillary bed, the glomerulus, filters blood, and the filtrate is captured by Bowman's capsule. A portal system is formed when the blood flows through a second capillary bed surrounding the proximal and distal convoluted tubules and the loop of Henle. Most water and solutes are recovered by this second capillary bed. This filtrate is processed and finally gathered by collecting ducts that drain into the minor calyces, which merge to form major calyces; the filtrate then proceeds to the renal pelvis and finally the ureters.

24.4 Microscopic Anatomy of the Kidney

The functional unit of the kidney, the nephron, consists of the renal corpuscle, PCT, loop of Henle, and DCT. Cortical nephrons have short loops of Henle, whereas juxtamedullary nephrons have long loops of Henle extending into the medulla. About 15 percent of nephrons are juxtamedullary. The glomerulus is a capillary bed that filters blood principally based on particle size. The filtrate is captured by Bowman's capsule and directed to the PCT. A filtration membrane is formed by the fused basement membranes of the podocytes and the capillary endothelial cells that they embrace. Contractile mesangial cells further perform a role in regulating the rate at which the blood is filtered. Specialized cells in the JGA produce paracrine signals to regulate blood flow and filtration rates of the glomerulus. Other JGA cells produce the enzyme renin, which plays a central role in blood pressure regulation. The filtrate enters the PCT, where absorption and secretion of several substances occur. The descending and ascending limbs of the loop of Henle consist of thick and thin segments. Absorption and secretion continue in the DCT but to a lesser extent than in the PCT. Each collecting duct collects forming urine from several nephrons and responds to the posterior pituitary hormone ADH by inserting aquaporin water channels into the cell membrane to fine-tune water recovery.

24.5 Physiology of Urine Formation

The entire volume of the blood is filtered through the kidneys about 300 times per day, and 99 percent of the water filtered is recovered. The GFR is influenced by hydrostatic pressure and colloid osmotic pressure.

Under normal circumstances, hydrostatic pressure is significantly greater and filtration occurs. The hydrostatic pressure of the glomerulus depends on systemic blood pressure, autoregulatory mechanisms, sympathetic nervous activity, and paracrine hormones. The kidney can function normally under a wide range of blood pressures due to the autoregulatory nature of smooth muscle.

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24.6 Tubular Reabsorption

The kidney regulates water recovery and blood pressure by producing the enzyme renin. It is renin that starts a series of reactions leading to the production of the vasoconstrictor angiotensin II and the salt-retaining steroid aldosterone. Water recovery is also powerfully and directly influenced by the hormone ADH. Even so, it only influences the last 10 percent of water available for recovery after filtration at the glomerulus, because 90 percent of water is recovered before reaching the collecting ducts. Depending on the body's fluid status at any given time, the collecting ducts can recover none or almost all of the water reaching them.

Mechanisms of solute recovery include active transport, simple diffusion, and facilitated diffusion. Most filtered substances are reabsorbed. Urea, NH_3, creatinine, and some drugs are filtered or secreted as wastes. H^+ and HCO_3- are secreted or reabsorbed as needed to maintain acid-base balance. Movement of water from the glomerulus is primarily due to pressure, whereas that of peritubular capillaries and vasa recta is due to osmolarity and concentration gradients. The PCT is the most metabolically active part of the nephron and uses a wide array of protein micromachines to maintain homeostasis—symporters, antiporters, and ATPase active transporters—in conjunction with diffusion, both simple and facilitated. Almost 100 percent of glucose, amino acids, and vitamins are recovered in the PCT. Bicarbonate (HCO−) is recovered using the same enzyme, carbonic anhydrase (CA), found in erythrocytes. The recovery of solutes creates an osmotic gradient to promote the recovery of water. The descending loop of the juxtaglomerular nephrons reaches an osmolarity of up to 1,200 mOsmol/kg, promoting the recovery of water. The ascending loop is impervious to water but actively recovers Na^+, reducing filtrate osmolarity to 50–100 mOsmol/kg. The descending and ascending loop and vasa recta form a countercurrent multiplier system to increase Na^+ concentration in the kidney medulla. The collecting ducts actively pump urea into the medulla, further contributing to the high osmotic environment. The vasa recta recover the solute and water in the medulla, returning them to the circulation. Nearly 90 percent of water is recovered before the forming urine reaches the DCT, which will recover another 10 percent. Calcium recovery in the DCT is influenced by PTH and active vitamin D. In the collecting ducts, ADH stimulates aquaporin channel insertion to increase water recovery and thereby regulate osmolarity of the blood. Aldosterone stimulates Na^+ recovery by the collecting duct.

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24.7 Regulation of Renal Blood Flow

The kidneys are innervated by sympathetic nerves of the autonomic nervous system. Sympathetic nervous activity decreases blood flow to the kidney, making more blood available to other areas of the body during times of stress. The arteriolar myogenic mechanism maintains a steady blood flow by causing arteriolar smooth muscle to contract when blood pressure increases and causing it to relax when blood pressure decreases. Tubuloglomerular feedback involves paracrine signalling at the JGA to cause vasoconstriction or vasodilation to maintain a steady rate of blood flow.

24.8 Endocrine Regulation of Kidney Function

Endocrine hormones act from a distance, and paracrine hormones act locally. The renal enzyme renin converts angiotensinogen into angiotensin I. The lung enzyme ACE converts angiotensin I into active angiotensin II. Angiotensin II is an active vasoconstrictor that increases blood pressure. Angiotensin II also stimulates aldosterone release from the adrenal cortex, causing the collecting duct to retain Na^+, which promotes water retention and a longer-term rise in blood pressure. ADH promotes water recovery by the collecting ducts by stimulating the insertion of aquaporin water channels into cell membranes.

Endothelins are elevated in cases of diabetic kidney disease, increasing Na^+ retention and decreasing GFR. Natriuretic hormones, released primarily from the atria of the heart in response to stretching of the atrial walls, stimulate Na^+ excretion and thereby decrease blood pressure. PTH stimulates the final step in the formation of active vitamin D3 and reduces phosphate reabsorption, resulting in higher circulating Ca^{++} levels.

24.9 The Urinary System and Homeostasis

The effects of failure of parts of the urinary system may range from inconvenient (incontinence) to fatal (loss of filtration and many others). The kidneys catalyze the final reaction in the synthesis of active vitamin D that in turn helps regulate Ca^{++}. The kidney hormone EPO stimulates erythrocyte development and promotes adequate O_2 transport. The kidneys help regulate blood pressure through Na^+ and water retention and loss. The kidneys work with the adrenal cortex, lungs, and liver in the renin-angiotensin-aldosterone system to regulate blood pressure. They regulate osmolarity of the blood by regulating both solutes and water. Three electrolytes are more closely regulated than others: Na^+, Ca^{++}, and K^+. The kidneys share pH regulation with the lungs and plasma buffers so that proteins can preserve their three-dimensional conformation and thus their function.

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25

Fluid, Electrolyte, and Acid-Base Balance

Chapter Objectives

After studying this chapter, you will be able to:

- Identify the body's main fluid compartments
- Define plasma osmolality and identify two ways in which plasma osmolality is maintained
- Identify the six ions most important to the function of the body
- Define *buffer* and discuss the role of buffers in the body
- Explain why bicarbonate must be conserved rather than reabsorbed in the kidney
- Identify the normal range of blood pH and name the conditions where one has a blood pH that is either too high or too low

Homeostasis, or the maintenance of constant conditions in the body, is a fundamental property of all living things. In the human body, the substances that participate in chemical reactions must remain within narrow ranges of concentration. Too much or too little of a single substance can disrupt your bodily functions.

Because metabolism relies on reactions that are all interconnected, any disruption might affect multiple organs or even organ systems. Water is the most ubiquitous substance in the chemical reactions of life. The interactions of various aqueous solutions—solutions in which water is the solvent—are continuously monitored and adjusted by a large suite of interconnected feedback systems in your body. Understanding the ways in which the body maintains these critical balances is key to understanding good health.

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25.1 Body Fluids and Fluid Compartments

Learning Objectives

By the end of this section, you will be able to:

- Explain the importance of water in the body
- Contrast the composition of the intracellular fluid with that of the extracellular fluid
- Explain the importance of protein channels in the movement of solutes

The chemical reactions of life take place in aqueous solutions. The dissolved substances in a solution are called solutes. In the human body, solutes vary in different parts of the body but may include proteins—such as those that transport lipids, carbohydrates, and very importantly, electrolytes. Often in medicine, a mineral dissociated from a salt that carries an electrical charge (an ion) is called an electrolyte. For instance, sodium ions (Na^+) and chloride ions (Cl^-) are often referred to as electrolytes.

In the body, water moves through semipermeable membranes of cells and from one compartment of the body to another by a process called osmosis. Osmosis is basically the diffusion of water from regions of higher concentration of water to regions of lower concentration of water along an osmotic gradient across a semipermeable membrane. As a result, water will move into and out of cells and tissues depending on the relative concentrations of the water and solutes found there. An appropriate balance of solutes inside and outside of cells must be maintained to ensure normal function.

Body Water Content

Human beings are mostly water, ranging from about 75 percent of body mass in infants to about 50–60 percent in adults to as low as 45 percent in old age. The percent of body water changes with development, because the proportions of the body given over to each organ and to muscles, fat, bone, and other tissues change from infancy to adulthood (Figure 25.1). Your brain and kidneys have the highest proportions of water, which comprises 80–85 percent of their mass. In contrast, teeth have the lowest proportion of water, at 8–10 percent.

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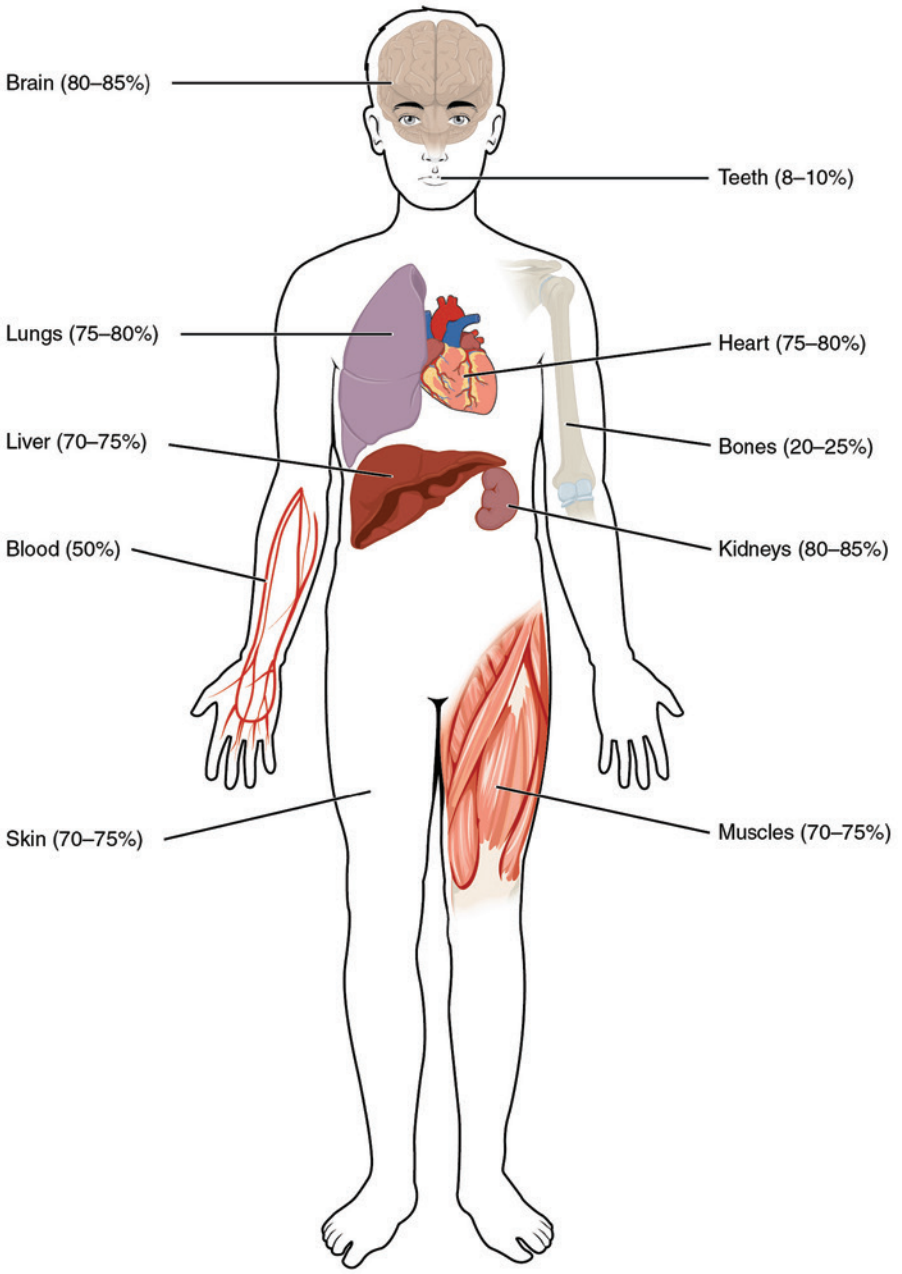


Figure 25.1 Water Content of the Body's Organs and Tissues. Water content varies in different body organs and tissues, from as little as 8 percent in the teeth to as much as 85 percent in the brain.

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Fluid Compartments

Body fluids can be discussed in terms of their specific **fluid compartment**, a location that is largely separate from another compartment by some form of physical barrier. The **intracellular fluid** (**ICF**) compartment is the system that includes all fluid enclosed in cells by their plasma membranes. **Extracellular fluid** (**ECF**) surrounds all cells in the body. Extracellular fluid has two primary constituents: the fluid component of the blood, called **plasma**, and the **interstitial fluid** (**IF**) that surrounds all cells (Figure 25.2).

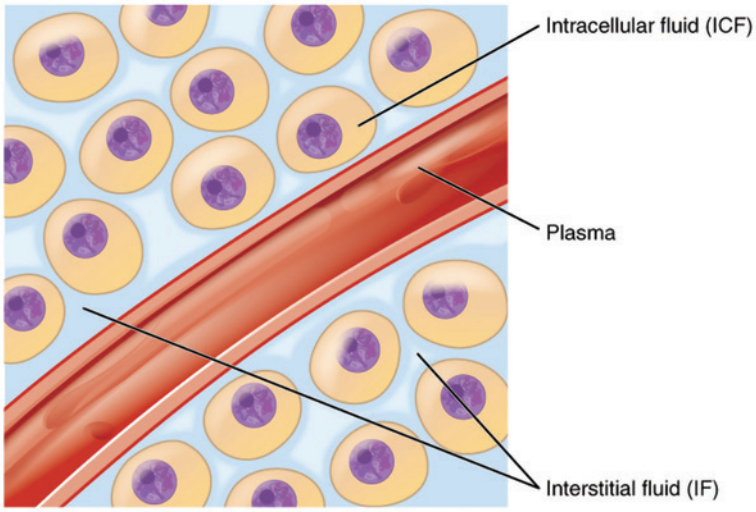


Figure 25.2 Fluid Compartments in the Human Body. The intracellular fluid (ICF) is the fluid within cells. The interstitial fluid (IF) is part of the extracellular fluid (ECF) between the cells. Blood plasma is the second part of the ECF. Materials travel between cells and the plasma in capillaries through the IF.

Intracellular Fluid

The ICF lies within cells and is the principal component of the cytosol/cytoplasm. The ICF makes up about 60 percent of the total water in the human body, and in an average-size adult male, the ICF accounts for about 25 L of fluid (Figure 25.3). This fluid volume tends to be very stable because the amount of water in living cells is closely regulated. If the amount of water inside a cell falls to a value that is too low, the cytosol becomes too concentrated with solutes to carry on normal cellular activities; if too much water enters a cell, the cell may burst and be destroyed.

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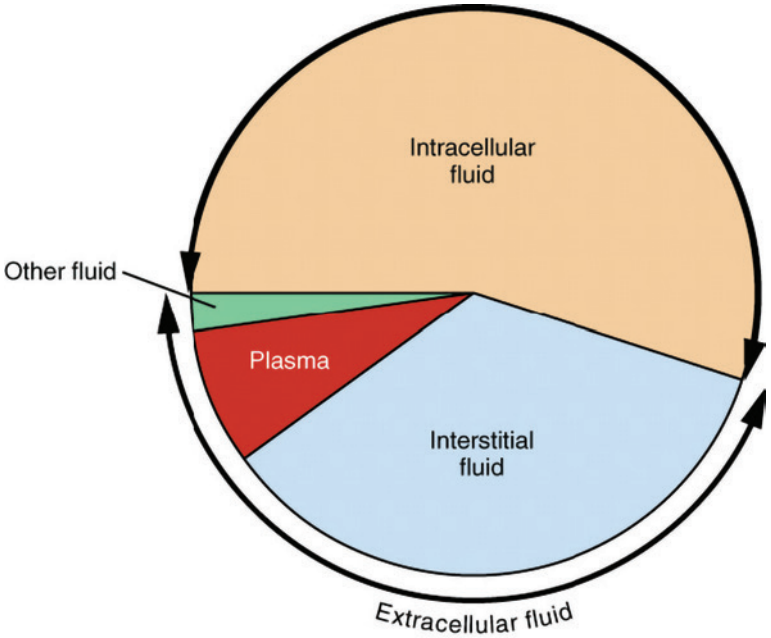


Figure 25.3 Proportion of Total Body Fluid in Each of the Body's Fluid Compartments. Most of the water in the body is intracellular fluid. The second largest volume is the interstitial fluid, which surrounds cells that are not blood cells.

Extracellular Fluid

The ECF accounts for the other one-third of the body's water content. Approximately 20 percent of the ECF is found in plasma. Plasma travels through the body in blood vessels and transports a range of materials, including blood cells, proteins (including clotting factors and antibodies), electrolytes, nutrients, gases, and wastes. Gases, nutrients, and waste materials travel between capillaries and cells through the IF. Cells are separated from the IF by a selectively permeable cell membrane that helps regulate the passage of materials between the IF and the interior of the cell.

The body has other water-based ECFs. These include the cerebrospinal fluid that bathes the brain and spinal cord, lymph, the synovial fluid in joints, the pleural fluid in the pleural cavities, the pericardial fluid in the cardiac sac, the peritoneal fluid in the peritoneal cavity, and the aqueous and vitreous humours of the eye. Because these fluids are outside of cells, these fluids are also considered components of the ECF compartment.

Composition of Body Fluids

The compositions of the two components of the ECF—plasma and IF—are more similar to each other than either is to the ICF. Blood plasma has high

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concentrations of sodium, chloride, bicarbonate, and protein. The IF has high concentrations of sodium, chloride, and bicarbonate but a relatively lower concentration of protein. In contrast, the ICF has elevated amounts of potassium, phosphate, magnesium, and protein. Overall, the ICF contains high concentrations of potassium and phosphate (HPO_4^{2-}), whereas both plasma and the ECF contain high concentrations of sodium and chloride.

Interactive Link 25.1

Watch this video (http://oer.aupress.ca/oer-202505/25.1) to learn more about body fluids, fluid compartments, and electrolytes. When blood volume decreases due to sweating, from what source is water taken in by the blood?

Most body fluids are neutral in charge. Thus, cations, or positively charged ions, and anions, or negatively charged ions, are balanced in fluids. Sodium (Na^+) ions and chloride (Cl-) ions are concentrated in the ECF of the body, whereas potassium (K^+) ions are concentrated inside cells. Although sodium and potassium can "leak" through "pores" into and out of cells, respectively, the high levels of potassium and low levels of sodium in the ICF are maintained by sodium-potassium pumps in the cell membranes. These pumps use the energy supplied by ATP to pump sodium out of the cell and potassium into the cell (Figure 25.4).

Fluid Movement Between Compartments

Hydrostatic pressure, the force exerted by a fluid against a wall, produces movement of fluid between compartments. The hydrostatic pressure of blood is the pressure exerted by blood against the walls of blood vessels by the pumping action of the heart. In capillaries, hydrostatic pressure (also known as capillary blood pressure) is higher than the opposing "colloid osmotic pressure" in blood—a "constant" pressure primarily produced by circulating albumin—at the arteriolar end of the capillary (Figure 25.5). This pressure forces plasma and nutrients out of the capillaries and into surrounding tissues. Fluid and the cellular wastes in the tissues enter the capillaries at the venule end, where the hydrostatic pressure is less than the osmotic pressure in the vessel. Filtration pressure squeezes fluid from the plasma in the blood to the IF surrounding the tissue cells. The surplus fluid in the interstitial space that is not returned directly back to the capillaries is drained from tissues by the lymphatic system and then reenters the vascular system at the subclavian veins.

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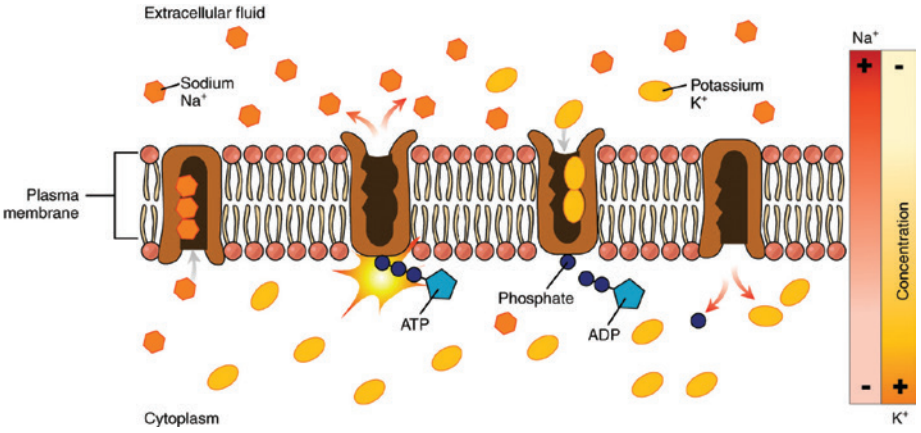


Figure 25.4 The Sodium-Potassium Pump. The sodium-potassium pump is powered by ATP to transfer sodium out of the cytoplasm and into the ECF. The pump also transfers potassium out of the ECF and into the cytoplasm. (credit: modification of work by Mariana Ruiz Villarreal)

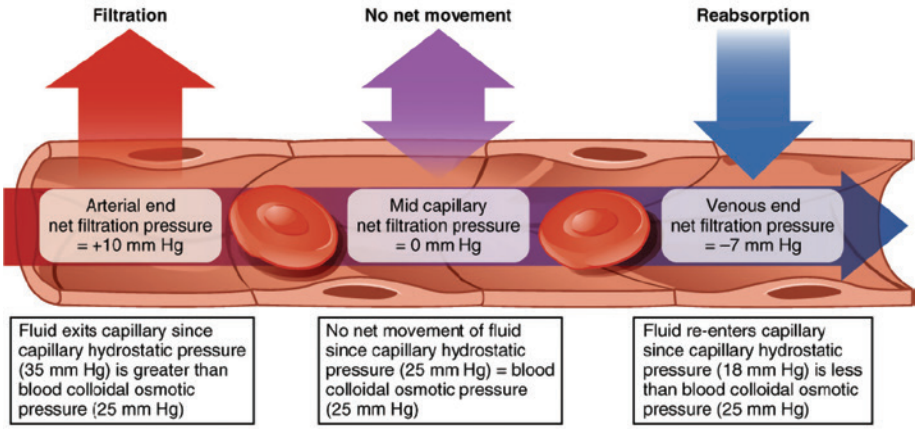


Figure 25.5 Capillary Exchange. Net filtration occurs near the arterial end of the capillary, since capillary hydrostatic pressure (CHP) is greater than blood colloidal osmotic pressure (BCOP). There is no net movement of fluid near the midpoint of the capillary, since CHP = BCOP. Net reabsorption occurs near the venous end of the capillary, since BCOP is greater than CHP.

Interactive Link 25.2

Watch this video (http://oer.aupress.ca/oer-202505/25.2) to see an explanation of the dynamics of fluid in the body's compartments. What happens in the tissue when capillary blood pressure is less than osmotic pressure?

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Hydrostatic pressure is especially important in governing the movement of water in the nephrons of the kidneys to ensure proper filtering of the blood to form urine. As hydrostatic pressure in the kidneys increases, the amount of water leaving the capillaries also increases, and more urine filtrate is formed. If hydrostatic pressure in the kidneys drops too low, as can happen in dehydration, the functions of the kidneys will be impaired, and less nitrogenous wastes will be removed from the bloodstream. Extreme dehydration can result in kidney failure.

Fluid also moves between compartments along an osmotic gradient. Recall that an osmotic gradient is produced by the difference in concentration of all solutes on either side of a semipermeable membrane. The magnitude of the osmotic gradient is proportional to the difference between the concentration of solutes on one side of the cell membrane and that on the other side. Water will move by osmosis from the side where its concentration is high (and the concentration of solute is low) to the side of the membrane where its concentration is low (and the concentration of solute is high). In the body, water moves by osmosis from plasma to the IF (and the reverse) and from the IF to the ICF (and the reverse). Water moves constantly into and out of fluid compartments as conditions change in different parts of the body.

For example, if you are sweating, you will lose water through your skin. Sweating depletes your tissues of water and increases the solute concentration in those tissues. As this happens, water diffuses from your blood into sweat glands and surrounding skin tissues that have become dehydrated because of the osmotic gradient. Additionally, as water leaves the blood, it is replaced by the water in other tissues throughout your body that are not dehydrated. If this continues, dehydration spreads throughout the body. When a dehydrated person drinks water and rehydrates, the water is redistributed by the same gradient, but in the opposite direction, replenishing water in all of the tissues.

Solute Movement Between Compartments

The movement of some solutes between compartments is active, which consumes energy and is an active transport process, whereas the movement of other solutes is passive, which does not require energy. Active transport allows cells to move a specific substance against its concentration gradient through a membrane protein, requiring energy in the form of ATP.

For example, the sodium-potassium pump employs active transport to pump sodium out of cells and potassium into cells, with both substances moving against their concentration gradients.

Passive transport of a molecule or ion depends on its ability to pass through the membrane as well as the existence of a concentration gradient that allows the

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molecules to diffuse from an area of higher concentration to an area of lower concentration. Some molecules, like gases, lipids, and water itself (which also utilizes water channels in the membrane called aquaporins), slip fairly easily through the cell membrane; others, including polar molecules like glucose, amino acids, and ions, do not. Some of these molecules enter and leave cells using facilitated transport, whereby the molecules move down a concentration gradient through specific protein channels in the membrane.

This process does not require energy.

For example, glucose is transferred into cells by glucose transporters that use facilitated transport (Figure 25.6).

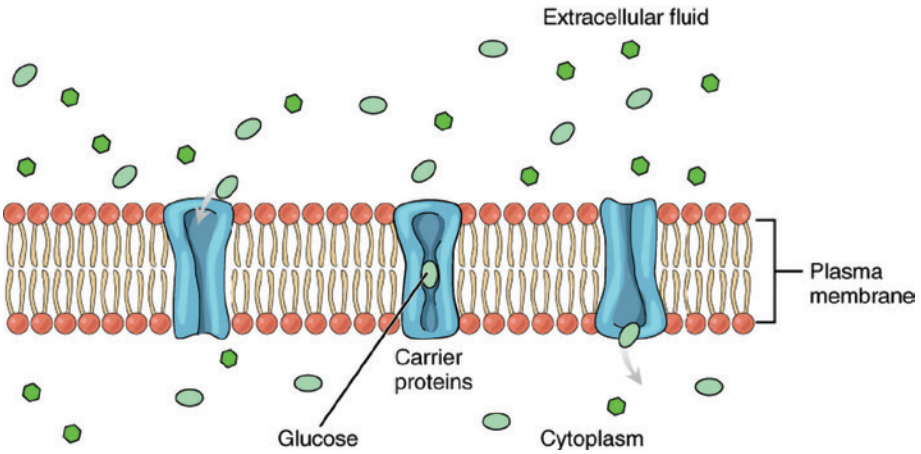


Figure 25.6 Facilitated Diffusion. Glucose molecules use facilitated diffusion to move down a concentration gradient through the carrier protein channels in the membrane. (credit: modification of work by Mariana Ruiz Villarreal)

25.2 Water Balance

Learning Objectives

By the end of this section, you will be able to:

- Explain how water levels in the body influence the thirst cycle
- Identify the main route by which water leaves the body
- Describe the role of ADH and its effect on body water levels
- Define dehydration and identify common causes of dehydration

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On a typical day, the average adult will take in about 2,500 mL of aqueous fluids. Although most of the intake comes through the digestive tract, about 230 mL per day is generated metabolically, in the last steps of aerobic respiration. Additionally, each day about the same volume (2,500 mL) of water leaves the body by different routes; most of this lost water is removed as urine. The kidneys also can adjust blood volume through mechanisms that draw water out of the filtrate and urine. The kidneys can regulate water levels in the body; they conserve water if you are dehydrated, and they can make urine more dilute to expel excess water if necessary.

Water is lost through the skin through evaporation from the skin surface without overt sweating and from air expelled from the lungs. This type of water loss is called insensible water loss because a person is usually unaware of it.

Regulation of Water Intake

Plasma osmolality is the ratio of solutes to water found in blood plasma. A person's plasma osmolality value reflects the state of hydration. A healthy body maintains plasma osmolality within a narrow range by employing several mechanisms that regulate both water intake and output.

Drinking water is considered voluntary. So how is water intake regulated by the body? Consider someone who is experiencing **dehydration**, a net loss of water that results in insufficient water in blood and other tissues. The water that leaves the body as exhaled air, sweat, or urine is ultimately extracted from blood plasma. As the blood becomes more concentrated, the thirst response—a sequence of physiological processes—is triggered (Figure 25.7). Osmoreceptors are sensory receptors in the thirst centre in the hypothalamus that monitor the concentration of solutes (osmolality) in the blood. If blood osmolality increases above its ideal value, the hypothalamus transmits signals that result in a conscious awareness of thirst. The person should (and normally does) respond by drinking water. The hypothalamus of a dehydrated person also releases antidiuretic hormone (ADH) through the posterior pituitary gland. ADH signals the kidneys to recover water from urine, effectively diluting the blood plasma. To conserve water, the hypothalamus of a dehydrated person also sends signals via the sympathetic nervous system to the salivary glands in the mouth. The signals result in a decrease in watery, serous output (and an increase in stickier, thicker mucus output). These changes in secretions result in a "dry mouth" and the sensation of thirst.

Decreased blood volume resulting from water loss has two additional effects. First, baroreceptors, blood-pressure receptors in the arch of the aorta and the carotid arteries in the neck, detect a decrease in blood pressure that results from

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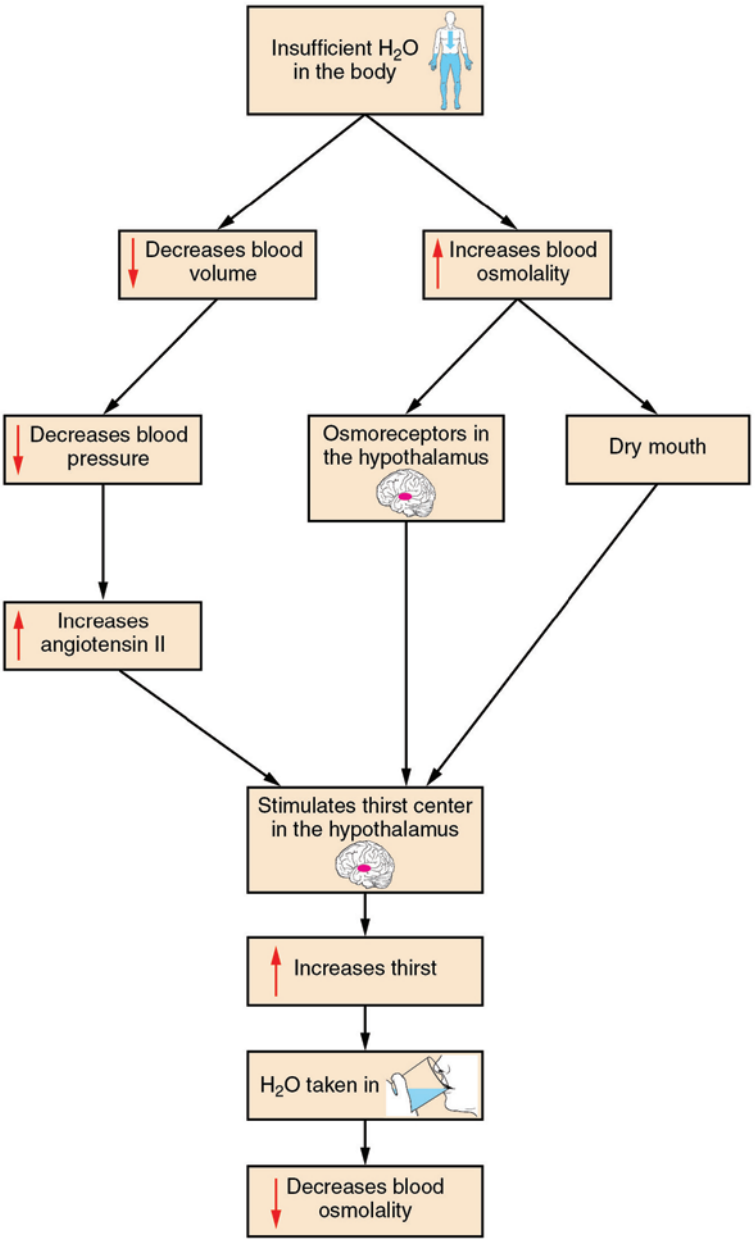


Figure 25.7 A Flowchart Showing the Thirst Response. The thirst response begins when osmoreceptors detect a decrease in water levels in the blood.

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decreased blood volume. The heart is ultimately signalled to increase its rate and/or strength of contractions to compensate for the lowered blood pressure.

Second, the kidneys have a renin-angiotensin hormonal system that increases the production of the active form of the hormone angiotensin II, which helps stimulate thirst but also stimulates the release of the hormone aldosterone from the adrenal glands. Aldosterone increases the reabsorption of sodium in the distal tubules of the nephrons in the kidneys, and water follows this reabsorbed sodium back into the blood.

If adequate fluids are not consumed, dehydration results, and a person's body contains too little water to function correctly. A person who repeatedly vomits or who has diarrhea may become dehydrated, and infants, because their body mass is so low, can become dangerously dehydrated very quickly. Endurance athletes such as distance runners often become dehydrated during long races. Dehydration can be a medical emergency, and a dehydrated person may lose consciousness, become comatose, or die if their body is not rehydrated quickly.

Regulation of Water Output

Water loss from the body occurs predominantly through the renal system. A person produces an average of 1.5 L of urine per day. Although the volume of urine varies in response to hydration levels, there is a minimum volume of urine production required for proper bodily functions. The kidney excretes 100 to 1,200 milliosmoles of solutes per day to rid the body of a variety of excess salts and other water-soluble chemical wastes, most notably creatinine, urea, and uric acid. Failure to produce the minimum volume of urine means that metabolic wastes cannot be effectively removed from the body, a situation that can impair organ function. The minimum level of urine production necessary to maintain normal function is about 0.47 L per day.

The kidneys also must make adjustments in the event of ingestion of too much fluid. **Diuresis**, which is the production of urine in excess of normal levels, begins about 30 minutes after drinking a large quantity of fluid. Diuresis reaches a peak after about 1 hour, and normal urine production is reestablished after about 3 hours.

Role of ADH

Antidiuretic hormone (**ADH**), also known as vasopressin, controls the amount of water reabsorbed from the collecting ducts and tubules in the kidney. This hormone is produced in the hypothalamus and is delivered to the posterior pituitary for storage and release (Figure 25.8). When the osmoreceptors in the hypothalamus detect an increase in the concentration of blood plasma, the hypothalamus signals the release of ADH from the posterior pituitary into the blood.

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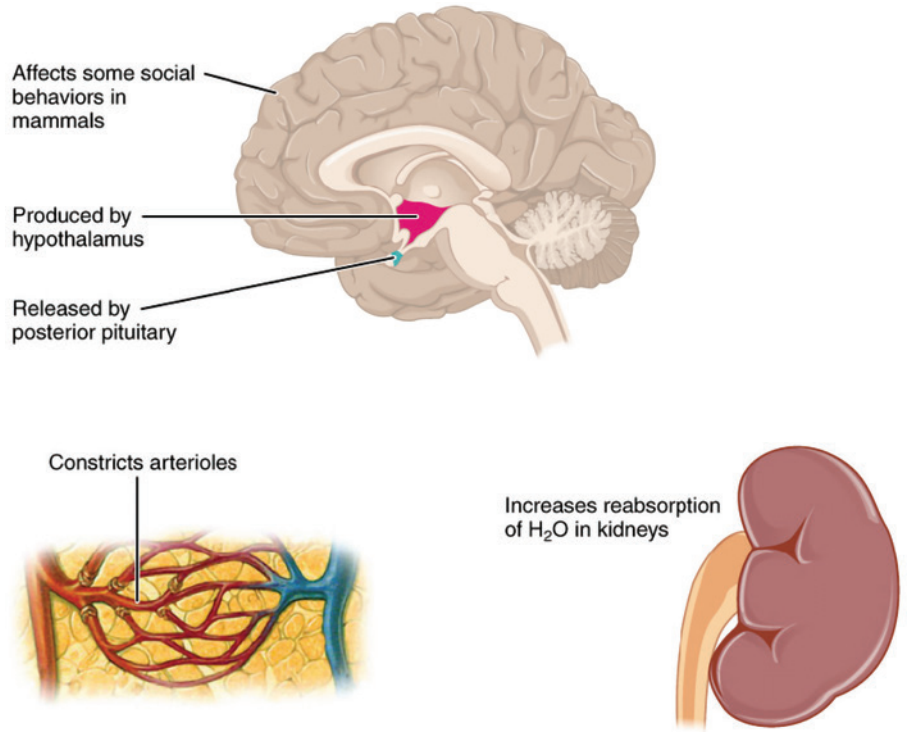


Figure 25.8 Antidiuretic Hormone (ADH). ADH is produced in the hypothalamus and released by the posterior pituitary gland. It causes the kidneys to retain water, constricts arterioles in the peripheral circulation, and affects some social behaviours in mammals.

ADH has two major effects. It constricts the arterioles in the peripheral circulation, which reduces the flow of blood to the extremities and thereby increases the blood supply to the core of the body. ADH also causes the epithelial cells that line the renal collecting tubules to move water channel proteins, called aquaporins, from the interior of the cells to the apical surface, where these proteins are inserted into the cell membrane (Figure 25.9). The result is an increase in the water permeability of these cells and, thus, a large increase in water passage from the urine through the walls of the collecting tubules, leading to more reabsorption of water into the bloodstream. When the blood plasma becomes less concentrated and the level of ADH decreases, aquaporins are removed from collecting tubule cell membranes, and the passage of water out of urine and into the blood decreases.

A diuretic is a compound that increases urine output and therefore decreases water conservation by the body. Diuretics are used to treat hypertension, congestive heart failure, and fluid retention associated with menstruation. Alcohol acts as a diuretic by inhibiting the release of ADH.

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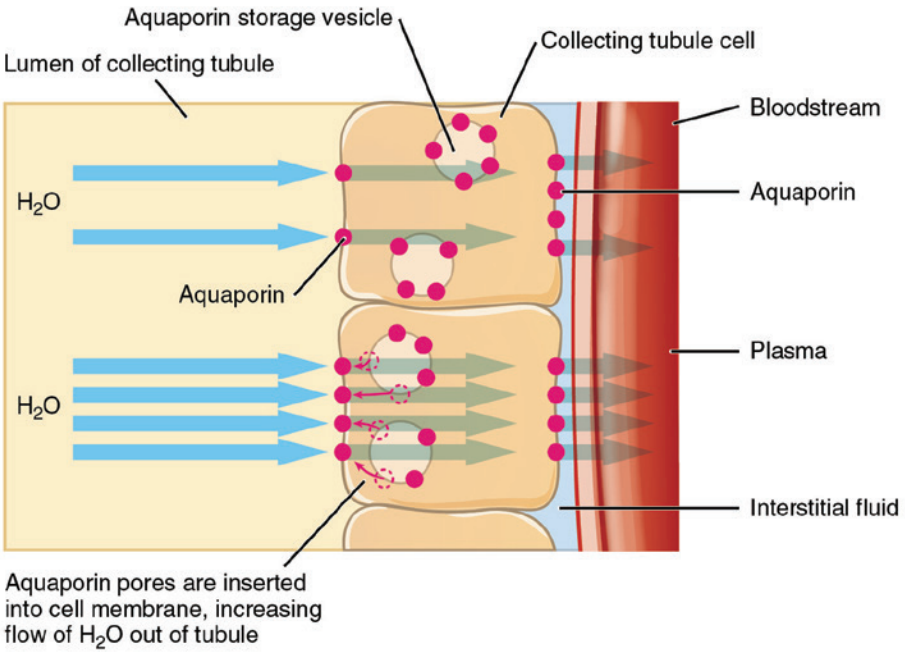


Figure 25.9 Aquaporins. The binding of ADH to receptors on the cells of the collecting tubule results in aquaporins being inserted into the plasma membrane, shown in the lower cell. This dramatically increases the flow of water out of the tubule and into the bloodstream.

25.3 Electrolyte Balance

Learning Objectives

By the end of this section, you will be able to:

- List the role of the six most important electrolytes in the body
- Name the disorders associated with abnormally high and low levels of the six electrolytes
- Identify the predominant extracellular anion
- Describe the role of aldosterone in the level of water in the body

The body contains a large variety of ions, or electrolytes, which perform a variety of functions. Some ions assist in the transmission of electrical impulses along cell membranes in neurons and muscles. Other ions help stabilize protein structures in enzymes. Still others aid in releasing hormones from endocrine glands. All of the ions in plasma contribute to the osmotic balance that controls the movement of water between cells and their environment.

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Electrolytes in living systems include sodium, potassium, chloride, bicarbonate, calcium, phosphate, magnesium, copper, zinc, iron, manganese, molybdenum, copper, and chromium. In terms of body functioning, six electrolytes are most important: sodium, potassium, chloride, bicarbonate, calcium, and phosphate.

Roles of Electrolytes

These six ions aid in nerve excitability, endocrine secretion, membrane permeability, buffering of body fluids, and controlling the movement of fluids between compartments. These ions enter the body through the digestive tract. More than 90 percent of the calcium and phosphate that enters the body is incorporated into bones and teeth, with bone serving as a mineral reserve for these ions. In the event that calcium and phosphate are needed for other functions, bone tissue can be broken down to supply the blood and other tissues with these minerals. Phosphate is a normal constituent of nucleic acids; hence, blood levels of phosphate will increase whenever nucleic acids are broken down.

Excretion of ions occurs mainly through the kidneys, with lesser amounts lost in sweat and in feces. Excessive sweating may cause a significant loss, especially of sodium and chloride. Severe vomiting or diarrhea will cause a loss of chloride and bicarbonate ions. Adjustments in respiratory and renal functions allow the body to regulate the levels of these ions in the ECF.

Sodium

Sodium is the major cation of the extracellular fluid. It is responsible for one-half of the osmotic pressure gradient that exists between the interior of cells and their surrounding environment. People eating a typical Western diet, which is very high in NaCl, routinely take in 130 to 160 mmol/day of sodium, but humans require only 1 to 2 mmol/day. This excess sodium appears to be a major factor in hypertension (high blood pressure) in some people.

Excretion of sodium is accomplished primarily by the kidneys. Sodium is freely filtered through the glomerular capillaries of the kidneys, and although much of the filtered sodium is reabsorbed in the proximal convoluted tubule, some remains in the filtrate and urine and is normally excreted.

Hyponatremia is a lower-than-normal concentration of sodium, usually associated with excess water accumulation in the body, which dilutes the sodium. An absolute loss of sodium may be due to a decreased intake of the ion coupled with its continual excretion in the urine. An abnormal loss of sodium from the body can result from several conditions, including excessive sweating, vomiting,

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or diarrhea; the use of diuretics; excessive production of urine, which can occur in diabetes; and acidosis, either metabolic acidosis or diabetic ketoacidosis.

A relative decrease in blood sodium can occur because of an imbalance of sodium in one of the body's other fluid compartments, like IF, or from a dilution of sodium due to water retention related to edema or congestive heart failure. At the cellular level, hyponatremia results in increased entry of water into cells by osmosis, because the concentration of solutes within the cell exceeds the concentration of solutes in the now-diluted ECF. The excess water causes swelling of the cells; the swelling of red blood cells—decreasing their oxygen-carrying efficiency and making them potentially too large to fit through capillaries—along with the swelling of neurons in the brain can result in brain damage or even death.

Hypernatremia is an abnormal increase of blood sodium. It can result from water loss from the blood, leading to the hemoconcentration of all blood constituents. Hormonal imbalances involving ADH and aldosterone may also result in higher-than-normal sodium levels.

Potassium

Potassium is the major intracellular cation. It helps establish the resting membrane potential in neurons and muscle fibres after membrane depolarization and action potentials. In contrast to sodium, potassium has very little effect on osmotic pressure. The low levels of potassium in blood and CSF are due to the sodium-potassium pumps in cell membranes, which maintain the normal potassium concentration gradients between the ICF and ECF. The recommended daily intake/consumption of potassium is 4,700 mg. Potassium is excreted, both actively and passively, through the renal tubules, especially the distal convoluted tubule and collecting ducts. Potassium participates in an exchange with sodium in the renal tubules under the influence of aldosterone; this exchange depends on basolateral sodium-potassium pumps.

Hypokalemia is an abnormally low potassium blood level. Similar to the situation with hyponatremia, hypokalemia can occur because of either an absolute reduction of potassium in the body or a relative reduction of potassium in the blood due to the redistribution of potassium. An absolute loss of potassium can arise from decreased intake, frequently related to starvation. It can also come about from vomiting, diarrhea, or alkalosis.

Some insulin-dependent diabetic patients experience a relative reduction of potassium in the blood from the redistribution of potassium. When insulin is administered and glucose is taken up by cells, potassium passes through the cell membrane along with glucose, decreasing the amount of potassium

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in the blood and IF, which can cause hyperpolarization of the cell membranes of neurons, reducing their responses to stimuli.

Hyperkalemia, an elevated potassium blood level, also can impair the function of skeletal muscles, the nervous system, and the heart. Hyperkalemia can result from increased dietary intake of potassium. In such a situation, potassium from the blood ends up in the ECF in abnormally high concentrations. This can result in a partial depolarization (excitation) of the plasma membrane of skeletal muscle fibres, neurons, and cardiac cells of the heart and can also lead to an inability of cells to repolarize. For the heart, this means that it won't relax after a contraction and will effectively "seize" and stop pumping blood, which is fatal within minutes. Because of such effects on the nervous system, a person with hyperkalemia may also exhibit mental confusion, numbness, and weakened respiratory muscles.

Chloride

Chloride is the predominant extracellular anion. Chloride is a major contributor to the osmotic pressure gradient between the ICF and ECF and plays an important role in maintaining proper hydration. Chloride functions to balance cations in the ECF, maintaining the electrical neutrality of this fluid. The paths of secretion and reabsorption of chloride ions in the renal system follow the paths of sodium ions.

Hypochloremia, or lower-than-normal blood chloride levels, can occur because of defective renal tubular absorption. Vomiting, diarrhea, and metabolic acidosis can also lead to hypochloremia. **Hyperchloremia**, or higher-than-normal blood chloride levels, can occur due to dehydration, excessive intake of dietary salt (NaCl) or swallowing of seawater, aspirin intoxication, congestive heart failure, and the hereditary, chronic lung disease cystic fibrosis. In people who have cystic fibrosis, chloride levels in sweat are two to five times those of normal levels, and analysis of sweat is often used in the diagnosis of the disease.

Interactive Link 25.3

Read this article (http://oer.aupress.ca/oer-202505/25.3) for an explanation of the effect of seawater on humans. What effect does drinking seawater have on the body?

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Bicarbonate

Bicarbonate is the second most abundant anion in the blood. Its principal function is to maintain your body's acid-base balance by being part of buffer systems. This role will be discussed in section 25.4 Acid-Base Balance.

$$+ H^+$$

Bicarbonate ions result from a chemical reaction that starts with carbon dioxide (CO_2) and water, two molecules that are produced at the end of aerobic metabolism. Only a small amount of CO_2 can be dissolved in body fluids. Thus, over 90 percent of the CO_2 is converted into bicarbonate ions, HCO_3^-, through the following reactions:

$$CO_2 + H_2O \leftrightarrow H_2CO_3 \leftrightarrow HCO_3^-$$

The bidirectional arrows indicate that the reactions can go in either direction, depending on the concentrations of the reactants and products. Carbon dioxide is produced in large amounts in tissues that have a high metabolic rate. Carbon dioxide is converted into bicarbonate in the cytoplasm of red blood cells through the action of an enzyme called carbonic anhydrase. Bicarbonate is transported in the blood. Once in the lungs, the reactions reverse direction, and CO_2 is regenerated from bicarbonate to be exhaled as metabolic waste.

Calcium

About two pounds of calcium in your body are bound up in bone, which provides hardness to the bone and serves as a mineral reserve for calcium and its salts for the rest of the tissues. Teeth also have a high concentration of calcium within them. A little more than one-half of blood calcium is bound to proteins, leaving the rest in its ionized form.

Calcium ions, Ca^{2+}, are necessary for muscle contraction, enzyme activity, and blood coagulation. In addition, calcium helps stabilize cell membranes and is essential for the release of neurotransmitters from neurons and of hormones from endocrine glands.

Calcium is absorbed through the intestines under the influence of activated vitamin D. A deficiency of vitamin D leads to a decrease in absorbed calcium and, eventually, a depletion of calcium stores from the skeletal system, potentially leading to rickets in children and osteomalacia in adults, contributing to osteoporosis.

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Hypocalcemia, or abnormally low calcium blood levels, is seen in hypoparathyroidism, which may follow the removal of the thyroid gland, because the four nodules of the parathyroid gland are embedded in it. **Hypercalcemia**, or abnormally high calcium blood levels, is seen in primary hyperparathyroidism. Some malignancies may also result in hypercalcemia.

Phosphate

Phosphate is present in the body in three ionic forms: H_2PO_4, HPO_4^{2-}, and PO_4^{3-}. The most common form is HPO_4^{2-}. Bone and teeth bind up 85 percent of the body's phosphate as part of calcium-phosphate salts. Phosphate is found in phospholipids, such as those that make up the cell membrane, and in ATP, nucleotides, and buffers.

Hypophosphatemia, or abnormally low phosphate blood levels, occurs with heavy use of antacids, during alcohol withdrawal, and during malnourishment. In the face of phosphate depletion, the kidneys usually conserve phosphate, but during starvation, this conservation is impaired greatly. **Hyperphosphatemia**, or abnormally increased levels of phosphates in the blood, occurs if there is decreased renal function or in cases of acute lymphocytic leukemia. Additionally, because phosphate is a major constituent of the ICF, any significant destruction of cells can result in the dumping of phosphate into the ECF.

Regulation of Sodium and Potassium

Sodium is reabsorbed from the renal filtrate, and potassium is excreted into the filtrate in the renal collecting tubule. The control of this exchange is governed principally by two hormones—aldosterone and angiotensin II.

Aldosterone

Recall that aldosterone increases the excretion of potassium and the reabsorption of sodium in the distal tubule. Aldosterone is released if blood levels of potassium increase, if blood levels of sodium severely decrease, or if blood pressure decreases. Its net effect is to conserve and increase water levels in the plasma by reducing the excretion of sodium, and thus water, from the kidneys. In a negative-feedback loop, increased osmolality of the ECF (which follows aldosterone-stimulated sodium absorption) inhibits the release of the hormone (Figure 25.10).

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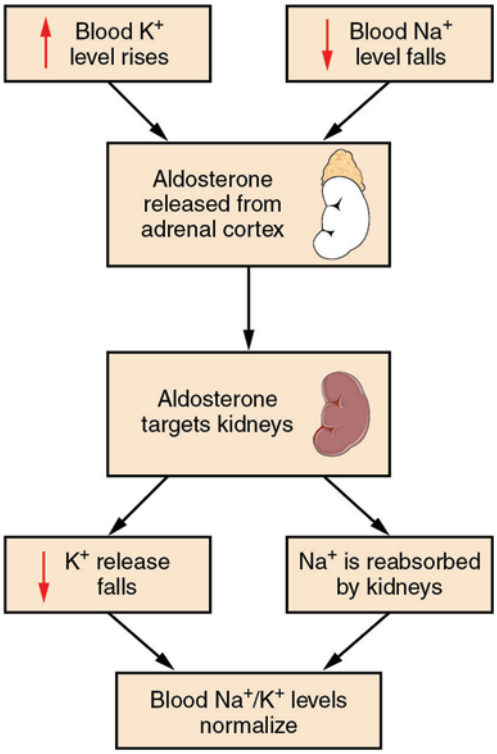


Figure 25.10 The Aldosterone Feedback Loop. Aldosterone, which is released by the adrenal gland, facilitates reabsorption of Na^+ and thus the reabsorption of water.

Angiotensin II

Angiotensin II causes vasoconstriction, resulting in an increase in systemic blood pressure. This action increases the glomerular filtration rate, resulting in more material filtered out of the glomerular capillaries and into Bowman's capsule. Angiotensin II also signals an increase in the release of aldosterone from the adrenal cortex.

In the distal convoluted tubules and collecting ducts of the kidneys, aldosterone stimulates the synthesis and activation of the sodium-potassium pump (Figure 25.11). Sodium passes from the filtrate into and through the cells of the tubules and ducts, into the ECF, and then into capillaries. Water follows the sodium due to osmosis. Thus, aldosterone causes an increase in blood sodium levels and blood volume. Aldosterone's effect on potassium is the reverse of that of sodium; under its influence, excess potassium is pumped into the renal filtrate for excretion from the body.

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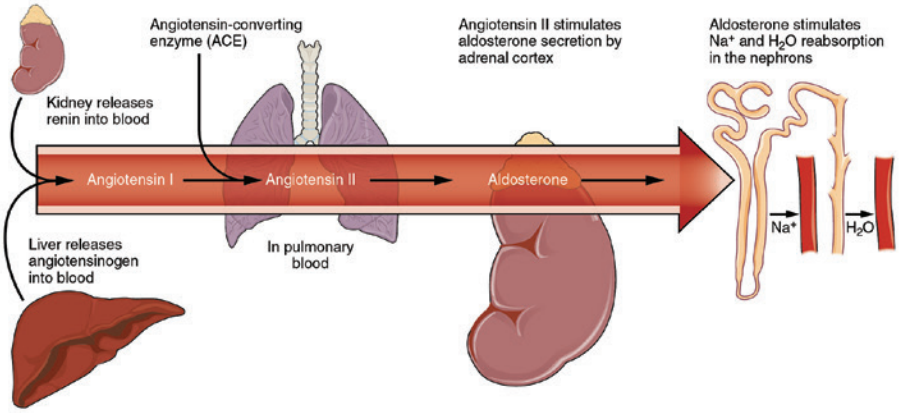


Figure 25.11 The Renin-Angiotensin-Alderosterone System. Angiotensin II stimulates the release of aldosterone from the adrenal cortex.

Regulation of Calcium and Phosphate

Calcium and phosphate are both regulated through the actions of three hormones: parathyroid hormone (PTH), dihydroxyvitamin D (calcitriol), and calcitonin. All three are released or synthesized in response to the blood levels of calcium.

PTH is released from the parathyroid gland in response to a decrease in the concentration of blood calcium. The hormone activates osteoclasts to break down bone matrix and release inorganic calcium-phosphate salts. PTH also increases the gastrointestinal absorption of dietary calcium by converting vitamin D into **dihydroxyvitamin D** (**calcitriol**), an active form of vitamin D that intestinal epithelial cells require to absorb calcium.

PTH raises blood calcium levels by inhibiting the loss of calcium through the kidneys. PTH also increases the loss of phosphate through the kidneys.

Calcitonin is released from the thyroid gland in response to elevated blood levels of calcium. The hormone increases the activity of osteoblasts, which removes calcium from the blood and incorporates calcium into the bony matrix.

25.4 Acid-Base Balance

Learning Objectives

By the end of this section, you will be able to:

- Identify the most powerful buffer system in the body
- Explain the way in which the respiratory system affects blood pH

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Proper physiological functioning depends on a very tight balance between the concentrations of acids and bases in the blood. Acid-base balance is measured using the pH scale. A variety of buffering systems permits blood and other bodily fluids to maintain a narrow pH range, even in the face of perturbations. A buffer is a chemical system that prevents a radical change in fluid pH by dampening the change in hydrogen ion concentrations in the case of excess acid or base. Most commonly, the substance that absorbs the ions is either a weak acid, which takes up hydroxyl ions, or a weak base, which takes up hydrogen ions.

Buffer Systems in the Body

The buffer systems in the human body are extremely efficient, and different systems work at different rates. It takes only seconds for the chemical buffers in the blood to make adjustments to pH. The respiratory tract can adjust the blood pH upward in minutes by exhaling CO_2 from the body. The renal system can also adjust blood pH through the excretion of hydrogen ions (H^+) and the conservation of bicarbonate, but this process takes hours to days to have an effect.

The buffer systems functioning in blood plasma include plasma proteins, phosphate, and bicarbonate—carbonic acid buffers. The kidneys help control acid-base balance by excreting hydrogen ions and generating bicarbonate that helps maintain blood plasma pH within a normal range. Protein buffer systems work predominantly inside cells.

Protein Buffers in Blood Plasma and Cells

Nearly all proteins can function as buffers. Proteins are made up of amino acids, which contain positively charged amino groups and negatively charged carboxyl groups. The charged regions of these molecules can bind hydrogen and hydroxyl ions and thus function as buffers. Buffering by proteins accounts for two-thirds of the buffering power of the blood and most of the buffering within cells.

Hemoglobin as a Buffer

Hemoglobin is the principal protein inside red blood cells and accounts for one-third of the mass of the cell. During the conversion of CO_2 into bicarbonate, hydrogen ions liberated in the reaction are buffered by hemoglobin, which is reduced by the dissociation of oxygen. This buffering helps maintain normal pH. The process is reversed in the pulmonary capillaries to reform CO_2, which then can diffuse into the air sacs to be exhaled into the atmosphere. This process is discussed in detail in chapter 21 on the respiratory system.

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Phosphate Buffer

Phosphates are found in the blood in two forms: sodium dihydrogen phosphate (NaH_2PO_4), which is a weak acid, and sodium monohydrogen phosphate (Na_2HPO_4), which is a weak base. When Na_2HPO_4 comes into contact with a strong acid, such as HCl, the base picks up a second hydrogen ion to form the weak acid NaH_2PO_4 and sodium chloride, NaCl. When $NaHPO_4$ (the weak acid) comes into contact with a strong base, such as sodium hydroxide (NaOH), the weak acid reverts back to the weak base and produces water. Acids and bases are still present, but they hold onto the ions.

Bicarbonate-Carbonic Acid Buffer

The bicarbonate-carbonic acid buffer works in a fashion similar to phosphate buffers. The bicarbonate is regulated in the blood by sodium, as are the phosphate ions. When sodium bicarbonate ($NaHCO_3$) comes into contact with a strong acid, such as HCl, carbonic acid (H_2CO_3), which is a weak acid, and NaCl are formed. When carbonic acid comes into contact with a strong base, such as NaOH, bicarbonate and water are formed.

As with the phosphate buffer, a weak acid or weak base captures the free ions, and a significant change in pH is prevented. Bicarbonate ions and carbonic acid are present in the blood in a 20:1 ratio if the blood pH is within the normal range. With 20 times more bicarbonate than carbonic acid, this capture system is most efficient at buffering changes that would make the blood more acidic. This is useful because most of the body's metabolic wastes, such as lactic acid and ketone bodies, are acids. Carbonic acid levels in the blood are controlled by the expiration of CO_2 through the lungs. In red blood cells, carbonic anhydrase forces the dissociation of the acid, rendering the blood less acidic. Because of this acid dissociation, CO_2 is exhaled (see equations above). The level of bicarbonate in the blood is controlled through the renal system, where bicarbonate ions in the renal filtrate are conserved and passed back into the blood. However, the bicarbonate buffer is the primary buffering system of the IF surrounding the cells in tissues throughout the body.

Respiratory Regulation of Acid-Base Balance

The respiratory system contributes to the balance of acids and bases in the body by regulating the blood levels of carbonic acid (Figure 25.12). CO_2 in the blood readily reacts with water to form carbonic acid, and the levels of CO_2 and carbonic acid in the blood are in equilibrium. When the CO_2 level in the blood rises (as it does when you hold your breath), the excess CO_2 reacts with water to form additional carbonic acid, lowering blood pH. Increasing the rate and/or depth

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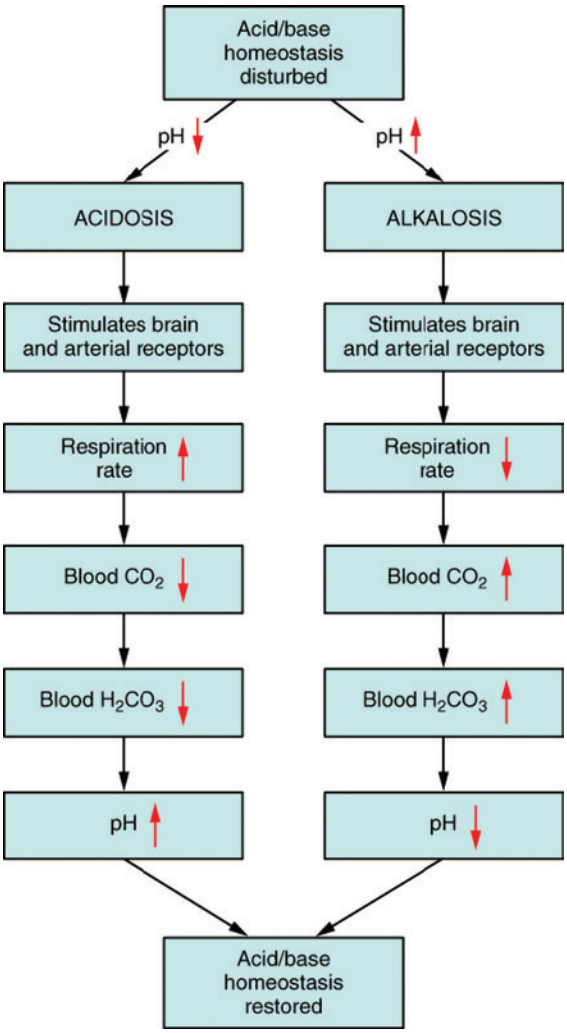


Figure 25.12 Respiratory Regulation of Blood pH. The respiratory system can reduce blood pH by removing CO_2 from the blood.

of respiration (which you might feel the "urge" to do after holding your breath) allows you to exhale more CO_2. The loss of CO_2 from the body reduces blood levels of carbonic acid and thereby adjusts the pH upward, toward normal levels. As you might have surmised, this process also works in the opposite direction.

Excessive deep and rapid breathing (as in hyperventilation) rids the blood of CO_2 and reduces the level of carbonic acid, making the blood too alkaline. This brief alkalosis can be remedied by rebreathing air that has been exhaled into a paper bag. Rebreathing exhaled air will rapidly bring blood pH down toward normal.

The chemical reactions that regulate the levels of CO_2 and carbonic acid occur in the lungs when blood travels through the lung's pulmonary capillaries.

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Minor adjustments in breathing are usually sufficient to adjust the pH of the blood by changing how much CO_2 is exhaled. In fact, doubling the respiratory rate for less than 1 minute, removing "extra" CO_2, would increase the blood pH by 0.2. This situation is common if you are exercising strenuously over a period of time. To keep up the necessary energy production, you would produce excess CO_2 (and lactic acid if exercising beyond your aerobic threshold). In order to balance the increased acid production, the respiration rate goes up to remove the CO_2. This helps keep you from developing acidosis.

The body regulates the respiratory rate by the use of chemoreceptors, which primarily use CO_2 as a signal. Peripheral blood sensors are found in the walls of the aorta and carotid arteries. These sensors signal the brain to provide immediate adjustments to the respiratory rate if CO_2 levels rise or fall. Yet other sensors are found in the brain itself. Changes in the pH of CSF affect the respiratory centre in the medulla oblongata, which can directly modulate breathing rate to bring the pH back into the normal range.

Hypercapnia, or abnormally elevated blood levels of CO_2, occurs in any situation that impairs respiratory functions, including pneumonia and congestive heart failure. Reduced breathing (hypoventilation) due to drugs such as morphine, barbiturates, or ethanol (or even just holding one's breath) can also result in hypercapnia. **Hypocapnia**, or abnormally low blood levels of CO_2, occurs with any cause of hyperventilation that drives off the CO_2, such as salicylate toxicity, elevated room temperatures, fever, or hysteria.

Renal Regulation of Acid-Base Balance

The renal regulation of the body's acid-base balance addresses the metabolic component of the buffering system.

Whereas the respiratory system (together with breathing centres in the brain) controls the blood levels of carbonic acid by controlling the exhalation of CO_2, the renal system controls the blood levels of bicarbonate. A decrease of blood bicarbonate can result from the inhibition of carbonic anhydrase by certain diuretics or from excessive bicarbonate loss due to diarrhea. Blood bicarbonate levels are also typically lower in people who have Addison's disease (chronic adrenal insufficiency), in which aldosterone levels are reduced, and in people who have renal damage, such as chronic nephritis. Finally, low bicarbonate blood levels can result from elevated levels of ketones (common in unmanaged diabetes mellitus), which bind bicarbonate in the filtrate and prevent its conservation.

Bicarbonate ions, HCO_3^-, found in the filtrate, are essential to the bicarbonate buffer system, yet the cells of the tubule are not permeable to bicarbonate ions. The steps involved in supplying bicarbonate ions to the system are summarized as follows:

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- Step 1: Sodium ions are reabsorbed from the filtrate in exchange for H^+ by an antiport mechanism in the apical membranes of cells lining the renal tubule.
- Step 2: The cells produce bicarbonate ions that can be shunted to peritubular capillaries.
- Step 3: When CO_2 is available, the reaction is driven to the formation of carbonic acid, which dissociates to form a bicarbonate ion and a hydrogen ion.
- Step 4: The bicarbonate ion passes into the peritubular capillaries and returns to the blood. The hydrogen ion is secreted into the filtrate, where it can become part of new water molecules and be reabsorbed as such, or removed in the urine.

It is also possible that salts in the filtrate, such as sulfates, phosphates, or ammonia, will capture hydrogen ions. If this occurs, the hydrogen ions will not be available to combine with bicarbonate ions and produce CO_2. In such cases, bicarbonate ions are not conserved from the filtrate to the blood, which will also contribute to a pH imbalance and acidosis.

The hydrogen ions also compete with potassium to exchange with sodium in the renal tubules. If more potassium is present than normal, potassium, rather than the hydrogen ions, will be exchanged, and increased potassium enters the filtrate. When this occurs, fewer hydrogen ions in the filtrate participate in the conversion of bicarbonate into CO_2 and less bicarbonate is conserved. If there is less potassium, more hydrogen ions enter the filtrate to be exchanged with sodium and more bicarbonate is conserved.

Chloride ions are important in neutralizing positive ion charges in the body. If chloride is lost, the body uses bicarbonate ions in place of the lost chloride ions. Thus, lost chloride results in an increased reabsorption of bicarbonate by the renal system.

25.5 Disorders of Acid-Base Balance

Learning Objectives

By the end of this section, you will be able to:

- Identify the three blood variables considered when making a diagnosis of acidosis or alkalosis
- Identify the source of compensation for blood pH problems of a respiratory origin

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- Identify the source of compensation for blood pH problems of a metabolic/renal origin

Normal arterial blood pH is restricted to a very narrow range of 7.35 to 7.45. A person who has a blood pH below 7.35 is considered to be in acidosis (actually, "physiological acidosis," because blood is not truly acidic until its pH drops below 7), and a continuous blood pH below 7.0 can be fatal. Acidosis has several symptoms, including headache and confusion, and the individual can become lethargic and easily fatigued (Figure 25.13). A person who has a blood pH above 7.45 is considered to be in alkalosis, and a pH above 7.8 is fatal. Some symptoms of alkalosis include cognitive impairment (which can progress to unconsciousness), tingling or numbness in the extremities, muscle twitching and spasm, and nausea and vomiting. Both acidosis and alkalosis can be caused by either metabolic or respiratory disorders.

As discussed earlier in this chapter, the concentration of carbonic acid in the blood is dependent on the level of CO_2 in the body and the amount of CO_2 gas exhaled through the lungs. Thus, the respiratory contribution to acid-base balance is usually discussed in terms of CO_2 (rather than of carbonic acid). Remember that a molecule of carbonic acid is lost for every molecule of CO_2 exhaled, and a molecule of carbonic acid is formed for every molecule of CO_2 retained.

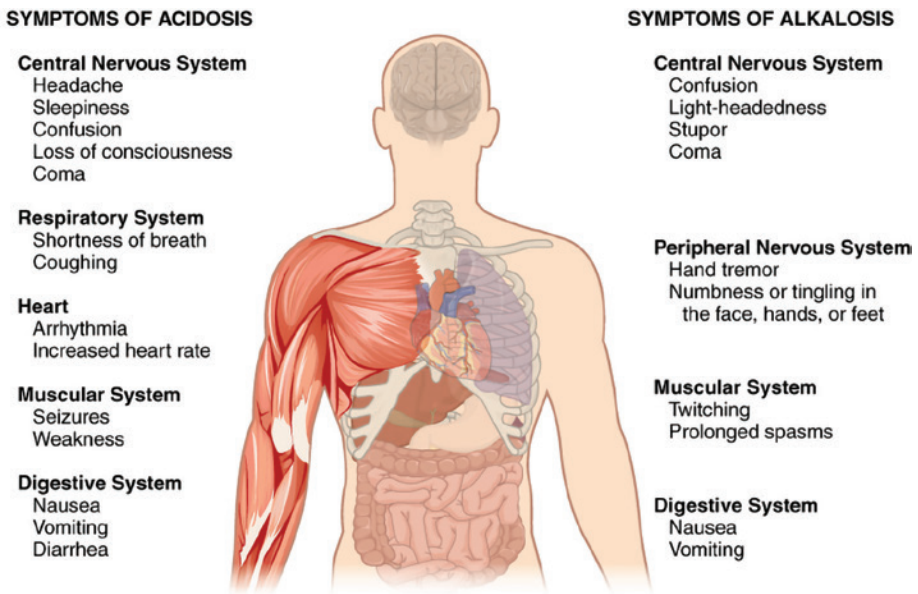


Figure 25.13 Symptoms of Acidosis and Alkalosis. Symptoms of acidosis affect several organ systems. Both acidosis and alkalosis can be diagnosed using a blood test.

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Metabolic Acidosis: Primary Bicarbonate Deficiency

Metabolic acidosis occurs when the blood is too acidic (pH below 7.35) due to too little bicarbonate, a condition called primary bicarbonate deficiency. At the normal pH of 7.40, the ratio of bicarbonate to carbonic acid buffer is 20:1. If a person's blood pH drops below 7.35, then the person is in metabolic acidosis. The most common cause of metabolic acidosis is the presence of organic acids or excessive ketone bodies in the blood. Table 25.1 lists some other causes of metabolic acidosis.

Table 25.1 Common Causes of Metabolic Acidosis and Blood Metabolites

Cause	Metabolite
Diarrhea	Bicarbonate
Uremia	Phosphoric, sulfuric, and lactic acids
Diabetic ketoacidosis	Increased ketone bodies
Strenuous exercise	Lactic acid
Methanol	Formic acid*
Paraldehyde	β-Hydroxybutyric acid*
Isopropanol	Propionic acid*
Ethylene glycol	Glycolic acid, and some oxalic and formic acids*
Salicylate/aspirin	Sulfosalicylic acid (SSA)*

* Acid metabolites from ingested chemical.

The first three of the nine causes of metabolic acidosis listed are medical (or unusual physiological) conditions.

Strenuous exercise can cause temporary metabolic acidosis due to the production of lactic acid. The last five causes result from the ingestion of specific substances. The active form of aspirin is its metabolite, sulfosalicylic acid. An overdose of aspirin causes acidosis due to the acidity of this metabolite. Metabolic acidosis can also result from uremia, which is the retention of urea and uric acid. Metabolic acidosis can also arise from diabetic ketoacidosis, wherein an excess of ketone bodies is present in the blood. Other causes of metabolic acidosis are a decrease in the excretion of hydrogen ions, which inhibits the conservation of bicarbonate ions, and excessive loss of bicarbonate ions through the gastrointestinal tract due to diarrhea.

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Metabolic Alkalosis: Primary Bicarbonate Excess

Metabolic alkalosis is the opposite of metabolic acidosis. It occurs when the blood is too alkaline (pH above 7.45) due to too much bicarbonate (called primary bicarbonate excess).

A transient excess of bicarbonate in the blood can follow ingestion of excessive amounts of bicarbonate, citrate, or antacids for conditions such as stomach acid reflux—known as heartburn. Cushing's disease, which is the chronic hypersecretion of adrenocorticotropic hormone (ACTH) by the anterior pituitary gland, can cause chronic metabolic alkalosis. The oversecretion of ACTH results in elevated aldosterone levels and an increased loss of potassium by urinary excretion. Other causes of metabolic alkalosis include the loss of hydrochloric acid from the stomach through vomiting, potassium depletion due to the use of diuretics for hypertension, and the excessive use of laxatives.

Respiratory Acidosis: Primary Carbonic Acid/CO_2 Excess

Respiratory acidosis occurs when the blood is overly acidic due to an excess of carbonic acid, resulting from too much CO_2 in the blood. Respiratory acidosis can result from anything that interferes with respiration, such as pneumonia, emphysema, or congestive heart failure.

Respiratory Alkalosis: Primary Carbonic Acid/CO_2 Deficiency

Respiratory alkalosis occurs when the blood is overly alkaline due to a deficiency in carbonic acid and CO_2 levels in the blood. This condition usually occurs when too much CO_2 is exhaled from the lungs, as occurs in hyperventilation, which is breathing that is deeper or more frequent than normal. An elevated respiratory rate leading to hyperventilation can be due to extreme emotional upset or fear, fever, infections, hypoxia, or abnormally high levels of catecholamines, such as epinephrine and norepinephrine. Surprisingly, aspirin overdose—salicylate toxicity—can result in respiratory alkalosis as the body tries to compensate for initial acidosis.

Interactive Link 25.4

Watch this video (http://oer.aupress.ca/oer-202505/25.4) to see a demonstration of the effect altitude has on blood pH. What effect does high altitude have on blood pH, and why?

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Compensation Mechanisms

Various compensatory mechanisms exist to maintain blood pH within a narrow range, including buffers, respiration, and renal mechanisms. Although compensatory mechanisms usually work very well, when one of these mechanisms is not working properly (like in kidney failure or respiratory disease), they have their limits. If the pH and bicarbonate to carbonic acid ratio are changed too drastically, the body may not be able to compensate. Moreover, extreme changes in pH can denature proteins. Extensive damage to proteins in this way can result in disruption of normal metabolic processes, serious tissue damage, and ultimately death.

Respiratory Compensation

Respiratory compensation for metabolic acidosis increases the respiratory rate to drive off CO_2 and readjust the bicarbonate to carbonic acid ratio to the 20:1 level. This adjustment can occur within minutes. Respiratory compensation for metabolic alkalosis is not as adept as its compensation for acidosis. The normal response of the respiratory system to elevated pH is to increase the amount of CO_2 in the blood by decreasing the respiratory rate to conserve CO_2. There is a limit to the decrease in respiration, however, that the body can tolerate. Hence the respiratory route is less efficient at compensating for metabolic alkalosis than for acidosis.

Metabolic Compensation

Metabolic and renal compensation for respiratory diseases that can create acidosis revolves around the conservation of bicarbonate ions. In cases of respiratory acidosis, the kidney increases the conservation of bicarbonate and secretion of H^+ through the exchange mechanism discussed earlier. These processes increase the concentration of bicarbonate in the blood, reestablishing the proper relative concentrations of bicarbonate and carbonic acid. In cases of respiratory alkalosis, the kidneys decrease the production of bicarbonate and reabsorb H^+ from the tubular fluid. These processes can be limited by the exchange of potassium by the renal cells, which use a K^+-H^+ exchange mechanism (antiporter).

Diagnosing Acidosis and Alkalosis

Lab tests for pH, CO_2 partial pressure (PCO_2), and HCO_3^- can identify acidosis and alkalosis, indicating whether the imbalance is respiratory or metabolic, and the extent to which compensatory mechanisms are working. The blood pH value, as shown in Table 25.2, indicates whether the blood is in acidosis, the

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normal range, or alkalosis. The PCO_2 and total HCO_3– values aid in determining whether the condition is metabolic or respiratory and whether the patient has been able to compensate for the problem. Table 25.2 lists the conditions and laboratory results that can be used to classify these conditions. Metabolic acid-base imbalances typically result from kidney disease, and the respiratory system usually responds to compensate.

Table 25.2 Types of Acidosis and Alkalosis

	pH	PCO_2	Total HCO_3–
Metabolic acidosis	↓	N, then ↓	↓
Respiratory acidosis	↓	↑	N, then ↑
Metabolic alkalosis	↑	N, then↑	↑
Respiratory alkalosis	↑	↓	N, then ↓

Reference values (arterial): pH: 7.35–7.45; pCO_2: male: 35–48 mm Hg, female: 32–45 mm Hg; total venous bicarbonate: 22–29 mM. N denotes normal; ↑ denotes a rising or increased value; and ↓ denotes a falling or decreased value.

Metabolic acidosis is problematic, as lower-than-normal amounts of bicarbonate are present in the blood. The PCO_2 would be normal at first, but if compensation has occurred, it would decrease as the body reestablishes the proper ratio of bicarbonate and carbonic acid/CO_2.

Respiratory acidosis is problematic, as excess CO_2 is present in the blood. Bicarbonate levels would be normal at first, but if compensation has occurred, they would increase in an attempt to reestablish the proper ratio of bicarbonate and carbonic acid/CO_2.

Alkalosis is characterized by a higher-than-normal pH. Metabolic alkalosis is problematic, as elevated pH and excess bicarbonate are present. The PCO_2 would again be normal at first, but if compensation has occurred, it would increase as the body attempts to reestablish the proper ratios of bicarbonate and carbonic acid/CO_2.

Respiratory alkalosis is problematic, as CO_2 deficiency is present in the bloodstream. The bicarbonate concentration would be normal at first. When renal compensation occurs, however, the bicarbonate concentration in blood decreases as the kidneys attempt to reestablish the proper ratios of bicarbonate and carbonic acid/CO_2 by eliminating more bicarbonate to bring the pH into the physiological range.

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Key Terms

antidiuretic hormone (ADH): Also known as vasopressin, a hormone that increases the volume of water reabsorbed from the collecting tubules of the kidney.

dehydration: State of containing insufficient water in blood and other tissues.

dihydroxyvitamin D (calcitriol): Active form of vitamin D required by the intestinal epithelial cells for the absorption of calcium.

diuresis: Excess production of urine.

extracellular fluid (ECF): Fluid exterior to cells; includes the interstitial fluid, blood plasma, and fluids found in other reservoirs in the body.

fluid compartment: Fluid inside all cells of the body constitutes a compartment system that is largely segregated from other systems.

hydrostatic pressure: Pressure exerted by a fluid against a wall, caused by its own weight or pumping force.

hypercalcemia: Abnormally increased blood levels of calcium.

hypercapnia: Abnormally elevated blood levels of CO_2.

hyperchloremia: Higher-than-normal blood chloride levels.

hyperkalemia: Higher-than-normal blood potassium levels.

hypernatremia: Abnormal increase in blood sodium levels.

hyperphosphatemia: Abnormally increased blood phosphate levels.

hypocalcemia: Abnormally low blood levels of calcium.

hypocapnia: Abnormally low blood levels of CO_2.

hypochloremia: Lower-than-normal blood chloride levels.

hypokalemia: Abnormally decreased blood levels of potassium.

hyponatremia: Lower-than-normal levels of sodium in the blood.

hypophosphatemia: Abnormally low blood phosphate levels.

interstitial fluid (IF): Fluid in the small spaces between cells not contained within blood vessels.

intracellular fluid (ICF): Fluid in the cytosol of cells.

metabolic acidosis: Condition wherein a deficiency of bicarbonate causes the blood to be overly acidic.

metabolic alkalosis: Condition wherein an excess of bicarbonate causes the blood to be overly alkaline.

plasma: Fluid component of the blood.

plasma osmolality: Ratio of solutes to a volume of solvent in the plasma; plasma osmolality reflects a person's state of hydration.

respiratory acidosis: Condition wherein an excess of carbonic acid or CO_2 causes the blood to be overly acidic.

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respiratory alkalosis: Condition wherein a deficiency of carbonic acid/CO_2 levels causes the blood to be overly alkaline.

Chapter Review

25.1 Body Fluids and Fluid Compartments

Your body is mostly water. Body fluids are aqueous solutions with differing concentrations of materials called solutes. An appropriate balance of water and solute concentrations must be maintained to ensure cellular functions. If the cytosol becomes too concentrated due to water loss, cell functions deteriorate. If the cytosol becomes too dilute due to water intake by cells, cell membranes can be damaged, and the cell can burst. Hydrostatic pressure is the force exerted by a fluid against a wall and causes movement of fluid between compartments. Fluid can also move between compartments along an osmotic gradient.

Active transport processes require ATP to move some solutes against their concentration gradients between compartments. Passive transport of a molecule or ion depends on its ability to pass easily through the membrane as well as the existence of a high to low concentration gradient.

25.2 Water Balance

Homeostasis requires that water intake and output be balanced. Most water intake comes through the digestive tract via liquids and food, but roughly 10 percent of water available to the body is generated at the end of aerobic respiration during cellular metabolism. Urine produced by the kidneys accounts for the largest amount of water leaving the body. The kidneys can adjust the concentration of the urine to reflect the body's water needs, conserving water if the body is dehydrated or making urine more dilute to expel excess water when necessary. ADH is a hormone that helps the body retain water by increasing water reabsorption by the kidneys.

25.3 Electrolyte Balance

Electrolytes serve various purposes, such as helping conduct electrical impulses along cell membranes in neurons and muscles, stabilizing enzyme structures, and releasing hormones from endocrine glands. The ions in plasma also contribute to the osmotic balance that controls the movement of water between cells and their environment. Imbalances of these ions can result in various problems in the body, and their concentrations are tightly regulated. Aldosterone and angiotensin II control the exchange of sodium and potassium between the renal filtrate and the renal collecting tubule. Calcium and phosphate are regulated by PTH, calcitriol, and calcitonin.

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25.4 Acid-Base Balance

A variety of buffering systems exist in the body that helps maintain the pH of the blood and other fluids within a narrow range—between pH 7.35 and 7.45. A buffer is a substance that prevents a radical change in fluid pH by absorbing excess hydrogen or hydroxyl ions. Most commonly, the substance that absorbs the ion is either a weak acid, which takes up a hydroxyl ion (OH-), or a weak base, which takes up a hydrogen ion (H^+). Several substances serve as buffers in the body, including cell and plasma proteins, hemoglobin, phosphates, bicarbonate ions, and carbonic acid. The bicarbonate buffer is the primary buffering system of the IF surrounding the cells in tissues throughout the body. The respiratory and renal systems also play major roles in acid-base homeostasis by removing CO_2 and hydrogen ions, respectively, from the body.

25.5 Disorders of Acid-Base Balance

Acidosis and alkalosis describe conditions in which a person's blood is, respectively, too acidic (pH below 7.35) and too alkaline (pH above 7.45). Each of these conditions can be caused either by metabolic problems related to bicarbonate levels or by respiratory problems related to carbonic acid and CO_2 levels.

Several compensatory mechanisms allow the body to maintain a normal pH.

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PART 6

Human Development and the Continuity of Life

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26

The Reproductive System

Chapter Objectives

After studying this chapter, you will be able to:

- Describe the anatomy of the reproductive systems, including their accessory structures
- Explain the role of hypothalamic and pituitary hormones in reproductive function
- Trace the path of a sperm cell from its initial production through fertilization of an oocyte
- Explain the events in the ovary prior to ovulation

Small, uncoordinated, and slick with amniotic fluid, a newborn encounters the world outside of the womb. We do not often consider that a child's birth is proof of the healthy functioning of reproductive systems. Moreover, endocrine systems had to secrete the appropriate regulating hormones to induce the production and release of unique male and female gametes, reproductive cells containing genetic material (one set of 23 chromosomes). Reproductive behaviour or medical innovation had to facilitate the transfer of male gametes—the sperm—to the female gamete, an oocyte (egg). Finally, combination of the gametes (fertilization) had to occur, followed by implantation and development. In this chapter, you will explore the reproductive systems, whose functioning can culminate in the powerful sound of a newborn's first cry.

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26.1 Anatomy and Physiology of the Testicular Reproductive System

Learning Objectives

By the end of this section, you will be able to:

- Describe the structure and function of the organs of the testicular reproductive system
- Describe the structure and function of the sperm cell
- Explain the events during spermatogenesis that produce haploid sperm from diploid cells
- Identify the importance of testosterone in reproductive function

People often use the words *female* and *male* to describe two different concepts: our sense of gender identity and our biological sex as determined by our X/Y chromosomes, hormones, sex organs, and other physical characteristics. For some people, gender identity is different from biological sex or their sex assigned at birth. In this chapter and the next chapter, *female* and *male* refer to sex only, and the typical reproductive anatomy of XX and XY individuals is discussed.

Unique for its role in reproduction, a **gamete** is a specialized sex cell, which in humans carries 23 chromosomes—one-half the number in body cells. In almost all sexually reproducing species, these two haploid cells differ in size; the smaller gamete is called the male gamete, and the larger one is called the female gamete. At fertilization, the chromosomes in one male gamete, called a **sperm** (or spermatozoon), combine with the chromosomes in one female gamete, called an oocyte. The function of the male, or testicular, reproductive system (Figure 26.1) is to produce sperm and transfer them to the female reproductive tract. The paired testes are a crucial component in this process, as they produce both sperm and androgens, the hormones that support male reproductive physiology. In male humans, the most important androgen is testosterone. For people with a penis, several accessory organs and ducts aid the process of sperm maturation and transport the sperm and other seminal components to the penis, which may deliver sperm to the female reproductive tract. In this section, we examine each of these different structures and discuss the process of sperm production and transport.

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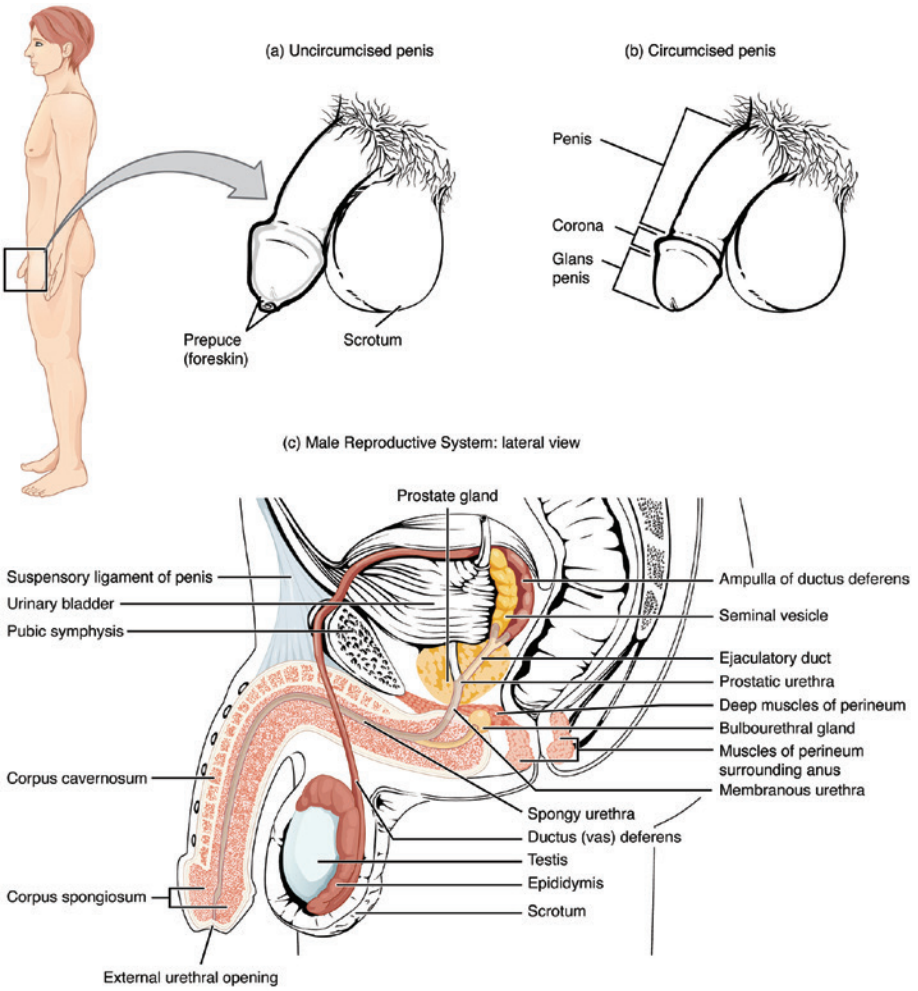


Figure 26.1 Testicular Reproductive System. The structures of the testicular reproductive system include the testes, the epididymides, the penis, and the ducts and glands that produce and carry semen. Sperm exit the scrotum through the ductus deferens, which is bundled in the spermatic cord. The seminal vesicles and prostate gland add fluids to the sperm to create semen.

Scrotum

The testes are located in a skin-covered, highly pigmented, muscular sack called the **scrotum** that extends from the body behind the penis (see Figure 26.1). This location is important in sperm production, which occurs within the testes, and proceeds more efficiently when the testes are kept 2°C to 4°C below core body temperature.

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The dartos muscle makes up the subcutaneous muscle layer of the scrotum (Figure 26.2). It continues internally to make up the scrotal septum, a wall that divides the scrotum into two compartments, each housing one testis.

Descending from the internal oblique muscle of the abdominal wall are the two cremaster muscles, which cover each testis like a muscular net. By contracting simultaneously, the dartos and cremaster muscles can elevate the testes in cold weather (or water), moving the testes closer to the body and decreasing the surface area of the scrotum to retain heat. Alternatively, as the environmental temperature increases, the scrotum relaxes, moving the testes farther from the body core and increasing scrotal surface area, which promotes heat loss. Externally, the scrotum has a raised medial thickening on the surface called the raphae.

Testes

The **testes** (singular = testis) are the male **gonads**—that is, the male reproductive organs. They produce both sperm and androgens, such as testosterone, and are active throughout the reproductive lifespan.

Paired ovals, adult testes are each approximately 4 to 5 cm in length and are housed within the scrotum (see Figure 26.2). They are surrounded by two distinct layers of protective connective tissue (Figure 26.3). The outer tunica vaginalis is a serous membrane that has both a parietal and a thin visceral layer. Beneath the tunica vaginalis is the tunica albuginea, a tough, white, dense connective tissue layer covering the testis itself. Not only does the tunica albuginea cover the outside of the testis; it also invaginates to form septa that divide the testis into 300 to 400 structures called lobules. Within the lobules, sperm develop in structures called **seminiferous tubules**. During the seventh

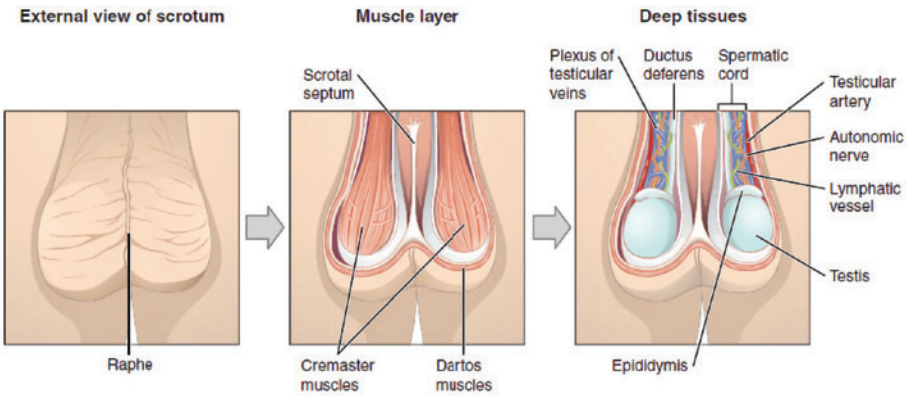


Figure 26.2 The Scrotum and Testes. This anterior view shows the structures of the scrotum and testes.

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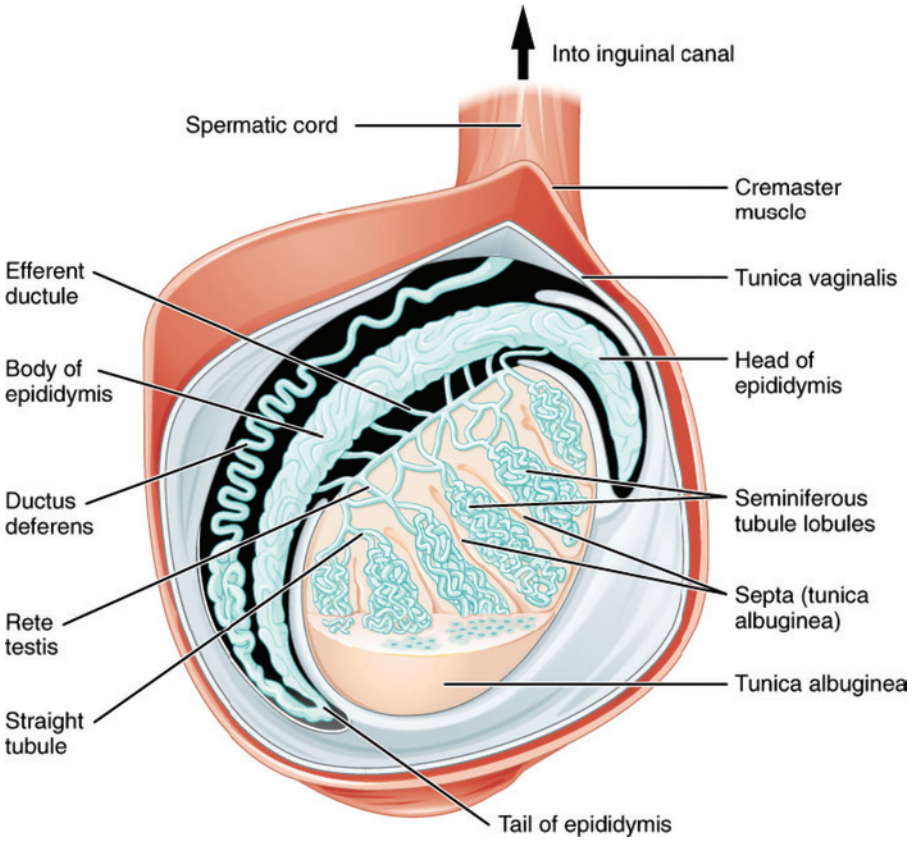


Figure 26.3 Anatomy of the Testis. This sagittal view shows the seminiferous tubules, the site of sperm production. Formed sperm are transferred to the epididymis, where they mature. They leave the epididymis during an ejaculation via the ductus deferens.

month of the developmental period of a male fetus, each testis moves through a passageway (called the inguinal canal) in the abdominal musculature to descend from the pelvic cavity into the scrotal cavity. This is called the "descent of the testis." Cryptorchidism is the clinical term used when one or both of the testes fail to descend into the scrotum prior to birth.

The tightly coiled **seminiferous tubules** form the bulk of each testis. They are composed of developing sperm cells surrounding a lumen, the hollow centre of the tubule, where formed sperm are released into the duct system of the testis. Specifically, from the lumens of the seminiferous tubules, sperm move into the straight tubules (or tubuli recti) and from there into a fine meshwork of tubules called the rete testes. Sperm leave the rete testes, and the testis itself, through the 15 to 20 efferent ductules that cross the tunica albuginea.

Inside the seminiferous tubules are six different cell types. These include supporting cells called sustentacular cells as well as five types of developing

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sperm cells called germ cells. Germ cell development progresses from the basement membrane—at the perimeter of the tubule—toward the lumen. Let's look more closely at these cell types.

Sertoli Cells

Surrounding all stages of the developing sperm cells are elongate, branching **Sertoli cells**. Sertoli cells are a type of supporting cell called a sustentacular cell, or sustentocyte, that are typically found in epithelial tissue. Sertoli cells secrete signalling molecules that promote sperm production and can control whether germ cells live or die. They extend physically around the germ cells from the peripheral basement membrane of the seminiferous tubules to the lumen. Tight junctions between these sustentacular cells create the **blood-testis barrier**, which keeps blood-borne substances from reaching the germ cells and, at the same time, keeps surface antigens on developing germ cells from escaping into the bloodstream and prompting an autoimmune response.

Germ Cells

The least mature cells, the **spermatogonia** (singular = spermatogonium), line the basement membrane inside the tubule. Spermatogonia are the stem cells of the testis, which means that they are still able to differentiate into a variety of different cell types throughout adulthood. Spermatogonia divide to produce primary and secondary spermatocytes, then spermatids, which finally produce formed sperm. The process that begins with spermatogonia and concludes with the production of sperm is called **spermatogenesis**.

Spermatogenesis

As just noted, spermatogenesis occurs in the seminiferous tubules that form the bulk of each testis (see Figure 26.3). The process begins at puberty, after which time sperm are produced constantly throughout a male's life. One production cycle, from spermatogonia through formed sperm, takes approximately 64 days. A new cycle starts approximately every 16 days, although this timing is not synchronous across the seminiferous tubules. Sperm counts—the total number of sperm a person produces—slowly decline after age 35, and some studies suggest that smoking can lower sperm counts irrespective of age.

The process of spermatogenesis begins with mitosis of the diploid spermatogonia (Figure 26.4). Because these cells are diploid ($2n$), they each have a complete copy of the person's genetic material, or 46 chromosomes. However, mature gametes are haploid ($1n$), containing 23 chromosomes—meaning that daughter cells of spermatogonia must undergo a second cellular division through the process of meiosis.

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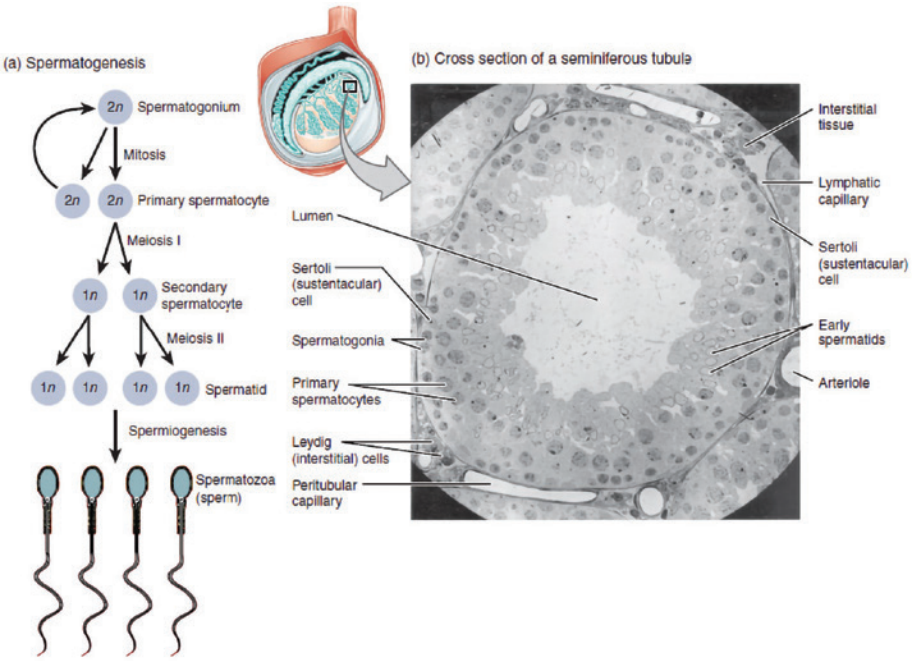


Figure 26.4 Spermatogenesis. (a) Mitosis of a spermatogonial stem cell involves a single cell division that results in two identical, diploid daughter cells (spermatogonia to primary spermatocyte). Meiosis has two rounds of cell division: primary spermatocyte to secondary spermatocyte and then secondary spermatocyte to spermatid. This produces four haploid daughter cells (spermatids). (b) In this electron micrograph of a cross section of a seminiferous tubule from a rat, the lumen is the light-shaded area in the centre of the image. The location of the primary spermatocytes is near the basement membrane, and the early spermatids are approaching the lumen (tissue source: rat). EM × 900. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

Two identical diploid cells result from spermatogonia mitosis. One of these cells remains a spermatogonium, and the other becomes a **primary spermatocyte**, the next stage in the process of spermatogenesis. As in mitosis, DNA is replicated in a primary spermatocyte before it undergoes a cell division called meiosis I. During meiosis I, each of the 23 pairs of chromosomes separates. This results in two cells, called **secondary spermatocytes**, each with only half the number of chromosomes. Now a second round of cell division (meiosis II) occurs in both of the secondary spermatocytes. During meiosis II, each of the 23 replicated chromosomes divides, similar to what happens during mitosis. Thus, meiosis results in separating the chromosome pairs. This second meiotic division results in a total of four cells with only half of the number of chromosomes. Each of these new cells is a **spermatid**. Although haploid, early spermatids look very similar to cells in the earlier stages of spermatogenesis, with a round shape, central nucleus, and large amount of cytoplasm.

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A process called **spermiogenesis** transforms these early spermatids, reducing the cytoplasm and beginning the formation of the parts of a true sperm. The fifth stage of germ cell formation—**spermatozoa**, or formed sperm—is the end result of this process, which occurs in the portion of the tubule nearest the lumen. Eventually, the sperm are released into the lumen and are moved along a series of ducts in the testis toward a structure called the epididymis for the next step of sperm maturation.

Structure of Formed Sperm

Sperm are smaller than most cells in the body; in fact, the volume of a sperm cell is 85,000 times less than that of the female gamete. Approximately 100 to 300 million sperm are produced each day, whereas females typically ovulate only one oocyte per month. As is true for most cells in the body, the structure of sperm cells speaks to their function. Sperm have a distinctive head, mid-piece, and tail region (Figure 26.5). The head of the sperm contains the extremely compact haploid nucleus with very little cytoplasm. These qualities contribute to the overall small size of the sperm (the head is only 5 μm long). A structure called the acrosome covers most of the head of the sperm cell as a "cap" that is filled with lysosomal enzymes important for preparing sperm to participate in fertilization. Tightly packed mitochondria fill the mid-piece of the sperm. ATP produced by these mitochondria will power the flagellum, which extends from the neck and the mid-piece through the tail of the sperm, enabling it to move the entire sperm cell. The central strand of the flagellum, the axial filament, is formed from one centriole inside the maturing sperm cell during the final stages of spermatogenesis.

Sperm Transport

To fertilize an egg without medical intervention, sperm must be moved from the seminiferous tubules in the testes, through the epididymis, and—later during ejaculation—along the length of the penis and out into the female reproductive tract.

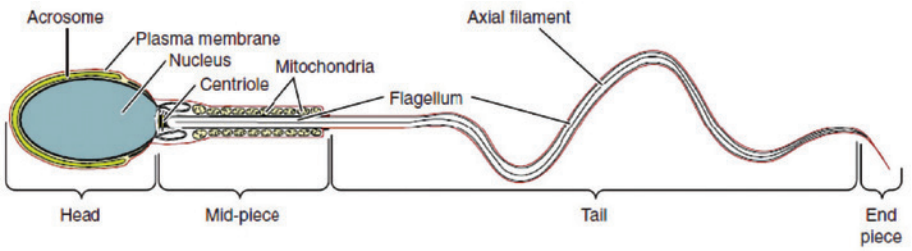


Figure 26.5 Structure of Sperm. Sperm cells are divided into a head, containing DNA; a mid-piece, containing mitochondria; and a tail, providing motility. The acrosome is oval and somewhat flattened.

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Role of the Epididymis

From the lumen of the seminiferous tubules, the immotile sperm are surrounded by testicular fluid and moved to the **epididymis** (plural = epididymides), a coiled tube attached to the testis where newly formed sperm continue to mature (see Figure 26.3). Though the epididymis does not take up much room in its tightly coiled state, it would be approximately 6 m long if straightened. It takes an average of 12 days for sperm to move through the coils of the epididymis, with the shortest recorded transit time in humans being 1 day. Sperm enter the head of the epididymis and are moved along predominantly by the contraction of smooth muscles lining the epididymal tubes. As they are moved along the length of the epididymis, the sperm further mature and acquire the ability to move under their own power. Once inside the female reproductive tract, they will use this ability to move independently toward the unfertilized egg. The more mature sperm are then stored in the tail of the epididymis (the final section) until ejaculation occurs.

Duct System

During ejaculation, sperm exit the tail of the epididymis and are pushed by smooth muscle contraction to the **ductus deferens** (also called the vas deferens). The ductus deferens is a thick, muscular tube that is bundled together inside the scrotum with connective tissue, blood vessels, and nerves into a structure called the **spermatic cord** (see Figure 26.1 and Figure 26.2). Because the ductus deferens is physically accessible within the scrotum, surgical sterilization to interrupt sperm delivery can be performed by cutting and sealing a small section of the ductus (vas) deferens. This procedure is called a vasectomy, and it is an effective form of birth control. Although it may be possible to reverse a vasectomy, clinicians consider the procedure permanent and advise people to undergo it only if they are certain they no longer wish to have children.

Interactive Link 26.1

Watch this video (http://oer.aupress.ca/oer-202505/26.1) to learn about a vasectomy. As described in this video, a vasectomy is a procedure in which a small section of the ductus (vas) deferens is removed from the scrotum. This interrupts the path taken by sperm through the ductus deferens. If sperm do not exit through the vas, because the person either has had a vasectomy or has not ejaculated, in what region of the testis do they remain?

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From each epididymis, each ductus deferens extends superiorly into the abdominal cavity through the **inguinal canal** in the abdominal wall. From here, the ductus deferens continues posteriorly to the pelvic cavity, ending posterior to the bladder, where it dilates in a region called the ampulla.

Sperm make up only 5 percent of the final volume of **semen**, the thick, milky fluid that is ejaculated. The bulk of semen is produced by accessory glands of the male reproductive system: the seminal vesicles, the prostate, and the bulbourethral glands.

Seminal Vesicles

As sperm pass through the ampulla of the ductus deferens at ejaculation, they mix with fluid from the associated **seminal vesicle** (see Figure 26.1). The paired seminal vesicles are glands that contribute approximately 60 percent of the semen volume. Seminal vesicle fluid contains large amounts of fructose, which is used by the sperm mitochondria to generate ATP to allow movement through the female reproductive tract.

The fluid, now containing both sperm and seminal vesicle secretions, next moves into the associated **ejaculatory duct**, a short structure formed from the ampulla of the ductus deferens and the duct of the seminal vesicle. The paired ejaculatory ducts transport the seminal fluid into the prostatic urethra located within the prostate gland.

Prostate Gland

As shown in Figure 26.1, the centrally located **prostate gland, or prostate**, sits anterior to the rectum at the base of the bladder surrounding the prostatic urethra (the portion of the urethra that runs within the prostate). About the size of a walnut, the prostate is formed of both muscular and glandular tissues. It secretes an alkaline, milky fluid to the passing seminal fluid—now called semen—that is critical to first coagulate and then decoagulate the semen following ejaculation. The temporary thickening of semen helps retain it within the female reproductive tract, providing time for sperm to utilize the fructose provided by seminal vesicle secretions. When the semen regains its fluid state, sperm can then pass farther into the female reproductive tract.

The prostate normally doubles in size during puberty. At approximately age 25, it gradually begins to enlarge again. This enlargement does not usually cause problems; however, abnormal growth of the prostate, or benign prostatic hyperplasia (BPH), can cause constriction of the urethra as it passes through the middle of the prostate gland, leading to a number of lower urinary tract symptoms, such as a frequent and intense urge to urinate, a weak stream, and a

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sensation that the bladder has not emptied completely. By age 60, approximately 40 percent of males have some degree of BPH. By age 80, the number of affected individuals has jumped to as many as 80 percent.

Treatments for BPH attempt to relieve the pressure on the urethra so that urine can flow more normally. Mild to moderate symptoms are treated with medication, whereas severe enlargement of the prostate is treated by surgery in which a portion of the prostate tissue is removed.

Another common disorder involving the prostate is prostate cancer. According to the Centers for Disease Control and Prevention (CDC), prostate cancer is the second most common cancer in males. However, some forms of prostate cancer grow very slowly and thus may not ever require treatment. Aggressive forms of prostate cancer, in contrast, involve metastasis to vulnerable organs like the lungs and brain. There is no link between BPH and prostate cancer, but the symptoms are similar. Prostate cancer is detected by a medical history, a blood test, and a rectal exam that allows physicians to palpate the prostate and check for unusual masses. If a mass is detected, the cancer diagnosis is confirmed by biopsy of the cells.

Bulbourethral Glands

The final addition to semen is made by two **bulbourethral glands** (or Cowper's glands) that release a thick, salty fluid that lubricates the end of the urethra and the vagina and helps clean urine residues from the penile urethra. The fluid from these accessory glands is released after the male becomes sexually aroused and shortly before the release of the semen. It is therefore sometimes called pre-ejaculate. It is important to note that, in addition to the lubricating proteins, it is possible for bulbourethral fluid to pick up sperm already present in the urethra, and therefore it may be able to cause pregnancy.

Interactive Link 26.2

Watch this video (http://oer.aupress.ca/oer-202505/26.2) to explore the structures of the male reproductive system and the path of sperm, which starts in the testes and ends as the sperm leave the penis through the urethra. Where are sperm deposited after they leave the ejaculatory duct?

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The Penis

The **penis** is the male organ of copulation (sexual intercourse). It is flaccid for nonsexual actions, such as urination, and turgid and rodlike with sexual arousal. When erect, the stiffness of the organ allows it to penetrate into the vagina and deposit semen into the female reproductive tract.

The shaft of the penis surrounds the urethra (Figure 26.6). The shaft is composed of three column-like chambers of **erectile tissue** that span the length of the shaft. Each of the two larger lateral chambers is called a **corpus cavernosum** (plural = corpora cavernosa). Together, these make up the bulk of the penis. The **corpus spongiosum**, which can be felt as a raised ridge on the erect penis, is a smaller chamber that surrounds the spongy, or penile, urethra. The slightly enlarged distal end of the penis, called the **glans penis**, has a high concentration of nerve endings, resulting in very sensitive skin that influences the likelihood of ejaculation (see Figure 26.1). The skin from the shaft extends down over the glans and forms a collar called the **prepuce** (or

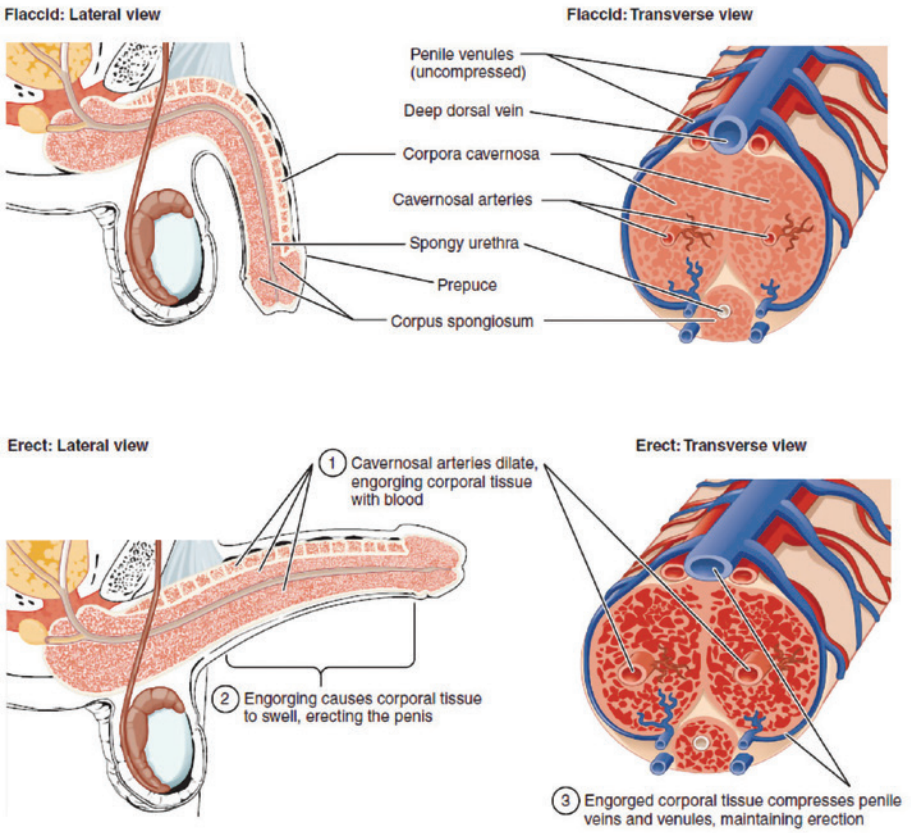


Figure 26.6 Cross-Sectional Anatomy of the Penis. Three columns of erectile tissue make up most of the volume of the penis.

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foreskin). The foreskin also contains a dense concentration of nerve endings, and both lubricate and protect the sensitive skin of the glans penis. A surgical procedure called circumcision, often performed for religious or social reasons, removes the prepuce, typically within days of birth.

Both sexual arousal and REM sleep (during which dreaming occurs) can induce an erection. Penile erections are the result of vasocongestion, or engorgement of the tissues because of more arterial blood flowing into the penis than is leaving in the veins. During sexual arousal, nitric oxide (NO) is released from nerve endings near blood vessels within the corpora cavernosa and spongiosum. Release of NO activates a signalling pathway that results in relaxation of the smooth muscles that surround the penile arteries, causing them to dilate. This dilation increases the amount of blood that can enter the penis and induces the endothelial cells in the penile arterial walls to also secrete NO and perpetuate the vasodilation. The rapid increase in blood volume fills the erectile chambers, and the increased pressure of the filled chambers compresses the thin-walled penile venules, preventing venous drainage of the penis. The result of this increased blood flow to the penis and reduced blood return from the penis is erection. Depending on the flaccid dimensions of a penis, it can increase in size slightly or greatly during erection, with the average length of an erect penis measuring approximately 15 cm.

Testosterone

Testosterone, an androgen, is a steroid hormone produced by **Leydig cells**. The alternate term for Leydig cells, interstitial cells, reflects their location between the seminiferous tubules in the testes. In male embryos, testosterone is secreted by Leydig cells by the seventh week of development, with peak concentrations reached in the second trimester. This early release of testosterone results in the anatomical differentiation of the male sexual organs. In childhood, testosterone concentrations are low. They increase during puberty, activating characteristic physical changes and initiating spermatogenesis.

Functions of Testosterone

The continued presence of testosterone is necessary to keep the male reproductive system working properly, and Leydig cells produce approximately 6 to 7 mg of testosterone per day. Testicular steroidogenesis (the manufacture of androgens, including testosterone) results in testosterone concentrations that are 100 times higher in the testes than in the circulation. Maintaining these normal concentrations of testosterone promotes spermatogenesis, whereas low levels of testosterone can lead to infertility. In addition to intratesticular secretion, testosterone is also released into the systemic circulation and plays

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an important role in muscle development, bone growth, the development of secondary sex characteristics, and maintaining libido (sex drive) in both males and females. In females, the ovaries secrete small amounts of testosterone, although most is converted to estradiol. A small amount of testosterone is also secreted by the adrenal glands in both sexes.

Control of Testosterone

The regulation of testosterone concentrations throughout the body is critical for male reproductive function. The intricate interplay between the endocrine system and the reproductive system is shown in Figure 26.7.

The regulation of Leydig cell production of testosterone begins outside of the testes. The hypothalamus and the pituitary gland in the brain integrate external and internal signals to control testosterone synthesis and secretion. The regulation begins in the hypothalamus. Pulsatile release of a hormone called **gonadotropin-releasing hormone** (**GnRH**) from the hypothalamus stimulates the endocrine release of hormones from the pituitary gland. Binding of GnRH to its receptors on the anterior pituitary gland stimulates release of the two gonadotropins: luteinizing hormone (LH) and follicle-stimulating hormone (FSH). These two hormones are critical for reproductive function in all humans. In the testes, FSH binds predominantly to the Sertoli cells within the seminiferous tubules to promote spermatogenesis. FSH also stimulates the Sertoli cells to produce hormones called **inhibins**, which function to inhibit FSH release from the pituitary, thus reducing testosterone secretion. These polypeptide hormones correlate directly with Sertoli cell function and sperm number; inhibin B can be used as a marker of spermatogenic activity. LH binds to receptors on Leydig cells in the testes and upregulates the production of testosterone.

A negative-feedback loop predominantly controls the synthesis and secretion of both FSH and LH. Low blood concentrations of testosterone stimulate the hypothalamic release of GnRH. GnRH then stimulates the anterior pituitary to secrete LH into the bloodstream. In the testis, LH binds to LH receptors on Leydig cells and stimulates the release of testosterone. When concentrations of testosterone in the blood reach a critical threshold, testosterone itself will bind to androgen receptors on both the hypothalamus and the anterior pituitary, inhibiting the synthesis and secretion of GnRH and LH, respectively. When the blood concentrations of testosterone once again decline, testosterone no longer interacts with the receptors to the same degree, and GnRH and LH are once again secreted, stimulating more testosterone production. This same process occurs with FSH and inhibin to control spermatogenesis.

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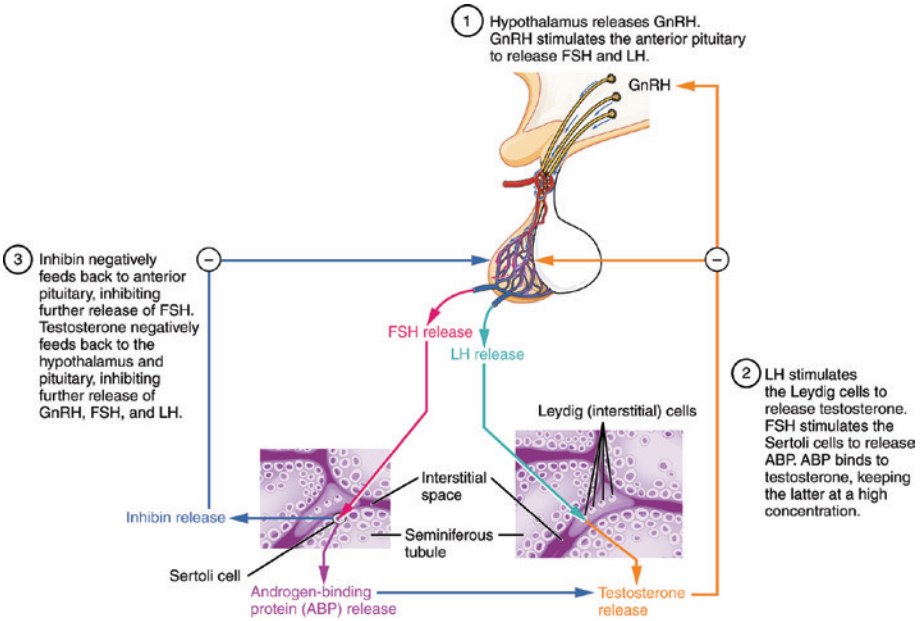


Figure 26.7 Regulation of Testosterone Production. The hypothalamus and pituitary gland regulate the production of testosterone and the cells that assist in spermatogenesis. GnRH activates the anterior pituitary to produce LH and FSH, which in turn stimulate Leydig cells and Sertoli cells, respectively. The system is a negative-feedback loop because the end products of the pathway, testosterone and inhibin, interact with the activity of GnRH to inhibit their own production.

26.2 Anatomy and Physiology of the Ovarian Reproductive System

Learning Objectives

By the end of this section, you will be able to:

- Describe the structure and function of the organs of the ovarian reproductive system
- List the steps of oogenesis
- Describe the hormonal changes that occur during the ovarian and menstrual cycles
- Trace the path of an oocyte from ovary to fertilization

The female, or ovarian, reproductive system functions to produce gametes and reproductive hormones, just like the male reproductive system; however, it also has the additional task of supporting the developing fetus and delivering

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it to the outside world. Unlike its male counterpart, the female reproductive system is located primarily inside the pelvic cavity (Figure 26.8). Recall that the ovaries are the female gonads. The gamete they produce is called an **oocyte**. We'll discuss the production of oocytes in detail shortly. First, let's look at some of the structures of the female reproductive system.

External Female Genitals

The external female reproductive structures are referred to collectively as the **vulva** (Figure 26.9). The **mons pubis** is a pad of fat that is located at the

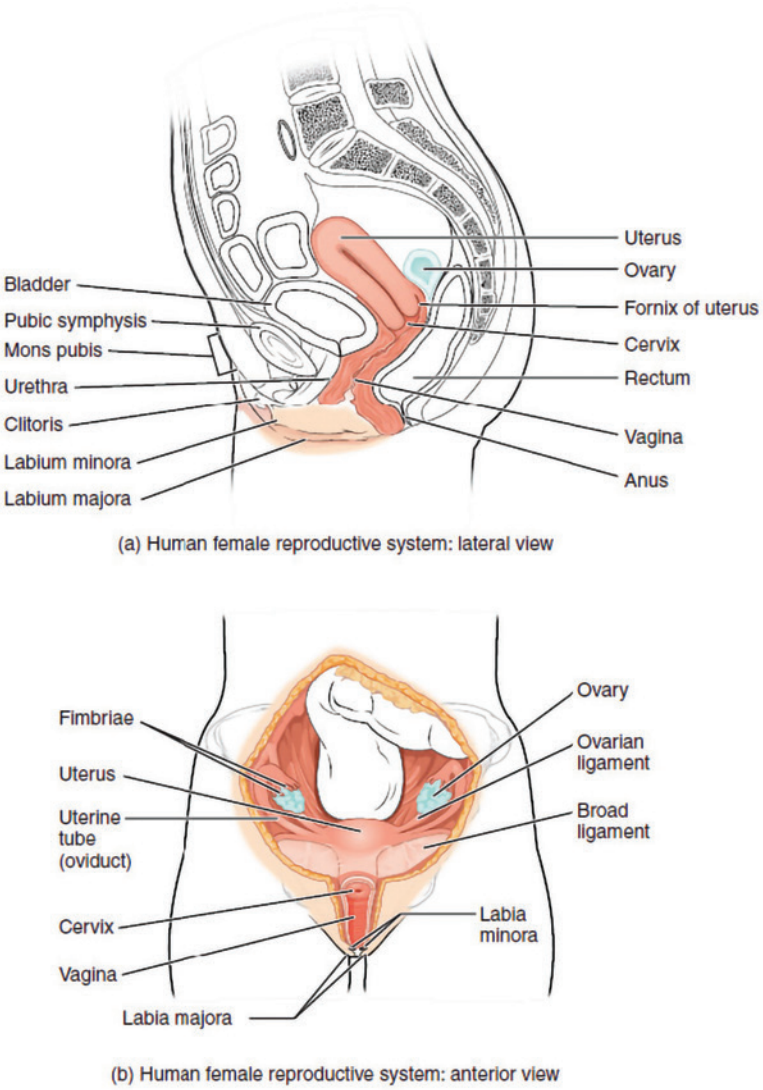


Figure 26.8 Female Reproductive System. The major organs of the female reproductive system are located inside the pelvic cavity.

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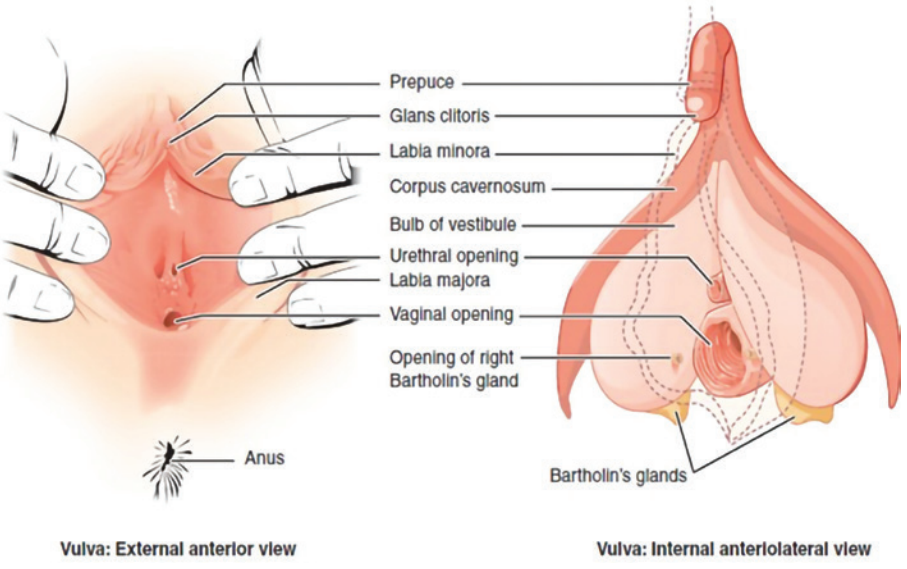


Figure 26.9 The Vulva. The external female genitalia are referred to collectively as the vulva.

anterior, over the pubic bone. After puberty, it becomes covered in pubic hair. The **labia majora** (*labia* = "lips"; *majora* = "larger") are folds of hair-covered skin that begin just posterior to the mons pubis. The thinner and more pigmented **labia minora** (*labia* = "lips"; *minora* = "smaller") extend medial to the labia majora. Although they naturally vary in shape and size from person to person, the labia minora serve to protect the urethra and the entrance to the reproductive tract.

The superior, anterior portions of the labia minora come together to encircle the **clitoris** (or glans clitoris), an organ that originates from the same cells as the glans penis and has abundant nerves that make it important in sexual sensation and orgasm. The **hymen** is a thin membrane that sometimes partially covers the entrance to the vagina. An intact hymen cannot be used as an indication of "virginity"; even at birth, this is only a partial membrane, as menstrual fluid and other secretions must be able to exit the body, regardless of penile-vaginal intercourse. The vaginal opening is located between the opening of the urethra and the anus. It is flanked by outlets to the **Bartholin's glands** (or greater vestibular glands).

Vagina

The **vagina**, shown at the bottom of Figure 26.8 and Figure 26.9, is a muscular canal (approximately 10 cm long) that serves as the entrance to the reproductive tract. It also serves as the exit from the uterus during menses and childbirth. The outer walls of the anterior and posterior vagina are formed into

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longitudinal columns, or ridges, and the superior portion of the vagina—called the fornix—meets the protruding uterine cervix. The walls of the vagina are lined with an outer fibrous adventitia; a middle layer of smooth muscle; and an inner mucous membrane with transverse folds called **rugae**. Together, the middle and inner layers allow the expansion of the vagina to accommodate intercourse and childbirth. The thin, perforated hymen can partially surround the opening to the vaginal orifice. The hymen can be ruptured with strenuous physical exercise, penile-vaginal intercourse, and childbirth. The Bartholin's glands and the lesser vestibular glands (located near the clitoris) secrete mucus, which keeps the vestibular area moist.

The vagina is home to a normal population of microorganisms that help protect against infection by pathogenic bacteria, yeast, or other organisms that can enter the vagina. In a healthy person, the most predominant type of vaginal bacteria is from the genus *Lactobacillus*. This family of beneficial bacterial flora secretes lactic acid and thus protects the vagina by maintaining an acidic pH (below 4.5). Potential pathogens are less likely to survive in these acidic conditions. Lactic acid, in combination with other vaginal secretions, makes the vagina a self-cleansing organ. However, douching—or washing out the vagina with fluid—can disrupt the normal balance of healthy microorganisms and actually increase risk for infections and irritation. Indeed, the American College of Obstetricians and Gynecologists recommend that people do not douche and that they allow the vagina to maintain its normal healthy population of protective microbial flora.

Ovaries

The **ovaries** are the female gonads (see Figure 26.8). Paired ovals, they are each about 2 to 3 cm in length, about the size of an almond. The ovaries are located within the pelvic cavity and are supported by the mesovarium, an extension of the peritoneum that connects the ovaries to the **broad ligament**. Extending from the mesovarium itself is the suspensory ligament that contains the ovarian blood and lymph vessels. Finally, the ovary itself is attached to the uterus via the ovarian ligament.

The ovary comprises an outer covering of cuboidal epithelium called the ovarian surface epithelium that is superficial to a dense connective tissue covering called the tunica albuginea. Beneath the tunica albuginea is the cortex, or outer portion, of the organ. The cortex is composed of a tissue framework called the ovarian stroma that forms the bulk of the adult ovary. Oocytes develop within the outer layer of this stroma, each surrounded by supporting cells. This grouping of an oocyte and its supporting cells is called a **follicle**. The growth

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and development of ovarian follicles will be described shortly. Beneath the cortex lies the inner ovarian medulla, the site of blood vessels, lymph vessels, and the nerves of the ovary. You will learn more about the overall anatomy of the female reproductive system in the rest of this chapter.

The Ovarian Cycle

The **ovarian cycle** is a set of predictable changes in oocytes and ovarian follicles. During the reproductive years, it is a roughly 28-day cycle that can be correlated with, but is not the same as, the menstrual cycle (discussed shortly). The cycle includes two interrelated processes: oogenesis (the production of gametes) and folliculogenesis (the growth and development of ovarian follicles).

Oogenesis

Gametogenesis in females is called **oogenesis**. The process begins with the ovarian stem cells, or **oogonia** (Figure 26.10). Oogonia are formed during fetal development and divide via mitosis, much like spermatogonia in the testis. Unlike spermatogonia, however, oogonia form **primary oocytes** in the fetal ovary prior to birth. These primary oocytes are then arrested in this stage of meiosis I, only to resume it years later, beginning at puberty and continuing until the person is near menopause (the cessation of a female's reproductive functions). The number of primary oocytes present in the ovaries declines from 1 to 2 million in an infant, to approximately 400,000 at puberty, to 0 by the end of menopause.

The initiation of **ovulation**—the release of an oocyte from the ovary—marks the transition from puberty into reproductive maturity. From then on, throughout the reproductive years, ovulation occurs approximately once every 28 days. Just prior to ovulation, a surge of luteinizing hormone triggers the resumption of meiosis in a primary oocyte. This initiates the transition from primary to secondary oocyte. However, as you can see in Figure 26.10, this cell division does not result in two identical cells. Instead, the cytoplasm is divided unequally, and one daughter cell is much larger than the other. This larger cell, the **secondary oocyte**, eventually leaves the ovary during ovulation.

The smaller cell, called the first **polar body**, may or may not complete meiosis and produce second polar bodies; in either case, it eventually disintegrates. Therefore, even though oogenesis produces up to four cells, only one survives.

How does the secondary oocyte become an **ovum**—the haploid female gamete? Meiosis of a secondary oocyte is completed only if a sperm succeeds in penetrating its barriers. Meiosis II then resumes, producing a haploid polar body and one haploid ovum that, at the instant of fertilization by a (haploid)

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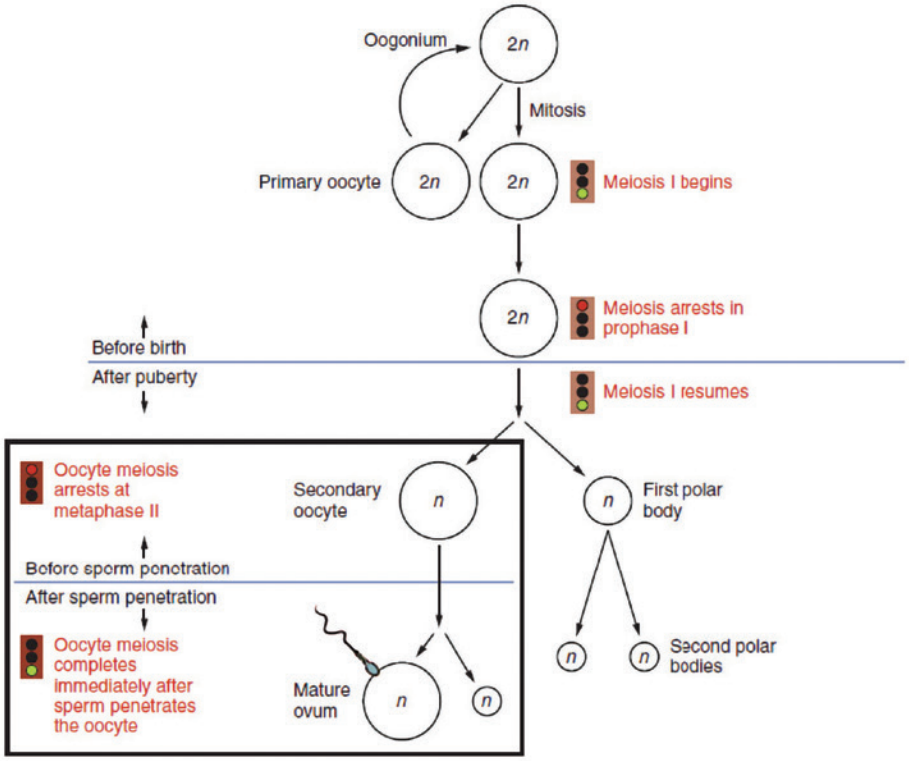


Figure 26.10 Oogenesis. The unequal cell division of oogenesis produces one to three polar bodies that later degrade as well as a single haploid ovum, which is produced only if there is penetration of the secondary oocyte by a sperm cell.

sperm, becomes the first diploid cell of the new offspring (a zygote). Thus, the ovum can be thought of as a brief, transitional, haploid stage between the diploid oocyte and diploid zygote.

The larger amount of cytoplasm contained in the female gamete is used to supply the developing zygote with nutrients during the period between fertilization and implantation into the uterus. Interestingly, sperm contribute only DNA at fertilization—not cytoplasm. Therefore, the cytoplasm and all of the cytoplasmic organelles in the developing embryo are of egg-derived origin. This includes mitochondria, which contain their own DNA. Scientific research in the 1980s determined that mitochondrial DNA was maternally inherited, meaning that you can trace your mitochondrial DNA directly to your biological mother, her mother, and so on back through your female ancestors.

Folliculogenesis

Again, ovarian follicles are oocytes and their supporting cells. They grow and develop in a process called **folliculogenesis**, which typically leads to ovulation

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of one follicle approximately every 28 days, along with death to multiple other follicles. The death of ovarian follicles is called atresia and can occur at any point during follicular development. Recall that a female infant at birth will have one to two million oocytes within the ovarian follicles and that this number declines throughout life until menopause, when no follicles remain. As you'll see next, follicles progress from primordial, to primary, to secondary and tertiary stages prior to ovulation—with the oocyte inside the follicle remaining as a primary oocyte until right before ovulation.

Folliculogenesis begins with follicles in a resting state. These small **primordial follicles** are present in newborn females and are the prevailing follicle type in the adult ovary (Figure 26.11). Primordial follicles have only a single flat layer of support cells, called **granulosa cells**, that surround the primary oocyte, and they can stay in this resting state for years—some until right before menopause.

After puberty, a few primordial follicles will respond to a recruitment signal each day and will join a pool of immature growing follicles called **primary follicles**. Primary follicles start with a single layer of granulosa cells, but the granulosa cells then become active and transition from a flat or squamous shape to a rounded, cuboidal shape as they increase in size and proliferate. As the granulosa cells divide, the follicles—now called **secondary follicles** (see Figure 26.11)—increase in diameter, adding a new outer layer of connective tissue, blood vessels, and **theca cells**—cells that work with the granulosa cells to produce estrogens.

Within the growing secondary follicle, the primary oocyte now secretes a thin acellular membrane called the **zona pellucida** that will play a critical role in fertilization. A thick fluid, called follicular fluid, that has formed between the granulosa cells also begins to collect into one large pool, or **antrum**. Follicles in which the antrum has become large and fully formed are considered **tertiary follicles** (or antral follicles). Several follicles reach the tertiary stage at the same time, and most of these will undergo atresia. The one that does not die will continue to grow and develop until ovulation, when it will expel its secondary oocyte surrounded by several layers of granulosa cells from the ovary.

Keep in mind that most follicles don't make it to this point. In fact, roughly 99 percent of the follicles in the ovary will undergo atresia, which can occur at any stage of folliculogenesis.

Hormonal Control of the Ovarian Cycle

The process of development that we have just described, from primordial follicle to early tertiary follicle, takes approximately 2 months in humans. The final stages of development of a small cohort of tertiary follicles, ending with ovulation of a secondary oocyte, occur over a course of approximately 28 days.

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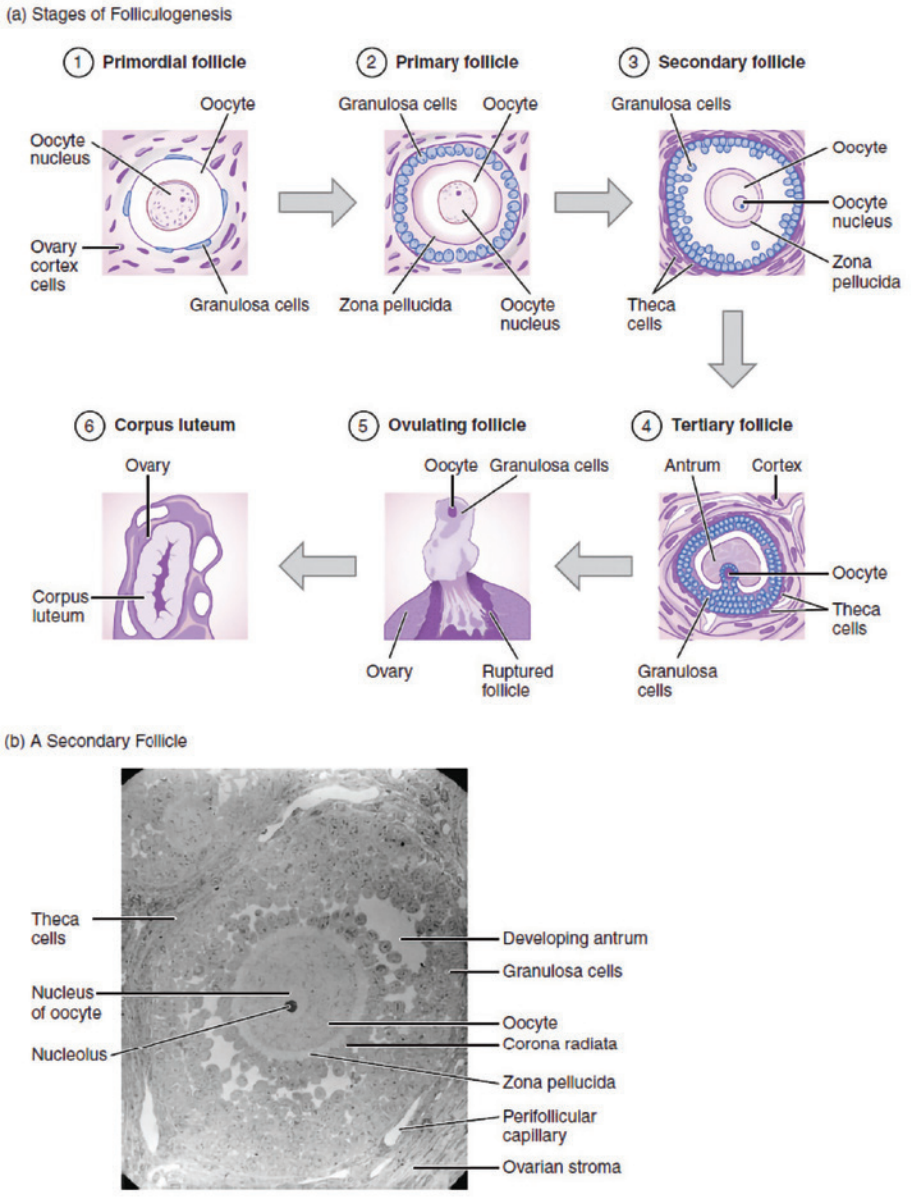


Figure 26.11 Folliculogenesis. (a) The maturation of a follicle is shown in a clockwise direction proceeding from the primordial follicles. FSH stimulates the growth of a tertiary follicle, and LH stimulates the production of estrogen by granulosa and theca cells. Once the follicle is mature, it ruptures and releases the oocyte. Cells remaining in the follicle then develop into the corpus luteum. (b) In this electron micrograph of a secondary follicle, the oocyte, theca cells (thecae folliculi), and developing antrum are clearly visible. EM × 1100. (Micrograph provided by the Regents of University of Michigan Medical School © 2012)

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These changes are regulated by many of the same hormones that regulate the male reproductive system, including GnRH, LH, and FSH.

As in males, the hypothalamus produces GnRH, a hormone that signals the anterior pituitary gland to produce the gonadotropins FSH and LH (Figure 26.12). These gonadotropins leave the pituitary and travel through the bloodstream to the ovaries, where they bind to receptors on the granulosa and theca cells of the follicles. FSH stimulates the follicles to grow (hence its name of follicle-stimulating hormone), and the five or six tertiary follicles expand in diameter. The release of LH also stimulates the granulosa and theca cells of the follicles to produce the sex steroid hormone estradiol, a type of estrogen. This phase of the ovarian cycle, when the tertiary follicles are growing and secreting estrogen, is known as the **follicular phase**.

The more granulosa and theca cells a follicle has (that is, the larger and more developed it is), the more estrogen it will produce in response to LH stimulation. As a result of these large follicles producing large amounts of estrogen, systemic plasma estrogen concentrations increase. Following a classic negative-feedback loop, the high concentrations of estrogen will stimulate the hypothalamus and pituitary to reduce the production of GnRH, LH, and FSH. Because the large tertiary follicles require FSH to grow and survive at this point, this decline in FSH caused by negative feedback leads most of them to die (atresia).

Typically only one follicle, now called the dominant follicle, will survive this reduction in FSH, and this follicle will be the one that releases an oocyte. Scientists have studied many factors that lead to a particular follicle becoming dominant: Size, the number of granulosa cells, and the number of FSH receptors on those granulosa cells all contribute to a follicle becoming the one surviving dominant follicle.

When only the one dominant follicle remains in the ovary, it again begins to secrete estrogen. It produces more estrogen than all of the developing follicles did together before the negative feedback occurred. It produces so much estrogen that the normal negative feedback doesn't occur. Instead, these extremely high concentrations of systemic plasma estrogen trigger a regulatory switch in the anterior pituitary that responds by secreting large amounts of LH and FSH into the bloodstream (see Figure 26.12). The positive feedback loop by which more estrogen triggers release of more LH and FSH only occurs at this point in the cycle.

It is this large burst of LH (called the LH surge) that leads to **ovulation** of the dominant follicle. The LH surge induces many changes in the dominant follicle, including stimulating the resumption of meiosis of the primary oocyte to a secondary oocyte. As noted earlier, the polar body that results from unequal cell division simply degrades. The LH surge also triggers proteases (enzymes

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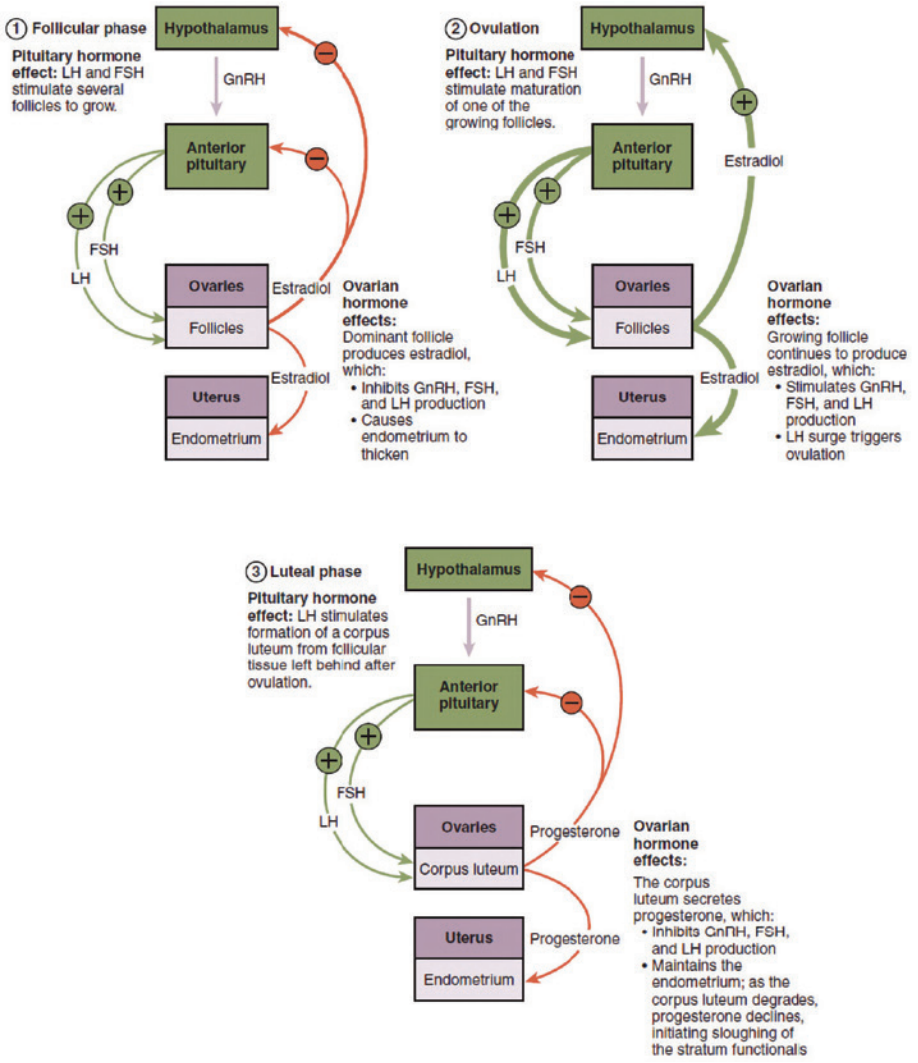


Figure 26.12 Hormonal Regulation of Ovulation. The hypothalamus and pituitary gland regulate the ovarian cycle and ovulation. GnRH activates the anterior pituitary to produce LH and FSH, which stimulate the production of estrogen and progesterone by the ovaries.

that cleave proteins) to break down structural proteins in the ovary wall on the surface of the bulging dominant follicle. This degradation of the wall, combined with pressure from the large, fluid-filled antrum, results in the expulsion of the oocyte surrounded by granulosa cells into the peritoneal cavity.

This release is ovulation.

In the next section, you will follow the ovulated oocyte as it travels toward the uterus, but there is one more important event that occurs in the ovarian cycle. The surge of LH also stimulates a change in the granulosa and theca cells that remain in the follicle after the oocyte has been ovulated. This change is

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called luteinization (recall that the full name of LH is luteinizing hormone), and it transforms the collapsed follicle into a new endocrine structure called the **corpus luteum**, a term meaning "yellowish body" (see Figure 26.11). Instead of estrogen, the luteinized granulosa and theca cells of the corpus luteum begin to produce large amounts of the sex steroid hormone progesterone, a hormone that is critical for the establishment and maintenance of pregnancy.

Progesterone triggers negative feedback at the hypothalamus and pituitary, which keeps GnRH, LH, and FSH secretions low, so no new dominant follicles develop at this time.

The postovulatory phase of progesterone secretion is known as the **luteal phase** of the ovarian cycle. If pregnancy does not occur within 10 to 12 days, the corpus luteum will stop secreting progesterone and degrade into the **corpus albicans**, a nonfunctional "whitish body" that will disintegrate in the ovary over a period of several months. During this time of reduced progesterone secretion, FSH and LH are once again stimulated, and the follicular phase begins again with a new cohort of early tertiary follicles beginning to grow and secrete estrogen.

The Uterine Tubes

The **uterine tubes** (also called fallopian tubes or oviducts) serve as the conduit of the oocyte from the ovary to the uterus (Figure 26.13). Each of the two uterine tubes is close to, but not directly connected to, the ovary and divided into sections. The **isthmus** is the narrow medial end of each uterine tube that is

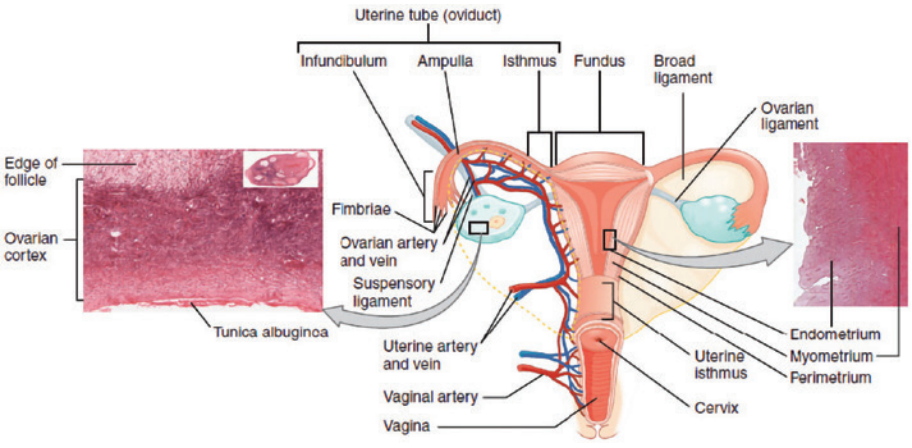


Figure 26.13 Ovaries, Uterine Tubes, and Uterus. This anterior view shows the relationship of the ovaries, uterine tubes (oviducts), and uterus. Sperm enter through the vagina, and fertilization of an ovulated oocyte usually occurs in the distal uterine tube. From left to right, LM × 400, LM × 20. (Micrographs provided by the Regents of University of Michigan Medical School © 2012)

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connected to the uterus. The wide distal **infundibulum** flares out with slender, fingerlike projections called **fimbriae**. The middle region of the tube, called the **ampulla**, is where fertilization often occurs. The uterine tubes also have three layers: an outer serosa, a middle smooth muscle layer, and an inner mucosal layer. In addition to its mucus-secreting cells, the inner mucosa contains ciliated cells that beat in the direction of the uterus, producing a current that will be critical to move the oocyte.

Following ovulation, the secondary oocyte surrounded by a few granulosa cells is released into the peritoneal cavity. The nearby uterine tube, either left or right, receives the oocyte. Unlike sperm, oocytes lack flagella and therefore cannot move on their own. So how do they travel into the uterine tube and toward the uterus? High concentrations of estrogen that occur around the time of ovulation induce contractions of the smooth muscle along the length of the uterine tube. These contractions occur every 4 to 8 seconds, and the result is a coordinated movement that sweeps the surface of the ovary and the pelvic cavity. Current flowing toward the uterus is generated by coordinated beating of the cilia that line the lumen of the length of the uterine tube. These cilia beat more strongly in response to the high estrogen concentrations that occur around the time of ovulation. As a result of these mechanisms, the oocyte-granulosa cell complex is pulled into the interior of the tube. Once inside, the muscular contractions and beating cilia move the oocyte slowly toward the uterus. When fertilization does occur, sperm typically meet the egg while it is still moving through the ampulla.

Interactive Link 26.3

Watch this video (http://oer.aupress.ca/oer-202505/26.3) to observe ovulation and its initiation in response to the release of FSH and LH from the pituitary gland. What specialized structures help guide the oocyte from the ovary into the uterine tube?

If the oocyte is successfully fertilized, the resulting zygote will begin to divide into two cells, then four, and so on to develop into an **embryo** as it makes its way through the uterine tube and into the uterus. There, it will implant and continue to grow. If the egg is not fertilized, it will simply degrade—either in the uterine tube or in the uterus, where it may be shed with the next menstrual period.

The open-ended structure of the uterine tubes can have significant health consequences if bacteria or other contagions enter through the vagina and move through the uterus, into the tubes, and then into the pelvic cavity. If this is left unchecked, a bacterial infection (sepsis) could quickly become life threatening.

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The spread of an infection in this manner is of special concern when unskilled practitioners perform abortions in nonsterile conditions. Sepsis is also associated with sexually transmitted bacterial infections, especially gonorrhea and chlamydia. These increase a person's risk for pelvic inflammatory disease (PID), infection of the uterine tubes or other reproductive organs. Even when resolved, PID can leave scar tissue in the tubes, leading to infertility.

Interactive Link 26.4

Watch this series of videos (http://oer.aupress.ca/oer-202505/26.4) to look at the movement of the oocyte through the ovary. The cilia in the uterine tube promote movement of the oocyte. What would likely occur if the cilia were paralyzed at the time of ovulation?

The Uterus and Cervix

The **uterus** is the muscular organ that nourishes and supports the growing embryo (see Figure 26.13). Its average size is approximately 5 cm wide by 7 cm long (approximately 2 in by 3 in) when a female is not pregnant. It has three sections. The portion of the uterus superior to the opening of the uterine tubes is called the **fundus**. The middle section of the uterus is called the **body of uterus** (or corpus). The **cervix** is the narrow inferior portion of the uterus that projects into the vagina. The cervix produces mucus secretions that become thin and stringy under the influence of high systemic plasma estrogen concentrations, and these secretions can facilitate sperm movement through the reproductive tract.

Several ligaments maintain the position of the uterus within the abdominopelvic cavity. The broad ligament is a fold of peritoneum that serves as a primary support for the uterus, extending laterally from both sides of the uterus and attaching it to the pelvic wall. The round ligament attaches to the uterus near the uterine tubes and extends to the labia majora. Finally, the uterosacral ligament stabilizes the uterus posteriorly by its connection from the cervix to the pelvic wall.

The wall of the uterus is made up of three layers. The most superficial layer is the serous membrane, or **perimetrium**, which consists of epithelial tissue and an underlying layer of loose connective tissue that covers the exterior portion of the uterus. The middle layer, or **myometrium**, is a thick layer of smooth muscle responsible for uterine contractions. Most of the uterus is myometrial tissue, and the muscle fibres run horizontally, vertically, and diagonally, allowing the powerful contractions that occur during labour and the less powerful contractions (or cramps) that help expel menstrual blood during a woman's period. Anteriorly directed myometrial contractions also occur near

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the time of ovulation and are thought to possibly facilitate the transport of sperm through the female reproductive tract.

The innermost layer of the uterus is called the **endometrium**. The endometrium contains a connective tissue lining, the lamina propria, which is covered by epithelial tissue that lines the lumen. Structurally, the endometrium consists of two layers: the **stratum basalis** and the **stratum functionalis** (the basal and functional layers). The stratum basalis layer is part of the lamina propria and is adjacent to the myometrium; this layer does not shed during menses. In contrast, the thicker stratum functionalis layer contains the glandular portion of the lamina propria and the endothelial tissue that lines the uterine lumen. It is the stratum functionalis that grows and thickens in response to increased levels of estrogen and progesterone. In the luteal phase of the menstrual cycle, special branches off of the uterine artery called spiral arteries supply the thickened stratum functionalis. This inner functional layer provides the proper site of **implantation** for the fertilized egg, and—should fertilization not occur—it is only the stratum functionalis layer of the endometrium that sheds during menstruation.

Recall that during the follicular phase of the ovarian cycle, the tertiary follicles are growing and secreting estrogen. At the same time, the stratum functionalis of the endometrium is thickening to prepare for a potential implantation. The postovulatory increase in progesterone, which characterizes the luteal phase, is key for maintaining a thick stratum functionalis. As long as a functional corpus luteum is present in the ovary, the endometrial lining is prepared for implantation. Indeed, if an embryo implants, signals are sent to the corpus luteum to continue secreting progesterone to maintain the endometrium and thus maintain the pregnancy. If an embryo does not implant, no signal is sent to the corpus luteum, and it degrades, ceasing progesterone production and ending the luteal phase.

Without progesterone, the endometrium thins, and under the influence of prostaglandins, the spiral arteries of the endometrium constrict and rupture, preventing oxygenated blood from reaching the endometrial tissue. As a result, endometrial tissue dies, and blood, pieces of the endometrial tissue, and white blood cells are shed through the vagina during menstruation, or the **menses**. The first menses after puberty, called **menarche**, can occur either before or after the first ovulation.

The Menstrual Cycle

Now that we have discussed the maturation of the cohort of tertiary follicles in the ovary, the buildup and then shedding of the endometrial lining in the uterus, and the function of the uterine tubes and vagina, we can put everything together

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to talk about the three phases of the **menstrual cycle**—the series of changes in which the uterine lining is shed, rebuilds, and prepares for implantation.

The timing of the menstrual cycle starts with the first day of menses, referred to as day 1 of a period. Cycle length is determined by counting the days between the onset of bleeding in two subsequent cycles. Because the average length of a menstrual cycle is 28 days, this is the time period used to identify the timing of events in the cycle.

However, the length of the menstrual cycle varies, even in the same person from one cycle to the next—typically from 21 to 32 days.

Just as the hormones produced by the granulosa and theca cells of the ovary "drive" the follicular and luteal phases of the ovarian cycle, they also control the three distinct phases of the menstrual cycle. These are the menses phase, the proliferative phase, and the secretory phase.

Menses Phase

The **menses phase** of the menstrual cycle is the phase during which the lining is shed—that is, the days that the person menstruates. Although it averages approximately 5 days, the menses phase can last from 2 to 7 days or longer. As shown in Figure 26.14, the menses phase occurs during the early days of the follicular phase of the ovarian cycle, when progesterone, FSH, and LH levels are low. Recall that progesterone concentrations decline as a result of the degradation of the corpus luteum, marking the end of the luteal phase. This decline in progesterone triggers the shedding of the stratum functionalis of the endometrium.

Proliferative Phase

Once menstrual flow ceases, the endometrium begins to proliferate again, marking the beginning of the **proliferative phase** of the menstrual cycle (see Figure 26.14). It occurs when the granulosa and theca cells of the tertiary follicles begin to produce increased amounts of estrogen. These rising estrogen concentrations stimulate the endometrial lining to rebuild.

Recall that the high estrogen concentrations will eventually lead to a decrease in FSH as a result of negative feedback, resulting in atresia of all but one of the developing tertiary follicles. The switch to positive feedback—which occurs with the elevated estrogen production from the dominant follicle—then stimulates the LH surge that will trigger ovulation. In a typical 28-day menstrual cycle, ovulation occurs on day 14. Ovulation marks the end of the proliferative phase as well as the end of the follicular phase.

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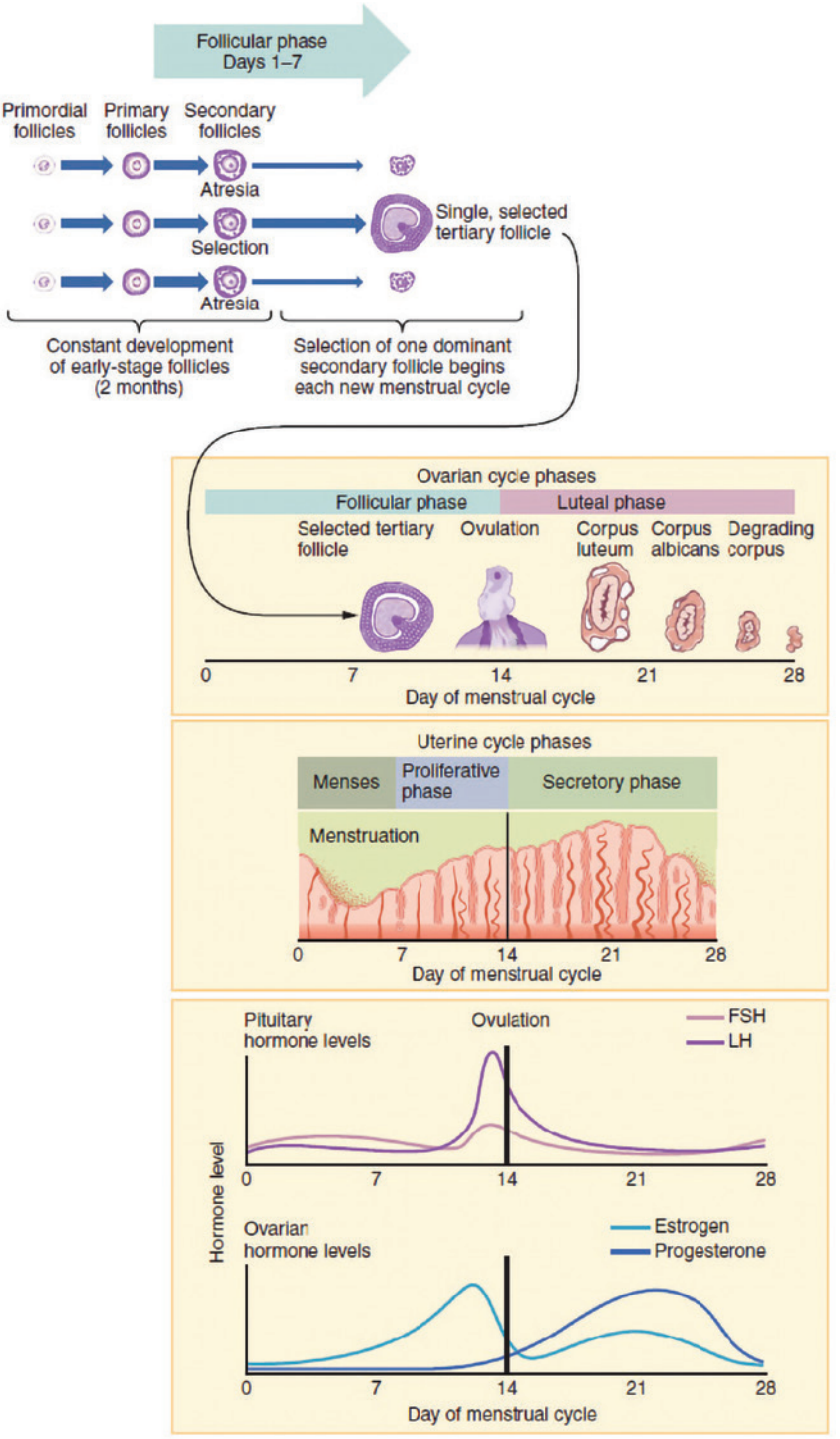


Figure 26.14 Hormone Levels in Ovarian and Menstrual Cycles. The correlation of the hormone levels and their effects on the female reproductive system is shown in this timeline of the ovarian and menstrual cycles. The menstrual cycle begins at day 1 with the start of menses. Ovulation occurs around day 14 of a 28-day cycle, triggered by the LH surge.

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Secretory Phase

In addition to prompting the LH surge, high estrogen levels increase the uterine tube contractions that facilitate the pickup and transfer of the ovulated oocyte. High estrogen levels also slightly decrease the acidity of the vagina, making it more hospitable to sperm. In the ovary, the luteinization of the granulosa cells of the collapsed follicle forms the progesterone-producing corpus luteum, marking the beginning of the luteal phase of the ovarian cycle. In the uterus, progesterone from the corpus luteum begins the **secretory phase** of the menstrual cycle, in which the endometrial lining prepares for implantation (see Figure 26.14). Over the next 10 to 12 days, the endometrial glands secrete a fluid rich in glycogen. If fertilization has occurred, this fluid will nourish the ball of cells now developing from the zygote. At the same time, the spiral arteries develop to provide blood to the thickened stratum functionalis.

If no pregnancy occurs within approximately 10 to 12 days, the corpus luteum will degrade into the corpus albicans. Levels of both estrogen and progesterone will fall, and the endometrium will grow thinner. Prostaglandins will be secreted that cause constriction of the spiral arteries, reducing oxygen supply. The endometrial tissue will die, resulting in menses—or the first day of the next cycle.

The Breasts

Whereas the breasts are located far from the other female reproductive organs, they are considered accessory organs of the female reproductive system. The function of the breasts is to supply milk to an infant in a process called **lactation**. The external features of the breast include a **nipple** surrounded by a pigmented **areola** (Figure 26.15), whose colouration may deepen during pregnancy. The areola is typically circular and can vary in size from 25 to 100 mm in diameter. The areolar region is characterized by small, raised areolar glands that secrete lubricating fluid during lactation to protect the nipple from chafing. When a baby nurses, or draws milk from the breast, the entire areolar region is taken into the mouth.

Breast milk is produced by the **mammary glands**, which are modified sweat glands. The milk itself exits the breast through the nipple via 15 to 20 **lactiferous ducts** that open on the surface of the nipple. These lactiferous ducts each extend to a **lactiferous sinus** that connects to a glandular **lobe** within the breast itself that contains groups of milk-secreting cells in clusters called **alveoli** (see Figure 26.15). The clusters can change in size depending on the amount of milk in the alveolar lumen. Once milk is made in the alveoli, stimulated myoepithelial cells that surround the alveoli contract to push the

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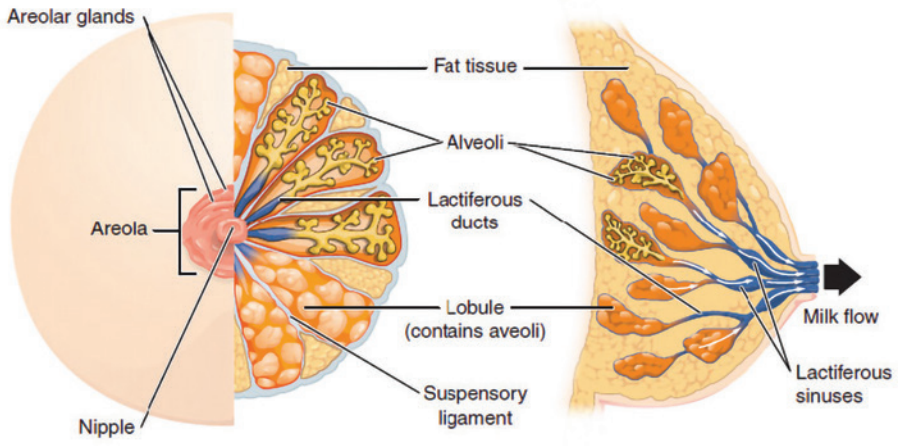


Figure 26.15 Anatomy of the Breast. During lactation, milk moves from the alveoli through the lactiferous ducts to the nipple.

milk to the lactiferous sinuses. From here, the baby can draw milk through the lactiferous ducts by suckling. The lobes themselves are surrounded by fat tissue, which determines the size of the breast; breast size differs between individuals and does not affect the amount of milk produced. Supporting the breasts are multiple bands of connective tissue called **suspensory ligaments** that connect the breast tissue to the dermis of the overlying skin.

During the normal hormonal fluctuations in the menstrual cycle, breast tissue responds to changing levels of estrogen and progesterone, which can lead to swelling and breast tenderness in some individuals, especially during the secretory phase. If pregnancy occurs, the increase in hormones leads to further development of the mammary tissue and enlargement of the breasts.

Hormonal Birth Control

Birth control pills take advantage of the negative-feedback system that regulates the ovarian and menstrual cycles to stop ovulation and prevent pregnancy. Typically, they work by providing a constant level of both estrogen and progesterone, which negatively feeds back onto the hypothalamus and pituitary, thus preventing the release of FSH and LH. Without FSH, the follicles do not mature, and without the LH surge, ovulation does not occur. Although the estrogen in birth control pills does stimulate some thickening of the endometrial wall, it is reduced compared with a normal cycle and is less likely to support implantation.

Some birth control pills contain 21 active pills containing hormones and 7 inactive pills (placebos). The decline in hormones during the week that the person takes the placebo pills triggers menses, although it is typically lighter

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than a normal menstrual flow because of the reduced endometrial thickening. Newer types of birth control pills have been developed that deliver low-dose estrogens and progesterone for the entire cycle (these are meant to be taken 365 days a year), and menses never occurs. While some people prefer to have the proof of a lack of pregnancy that a monthly period provides, menstruation every 28 days is not required for health reasons, and there are no reported adverse effects of not having a menstrual period in an otherwise healthy individual.

Because birth control pills function by providing constant estrogen and progesterone levels and disrupting negative feedback, skipping even just one or two pills at certain points of the cycle (or even being several hours late taking the pill) can lead to an increase in FSH and LH and result in ovulation. It is important, therefore, to follow the directions on the birth control pill package to successfully prevent pregnancy.

Key Terms

alveoli (of the breast): Milk-secreting cells in the mammary gland.

ampulla (of the uterine tube): Middle portion of the uterine tube in which fertilization often occurs.

antrum: Fluid-filled chamber that characterizes a mature tertiary (antral) follicle.

areola: Highly pigmented, circular area surrounding the raised nipple and containing areolar glands that secrete fluid important for lubrication during suckling.

Bartholin's glands (also greater vestibular glands): Glands that produce a thick mucus that maintains moisture in the vulva area; also referred to as the greater vestibular glands.

blood-testis barrier: Tight junctions between Sertoli cells that prevent blood-borne pathogens from gaining access to later stages of spermatogenesis and prevent the potential for an autoimmune reaction to haploid sperm.

body of uterus: Middle section of the uterus.

broad ligament: Wide ligament that supports the uterus by attaching laterally to both sides of the uterus and pelvic wall.

bulbourethral glands (also Cowper's glands): Glands that secrete a lubricating mucus that cleans and lubricates the urethra prior to and during ejaculation.

cervix: Elongate inferior end of the uterus where it connects to the vagina.

clitoris (also glans clitoris): Nerve-rich area of the vulva that contributes to sexual sensation during intercourse.

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corpus albicans: Nonfunctional structure remaining in the ovarian stroma following structural and functional regression of the corpus luteum.

corpus cavernosum: Either of two columns of erectile tissue in the penis that fill with blood during an erection.

corpus luteum: Transformed follicle after ovulation that secretes progesterone.

corpus spongiosum (plural = corpora cavernosa): Column of erectile tissue in the penis that fills with blood during an erection and surrounds the penile urethra on the ventral portion of the penis.

ductus deferens (also vas deferens): Duct that transports sperm from the epididymis through the spermatic cord and into the ejaculatory duct; also referred to as the vas deferens.

ejaculatory duct: Duct that connects the ampulla of the ductus deferens with the duct of the seminal vesicle at the prostatic urethra.

embryo: Oocyte successfully fertilized.

endometrium: Inner lining of the uterus, part of which builds up during the secretory phase of the menstrual cycle and then sheds with menses.

epididymis (plural = epididymides): Coiled tubular structure in which sperm start to mature and are stored until ejaculation.

erectile tissue: Located in the shaft of the penis and composed of three column-like chambers.

fimbriae: Fingerlike projections on the distal uterine tubes.

follicle: Ovarian structure of one oocyte and surrounding granulosa (and later theca) cells.

follicular phase: Phase of the ovarian cycle when the tertiary follicles are growing and secreting estrogen.

folliculogenesis: Development of ovarian follicles from primordial to tertiary under the stimulation of gonadotropins.

fundus (of the uterus): Domed portion of the uterus that is superior to the uterine tubes.

gamete: Haploid reproductive cell that contributes genetic material to form an offspring.

glans penis: Bulbous end of the penis that contains a large number of nerve endings.

gonadotropin-releasing hormone (GnRH): Hormone released by the hypothalamus that regulates the production of follicle-stimulating hormone and luteinizing hormone from the pituitary gland.

gonads: Reproductive organs (testes and ovaries) that produce gametes and reproductive hormones.

granulosa cells: Supportive cells in the ovarian follicle that produce estrogen.

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hymen: Membrane that covers part of the opening of the vagina.
implantation: When the developing zygote lodges into the uterus for development.
infundibulum (of the uterine tube): Wide, distal portion of the uterine tube terminating in fimbriae.
inguinal canal: Opening in abdominal wall that connects the testes to the abdominal cavity.
inhibins: Hormones produced by the Sertoli cells stimulated by FSH.
isthmus: Narrow, medial portion of the uterine tube that joins the uterus.
labia majora: Hair-covered folds of skin located behind the mons pubis.
labia minora: Thin, pigmented, hairless flaps of skin located medial and deep to the labia majora.
lactation: Function of the breasts to supply milk to an infant.
lactiferous ducts: Ducts that connect the mammary glands to the nipple and allow for the transport of milk.
lactiferous sinus: Area of milk collection between alveoli and lactiferous duct.
Leydig cells: Cells between the seminiferous tubules of the testes that produce testosterone; a type of interstitial cell.
lobe: Glandular tissue in the breast that contains groups of milk-secreting cells.
luteal phase: Postovulatory phase in the ovarian cycle of progesterone secretion.
mammary glands: Glands inside the breast that secrete milk.
menarche: First menstruation in a pubertal female.
menses: Shedding of the inner portion of the endometrium out through the vagina; also referred to as menstruation.
menses phase: Phase of the menstrual cycle in which the endometrial lining is shed.
menstrual cycle: Approximately 28-day cycle of changes in the uterus consisting of a menses phase, a proliferative phase, and a secretory phase.
mons pubis: Mound of fatty tissue located at the front of the vulva.
myometrium: Smooth muscle layer of the uterus that allows for uterine contractions during labour and expulsion of menstrual blood.
nipple: External features of the breast surrounded by a pigmented areola.
oocyte: Cell that results from the division of the oogonium and undergoes meiosis I at the LH surge and meiosis II at fertilization to become a haploid ovum.
oogenesis: Process by which oogonia divide by mitosis to primary oocytes, which undergo meiosis to produce the secondary oocyte and, upon fertilization, the ovum.

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oogonia: Ovarian stem cells that undergo mitosis during female fetal development to form primary oocytes.

ovarian cycle: Approximately 28-day cycle of changes in the ovary consisting of a follicular phase and a luteal phase.

ovaries: Female gonads that produce oocytes and sex steroid hormones (notably estrogen and progesterone).

ovulation: Release of a secondary oocyte and associated granulosa cells from an ovary.

ovum: Haploid female gamete resulting from completion of meiosis II at fertilization.

penis: Male organ of copulation.

perimetrium: Outer epithelial layer of the uterine wall.

polar body: Smaller cell produced during the process of meiosis in oogenesis.

prepuce (also foreskin): Flap of skin that forms a collar around, and thus protects and lubricates, the glans penis; also referred to as the foreskin.

primary follicles: Ovarian follicles with a primary oocyte and one layer of cuboidal granulosa cells.

primary oocytes: Formed from ogonia in the fetal ovary prior to birth.

primary spermatocyte: Cell that results from the division of spermatogonium and undergoes meiosis I and meiosis II to form spermatids.

primordial follicles: Least-developed ovarian follicles that consist of a single oocyte and a single layer of flat (squamous) granulosa cells.

proliferative phase: Phase of the menstrual cycle in which the endometrium proliferates.

prostate gland, or prostate: Doughnut-shaped gland at the base of the bladder surrounding the urethra and contributing fluid to semen during ejaculation.

rugae (of the vagina): Folds of skin in the vagina that allow it to stretch during intercourse and childbirth.

scrotum: External pouch of skin and muscle that houses the testes.

secondary follicles: Ovarian follicles with a primary oocyte and multiple layers of granulosa cells.

secondary oocyte: Daughter oocyte resulting from meiosis in a primary oocyte; leaves the ovary during ovulation.

secondary spermatocytes: Products of meiosis I in primary spermatocytes, where each of the 23 pairs of chromosomes separates resulting in two cells, each with only half the number of chromosomes.

secretory phase: Phase of the menstrual cycle in which the endometrium secretes a nutrient-rich fluid in preparation for implantation of an embryo.

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semen: Ejaculatory fluid composed of sperm and secretions from the seminal vesicles, prostate, and bulbourethral glands.

seminal vesicle: Gland that produces seminal fluid, which contributes to semen.

seminiferous tubules: Tube structures within the testes where spermatogenesis occurs.

Sertoli cells: Cells that support germ cells through the process of spermatogenesis; a type of sustentacular cell.

sperm (also spermatozoon): Male gamete.

spermatic cord: Bundle of nerves and blood vessels that supplies the testes; contains ductus deferens.

spermatid: Immature sperm cells produced by meiosis II of secondary spermatocytes.

spermatogenesis: Formation of new sperm; occurs in the seminiferous tubules of the testes.

spermatogonia (singular = spermatogonium): Diploid precursor cells that become sperm.

spermatozoa: Formed sperm that are the end result of spermiogenesis.

spermiogenesis: Transformation of spermatids to spermatozoa during spermatogenesis.

stratum basalis: Part of the lamina propria adjacent to the myometrium; does not shed during menses.

stratum functionalis: Contains the glandular portion of the lamina propria and the endothelial tissue that lines the uterine lumen.

suspensory ligaments: Bands of connective tissue that suspend the breast onto the chest wall by attachment to the overlying dermis.

tertiary follicles (also antral follicles): Ovarian follicles with a primary or secondary oocyte, multiple layers of granulosa cells, and a fully formed antrum.

testes (singular = testis): Male gonads.

theca cells: Estrogen-producing cells in a maturing ovarian follicle.

uterine tubes (also fallopian tubes or oviducts): Ducts that facilitate transport of an ovulated oocyte to the uterus.

uterus: Muscular hollow organ in which a fertilized egg develops into a fetus.

vagina: Tunnel-like organ that provides access to the uterus for the insertion of semen and from the uterus for the birth of a baby.

vulva: External female genitalia.

zona pellucida: Thin acellular membrane secreted by the primary oocyte.

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Chapter Review

26.1 Anatomy and Physiology of the Testicular Reproductive System

Gametes are the reproductive cells that combine to form offspring. Organs called gonads produce the gametes, along with the hormones that regulate human reproduction. The male gametes are called sperm. Spermatogenesis, the production of sperm, occurs within the seminiferous tubules that make up most of the testis. The scrotum is the muscular sac that holds the testes outside of the body cavity.

Spermatogenesis begins with mitotic division of spermatogonia (stem cells) to produce primary spermatocytes that undergo the two divisions of meiosis to become secondary spermatocytes, then the haploid spermatids. During spermiogenesis, spermatids are transformed into spermatozoa (formed sperm). Upon release from the seminiferous tubules, sperm are moved to the epididymis where they continue to mature. During ejaculation, sperm exit the epididymis through the ductus deferens, a duct in the spermatic cord that leaves the scrotum. The ampulla of the ductus deferens meets the seminal vesicle, a gland that contributes fructose and proteins, at the ejaculatory duct. The fluid continues through the prostatic urethra, where secretions from the prostate are added to form semen. These secretions help the sperm travel through the urethra and into the female reproductive tract. Secretions from the bulbourethral glands protect sperm and cleanse and lubricate the penile (spongy) urethra.

The penis is the male organ of copulation. Columns of erectile tissue called the corpora cavernosa and corpus spongiosum fill with blood when sexual arousal activates vasodilation in the blood vessels of the penis. Testosterone regulates and maintains the sex organs and sex drive and induces the physical changes of puberty. Interplay between the testes and the endocrine system precisely controls the production of testosterone with a negative feedback loop.

26.2 Anatomy and Physiology of the Ovarian Reproductive System

The external female genitalia are collectively called the vulva. The vagina is the pathway into and out of the uterus. The penis is inserted into the vagina to deliver sperm, and the baby exits the uterus through the vagina during childbirth.

The ovaries produce oocytes, the female gametes, in a process called oogenesis. As with spermatogenesis, meiosis produces the haploid gamete (in this case, an ovum); however, it is completed only in an oocyte that has been penetrated by a sperm. In the ovary, an oocyte surrounded by supporting cells is called a follicle. In folliculogenesis, primordial follicles develop into primary,

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secondary, and tertiary follicles. Early tertiary follicles with their fluid-filled antrum will be stimulated by an increase in FSH, a gonadotropin produced by the anterior pituitary, to grow during the early part of the ovarian cycle. Supporting granulosa and theca cells in the growing follicles produce estrogens, until the level of estrogen in the bloodstream is high enough that it triggers negative feedback at the hypothalamus and pituitary. This results in a reduction of FSH and LH, and most tertiary follicles in the ovary undergo atresia (they die). One follicle, usually the one with the most FSH receptors, survives this period and is now called the dominant follicle. The dominant follicle produces more estrogen, triggering positive feedback and the LH surge that will induce ovulation. Following ovulation, the granulosa cells of the empty follicle luteinize and transform into the progesterone-producing corpus luteum. The ovulated oocyte with its surrounding granulosa cells is picked up by the infundibulum of the uterine tube, and beating cilia help transport it through the tube toward the uterus. Fertilization occurs within the uterine tube, and the final stage of meiosis is completed.

The uterus has three regions: the fundus, the body, and the cervix. It has three layers: the outer perimetrium, the muscular myometrium, and the inner endometrium. The endometrium responds to estrogen released by the follicles during the menstrual cycle and grows thicker with an increase in blood vessels in preparation for pregnancy. If the egg is not fertilized, no signal is sent to extend the life of the corpus luteum, and it degrades, stopping progesterone production.

This decline in progesterone results in the sloughing of the inner portion of the endometrium in a process called menses, or menstruation.

The breasts are accessory organs that may be utilized after the birth of a child to produce milk in a process called lactation. Birth control pills provide constant levels of estrogen and progesterone to negatively feed back on the hypothalamus and pituitary and suppress the release of FSH and LH, which inhibits ovulation and prevents pregnancy.

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27

Development and Inheritance

Chapter Objectives

After studying this chapter, you will be able to:

- List and explain the steps involved in fertilization
- Describe the major events in embryonic development
- Describe the major events in fetal development
- Discuss the adaptations of the body to pregnancy
- Summarize the physiology of lactation

In approximately 9 months, a single cell—a fertilized egg—develops into a fully formed infant consisting of trillions of cells with myriad specialized functions. The dramatic changes of fertilization, embryonic development, and fetal development are followed by remarkable adaptations of the newborn to life outside the womb. An offspring's normal development depends on the appropriate synthesis of structural and functional proteins. This, in turn, is governed by the genetic material inherited from the egg and sperm as well as environmental factors.

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27.1 Fertilization

Learning Objectives

By the end of this section, you will be able to:

- Describe the obstacles that sperm must overcome to reach an oocyte
- Explain capacitation and its importance in fertilization
- Summarize the events that occur as a sperm fertilizes an oocyte

Fertilization occurs when a sperm and an oocyte (egg) combine and their nuclei fuse. Because each of these reproductive cells is a haploid cell containing half of the genetic material needed to form a human being, their combination forms a diploid cell. This new single cell, called a **zygote**, contains all of the genetic material needed to form a human—half from each biological parent.

Transit of Sperm

Fertilization is a numbers game. During ejaculation, hundreds of millions of sperm (spermatozoa) are released into the vagina. Almost immediately, millions of these sperm are overcome by the acidity of the vagina (approximately pH 3.8), and millions more may be blocked from entering the uterus by thick cervical mucus. Of those that do enter, thousands are destroyed by phagocytic uterine leukocytes. Thus, the race into the uterine tubes, which is the most typical site for sperm to encounter the oocyte, is reduced to a few thousand contenders. Their journey—thought to be facilitated by uterine contractions—usually takes from 30 minutes to 2 hours. If the sperm do not encounter an oocyte immediately, they can survive in the uterine tubes for another 3–5 days. Thus, fertilization can still occur if intercourse takes place a few days before ovulation. In comparison, an oocyte can survive independently for only approximately 24 hours following ovulation. Intercourse more than a day after ovulation will therefore usually not result in fertilization.

During the journey, fluids in the female reproductive tract prepare the sperm for fertilization through a process called **capacitation**, or priming. The fluids improve the motility of the spermatozoa. They also deplete cholesterol molecules embedded in the membrane of the head of the sperm, thinning the membrane in such a way that will help facilitate the release of the lysosomal (digestive) enzymes needed for the sperm to penetrate the oocyte's exterior once contact is made. Sperm must undergo the process of capacitation in order to have the "capacity" to fertilize an oocyte. If they reach the oocyte before capacitation is complete, they will be unable to penetrate the oocyte's thick outer layer of cells.

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Contact Between Sperm and Oocyte

Upon ovulation, the oocyte released by the ovary is swept into—and along—the uterine tube. Fertilization must occur in the distal uterine tube because an unfertilized oocyte cannot survive the 72-hour journey to the uterus. As you will recall from your study of oogenesis, this oocyte (specifically a secondary oocyte) is surrounded by two protective layers. The **corona radiata** is an outer layer of follicular (granulosa) cells that form around a developing oocyte in the ovary and remain with it upon ovulation. The underlying **zona pellucida** is a transparent, but thick, glycoprotein membrane that surrounds the cell's plasma membrane.

As it is swept along the distal uterine tube, the oocyte encounters the surviving capacitated sperm, which stream toward it in response to chemical attractants released by the cells of the corona radiata. To reach the oocyte itself, the sperm must penetrate the two protective layers. The sperm first burrow through the cells of the corona radiata. Then, upon contact with the zona pellucida, the sperm bind to receptors in the zona pellucida. This initiates a process called the **acrosomal reaction**, in which the enzyme-filled "cap" of the sperm, called the **acrosome**, releases its stored digestive enzymes. These enzymes clear a path through the zona pellucida that allows sperm to reach the oocyte. Finally, a single sperm makes contact with sperm-binding receptors on the oocyte's plasma membrane (Figure 27.1). The plasma membrane of that sperm then fuses with the oocyte's plasma membrane, and the head and mid-piece of the "winning" sperm enter the oocyte interior.

How do sperm penetrate the corona radiata? Some sperm undergo a spontaneous acrosomal reaction, which is an acrosomal reaction not triggered by contact with the zona pellucida. The digestive enzymes released by this reaction digest the extracellular matrix of the corona radiata. As you can see, the first sperm to reach the oocyte is never the one to fertilize it. Rather, hundreds of sperm cells must undergo the acrosomal reaction, each helping degrade the corona radiata and zona pellucida until a path is created to allow one sperm to contact and fuse with the plasma membrane of the oocyte. If you consider the loss of millions of sperm between entry into the vagina and degradation of the zona pellucida, you can understand why a low sperm count can cause male infertility.

When the first sperm fuses with the oocyte, the oocyte deploys two mechanisms to prevent **polyspermy**, which is penetration by more than one sperm. This is critical because if more than one sperm were to fertilize the oocyte, the resulting zygote would be a triploid organism with three sets of chromosomes. This is incompatible with life.

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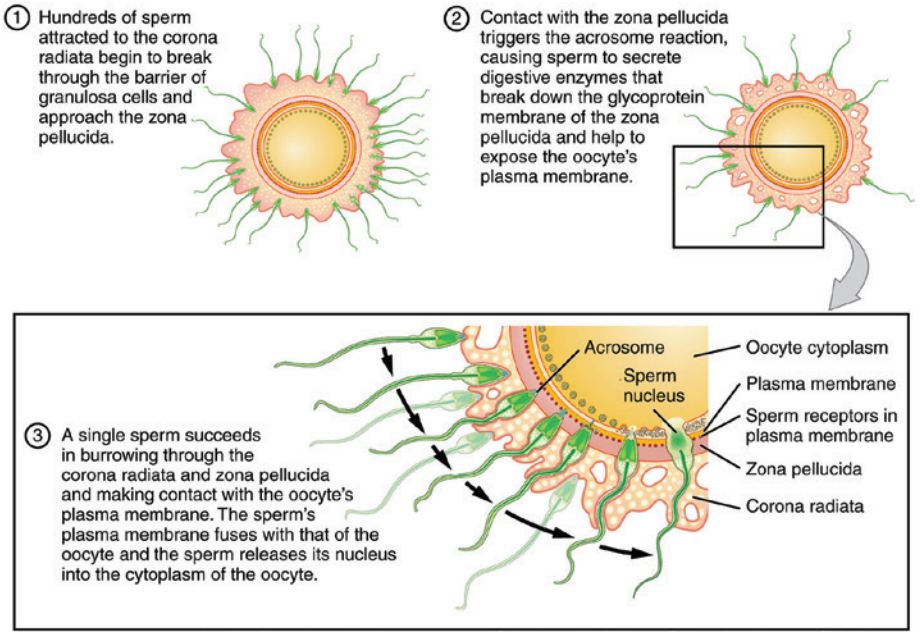


Figure 27.1 Sperm and the Process of Fertilization. Before fertilization, hundreds of capacitated sperm must break through the surrounding corona radiata and zona pellucida so that one can contact and fuse with the oocyte plasma membrane.

The first mechanism is the fast block, which involves a near instantaneous change in sodium ion permeability upon binding of the first sperm, depolarizing the oocyte plasma membrane and preventing the fusion of additional sperm cells. The fast block sets in almost immediately and lasts for about a minute, during which time an influx of calcium ions following sperm penetration triggers the second mechanism, the slow block. In this process, referred to as the **cortical reaction**, cortical granules sitting immediately below the oocyte plasma membrane fuse with the membrane and release zonal inhibiting proteins and mucopolysaccharides into the space between the plasma membrane and the zona pellucida. Zonal inhibiting proteins cause the release of any other attached sperm and destroy the oocyte's sperm receptors, thus preventing any more sperm from binding. The mucopolysaccharides then coat the nascent zygote in an impenetrable barrier that, together with the hardened zona pellucida, is called a **fertilization membrane**.

The Zygote

Recall that at the point of fertilization, the oocyte has not yet completed meiosis; all secondary oocytes remain arrested in metaphase of meiosis II

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until fertilization. Only upon fertilization does the oocyte complete meiosis. The unneeded complement of genetic material that results is stored in a second polar body that is eventually ejected. At this moment, the oocyte has become an ovum, the female haploid gamete. The two haploid nuclei derived from the sperm and oocyte and contained within the egg are referred to as pronuclei. They decondense, expand, and replicate their DNA in preparation for mitosis. The pronuclei then migrate toward each other, their nuclear envelopes disintegrate, and the male- and female-derived genetic material intermingles. This step completes the process of fertilization and results in a single-celled diploid zygote with all the genetic instructions it needs to develop into a human.

Most of the time, a person releases a single egg during an ovulation cycle. However, in approximately 1 percent of ovulation cycles, two eggs are released and both are fertilized. Two zygotes form, implant, and develop, resulting in the birth of dizygotic (or fraternal) twins. Because dizygotic twins develop from two eggs fertilized by two sperm, they are no more identical than siblings born at different times.

Much less commonly, a zygote can divide into two separate offspring during early development. This results in the birth of monozygotic (or identical) twins. Although the zygote can split as early as the two-cell stage, splitting occurs most commonly during the early blastocyst stage, with roughly 70–100 cells present. These two scenarios are distinct from each other in that the twin embryos that separated at the two-cell stage will have individual placentas, whereas twin embryos that form from separation at the blastocyst stage will share a placenta and a chorionic cavity.

Interactive Link 27.1

Go to this site (http://oer.aupress.ca/oer-202505/27.1) to view resources covering various aspects of fertilization, including movies and animations showing sperm structure and motility, ovulation, and fertilization.

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27.2 Embryonic Development

Learning Objectives

By the end of this section, you will be able to:

- Distinguish the stages of embryonic development that occur before implantation
- Describe the process of implantation
- List and describe four embryonic membranes
- Explain gastrulation
- Describe how the placenta is formed and identify its functions
- Explain how an embryo transforms from a flat disc of cells into a three-dimensional shape resembling a human
- Summarize the process of organogenesis

Throughout this chapter, we will express embryonic and fetal ages in terms of weeks from fertilization, commonly called conception. The period of time required for full development of a fetus in utero is referred to as **gestation**. It can be subdivided into distinct gestational periods. The first 2 weeks of prenatal development are referred to as the preembryonic stage. A developing human is referred to as an **embryo** during weeks 3–8, and a **fetus** from the ninth week of gestation until birth. In this section, we'll cover the preembryonic and embryonic stages of development, which are characterized by cell division, migration, and differentiation. By the end of the embryonic period, all of the organ systems are structured in rudimentary form, although the organs themselves are either nonfunctional or only semifunctional.

Preimplantation Embryonic Development

Following fertilization, the zygote and its associated membranes, together referred to as the **conceptus**, continue to be projected toward the uterus by peristalsis and beating cilia of the epithelial cells of the fallopian tube. During its journey to the uterus, the zygote undergoes five or six rapid mitotic cell divisions. Although each **cleavage** results in more cells, it does not increase the total volume of the conceptus (Figure 27.2). Each daughter cell produced by cleavage is called a **blastomere**.

Approximately 3 days after fertilization, a 16-cell conceptus reaches the uterus. The cells that had been loosely grouped are now compacted and look more like a solid mass. The name given to this structure is the **morula**. Once inside the uterus, the conceptus floats freely for several more days. It continues

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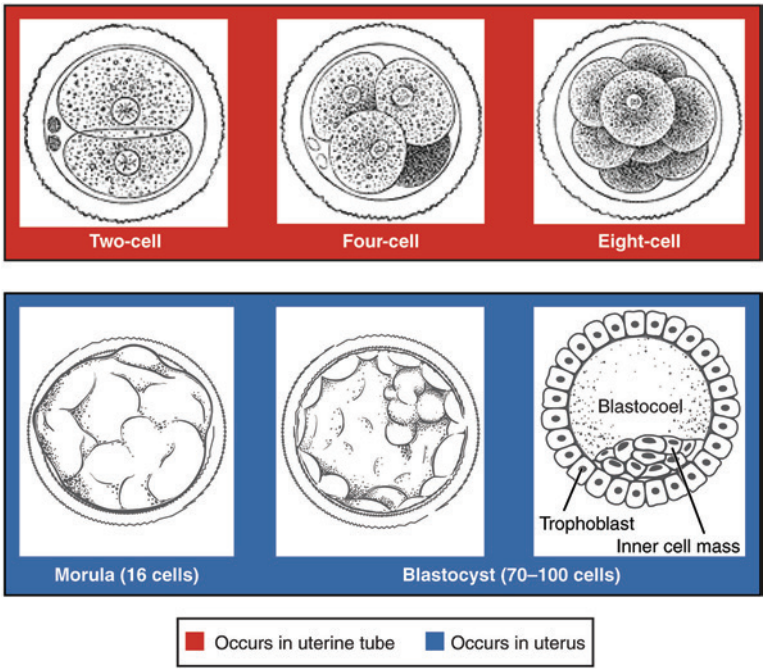


Figure 27.2 Preembryonic Cleavages. Preembryonic cleavages make use of the abundant cytoplasm of the conceptus as the cells rapidly divide without changing the total volume.

to divide, creating a ball of approximately 100 cells and consuming nutritive endometrial secretions called uterine milk while the uterine lining thickens.

The ball of now tightly bound cells starts to secrete fluid and organize around a fluid-filled cavity, the **blastocoel**. At this developmental stage, the conceptus is referred to as a **blastocyst**. Within this structure, a group of cells forms into an **inner cell mass**, which is fated to become the embryo. The cells that form the outer shell (**trophoblast**) are called **trophoblasts**. These cells will develop into the chorionic sac and the fetal portion of the **placenta** (the organ of nutrient, waste, and gas exchange between a pregnant person and the developing offspring).

The inner mass of embryonic cells is totipotent during this stage, meaning that each cell has the potential to differentiate into any cell type in the human body. Totipotency lasts for only a few days before the cells' fates are set as being the precursors to a specific lineage of cells.

As the blastocyst forms, the trophoblast secretes enzymes that begin to degrade the zona pellucida. In a process called "hatching," the conceptus breaks free of the zona pellucida in preparation for implantation.

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Interactive Link 27.2

View this time-lapse movie (http://oer.aupress.ca/oer-202505/27.2) of a conceptus starting at day 3. What is the first structure you see? At what point in the movie does the blastocoel first appear? What event occurs at the end of the movie?

Implantation

At the end of the first week, the blastocyst comes in contact with the uterine wall and adheres to it, embedding itself in the uterine lining via the trophoblast cells. Thus begins the process of **implantation**, which signals the end of the preembryonic stage of development (Figure 27.3). Implantation can be accompanied by minor bleeding. The blastocyst typically implants in the fundus of the uterus or on the posterior wall. However, if the endometrium is not fully

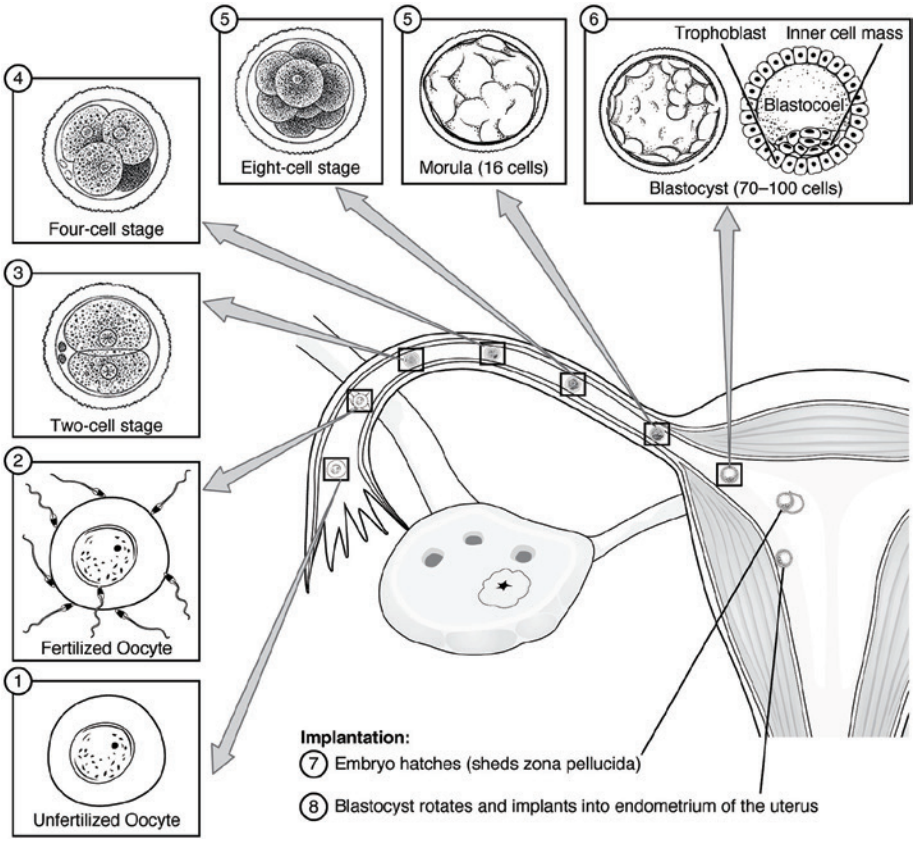


Figure 27.3 Preembryonic Development. Ovulation, fertilization, preembryonic development, and implantation occur at specific locations within the female reproductive system in a time span of approximately 1 week.

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developed and ready to receive the blastocyst, the blastocyst will detach and find a better spot. A significant percentage (50–75 percent) of blastocysts fail to implant; when this occurs, the blastocyst is shed with the endometrium during menses. The high rate of implantation failure is one reason why pregnancy typically requires several ovulation cycles to achieve.

When implantation succeeds and the blastocyst adheres to the endometrium, the superficial cells of the trophoblast fuse with each other, forming the **syncytiotrophoblast**, a multinucleated body that digests endometrial cells to firmly secure the blastocyst to the uterine wall. In response, the uterine mucosa rebuilds itself and envelops the blastocyst (Figure 27.4). The trophoblast secretes **human chorionic gonadotropin** (**hCG**), a hormone that directs the corpus luteum to survive, enlarge, and continue producing progesterone and estrogen to suppress menses.

These functions of hCG are necessary for creating an environment suitable for the developing embryo. As a result of this increased production, hCG accumulates in the maternal bloodstream and is excreted in the urine. Implantation is complete by the middle of the second week. Just a few days after implantation, the trophoblast has secreted enough hCG for an at-home urine pregnancy test to give a positive result.

Most of the time an embryo implants within the body of the uterus in a location that can support growth and development. However, in 1 to 2 percent of cases, the embryo implants either outside the uterus (an **ectopic pregnancy**) or in a region of the uterus that can create complications for the pregnancy. If the embryo implants in the inferior portion of the uterus, the placenta can potentially grow over the opening of the cervix, a condition called **placenta previa**.

Embryonic Membranes

During the second week of development, with the embryo implanted in the uterus, cells within the blastocyst start to organize into layers. Some grow to form the extraembryonic membranes needed to support and protect the growing embryo: the amnion, the yolk sac, the allantois, and the chorion.

At the beginning of the second week, the cells of the inner cell mass form into a two-layered **embryonic disc** composed of embryonic cells, and a space—the **amniotic cavity**—opens up between it and the trophoblast (Figure 27.5). Cells from the upper layer of the disc extend around the amniotic cavity, creating a membranous sac that forms into the **amnion** by the end of the second week. The amnion fills with **amniotic fluid** and eventually grows to surround the embryo. Early in development, amniotic fluid consists almost entirely of a filtrate of maternal plasma, but as the kidneys of the fetus begin to function at approximately the eighth week, they add urine to the volume of amniotic fluid.

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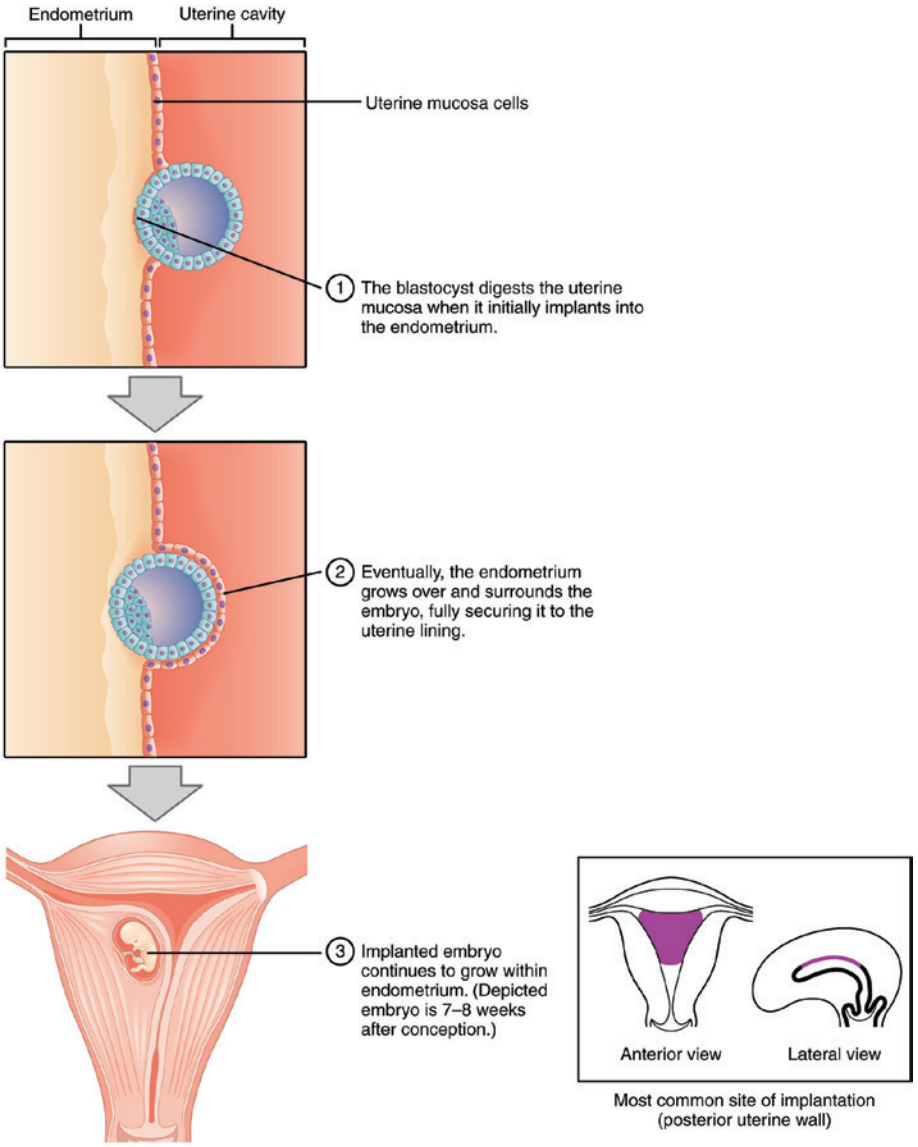


Figure 27.4 Implantation. During implantation, the trophoblast cells of the blastocyst adhere to the endometrium and digest endometrial cells until it is attached securely.

Floating within the amniotic fluid, the embryo—and later, the fetus—is protected from trauma and rapid temperature changes. It can move freely within the fluid and can prepare for swallowing and breathing outside of the uterus.

On the ventral side of the embryonic disc, opposite the amnion, cells in the lower layer of the embryonic disc extend into the blastocyst cavity and form a **yolk sac**. The yolk sac supplies some nutrients absorbed from the trophoblast and also provides primitive blood circulation to the developing embryo for the

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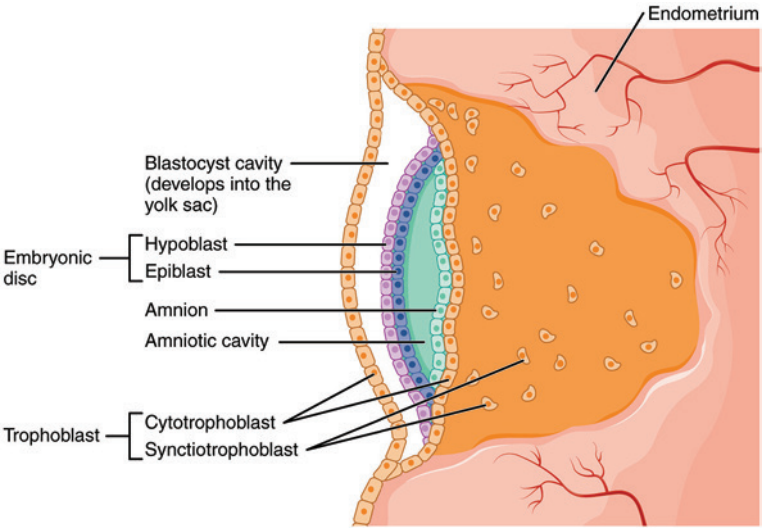


Figure 27.5 Development of the Embryonic Disc. Formation of the embryonic disc leaves spaces on either side that develop into the amniotic cavity and the yolk sac.

second and third weeks of development. When the placenta takes over nourishing the embryo at approximately week 4, the yolk sac has been greatly reduced in size, and its main function is to serve as the source of blood cells and germ cells (cells that will give rise to gametes). During week 3, a fingerlike outpocketing of the yolk sac develops into the **allantois**, a primitive excretory duct of the embryo that will become part of the urinary bladder. Together, the stalks of the yolk sac and allantois establish the outer structure of the umbilical cord.

The last of the extraembryonic membranes is the **chorion**, which is the one membrane that surrounds all others. The development of the chorion will be discussed in more detail shortly, as it relates to the growth and development of the placenta.

Embryogenesis

As the third week of development begins, the two-layered disc of cells becomes a three-layered disc through the process of **gastrulation**, during which the cells transition from totipotency to multipotency. The embryo, which takes the shape of an oval-shaped disc, forms an indentation called the **primitive streak** along the dorsal surface of the epiblast. A node at the caudal or "tail" end of the primitive streak emits growth factors that direct cells to multiply and migrate. Cells migrate toward and through the primitive streak and then move laterally to create two new layers of cells. The first layer is the **endoderm**, a sheet of cells that displaces the hypoblast and lies adjacent to the yolk sac.

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The second layer of cells fills in as the middle layer, or **mesoderm.** The cells of the epiblast that remain (not having migrated through the primitive streak) become the **ectoderm** (Figure 27.6).

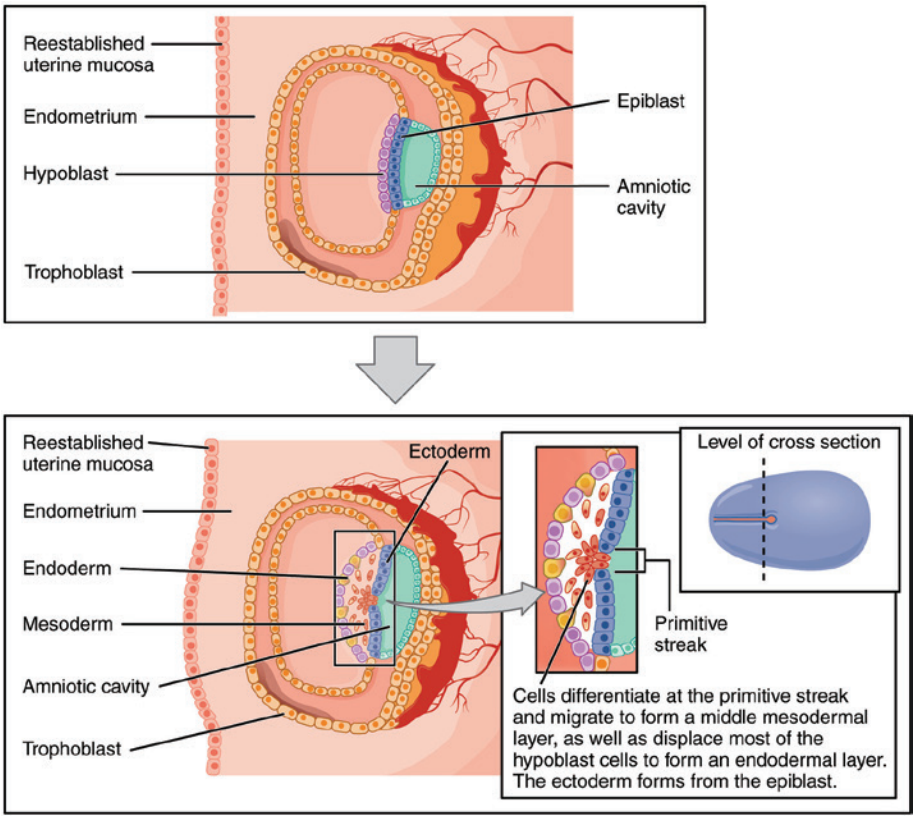


Figure 27.6 Germ Layers. Formation of the three primary germ layers occurs during the first 2 weeks of development. The embryo at this stage is only a few millimetres in length.

Each of the **primary germ layers** will develop into specific structures in the embryo. Whereas the ectoderm and endoderm form tightly connected epithelial sheets, the mesodermal cells are less organized and exist as a loosely connected cell community. The ectoderm gives rise to cell lineages that differentiate to become the central and peripheral nervous systems, sensory organs, epidermis, hair, and nails. Mesodermal cells ultimately become the skeleton, muscles, connective tissue, heart, blood vessels, and kidneys. The endoderm goes on to form the epithelial lining of the gastrointestinal tract, liver, and pancreas, as well as the lungs (Figure 27.7).

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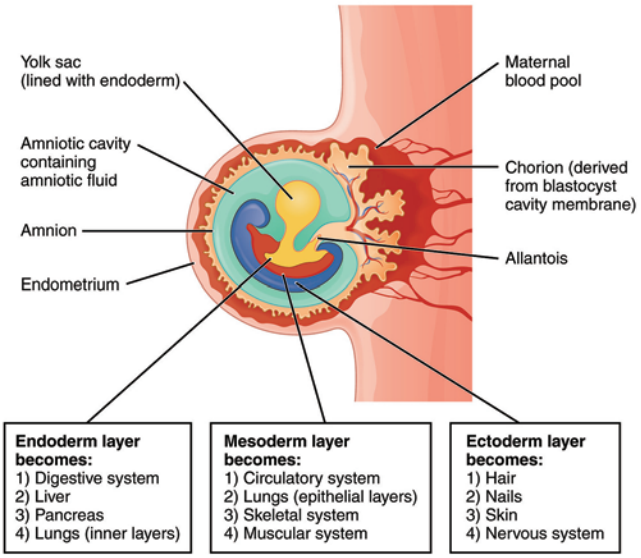


Figure 27.7 Fates of Germ Layers in Embryo. Following gastrulation of the embryo in the third week, embryonic cells of the ectoderm, mesoderm, and endoderm begin to migrate and differentiate into the cell lineages that will give rise to mature organs and organ systems in the infant.

Development of the Placenta

During the first several weeks of development, the cells of the endometrium—referred to as decidual cells—nourish the nascent embryo. During prenatal weeks 4–12, the developing placenta gradually takes over the role of feeding the embryo, and the decidual cells are no longer needed. The mature placenta is composed of tissues derived from the embryo as well as maternal tissues of the endometrium. The placenta connects to the conceptus via the **umbilical cord**, which carries deoxygenated blood and wastes from the fetus through two umbilical arteries; nutrients and oxygen are carried from the pregnant person to the fetus through the single umbilical vein. The umbilical cord is surrounded by the amnion, and the spaces within the cord around the blood vessels are filled with Wharton's jelly, a mucous connective tissue.

The maternal portion of the placenta develops from the deepest layer of the endometrium, the decidua basalis. To form the embryonic portion of the placenta, the syncytiotrophoblast and the underlying cells of the trophoblast (cytotrophoblast cells) begin to proliferate along with a layer of extraembryonic mesoderm cells. These form the **chorionic membrane**, which envelops the entire conceptus as the chorion. The chorionic membrane forms fingerlike structures called **chorionic villi** that burrow into the endometrium like tree roots, making up the fetal portion of the placenta. The cytotrophoblast cells perforate the

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chorionic villi, burrow farther into the endometrium, and remodel maternal blood vessels to augment maternal blood flow surrounding the villi. Meanwhile, fetal mesenchymal cells derived from the mesoderm fill the villi and differentiate into blood vessels, including the three umbilical blood vessels that connect the embryo to the developing placenta (Figure 27.8).

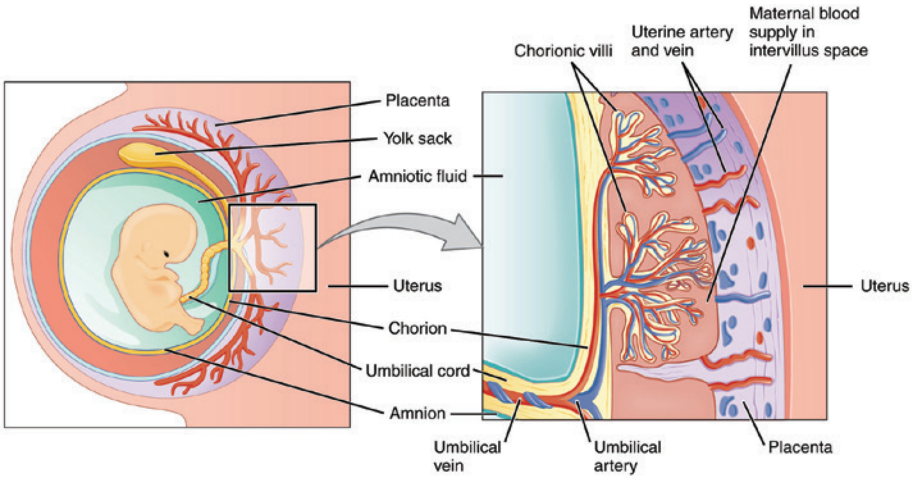


Figure 27.8 Cross Section of the Placenta. In the placenta, maternal and fetal blood components are conducted through the surface of the chorionic villi, but maternal and fetal bloodstreams never mix directly.

The placenta develops throughout the embryonic period and during the first several weeks of the fetal period; **placentation** is complete by weeks 14–16. As a fully developed organ, the placenta provides nutrition and excretion, respiration, and endocrine functions.

It receives blood from the fetus through the two umbilical arteries. Capillaries in the chorionic villi filter fetal wastes out of the blood and return clean, oxygenated blood to the fetus through a single umbilical vein. Nutrients and oxygen are transferred from maternal blood surrounding the villi through the capillaries and into the fetal bloodstream. Some substances move across the placenta by simple diffusion. Oxygen, carbon dioxide, and any other lipid-soluble substances take this route. Other substances move across by facilitated diffusion. This includes water-soluble glucose. The fetus has a high demand for amino acids and iron, and those substances are moved across the placenta by active transport.

Maternal and fetal blood do not commingle because blood cells cannot move across the placenta. This separation prevents the pregnant person's cytotoxic T cells from reaching and subsequently destroying the fetus, which

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bears "nonself" antigens. Further, it ensures the fetal red blood cells do not enter the pregnant person's circulation and trigger antibody development (if they carry "nonself" antigens)—at least until the final stages of pregnancy or birth. This is the reason that, even in the absence of preventive treatment, an Rh^- person doesn't develop antibodies that could cause hemolytic disease in their first Rh^+ fetus.

Although blood cells are not exchanged, the chorionic villi provide ample surface area for the two-way exchange of substances between maternal and fetal blood. The rate of exchange increases throughout gestation as the villi become thinner and increasingly branched. The placenta is permeable to lipid-soluble fetotoxic substances: alcohol, nicotine, barbiturates, antibiotics, certain pathogens, and many other substances that can be dangerous or fatal to the developing embryo or fetus. For these reasons, pregnant people should avoid fetotoxic substances.

Organogenesis

Following gastrulation, rudiments of the central nervous system develop from the ectoderm in the process of **neurulation**. Specialized neuroectodermal tissues along the length of the embryo thicken into the **neural plate**. During the fourth week, tissues on either side of the plate fold upward into a **neural fold**. The two folds converge to form the **neural tube**. The tube lies atop a rod-shaped, mesoderm-derived **notochord**, which eventually becomes the nucleus pulposus of intervertebral discs. Block-like structures called **somites** form on either side of the tube, eventually differentiating into the axial skeleton, skeletal muscle, and dermis. During the fourth and fifth weeks, the anterior neural tube dilates and subdivides to form vesicles that will become the brain structures.

The embryo, which begins as a flat sheet of cells, begins to acquire a cylindrical shape through the process of **embryonic folding**. The embryo folds laterally and again at either end, forming a C shape with distinct head and tail ends. The embryo envelops a portion of the yolk sac, which protrudes with the umbilical cord from what will become the abdomen. The folding essentially creates a tube, called the primitive gut, that is lined by the endoderm. The amniotic sac, which was sitting on top of the flat embryo, envelops the embryo as it folds. Within the first 8 weeks of gestation, a developing embryo establishes the rudimentary structures of all of its organs and tissues from the ectoderm, mesoderm, and endoderm. This process is called **organogenesis**.

The heart begins beating at the beginning of the fourth week, although it does not actually pump embryonic blood until a week later, when the oversized liver has begun producing red blood cells. During weeks 4–5, the eye pits form, limb buds become apparent, and the rudiments of the pulmonary system are

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formed. During the sixth week, uncontrolled fetal limb movements begin to occur. The gastrointestinal system develops too rapidly for the embryonic abdomen to accommodate it, and the intestines temporarily loop into the umbilical cord. Paddle-shaped hands and feet develop fingers and toes by the process of apoptosis (programmed cell death), which causes the tissues between the fingers to disintegrate. By week 7, the facial structure is more complex and includes nostrils, outer ears, and lenses. By the eighth week, the head is nearly as large as the rest of the embryo's body, and all major brain structures are in place. The external genitalia are apparent, but at this point, male and female embryos are indistinguishable. Bone begins to replace cartilage in the embryonic skeleton through the process of ossification. By the end of the embryonic period, the embryo is approximately 3 cm from crown to rump and weighs approximately 8 g.

Interactive Link 27.3

Watch this video (http://oer.aupress.ca/oer-202505/27.3) to view the process of embryogenesis from fertilization through pregnancy to birth. Can you identify when neurulation occurs in the embryo?

27.3 Fetal Development

Learning Objectives

By the end of this section, you will be able to:

- Differentiate between the embryonic period and the fetal period
- Briefly describe the process of sexual differentiation
- Describe the fetal circulatory system and explain the role of the shunts
- Trace the development of a fetus from the end of the embryonic period to birth

As you will recall, a developing human is called a fetus from the ninth week of gestation until birth. This 30-week period of development is marked by continued cell growth and differentiation, which fully develop the structures and functions of the immature organ systems formed during the embryonic period. The completion of fetal development results in a newborn who, although still immature in many ways, is capable of survival outside the womb.

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Sexual Differentiation

Sexual differentiation does not begin until the fetal period, during weeks 9–12. Embryonic males and females, though genetically distinguishable, are morphologically identical. Bipotential gonads, or gonads that can develop into male or female sexual organs, are connected to a central cavity called the cloaca via Müllerian ducts and Wolffian ducts. (The cloaca is an extension of the primitive gut.) Several events lead to sexual differentiation during this period.

During male fetal development, the bipotential gonads become the testes and associated epididymis. The Müllerian ducts degenerate. The Wolffian ducts become the vas deferens, and the cloaca becomes the urethra and rectum.

During female fetal development, the bipotential gonads develop into ovaries. The Wolffian ducts degenerate. The Müllerian ducts become the uterine tubes and uterus, and the cloaca divides and develops into a vagina, a urethra, and a rectum.

The Fetal Circulatory System

During prenatal development, the fetal circulatory system is integrated with the placenta via the umbilical cord so that the fetus receives both oxygen and nutrients from the placenta. However, after childbirth, the umbilical cord is severed, and the newborn's circulatory system must be reconfigured. When the heart first forms in the embryo, it exists as two parallel tubes derived from mesoderm and lined with endothelium, which then fuse together. As the embryo develops into a fetus, the tube-shaped heart folds and further differentiates into the four chambers present in a mature heart. Unlike a mature cardiovascular system, however, the fetal cardiovascular system also includes circulatory shortcuts, or shunts. A **shunt** is an anatomical (or sometimes surgical) diversion that allows blood flow to bypass immature organs such as the lungs and liver until childbirth.

The placenta provides the fetus with necessary oxygen and nutrients via the umbilical vein. (Remember that veins carry blood toward the heart. In this case, the blood flowing to the fetal heart is oxygenated because it comes from the placenta. The respiratory system is immature and cannot yet oxygenate blood on its own.) From the umbilical vein, the oxygenated blood flows toward the inferior vena cava, all but bypassing the immature liver, via the **ductus venosus** shunt (Figure 27.9). The liver receives just a trickle of blood, which is all that it needs in its immature, semifunctional state. Blood flows from the inferior vena cava to the right atrium, mixing with fetal venous blood along the way.

Although the fetal liver is semifunctional, the fetal lungs are nonfunctional. The fetal circulation therefore bypasses the lungs by shifting some of the blood

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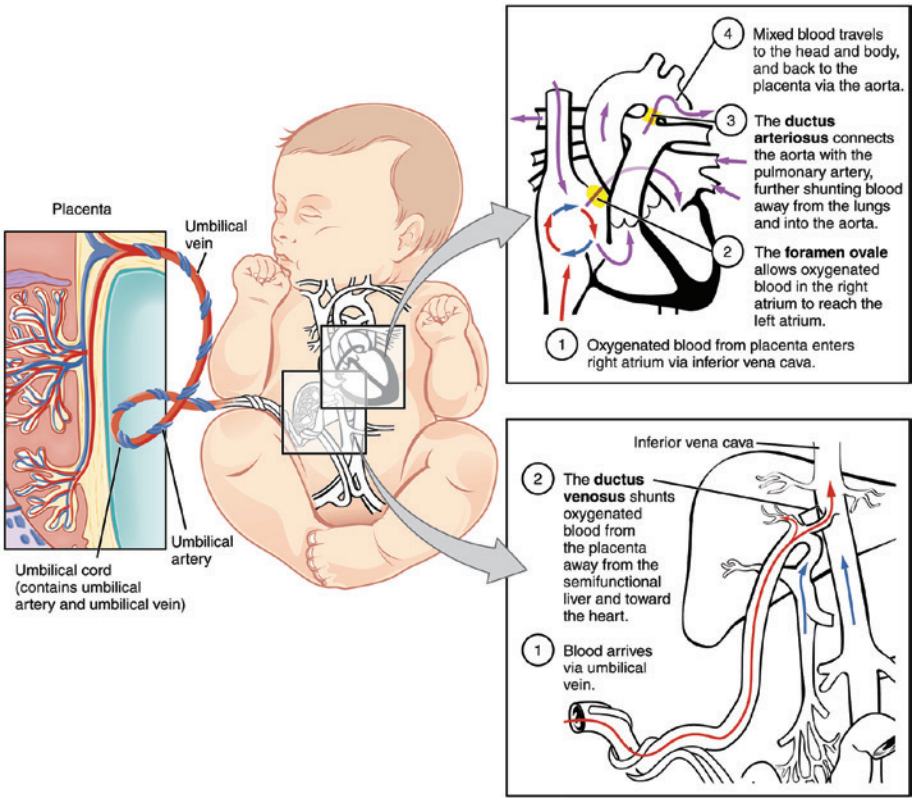


Figure 27.9 Fetal Circulatory System. The fetal circulatory system includes three shunts to divert blood from undeveloped and partially functioning organs as well as blood supply to and from the placenta.

through the **foramen ovale**, a shunt that directly connects the right and left atria and avoids the pulmonary trunk altogether. Most of the rest of the blood is pumped to the right ventricle and, from there, into the pulmonary trunk, which splits into pulmonary arteries. However, a shunt within the pulmonary artery, the **ductus arteriosus**, diverts a portion of this blood into the aorta. This ensures that only a small volume of oxygenated blood passes through the immature pulmonary circuit, which has only minor metabolic requirements. Blood vessels of uninflated lungs have high resistance to flow, a condition that encourages blood to flow to the aorta, which presents much lower resistance. The oxygenated blood moves through the foramen ovale into the left atrium, where it mixes with the now deoxygenated blood returning from the pulmonary circuit. This blood then moves into the left ventricle, where it is pumped into the aorta. Some of this blood moves through the coronary arteries into the myocardium, and some moves through the carotid arteries to the brain.

The descending aorta carries partially oxygenated and partially deoxygenated blood into the lower regions of the body. It eventually passes into the

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umbilical arteries through branches of the internal iliac arteries. The deoxygenated blood collects waste as it circulates through the fetal body and returns to the umbilical cord. Thus, the two umbilical arteries carry blood low in oxygen and high in carbon dioxide and fetal wastes. This blood is filtered through the placenta, where wastes diffuse into the maternal circulation. Oxygen and nutrients from the pregnant person diffuse into the placenta and from there into the fetal blood, and the process repeats.

Other Organ Systems

During weeks 9–12 of fetal development, the brain continues to expand, the body elongates, and ossification continues. Fetal movements are frequent during this period but are jerky and not well controlled. The bone marrow begins to take over the process of erythrocyte production—a task that the liver performed during the embryonic period. The liver now secretes bile. The fetus circulates amniotic fluid by swallowing it and producing urine. The eyes are well developed by this stage, but the eyelids are fused shut. The fingers and toes begin to develop nails. By the end of week 12, the fetus measures approximately 9 cm (3.5 in) from crown to rump.

Weeks 13–16 are marked by sensory organ development. The eyes move closer together; blinking motions begin, although the eyes remain sealed shut. The lips exhibit sucking motions. The ears move upward and lie flatter against the head. The scalp begins to grow hair. The excretory system is also developing: The kidneys are well formed, and **meconium**, or fetal feces, begins to accumulate in the intestines. Meconium consists of ingested amniotic fluid, cellular debris, mucus, and bile.

During approximately weeks 16–20, as the fetus grows and limb movements become more powerful, the pregnant person may begin to feel **quickening**, or fetal movements. However, space restrictions limit these movements and typically force the growing fetus into the "fetal position," with the arms crossed and the legs bent at the knees.

Sebaceous glands coat the skin with a waxy, protective substance called **vernix caseosa** that protects and moisturizes the skin and may provide lubrication during childbirth. A silky hair called **lanugo** also covers the skin during weeks 17–20, but it is shed as the fetus continues to grow. Extremely premature infants sometimes exhibit residual lanugo.

Developmental weeks 21–30 are characterized by rapid weight gain, which is important for maintaining a stable body temperature after birth. The bone marrow completely takes over erythrocyte synthesis, and the axons of the spinal cord begin to be myelinated, or coated in the electrically insulating glial cell sheaths that are necessary for efficient nervous system functioning. (The process

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of myelination is not completed until adolescence.) During this period, the fetus grows eyelashes. The eyelids are no longer fused and can be opened and closed. The lungs begin producing surfactant, a substance that reduces surface tension in the lungs and assists proper lung expansion after birth. Inadequate surfactant production in premature newborns may result in respiratory distress syndrome, and as a result, the newborn may require surfactant replacement therapy, supplemental oxygen, or maintenance in a continuous positive airway pressure (CPAP) chamber during their first days or weeks of life. In male fetuses, the testes descend into the scrotum near the end of this period. The fetus at 30 weeks measures 28 cm (11 in) from crown to rump and exhibits the approximate body proportions of a full-term newborn but still is much leaner.

Interactive Link 27.4

Visit this site (http://oer.aupress.ca/oer-202505/27.4) for a summary of the stages of pregnancy, as experienced by the pregnant person, and view the stages of development of the fetus throughout gestation. At what point in fetal development can a regular heartbeat be detected?

The fetus continues to lay down subcutaneous fat from week 31 until birth. The added fat fills out the hypodermis, and the skin transitions from red and wrinkled to soft and pink. Lanugo is shed, and the nails grow to the tips of the fingers and toes. Immediately before birth, the average crown-to-rump length is 35.5–40.5 cm (14–16 in), and the fetus weighs approximately 2.5–4 kg (5.5–8.8 lbs). Once born, the newborn is no longer confined to the fetal position, so subsequent measurements are made from head to toe instead of from crown to rump. At birth, the average length is approximately 51 cm (20 in).

27.4 Changes During Pregnancy, Labour, and Birth

Learning Objectives

By the end of this section, you will be able to:

- Explain how estrogen, progesterone, and hCG are involved in maintaining pregnancy
- List the contributors to weight gain during pregnancy
- Describe the major changes to the maternal digestive, circulatory, and integumentary systems during pregnancy

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- Summarize the events leading to labour
- Identify and describe each of the three stages of childbirth

A full-term pregnancy lasts approximately 270 days (approximately 38.5 weeks) from conception to birth. Because it is easier to remember the first day of the last menstrual period (LMP) than to estimate the date of conception, obstetricians set the due date as 284 days (approximately 40.5 weeks) from the LMP. This assumes that conception occurred on day 14 of the menstrual cycle, which is usually a good approximation. The 40 weeks of an average pregnancy are usually discussed in terms of three **trimesters**, each approximately 13 weeks. During the second and third trimesters, the prepregnancy uterus—about the size of a fist—grows dramatically to contain the fetus, causing a number of anatomical changes in the pregnant person (Figure 27.10).

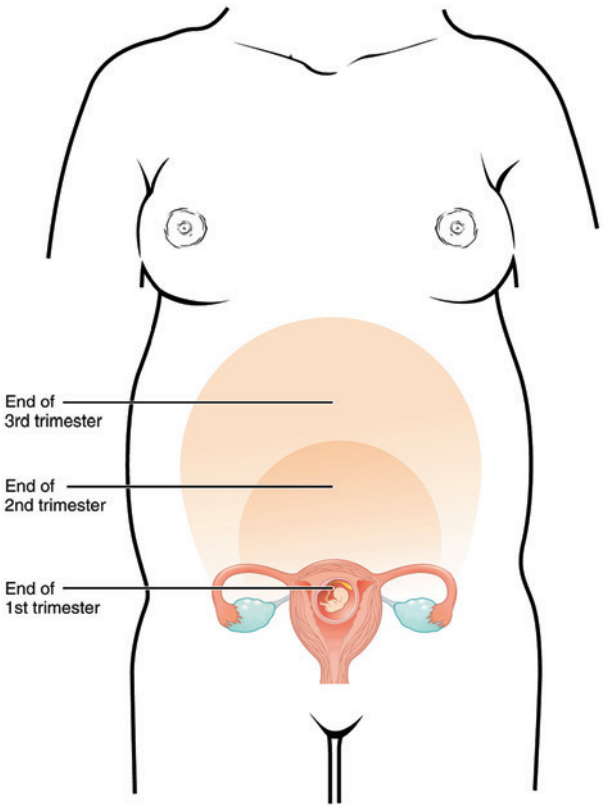


Figure 27.10 Size of Uterus Throughout Pregnancy. The uterus grows throughout pregnancy to accommodate the fetus.

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Effects of Hormones

Virtually all of the effects of pregnancy can be attributed in some way to the influence of hormones—particularly estrogens, progesterone, and hCG. During weeks 7–12 from the LMP, the pregnancy hormones are primarily generated by the corpus luteum. Progesterone secreted by the corpus luteum stimulates the production of decidual cells of the endometrium that nourish the blastocyst before placentation. As the placenta develops and the corpus luteum degenerates during weeks 12–17, the placenta gradually takes over as the endocrine organ of pregnancy.

The placenta converts weak androgens secreted by the maternal and fetal adrenal glands to estrogens, which are necessary for pregnancy to progress. Estrogen levels climb throughout the pregnancy, increasing 30-fold by childbirth. Estrogens have the following actions:

- They suppress FSH and LH production, effectively preventing ovulation. (This function is the biological basis of hormonal birth control pills.)
- They induce the growth of fetal tissues and are necessary for the maturation of the fetal lungs and liver.
- They promote fetal viability by regulating progesterone production and triggering fetal synthesis of cortisol, which helps with the maturation of the lungs, liver, and endocrine organs such as the thyroid gland and adrenal gland.
- They stimulate maternal tissue growth, leading to uterine enlargement and mammary duct expansion and branching.

Relaxin, another hormone secreted by the corpus luteum and then by the placenta, helps prepare the body for childbirth. It increases the elasticity of the symphysis pubis joint and pelvic ligaments, making room for the growing fetus and allowing expansion of the pelvic outlet for childbirth. Relaxin also helps dilate the cervix during labour.

The placenta takes over the synthesis and secretion of progesterone throughout pregnancy as the corpus luteum degenerates. Like estrogen, progesterone suppresses FSH and LH. It also inhibits uterine contractions, protecting the fetus from preterm birth. This hormone decreases in late gestation, allowing uterine contractions to intensify and eventually progress to true labour. The placenta also produces hCG. In addition to promoting survival of the corpus luteum, hCG stimulates the male fetal gonads to secrete testosterone, which is essential for the development of the male reproductive system.

The anterior pituitary enlarges and ramps up its hormone production during pregnancy, raising the levels of thyrotropin, prolactin, and adrenocorticotropic

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hormone (ACTH). Thyrotropin, in conjunction with placental hormones, increases the production of thyroid hormone, which raises the maternal metabolic rate. This can markedly augment a pregnant person's appetite and cause hot flashes. Prolactin stimulates enlargement of the mammary glands in preparation for milk production. ACTH stimulates maternal cortisol secretion, which contributes to fetal protein synthesis. In addition to the pituitary hormones, increased parathyroid levels mobilize calcium from maternal bones for fetal use.

Weight Gain

The second and third trimesters of pregnancy are associated with dramatic changes in maternal anatomy and physiology. The most obvious anatomical sign of pregnancy is the dramatic enlargement of the abdominal region, coupled with weight gain. This weight results from the growing fetus as well as the enlarged uterus, amniotic fluid, and placenta. Additional breast tissue and dramatically increased blood volume also contribute to weight gain. Surprisingly, fat storage accounts for only approximately 2.3 kg (5 lbs) in a normal pregnancy and serves as a reserve for the increased metabolic demand of breastfeeding.

During the first trimester, a pregnant person does not need to consume additional calories to maintain a healthy pregnancy. However, a weight gain of approximately 0.45 kg (1 lb) per month is common. During the second and third trimesters, the appetite increases, but it is only necessary to consume an additional 300 calories per day to support the growing fetus. Most pregnant people gain approximately 0.45 kg (1 lb) per week.

Changes in Organ Systems During Pregnancy

As the body adapts to pregnancy, characteristic physiologic changes occur. These changes can sometimes prompt symptoms often referred to collectively as the common discomforts of pregnancy.

Digestive and Urinary System Changes

Nausea and vomiting, sometimes triggered by an increased sensitivity to odours, are common during the first few weeks to months of pregnancy. This phenomenon is often referred to as "morning sickness," although the nausea may persist all day. The source of pregnancy nausea is thought to be the increased circulation of pregnancy-related hormones, specifically circulating estrogen, progesterone, and hCG. Decreased intestinal peristalsis may also contribute to nausea. By about week 12 of pregnancy, nausea typically subsides.

A common gastrointestinal complaint during the later stages of pregnancy is gastric reflux, or heartburn, which results from the upward, constrictive pressure of the growing uterus on the stomach. The same decreased peristalsis that

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may contribute to nausea in early pregnancy is also thought to be responsible for pregnancy-related constipation as pregnancy progresses.

The downward pressure of the uterus also compresses the urinary bladder, leading to frequent urination. The problem is exacerbated by increased urine production. In addition, the maternal urinary system processes both maternal and fetal wastes, further increasing the total volume of urine.

Circulatory System Changes

Blood volume increases substantially during pregnancy so that by childbirth, it exceeds its preconception volume by 30 percent, or approximately 1–2 L. The greater blood volume helps manage the demands of fetal nourishment and fetal waste removal. In conjunction with increased blood volume, the pulse and blood pressure also rise moderately during pregnancy. As the fetus grows, the uterus compresses underlying pelvic blood vessels, hampering venous return from the legs and pelvic region. As a result, many pregnant people develop varicose veins or hemorrhoids.

Respiratory System Changes

During the second half of pregnancy, the respiratory minute volume (volume of gas inhaled or exhaled by the lungs per minute) increases by 50 percent to compensate for the oxygen demands of the fetus and the increased maternal metabolic rate. The growing uterus exerts upward pressure on the diaphragm, decreasing the volume of each inspiration and potentially causing shortness of breath, or dyspnea. During the last several weeks of pregnancy, the pelvis becomes more elastic, and the fetus descends lower in a process called lightening. This typically ameliorates dyspnea.

The respiratory mucosa swells in response to increased blood flow during pregnancy, leading to nasal congestion and nose bleeds, particularly when the weather is cold and dry. Humidifier use and increased fluid intake are often recommended to counteract congestion.

Integumentary System Changes

The dermis stretches extensively to accommodate the growing uterus, breast tissue, and fat deposits on the thighs and hips. Torn connective tissue beneath the dermis can cause striae (stretch marks) on the abdomen, which appear as red or purple marks during pregnancy that fade to a silvery white colour in the months after childbirth.

An increase in melanocyte-stimulating hormone, in conjunction with estrogens, darkens the areolae and creates a line of pigment from the umbilicus to the pubis called the linea nigra.

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Physiology of Labour

Childbirth, or **parturition**, typically occurs within a week of the due date, unless the pregnancy involves more than one fetus, which usually causes labour to begin early. As a pregnancy progresses into its final weeks, several physiological changes occur in response to hormones that trigger labour.

First, recall that progesterone inhibits uterine contractions throughout the first several months of pregnancy. As the pregnancy enters its seventh month, progesterone levels plateau and then drop. Estrogen levels, however, continue to rise in the maternal circulation (Figure 27.11). The increasing ratio of estrogen to progesterone makes the myometrium (the uterine smooth muscle) more sensitive to stimuli that promote contractions (because progesterone no longer inhibits them). Moreover, in the eighth month of pregnancy, fetal cortisol rises, which boosts estrogen secretion by the placenta and further overpowers the uterine-calming effects of progesterone. Some people may feel the result of the decreasing levels of progesterone in late pregnancy as weak and irregular peristaltic **Braxton Hicks contractions**, also called false labour. These contractions can often be relieved with rest or hydration.

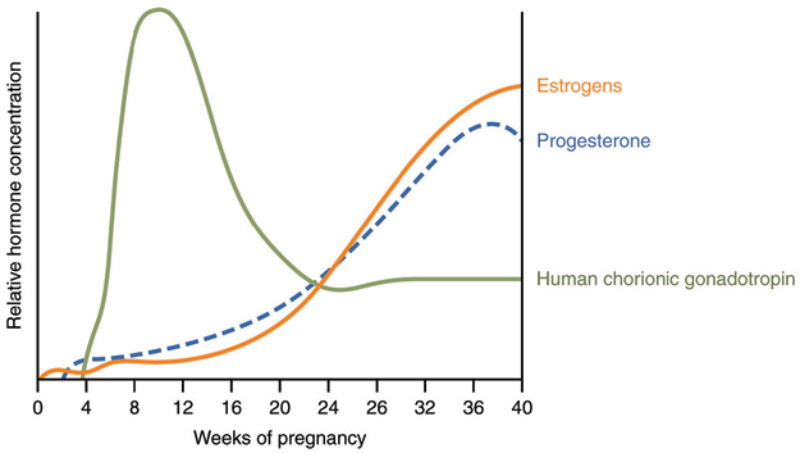


Figure 27.11 Hormones Initiating Labour. A positive feedback loop of hormones works to initiate labour.

A common sign that labour will be short is the so-called bloody show. During pregnancy, a plug of mucus accumulates in the cervical canal, blocking the entrance to the uterus. Approximately 1–2 days prior to the onset of true labour, this plug loosens and is expelled, along with a small amount of blood.

Meanwhile, the posterior pituitary has been boosting its secretion of **oxytocin**, a hormone that stimulates the contractions of labour. At the same time, the

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myometrium increases its sensitivity to oxytocin by expressing more receptors for this hormone. As labour nears, oxytocin begins to stimulate stronger, more painful uterine contractions, which—in a positive feedback loop—stimulate the secretion of prostaglandins from fetal membranes. Like oxytocin, prostaglandins also enhance uterine contractile strength. The fetal pituitary also secretes oxytocin, which increases prostaglandins even further. Given the importance of oxytocin and prostaglandins to the initiation and maintenance of labour, it is not surprising that when a pregnancy is not progressing to labour and needs to be induced, a pharmaceutical version of these compounds (called pitocin) is administered by intravenous drip.

Finally, stretching of the myometrium and cervix by a full-term fetus in the vertex (head-down) position is regarded as a stimulant to uterine contractions. The sum of these changes initiates the regular contractions known as **true labour**, which become more powerful and more frequent with time. The pain of labour is attributed to myometrial hypoxia during uterine contractions.

Stages of Childbirth

The process of childbirth can be divided into three stages: cervical dilation, expulsion of the newborn, and afterbirth (Figure 27.12).

Cervical Dilation

For vaginal birth to occur, the cervix must dilate fully to 10 cm in diameter—wide enough to deliver the newborn's head. The **dilation** stage is the longest stage of labour and typically takes 6–12 hours. However, it varies widely and may take minutes, hours, or days, depending in part on whether the person has given birth before; in each subsequent labour, this stage tends to be shorter.

True labour progresses in a positive feedback loop in which uterine contractions stretch the cervix, causing it to dilate and efface, or become thinner. Cervical stretching induces reflexive uterine contractions that dilate and efface the cervix further. In addition, cervical dilation boosts oxytocin secretion from the pituitary, which in turn triggers more powerful uterine contractions. When labour begins, uterine contractions may occur only every 3–30 minutes and last only 20–40 seconds; however, by the end of this stage, contractions may occur as frequently as every 1.5–2 minutes and last for a full minute.

Each contraction sharply reduces oxygenated blood flow to the fetus. For this reason, it is critical that a period of relaxation occur after each contraction. Fetal distress, measured as a sustained decrease or increase in the fetal heart rate, can result from severe contractions that are too powerful or lengthy for oxygenated blood to be restored to the fetus. Such a situation can be cause for an emergency birth with vacuum or forceps or surgically by Cesarean section.

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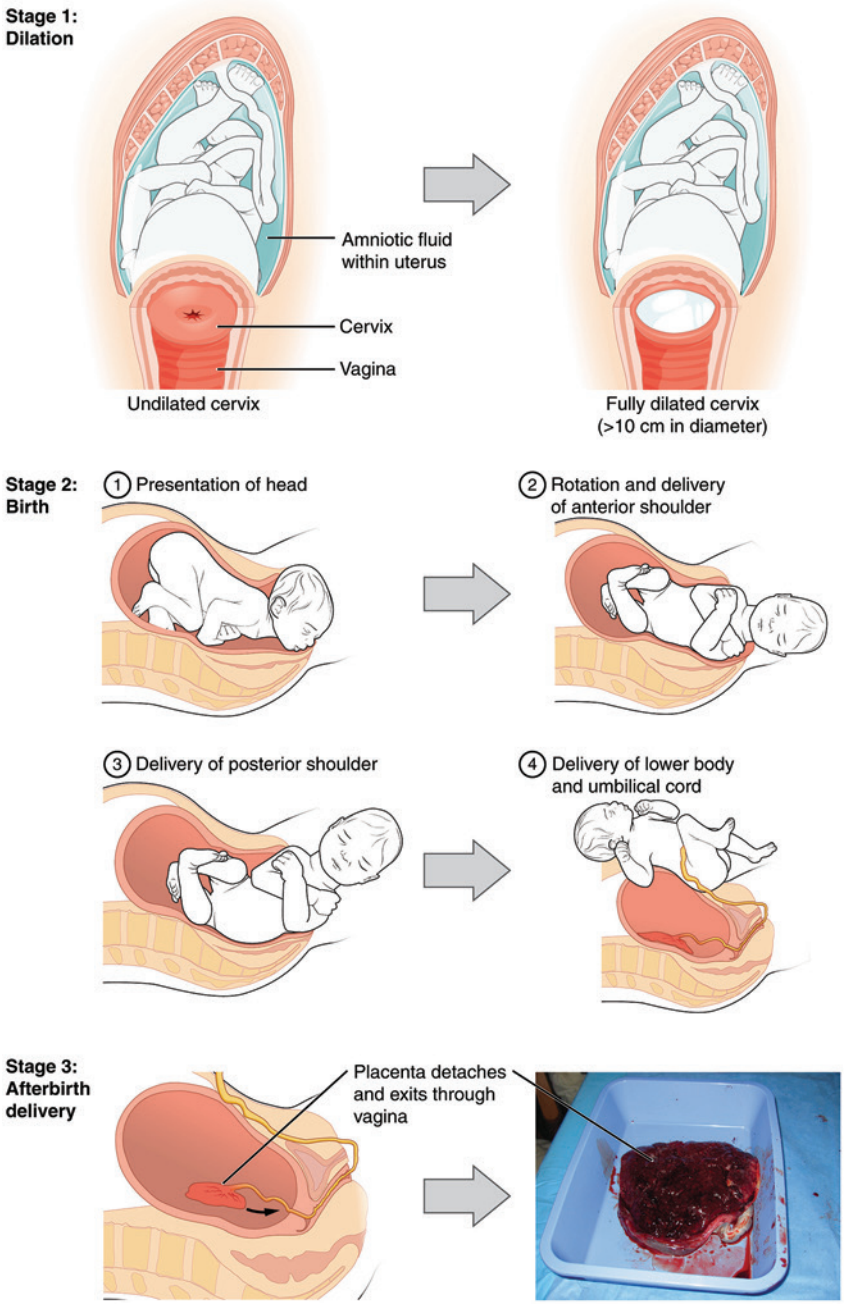


Figure 27.12 Stages of Childbirth. The stages of childbirth include Stage 1, early cervical dilation; Stage 2, full dilation and expulsion of the newborn; and Stage 3, delivery of the placenta and associated fetal membranes. (The position of the newborn's shoulder is described relative to the person giving birth.)

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The amniotic membranes rupture before the onset of labour in about 12 percent of people; they typically rupture at the end of the dilation stage in response to excessive pressure from the fetal head entering the birth canal.

Expulsion Stage

The **expulsion** stage begins when the fetal head enters the birth canal and ends with the birth of the newborn. It typically takes up to 2 hours, but it can last longer or be completed in minutes, depending in part on the orientation of the fetus. The vertex presentation known as the occiput anterior vertex is the most common presentation and is associated with the greatest ease of vaginal birth. The fetus faces the maternal spinal cord, and the smallest part of the head (the posterior aspect called the occiput) exits the birth canal first.

In fewer than 5 percent of births, the infant is oriented in the breech presentation, or buttocks down. In a complete breech, both legs are crossed and oriented downward. In a frank breech presentation, the legs are oriented upward. Before the 1960s, it was common for breech presentations to be delivered vaginally. Today, most breech births are accomplished by Cesarean section.

Vaginal birth is associated with significant stretching of the vaginal canal, the cervix, and the perineum. Until recent decades, it was routine procedure for an obstetrician to numb the perineum and perform an episiotomy, an incision in the posterior vaginal wall and perineum. The perineum is now more commonly allowed to tear on its own during birth. Both an episiotomy and a perineal tear need to be sutured shortly after birth to ensure optimal healing.

Although suturing the jagged edges of a perineal tear may be more difficult than suturing an episiotomy, tears heal more quickly, are less painful, and are associated with less damage to the muscles around the vagina and rectum.

Upon birth of the newborn's head, an obstetrician will aspirate mucus from the mouth and nose before the newborn's first breath. Once the head is birthed, the rest of the body usually follows quickly. The umbilical cord is then double clamped, and a cut is made between the clamps. This completes the second stage of childbirth.

Afterbirth

The delivery of the placenta and associated membranes, commonly referred to as the **afterbirth**, marks the final stage of childbirth. After expulsion of the newborn, the myometrium continues to contract. This movement shears the placenta from the back of the uterine wall. It is then easily delivered through the vagina. Continued uterine contractions then reduce blood loss from the site of the placenta. Delivery of the placenta marks the beginning of the postpartum period—the period of approximately 6 weeks immediately following

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childbirth during which the body gradually returns to a nonpregnant state. If the placenta does not birth spontaneously within approximately 30 minutes, it is considered retained, and the obstetrician may attempt manual removal. If this is not successful, surgery may be required.

It is important that the obstetrician examines the expelled placenta and fetal membranes to ensure that they are intact. If fragments of the placenta remain in the uterus, they can cause postpartum hemorrhage. Uterine contractions continue for several hours after birth to return the uterus to its prepregnancy size in a process called **involution**, which also allows the abdominal organs to return to their prepregnancy locations. Breastfeeding facilitates this process.

Although postpartum uterine contractions limit blood loss from the detachment of the placenta, the person who has recently given birth does experience a postpartum vaginal discharge called lochia. This is made up of uterine lining cells, erythrocytes, leukocytes, and other debris. Thick, dark lochia rubra (red lochia) typically continues for 2–3 days, and is replaced by lochia serosa, a thinner pinkish form that continues until about the tenth postpartum day. After this period, a scant, creamy, or watery discharge called lochia alba (white lochia) may continue for another 1–2 weeks.

27.5 Adjustments of the Infant at Birth and Postnatal Stages

Learning Objectives

By the end of this section, you will be able to:

- Discuss the importance of an infant's first breath
- Explain the closing of the cardiac shunts
- Describe thermoregulation in the newborn
- Summarize the importance of intestinal flora in the newborn

From a fetal perspective, the process of birth is a crisis. In the womb, the fetus was snuggled in a soft, warm, dark, and quiet world. The placenta provided nutrition and oxygen continuously. Suddenly, the contractions of labour and vaginal childbirth forcibly squeeze the fetus through the birth canal, limiting oxygenated blood flow during contractions and shifting the skull bones to accommodate the small space. After birth, the newborn's system must make drastic adjustments to a world that is colder, brighter, and louder and where they will experience hunger and thirst. The neonatal period spans the first to the thirtieth day of life outside of the uterus.

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Respiratory Adjustments

Although the fetus "practices" breathing by inhaling amniotic fluid in utero, there is no air in the uterus and thus no true opportunity to breathe. (There is also no need to breathe because the placenta supplies the fetus with all the oxygenated blood it needs.) During gestation, the partially collapsed lungs are filled with amniotic fluid and exhibit very little metabolic activity. Several factors stimulate newborns to take their first breath at birth. First, labour contractions temporarily constrict umbilical blood vessels, reducing oxygenated blood flow to the fetus and elevating carbon dioxide levels in the blood. High carbon dioxide levels cause acidosis and stimulate the respiratory centre in the brain, triggering the newborn to take a breath.

The first breath typically is taken within 10 seconds of birth, after mucus is aspirated from the infant's mouth and nose. The first breaths inflate the lungs to nearly full capacity and dramatically decrease lung pressure and resistance to blood flow, causing a major circulatory reconfiguration. Pulmonary alveoli open, and alveolar capillaries fill with blood. Amniotic fluid in the lungs drains or is absorbed, and the lungs immediately take over the task of the placenta, exchanging carbon dioxide for oxygen by the process of respiration.

Circulatory Adjustments

The process of clamping and cutting the umbilical cord collapses the umbilical blood vessels. In the absence of medical assistance, this occlusion would occur naturally within 20 minutes of birth because the Wharton's jelly within the umbilical cord would swell in response to the lower temperature outside of the mother's body, and the blood vessels would constrict. Natural occlusion has occurred when the umbilical cord is no longer pulsating. For the most part, the collapsed vessels atrophy and become fibrotic remnants, existing in the mature circulatory system as ligaments of the abdominal wall and liver. The ductus venosus degenerates to become the ligamentum venosum beneath the liver. Only the proximal sections of the two umbilical arteries remain functional, taking on the role of supplying blood to the upper part of the bladder (Figure 27.13).

The newborn's first breath is vital to initiate the transition from the fetal to the neonatal circulatory pattern. Inflation of the lungs decreases blood pressure throughout the pulmonary system as well as in the right atrium and ventricle. In response to this pressure change, the flow of blood temporarily reverses direction through the foramen ovale, moving from the left to the right atrium, and blocking the shunt with two flaps of tissue. Within 1 year, the tissue flaps usually fuse over the shunt, turning the foramen ovale into the fossa ovalis. The ductus arteriosus constricts as a result of increased oxygen concentration

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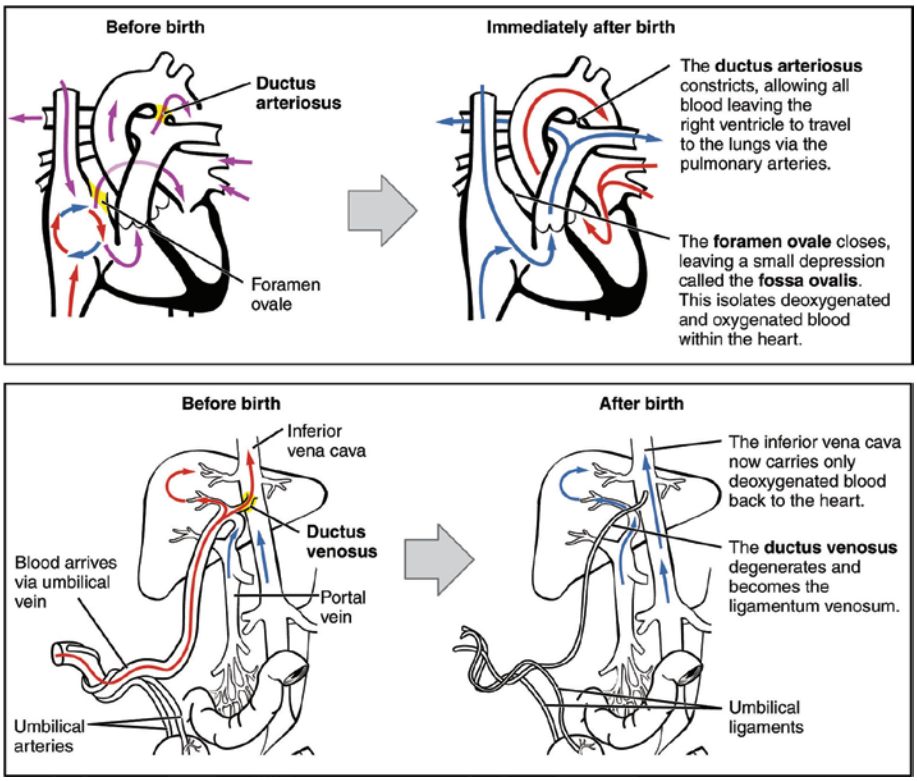


Figure 27.13 Neonatal Circulatory System. A newborn's circulatory system reconfigures immediately after birth. The three fetal shunts have been closed permanently, facilitating blood flow to the liver and lungs.

and becomes the ligamentum arteriosum. Closing of the ductus arteriosus ensures that all blood pumped to the pulmonary circuit will be oxygenated by the newly functional neonatal lungs.

Thermoregulatory Adjustments

The fetus floats in warm amniotic fluid that is maintained at a temperature of approximately 37°C with very little fluctuation. Birth exposes newborns to a cooler environment in which they have to regulate their own body temperature. Newborns have a higher ratio of surface area to volume than adults. This means that their body has less volume throughout which to produce heat and more surface area from which to lose heat. As a result, newborns produce heat more slowly and lose it more quickly. Newborns also have immature musculature that limits their ability to generate heat by shivering. Moreover, their nervous systems are underdeveloped, so they cannot quickly constrict superficial blood vessels in response to cold. They also have little subcutaneous fat for insulation. All these factors make it harder for newborns to maintain their body temperature.

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Newborns, however, do have a special method for generating heat: **non-shivering thermogenesis**, which involves the breakdown of **brown adipose tissue**, or brown fat, which is distributed over the back, chest, and shoulders. Brown fat differs from the more familiar white fat in two ways:

- It is highly vascularized. This allows for faster delivery of oxygen, which leads to faster cellular respiration.
- It is packed with a special type of mitochondria that are able to engage in cellular respiration reactions that produce less ATP and more heat than standard cellular respiration reactions.

The breakdown of brown fat occurs automatically upon exposure to cold, so it is an important heat regulator in newborns. During fetal development, the placenta secretes inhibitors that prevent metabolism of brown adipose fat and promote its accumulation in preparation for birth.

Gastrointestinal and Urinary Adjustments

In adults, the gastrointestinal tract harbors bacterial flora—trillions of bacteria that aid in digestion, produce vitamins, and protect from the invasion or replication of pathogens. In stark contrast, the fetal intestine is sterile. The first consumption of breast milk or formula floods the neonatal gastrointestinal tract with beneficial bacteria that begin to establish the bacterial flora.

The fetal kidneys filter blood and produce urine, but the neonatal kidneys are still immature and inefficient at concentrating urine. Therefore, newborns produce very dilute urine, making it particularly important for infants to obtain sufficient fluids from breast milk or formula.

27.6 Lactation

Learning Objectives

By the end of this section, you will be able to:

- Describe the structure of the lactating breast
- Summarize the process of lactation
- Explain how the composition of breast milk changes during the first days of lactation and in the course of a single feeding

Lactation is the process by which milk is synthesized and secreted from the mammary glands of the postpartum female breast in response to an infant sucking at the nipple. Breast milk provides ideal nutrition and passive immunity

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for the infant, encourages mild uterine contractions to return the uterus to its prepregnancy size (i.e., involution), and induces a substantial metabolic increase in the postpartum person, consuming the fat reserves stored during pregnancy.

Structure of the Lactating Breast

Mammary glands are modified sweat glands. The nonpregnant and nonlactating female breast is composed primarily of adipose and collagenous tissue, with mammary glands making up a very minor proportion of breast volume. The mammary gland is composed of milk-transporting lactiferous ducts, which expand and branch extensively during pregnancy in response to estrogen, growth hormone, cortisol, and prolactin. Moreover, in response to progesterone, clusters of breast alveoli bud from the ducts and expand outward toward the chest wall. Breast alveoli are balloon-like structures lined with milk-secreting cuboidal cells, or lactocytes, that are surrounded by a net of contractile myoepithelial cells. Milk is secreted from the lactocytes, fills the alveoli, and is squeezed into the ducts. Clusters of alveoli that drain to a common duct are called lobules; the lactating female has 12–20 lobules organized radially around the nipple. Milk drains from lactiferous ducts into lactiferous sinuses that meet at 4 to 18 perforations in the nipple called nipple pores. The small bumps of the areola (the darkened skin around the nipple) are called Montgomery glands. They secrete oil to cleanse the nipple opening and prevent chapping and cracking of the nipple during breastfeeding.

The Process of Lactation

The pituitary hormone **prolactin** is instrumental in the establishment and maintenance of breast milk supply. It also is important for the mobilization of maternal micronutrients for breast milk.

Near the fifth week of pregnancy, the level of circulating prolactin begins to increase, eventually rising to approximately 10–20 times the prepregnancy concentration. We noted earlier that during pregnancy, prolactin and other hormones prepare the breasts anatomically for the secretion of milk. The level of prolactin plateaus in late pregnancy at a level high enough to initiate milk production. However, estrogen, progesterone, and other placental hormones inhibit prolactin-mediated milk synthesis during pregnancy. It is not until the placenta is expelled that this inhibition is lifted and milk production commences.

After childbirth, the baseline prolactin level drops sharply, but it is restored for a 1-hour spike during each feeding to stimulate the production of milk for the next feeding. With each prolactin spike, estrogen and progesterone also increase slightly.

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When the infant suckles, sensory nerve fibres in the areola trigger a neuroendocrine reflex that results in milk secretion from lactocytes into the alveoli. The posterior pituitary releases, which stimulates myoepithelial cells to squeeze milk from the alveoli so it can drain into the lactiferous ducts, collect in the lactiferous sinuses, and discharge through the nipple pores. It takes less than 1 minute from the time when an infant begins suckling (the latent period) until milk is secreted (the letdown). Figure 27.14 summarizes the positive feedback loop of the **letdown reflex**.

The prolactin-mediated synthesis of milk changes with time. Frequent milk removal by breastfeeding (or pumping) will maintain high circulating prolactin levels for several months. However, even with continued breastfeeding, baseline prolactin will decrease over time to its prepregnancy level. In addition to prolactin and oxytocin, growth hormone, cortisol, parathyroid hormone, and

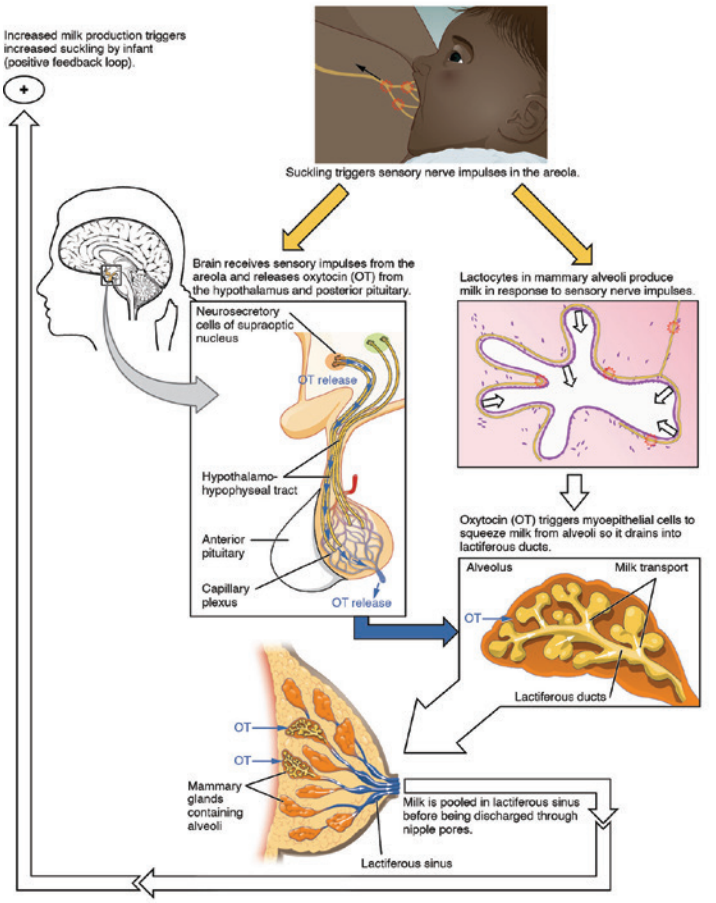


Figure 27.14 Letdown Reflex. A positive feedback loop ensures continued milk production as long as the infant continues to breastfeed.

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insulin contribute to lactation, in part by facilitating the transport of maternal amino acids, fatty acids, glucose, and calcium to breast milk.

Changes in the Composition of Breast Milk

In the final weeks of pregnancy, the alveoli swell with **colostrum**, a thick, yellowish substance that is high in protein but contains less fat and glucose than mature breast milk. Before childbirth, some people experience leakage of colostrum from the nipples. In contrast, mature breast milk does not leak during pregnancy and is not secreted until several days after childbirth.

Colostrum is secreted during the first 48–72 hours postpartum. Only a small volume of colostrum is produced—approximately 88 mL in a 24-hour period—but it is sufficient for the newborn in the first few days of life. Colostrum is rich with immunoglobulins, which confer gastrointestinal, and also likely systemic, immunity as the newborn adjusts to a nonsterile environment.

After about the third postpartum day, the breast secretes transitional milk that represents an intermediate between mature milk and colostrum. This is followed by mature milk from approximately postpartum day 10. Cow's milk is not a substitute for breast milk. It contains less lactose, less fat, and more protein and minerals. Moreover, the proteins in cow's milk are difficult for an infant's immature digestive system to metabolize and absorb.

The first few weeks of breastfeeding may involve leakage, soreness, and periods of milk engorgement as the relationship between milk supply and infant demand becomes established. Once this period is complete, the lactating person will produce approximately 1.5 L of milk per day for a single infant, and more if the person has twins or triplets. As the infant goes through growth spurts, the milk supply constantly adjusts to accommodate changes in demand. A person can continue to lactate for years, but once breastfeeding is stopped for approximately 1 week, any remaining milk will be reabsorbed; in most cases, no more will be produced, even if suckling or pumping is resumed.

Mature milk changes from the beginning to the end of a feeding. The early milk, called foremilk, is watery, translucent, and rich in lactose and protein. Its purpose is to quench the infant's thirst. Hindmilk is delivered toward the end of a feeding. It is opaque, creamy, and rich in fat, and serves to satisfy the infant's appetite.

During the first days of a newborn's life, it is important for meconium to be cleared from the intestines and for bilirubin to be kept low in the circulation. Recall that bilirubin, a product of erythrocyte breakdown, is processed by the liver and secreted in bile. It enters the gastrointestinal tract and exits the body in the stool. Breast milk has laxative properties that help expel meconium from the intestines and clear bilirubin through the excretion of bile. A high concentration

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of bilirubin in the blood causes jaundice. Some degree of jaundice is normal in newborns, but a high level of bilirubin—which is neurotoxic—can cause brain damage. Newborns, who do not yet have a fully functional blood-brain barrier, are highly vulnerable to the bilirubin circulating in the blood. Indeed, hyperbilirubinemia, a high level of circulating bilirubin, is the most common condition requiring medical attention in newborns. Newborns with hyperbilirubinemia are treated with phototherapy because UV light helps break down the bilirubin quickly.

Key Terms

acrosomal reaction: Release of digestive enzymes by sperm that enables them to burrow through the corona radiata and penetrate the zona pellucida of an oocyte prior to fertilization.

acrosome: Cap-like vesicle located at the anterior-most region of a sperm that is rich with lysosomal enzymes capable of digesting the protective layers surrounding the oocyte.

afterbirth: Third stage of childbirth in which the placenta and associated fetal membranes are expelled.

allantois: Fingerlike outpocketing of yolk sac that forms the primitive excretory duct of the embryo; precursor to the urinary bladder.

amnion: Transparent membranous sac that encloses the developing fetus and fills with amniotic fluid.

amniotic cavity: Cavity that opens up between the inner cell mass and the trophoblast; develops into amnion.

amniotic fluid: Filtrate of maternal plasma and urine.

blastocoel: Fluid-filled cavity of the blastocyst.

blastocyst: Term for the conceptus at the developmental stage that consists of about 100 cells shaped into an inner cell mass that is fated to become the embryo and an outer trophoblast that is fated to become the associated fetal membranes and placenta.

blastomere: Daughter cell of a cleavage.

Braxton Hicks contractions: Weak and irregular peristaltic contractions that can occur in the second and third trimesters; they do not indicate that childbirth is imminent.

brown adipose tissue: Highly vascularized fat tissue packed with mitochondria; these properties confer the ability to oxidize fatty acids to generate heat.

capacitation: Process that occurs in the female reproductive tract in which sperm are prepared for fertilization; leads to increased motility and

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changes in their outer membrane that improve their ability to release enzymes capable of digesting an oocyte's outer layers.

chorion: Membrane that develops from the syncytiotrophoblast, cytotrophoblast, and mesoderm; surrounds the embryo and forms the fetal portion of the placenta through the chorionic villi.

chorionic membrane: Precursor to the chorion; forms from extraembryonic mesoderm cells.

chorionic villi: Projections of the chorionic membrane that burrow into the endometrium and develop into the placenta.

cleavage: Form of mitotic cell division in which the cell divides but the total volume remains unchanged; this process serves to produce smaller and smaller cells.

colostrum: Thick, yellowish substance secreted from a mother's breasts in the first postpartum days; rich in immunoglobulins.

conceptus: Preimplantation stage of a fertilized egg and its associated membranes.

corona radiata: In an oocyte, a layer of granulosa cells that surrounds the oocyte and that must be penetrated by sperm before fertilization can occur.

cortical reaction: Following fertilization, the release of cortical granules from the oocyte's plasma membrane into the zona pellucida, creating a fertilization membrane that prevents any further attachment or penetration of sperm; part of the slow block to polyspermy.

dilation: First stage of childbirth, involving an increase in cervical diameter.

ductus arteriosus: Shunt in the pulmonary trunk that diverts oxygenated blood back to the aorta.

ductus venosus: Shunt that causes oxygenated blood to bypass the fetal liver on its way to the inferior vena cava.

ectoderm: Primary germ layer that develops into the central and peripheral nervous systems, sensory organs, epidermis, hair, and nails.

ectopic pregnancy: Implantation of an embryo outside of the uterus.

embryo: Developing human during weeks 3–8.

embryonic disc: Composed of embryonic cells and the amniotic cavity.

embryonic folding: Process by which an embryo develops from a flat disc of cells to a three-dimensional shape resembling a cylinder.

endoderm: Primary germ layer that goes on to form the gastrointestinal tract, liver, pancreas, and lungs.

expulsion: Second stage of childbirth, during which the mother bears down with contractions; this stage ends in birth.

fertilization: Unification of genetic material from male and female haploid gametes.

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fertilization membrane: Impenetrable barrier that coats a nascent zygote; part of the slow block to polyspermy.

fetus: Developing human during the time from the end of the embryonic period (week 9) to birth.

foramen ovale: Shunt that directly connects the right and left atria and helps divert oxygenated blood from the fetal pulmonary circuit.

gastrulation: Process of cell migration and differentiation into three primary germ layers following cleavage and implantation.

gestation: In human development, the period required for embryonic and fetal development in utero; pregnancy.

human chorionic gonadotropin (hCG): Hormone that directs the corpus luteum to survive, enlarge, and continue producing progesterone and estrogen to suppress menses and secure an environment suitable for the developing embryo.

inner cell mass: Cluster of cells within the blastocyst that is fated to become the embryo.

involution: Postpartum shrinkage of the uterus back to its prepregnancy volume.

lactation: Process by which milk is synthesized and secreted from the mammary glands of the postpartum female breast in response to sucking at the nipple.

lanugo: Silk-like hairs that coat the fetus; shed later in fetal development.

letdown reflex: Release of milk from the alveoli triggered by infant suckling.

meconium: Fetal wastes consisting of ingested amniotic fluid, cellular debris, mucus, and bile.

mesoderm: Primary germ layer that becomes the skeleton, muscles, connective tissue, heart, blood vessels, and kidneys.

morula: Tightly packed sphere of blastomeres that has reached the uterus but has not yet implanted itself.

neural fold: Elevated edge of the neural groove.

neural plate: Thickened layer of neuroepithelium that runs longitudinally along the dorsal surface of an embryo and gives rise to nervous system tissue.

neural tube: Precursor to structures of the central nervous system, formed by the invagination and separation of neuroepithelium.

neurulation: Embryonic process that establishes the central nervous system.

nonshivering thermogenesis: Process of breaking down brown adipose tissue to produce heat in the absence of a shivering response.

notochord: Rod-shaped, mesoderm-derived structure that provides support for the growing fetus.

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organogenesis: Development of the rudimentary structures of all of an embryo's organs from the germ layers.

oxytocin: Hormone released from the anterior pituitary gland that stimulates the contractions of labour.

parturition: Childbirth.

placenta: Organ that forms during pregnancy to nourish the developing fetus; also regulates waste and gas exchange between mother and fetus.

placenta previa: Low placement of fetus within the uterus that causes the placenta to partially or completely cover the opening of the cervix as it grows.

placentation: Formation of the placenta; complete by weeks 14–16 of pregnancy.

polyspermy: Penetration of an oocyte by more than one sperm.

primary germ layers: The endoderm, mesoderm, and ectoderm.

primitive streak: Indentation along the dorsal surface of the epiblast through which cells migrate to form the endoderm and mesoderm during gastrulation.

prolactin: Pituitary hormone that establishes and maintains the supply of breast milk; also important for the mobilization of maternal micronutrients for breast milk.

quickening: Fetal movements that are strong enough to be felt by the mother.

shunt: Circulatory shortcut that diverts the flow of blood from one region to another.

somite: One of the paired, repeating blocks of tissue located on either side of the notochord in the early embryo.

syncytiotrophoblast: Superficial cells of the trophoblast that fuse to form a multinucleated body that digests endometrial cells to firmly secure the blastocyst to the uterine wall.

trimester: Division of the duration of a pregnancy into three 3-month terms.

trophoblast: Fluid-filled shell of squamous cells destined to become the chorionic villi, placenta, and associated fetal membranes.

true labour: Regular contractions that immediately precede childbirth; they do not abate with hydration or rest, and they become more frequent and powerful with time.

umbilical cord: Connection between the developing conceptus and the placenta; carries deoxygenated blood and waste from the fetus and returns nutrients and oxygen from the mother.

vernix caseosa: Waxy, cheese-like substance that protects the delicate fetal skin until birth.

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yolk sac: Membrane associated with primitive circulation to the developing embryo; source of the first blood cells and germ cells and contributes to the umbilical cord structure.

zona pellucida: Thick, gel-like glycoprotein membrane that coats the oocyte and must be penetrated by sperm before fertilization can occur.

zygote: Fertilized egg; a diploid cell resulting from the fertilization of haploid gametes from the male and female lines.

Chapter Review

27.1 Fertilization

Hundreds of millions of sperm deposited in the vagina travel toward the oocyte, but only a few hundred actually reach it. The number of sperm that reach the oocyte is greatly reduced because of conditions within the female reproductive tract. Many sperm are overcome by the acidity of the vagina, others are blocked by mucus in the cervix, whereas others are attacked by phagocytic leukocytes in the uterus. Those sperm that do survive undergo a change in response to those conditions. They go through the process of capacitation, which improves their motility and alters the membrane surrounding the acrosome, the cap-like structure in the head of a sperm that contains the digestive enzymes needed for it to attach to and penetrate the oocyte.

The oocyte that is released by ovulation is protected by a thick outer layer of granulosa cells known as the corona radiata and by the zona pellucida, a thick glycoprotein membrane that lies just outside the oocyte's plasma membrane. When capacitated sperm make contact with the oocyte, they release the digestive enzymes in the acrosome (the acrosomal reaction) and are thus able to attach to the oocyte and burrow through to the oocyte's zona pellucida. One of the sperm will then break through to the oocyte's plasma membrane and release its haploid nucleus into the oocyte. The oocyte's membrane structure changes in response (cortical reaction), preventing any further penetration by another sperm and forming a fertilization membrane. Fertilization is complete upon unification of the haploid nuclei of the two gametes, producing a diploid zygote.

27.2 Embryonic Development

As the zygote travels toward the uterus, it undergoes numerous cleavages in which the number of cells doubles (blastomeres). Upon reaching the uterus, the conceptus has become a tightly packed sphere of cells called the morula, which then forms into a blastocyst consisting of an inner cell mass within a fluid-filled cavity surrounded by trophoblasts. The blastocyst implants in the uterine wall, the trophoblasts fuse to form a syncytiotrophoblast, and the conceptus is

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enveloped by the endometrium. Four embryonic membranes form to support the growing embryo: the amnion, the yolk sac, the allantois, and the chorion.

The chorionic villi of the chorion extend into the endometrium to form the fetal portion of the placenta. The placenta supplies the growing embryo with oxygen and nutrients; it also removes carbon dioxide and other metabolic wastes.

Following implantation, embryonic cells undergo gastrulation, in which they differentiate and separate into an embryonic disc and establish three primary germ layers (the endoderm, mesoderm, and ectoderm). Through the process of embryonic folding, the fetus begins to take shape. Neurulation starts the process of the development of structures of the central nervous system, and organogenesis establishes the basic plan for all organ systems.

27.3 Fetal Development

The fetal period lasts from the ninth week of development until birth. During this period, male and female gonads differentiate. The fetal circulatory system becomes much more specialized and efficient than its embryonic counterpart. It includes three shunts—the ductus venosus, the foramen ovale, and the ductus arteriosus—that enable it to bypass the semifunctional liver and pulmonary circuit until after childbirth. The brain continues to grow, and its structures differentiate. Facial features develop, the body elongates, and the skeleton ossifies. In the womb, the developing fetus moves, blinks, practices sucking, and circulates amniotic fluid. The fetus grows from an embryo measuring approximately 3.3 cm (1.3 in) and weighing 7 g (0.25 oz) to an infant measuring approximately 51 cm (20 in) and weighing an average of approximately 3.4 kg (7.5 lbs). Embryonic organ structures that were primitive and nonfunctional develop to the point that the newborn can survive in the outside world.

27.4 Changes During Pregnancy, Labour, and Birth

Hormones (especially estrogens, progesterone, and hCG) secreted by the corpus luteum and later by the placenta are responsible for most of the changes experienced during pregnancy. Estrogen maintains the pregnancy, promotes fetal viability, and stimulates tissue growth in the mother and developing fetus.

Progesterone prevents new ovarian follicles from developing and suppresses uterine contractility.

Pregnancy weight gain primarily occurs in the breasts and abdominal region. Nausea, heartburn, and frequent urination are common during pregnancy.

Maternal blood volume increases by 30 percent during pregnancy, and respiratory minute volume increases by 50 percent. The skin may develop stretch marks, and melanin production may increase.

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Toward the late stages of pregnancy, a drop in progesterone and stretching forces from the fetus lead to increasing uterine irritability and prompt labour.

Contractions serve to dilate the cervix and expel the newborn. Delivery of the placenta and associated fetal membranes follows.

27.5 Adjustments of the Infant at Birth and Postnatal Stages

The first breath a newborn takes at birth inflates the lungs and dramatically alters the circulatory system, closing the three shunts that directed oxygenated blood away from the lungs and liver during fetal life. Clamping and cutting the umbilical cord collapses the three umbilical blood vessels. The proximal umbilical arteries remain a part of the circulatory system, whereas the distal umbilical arteries and the umbilical vein become fibrotic. The newborn keeps warm by breaking down brown adipose tissue in the process of nonshivering thermogenesis. The first consumption of breast milk or formula floods the newborn's sterile gastrointestinal tract with beneficial bacteria that eventually establish themselves as the bacterial flora, which aid in digestion.

27.6 Lactation

The lactating mother supplies all the hydration and nutrients that a growing infant needs for the first 4–6 months of life. During pregnancy, the body prepares for lactation by stimulating the growth and development of branching lactiferous ducts and alveoli lined with milk-secreting lactocytes and by creating colostrum. These functions are attributable to the actions of several hormones, including prolactin. Following childbirth, suckling triggers oxytocin release, which stimulates myoepithelial cells to squeeze milk from alveoli. Breast milk then drains toward the nipple pores to be consumed by the infant. Colostrum, the milk produced in the first postpartum days, provides immunoglobulins that increase the newborn's immune defences.

Colostrum, transitional milk, and mature breast milk are ideally suited to each stage of the newborn's development, and breastfeeding helps the newborn's digestive system expel meconium and clear bilirubin. Mature milk changes from the beginning to the end of a feeding. Foremilk quenches the infant's thirst, whereas hindmilk satisfies the infant's appetite.

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Glossary

abdominal aorta: Portion of the aorta inferior to the aortic hiatus and superior to the common iliac arteries.

abdominopelvic cavity: Division of the anterior (ventral) cavity that houses the abdominal and pelvic viscera.

abducens nerve: Sixth cranial nerve; responsible for contraction of one of the extraocular muscles.

abduction: Movement in the coronal plane that moves a limb laterally away from the body; spreading of the fingers.

abductor: Moves the bone away from the midline.

ABO blood group: Blood-type classification based on the presence or absence of A and B glycoproteins on the erythrocyte membrane surface.

absolute refractory period: Time during an action period when another action potential cannot be generated because the voltage-gated Na^+ channel is inactivated.

absorption: Passage of digested products from the intestinal lumen through mucosal cells and into the bloodstream or lacteals.

absorptive state: Also called the fed state; the metabolic state occurring during the first few hours after ingesting food in which the body is digesting food and absorbing the nutrients.

accessory digestive organ: Includes teeth, tongue, salivary glands, gallbladder, liver, and pancreas.

accessory duct (also duct of Santorini): Duct that runs from the pancreas into the duodenum.

acetabulum: Large, cup-shaped cavity located on the lateral side of the hip bone; formed by the junction of the ilium, pubis, and ischium portions of the hip bone.

acetylcholine (ACh): Neurotransmitter that binds at a motor end-plate to trigger depolarization.

acetyl coenzyme A (acetyl CoA): Starting molecule of the Krebs cycle.

acid: Compound that releases hydrogen ions (H^+) in solution.

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acinus: Cluster of glandular epithelial cells in the pancreas that secretes pancreatic juice in the pancreas.

acromegaly: Disorder in adults caused when abnormally high levels of GH trigger growth of bones in the face, hands, and feet.

acromial (lateral) end of the clavicle: Lateral end of the clavicle that articulates with the acromion of the scapula.

acromion (acromial process): Flattened bony process that extends laterally from the scapular spine to form the bony tip of the shoulder.

acrosomal reaction: Release of digestive enzymes by sperm that enables them to burrow through the corona radiata and penetrate the zona pellucida of an oocyte prior to fertilization.

acrosome: Cap-like vesicle located at the anterior-most region of a sperm that is rich with lysosomal enzymes capable of digesting the protective layers surrounding the oocyte.

actin: Protein that makes up most of the thin myofilaments in a sarcomere muscle fibre.

action potential: Change in voltage of a cell membrane in response to a stimulus that results in transmission of an electrical signal; unique to neurons and muscle fibres.

activation energy: Amount of energy greater than the energy contained in the reactants, which must be overcome for a reaction to proceed.

activation gate: Part of the voltage-gated Na^+ channel that opens when the membrane voltage reaches threshold.

active immunity: Immunity developed from an individual's own immune system.

active transport: Form of transport across the cell membrane that requires input of cellular energy.

acute inflammation: Inflammation occurring for a limited time period; rapidly developing.

adaptive immune response: Relatively slow but very specific and effective immune response controlled by lymphocytes.

adduction: Movement in the coronal plane that moves a limb medially toward or across the midline of the body; bringing fingers together.

adductor: Moves the bone toward the midline.

adductor brevis: Muscle that adducts and medially rotates the thigh.

adductor longus: Muscle that adducts, medially rotates, and flexes the thigh.

adductor magnus: Muscle with an anterior fascicle that adducts, medially rotates, and flexes the thigh and a posterior fascicle that assists in thigh extension.

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adenosine triphosphate (ATP): Nucleotide containing ribose, an adenine base, and three phosphates; essential in energy transfer.

adenylyl cyclase: Membrane-bound enzyme that converts ATP to cyclic AMP, creating cAMP, as a result of G-protein activation.

adherens junction: Type of cell junction; uses adhesion proteins found in either desmosomes or hemidesmosomes, depending on whether they are linking to other cells or the matrix.

adipocytes: Lipid storage cells.

adipose tissue: Specialized areolar tissue rich in stored fat.

adrenal artery: Branch of the abdominal aorta; supplies blood to the adrenal (suprarenal) glands.

adrenal cortex: Outer region of the adrenal glands consisting of multiple layers of epithelial cells and capillary networks that produces mineralocorticoids and glucocorticoids.

adrenal glands: Endocrine glands located at the top of each kidney that are important for the regulation of the stress response, blood pressure and blood volume, water homeostasis, and electrolyte levels.

adrenal medulla: Inner layer of the adrenal glands that plays an important role in the stress response by producing epinephrine and norepinephrine.

adrenal vein: Drains the adrenal or suprarenal glands that are immediately superior to the kidneys; the right adrenal vein enters the inferior vena cava directly, and the left adrenal vein enters the left renal vein.

adrenergic: Synapse where norepinephrine is released, which binds to α- or β-adrenergic receptors.

adrenocorticotropic hormone (ACTH): Anterior pituitary hormone that stimulates the adrenal cortex to secrete corticosteroid hormones (also called corticotropin).

aerobic respiration: Production of ATP in the presence of oxygen.

afferent arterioles: Branches of high-pressure capillaries bringing blood to the glomerulus.

afferent branch: Component of a reflex arc that represents the input from a sensory neuron, for either a special or general sense.

afferent lymphatic vessels: Vessels that lead into a lymph node.

afterbirth: Third stage of childbirth in which the placenta and associated fetal membranes are expelled.

afterload: Force the ventricles must develop to effectively pump blood against the resistance in the vessels.

agglutination: Clustering of cells into masses linked by antibodies.

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agonist (also prime mover): Muscle whose contraction is responsible for producing a particular motion.

agranular leukocytes: Leukocytes with few granules in their cytoplasm; specifically, monocytes, lymphocytes, and NK cells.

ala (plural = alae): Small, flaring structure of a nostril that forms the lateral side of the nares.

alar cartilage: Cartilage that supports the apex of the nose and helps shape the nares; it is connected to the septal cartilage and connective tissue of the alae.

alarm reaction: The short-term stress, or fight-or-flight, response of stage one of the general adaptation syndrome mediated by the hormones epinephrine and norepinephrine.

albumin: Most abundant plasma protein, accounting for most of the osmotic pressure of plasma.

aldosterone: Hormone produced and secreted by the adrenal cortex that stimulates sodium and fluid retention and increases blood volume and blood pressure.

alimentary canal: Continuous muscular digestive tube that extends from the mouth to the anus.

alkaloid: Substance, usually from a plant source, that is chemically basic with respect to pH and will stimulate bitter receptors.

allantois: Fingerlike outpocketing of yolk sac that forms the primitive excretory duct of the embryo; precursor to the urinary bladder.

alpha (α)-adrenergic receptor: One of the receptors to which epinephrine and norepinephrine bind, which comes in two subtypes: α_1 and α_2.

alpha cell: Pancreatic islet cell type that produces the hormone glucagon.

α-dextrin: Breakdown product of starch.

α-dextrinase: Brush border enzyme that acts on α-dextrins.

alveolar dead space: Air space within alveoli that are unable to participate in gas exchange.

alveolar duct: Small tube that leads from the terminal bronchiole to the respiratory bronchiole and is the point of attachment for alveoli.

alveolar macrophage: Immune system cell of the alveolus that removes debris and pathogens.

alveolar pore: Opening that allows airflow between neighbouring alveoli.

alveolar process of the mandible: Upper border of the mandibular body that contains the lower teeth.

alveolar sac: Cluster of alveoli.

alveoli (of the breast): Milk-secreting cells in the mammary gland.

alveolus: Small, grape-like sac that performs gas exchange in the lungs.

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amacrine cell: Type of cell in the retina that connects to the bipolar cells near the outer synaptic layer and provides the basis for early image processing within the retina.

amino acid: Building block of proteins; characterized by an amino functional group, carboxyl functional groups, and a variable side chain.

aminopeptidase: Brush border enzyme that acts on proteins.

amnion: Transparent membranous sac that encloses the developing fetus and fills with amniotic fluid.

amniotic cavity: Cavity that opens up between the inner cell mass and the trophoblast; develops into amnion.

amniotic fluid: Filtrate of maternal plasma and urine.

amphiarthrosis: Slightly mobile joint.

amphipathic: Describes a molecule that exhibits a difference in polarity between its two ends, resulting in a difference in water solubility.

ampulla: In the ear, the structure at the base of a semicircular canal that contains the hair cells and cupula for transduction of rotational movement of the head.

ampulla (of the uterine tube): Middle portion of the uterine tube in which fertilization often occurs.

amygdala: Nucleus deep in the temporal lobe of the cerebrum that is related to memory and emotional behaviour.

anabolic hormones: Hormones that stimulate the synthesis of new, larger molecules.

anabolic reactions: Reactions that build smaller molecules into larger molecules.

anabolism: Assembly of more complex molecules from simpler molecules.

anaerobic metabolism: Process during periods of reduced oxygen when pyruvic acid is converted to lactic acid, which may contribute to muscle fatigue.

anal canal: Final segment of the large intestine.

anal column: Long fold of mucosa in the anal canal.

anal sinus: Recess between anal columns.

anaphase: Third stage of mitosis (and meiosis), during which sister chromatids separate into two new nuclear regions of a dividing cell.

anaphylactic shock: Type of shock that follows a severe allergic reaction and results from massive vasodilation.

anastomosis (plural = anastomoses): Area where vessels unite to allow blood to circulate even if there may be partial blockage in another branch.

anatomical dead space: Air space present in the airway that never reaches the alveoli and therefore never participates in gas exchange.

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anatomical neck: Line on the humerus located around the outside margin of the humeral head.

anatomical position: Standard reference position used for describing locations and directions on the human body.

anatomical sphincter: Smooth or skeletal muscle surrounding the lumen of a vessel or hollow organ that can restrict flow when contracted.

anatomy: Science that studies the form and composition of the body's structures.

anchoring junction: Mechanically attaches adjacent cells to each other or to the basement membrane.

anconeus: Small muscle on the lateral posterior elbow that extends the forearm.

angiotensin I: Protein produced by the enzymatic action of renin on angiotensinogen; inactive precursor of angiotensin II.

angiotensin II: Protein produced by the enzymatic action of ACE on inactive angiotensin I; actively causes vasoconstriction and stimulates aldosterone release by the adrenal cortex.

angiotensin-converting enzyme (ACE): Enzyme produced by the lungs that catalyzes the reaction of inactive angiotensin I into active angiotensin II.

angiotensinogen: Inactive protein in the circulation produced by the liver; precursor of angiotensin I; must be modified by the enzymes renin and ACE to be activated.

angle of the rib: Portion of a rib with the greatest curvature; together, the rib angles form the most posterior extent of the thoracic cage.

anion: Atom with a negative charge.

ankle joint: Joint that separates the leg and foot portions of the lower limb; formed by the articulations between the talus bone of the foot inferiorly, and the distal end of the tibia, medial malleolus of the tibia, and lateral malleolus of the fibula superiorly.

annular ligament: Intrinsic ligament of the elbow articular capsule that surrounds and supports the head of the radius at the proximal radioulnar joint.

antagonist: Muscle that opposes the action of an agonist.

anterior: Describes the front or direction toward the front of the body; also referred to as ventral.

anterior arch: Anterior portion of the ringlike C1 (atlas) vertebra.

anterior border of the tibia: Narrow, anterior margin of the tibia that extends inferiorly from the tibial tuberosity.

anterior cardiac veins: Vessels that parallel the small cardiac arteries and drain the anterior surface of the right ventricle, bypass the coronary sinus, and drain directly into the right atrium.

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anterior cavity: Larger body cavity located anterior to the posterior (dorsal) body cavity; includes the serous membrane–lined pleural cavities for the lungs, pericardial cavity for the heart, and peritoneal cavity for the abdominal and pelvic organs; also referred to as ventral cavity.

anterior column: White matter between the anterior horns of the spinal cord composed of many different groups of axons of both ascending and descending tracts.

anterior corticospinal tract: Division of the corticospinal pathway that travels through the ventral (anterior) column of the spinal cord and controls axial musculature through the medial motor neurons in the ventral (anterior) horn.

anterior cruciate ligament: Intracapsular ligament of the knee; extends from anterior, superior surface of the tibia to the inner aspect of the lateral condyle of the femur; resists hyperextension of knee.

anterior horn: Grey matter of the spinal cord containing multipolar motor neurons, sometimes referred to as the ventral horn.

anterior interventricular artery (also left anterior descending artery or LAD): Major branch of the left coronary artery that follows the anterior interventricular sulcus.

anterior interventricular sulcus: Sulcus located between the left and right ventricles on the anterior surface of the heart.

anterior median fissure: Deep midline feature of the anterior spinal cord, marking the separation between the right and left sides of the cord.

anterior pituitary (adenohypophysis): Produces two classes of regulatory hormones: releasing hormones, which stimulate the secretion of specific hormones from the anterior pituitary, and inhibiting hormones, which suppress their secretion.

anterior tibial artery: Branches from the popliteal artery; supplies blood to the anterior tibial region; becomes the dorsalis pedis artery.

antibodies (also immunoglobulins or gamma globulins): Antigen-specific proteins produced by specialized B lymphocytes that protect the body by binding to foreign objects such as bacteria and viruses.

antibody: Antigen-specific protein secreted by plasma cells; immunoglobulin.

anticoagulant: Substance such as heparin that opposes coagulation.

anticodon: Consecutive sequence of three nucleotides on a tRNA molecule that is complementary to a specific codon on an mRNA molecule.

antidiuretic hormone (ADH): Also known as vasopressin, a hormone that increases the volume of water reabsorbed from the collecting tubules of the kidney.

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antigen: Substance that the body does not recognize as belonging to the "self" and that therefore triggers a defensive response from the leukocytes of the immune system.

antigenic determinant (also epitope): One of the chemical groups recognized by a single type of lymphocyte antigen receptor.

antigen presentation: Binding of processed antigen to the protein-binding cleft of a major histocompatibility complex molecule.

antigen processing: Internalization and digestion of antigen in an antigen-presenting cell.

antigen receptor: Two-chain receptor by which lymphocytes recognize antigen.

antiporters: Secondary active transporters that transport substances in opposite directions.

antrum: Fluid-filled chamber that characterizes a mature tertiary (antral) follicle.

anulus fibrosus: Tough, fibrous outer portion of an intervertebral disc, which is strongly anchored to the bodies of the adjacent vertebrae.

anuria: Absence of urine produced; production of 50 mL or less per day.

aorta: Largest artery in the body, originating from the left ventricle and descending to the abdominal region, where it bifurcates into the common iliac arteries at the level of the fourth lumbar vertebra; arteries originating from the aorta distribute blood to virtually all tissues of the body.

aortic arch: Arch that connects the ascending aorta to the descending aorta; ends at the intervertebral disk between the fourth and fifth thoracic vertebrae.

aortic hiatus: Opening in the diaphragm that allows passage of the thoracic aorta into the abdominal region, where it becomes the abdominal aorta.

aortic sinuses: Small pockets in the ascending aorta near the aortic valve that are the locations of the baroreceptors (stretch receptors) and chemoreceptors that trigger a reflex that aids in the regulation of vascular homeostasis.

aortic valve (also aortic semilunar valve): Valve located at the base of the aorta.

apex (nose): Tip of the external nose.

apex (sacrum): The inferior tip of the sacrum.

apneustic centre: Network of neurons within the pons that stimulate the neurons in the dorsal respiratory group; controls the depth of inspiration.

apocrine secretion: Release of a substance along with the apical portion of the cell.

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apocrine sweat gland: Type of sweat gland that is associated with hair follicles in the armpits and genital regions.

aponeurosis: Broad, tendonlike sheet of connective tissue that attaches a skeletal muscle to another skeletal muscle or to a bone.

apoptosis: Programmed cell death.

appendicular: Of the arms and legs.

appendicular skeleton: All bones of the upper and lower limbs, plus the girdle bones that attach each limb to the axial skeleton.

appendix (vermiform appendix): Coiled tube attached to the cecum.

aquaporin: Protein-forming water channels through the lipid bilayer of the cell; allows water to cross; activation in the collecting ducts is under the control of ADH.

aqueous humour: Watery fluid that fills the anterior chamber containing the cornea, iris, ciliary body, and lens of the eye.

arachnoid mater: Middle layer of the meninges named for the spider-web–like trabeculae that extend between it and the pia mater.

areola: Highly pigmented, circular area surrounding the raised nipple and containing areolar glands that secrete fluid important for lubrication during suckling.

areolar tissue (also loose connective tissue): A type of connective tissue proper that shows little specialization with cells dispersed in the matrix.

arm: Region of the upper limb located between the shoulder and elbow joints; contains the humerus bone.

arrector pili: Smooth muscle that is activated in response to external stimuli that pull on hair follicles and make the hair "stand up."

arteriole (also resistance vessel): Very small artery that leads to a capillary.

arteriovenous anastomosis: Short vessel connecting an arteriole directly to a venule and bypassing the capillary beds.

artery: Blood vessel that conducts blood away from the heart; may be a conducting or distributing vessel.

articular capsule: Connective tissue structure that encloses the joint cavity of a synovial joint.

articular cartilage: Thin layer of cartilage covering an epiphysis; reduces friction and acts as a shock absorber.

articular disc: Meniscus; a fibrocartilage structure found between the bones of some synovial joints; provides padding or smooths movements between the bones; strongly unites the bones together.

articulation: Where two bone surfaces meet.

ascending aorta: Initial portion of the aorta, rising from the left ventricle for a distance of approximately 5 cm.

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ascending colon: First region of the colon.

ascending pathway: Fibre structure that relays sensory information from the periphery through the spinal cord and brain stem to other structures of the brain.

ascending tract: Central nervous system fibres carrying sensory information from the spinal cord or periphery to the brain.

association area: Region of cortex connected to a primary sensory cortical area that further processes the information to generate more complex sensory perceptions.

astrocyte: Star-shaped cell in the central nervous system that regulates ions and uptake and/or breakdown of some neurotransmitters and contributes to the formation of the blood-brain barrier.

atlantoaxial joint: Series of three articulations between the atlas (C1) vertebra and the axis (C2) vertebra, consisting of the joints between the inferior articular processes of C1 and the superior articular processes of C2, and the articulation between the dens of C2 and the anterior arch of C1.

atlanto-occipital joint: Articulation between the occipital condyles of the skull and the superior articular processes of the atlas (C1 vertebra).

atlas: First cervical (C1) vertebra.

atmospheric pressure: Amount of force exerted by gases in the air surrounding any given surface.

atom: Smallest unit of an element that retains the unique properties of that element.

atomic number: Number of protons in the nucleus of an atom.

atoms and molecules: The smallest unit of any pure substance (element) is an atom; molecules are the chemical building blocks of all body structures.

ATPase: Enzyme that hydrolyzes ATP to ADP.

ATP synthase: Protein pore complex that creates ATP.

atrial natriuretic peptide (ANP): Peptide hormone produced by the walls of the atria in response to high blood pressure, blood volume, or blood sodium that reduces the reabsorption of sodium and water in the kidneys and promotes vasodilation.

atrial reflex (also called Bainbridge reflex): Autonomic reflex that responds to stretch receptors in the atria that send impulses to the cardioaccelerator area to increase HR when venous flow into the atria increases.

atrioventricular (AV) node: Clump of myocardial cells located in the inferior portion of the right atrium within the atrioventricular septum;

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receives the impulse from the SA node, pauses, and then transmits it into specialized conducting cells within the interventricular septum.

atrioventricular bundle (also bundle of His): Group of specialized myocardial conductile cells that transmit the impulse from the AV node through the interventricular septum; form the left and right atrioventricular bundle branches.

atrioventricular bundle branches (also left or right bundle branches): Specialized myocardial conductile cells that arise from the bifurcation of the atrioventricular bundle and pass through the interventricular septum; lead to the Purkinje fibres and also to the right papillary muscle via the moderator band.

atrioventricular septum: Cardiac septum located between the atria and ventricles; atrioventricular valves are located here.

atrioventricular valves (AV valves): One-way valves located between the atria and ventricles; the valve on the right is called the tricuspid valve, and the one on the left is the mitral or bicuspid valve.

atrium (plural = atria): Upper or receiving chamber of the heart that pumps blood into the lower chambers just prior to their contraction; the right atrium receives blood from the systemic circuit that flows into the right ventricle; the left atrium receives blood from the pulmonary circuit that flows into the left ventricle.

audition: Sense of hearing.

auricle (ear): Fleshy external structure of the ear.

auricle (heart): Extension of an atrium visible on the superior surface of the heart.

autocrine: Chemical signal that elicits a response in the same cell that secreted it.

autolysis: Breakdown of cells by their own enzymatic action.

autonomic ganglia: Related to the autonomic nervous system, which is divided into the sympathetic and parasympathetic nervous systems.

autonomic nervous system (ANS): Functional division of the nervous system that is responsible for homeostatic reflexes that coordinate control of cardiac and smooth muscle, as well as glandular tissue.

autonomic tone: Tendency of an organ system to be governed by one division of the autonomic nervous system over the other, such as heart rate being lowered by parasympathetic input at rest.

autophagy: Lysosomal breakdown of a cell's own components.

autorhythmicity: Ability of cardiac muscle to initiate its own electrical impulse that triggers the mechanical contraction that pumps blood at a fixed pace without nervous or endocrine control.

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axial: Of the trunk and head.

axial skeleton: Central, vertical axis of the body, including the skull, vertebral column, and thoracic cage.

axillary artery: Continuation of the subclavian artery as it penetrates the body wall and enters the axillary region; supplies blood to the region near the head of the humerus (humeral circumflex arteries); the majority of the vessel continues into the brachium and becomes the brachial artery.

axillary nerve: Systemic nerve of the arm that arises from the brachial plexus.

axillary vein: Major vein in the axillary region; drains the upper limb and becomes the subclavian vein.

axis: Second cervical (C2) vertebra.

axon: Single process of the neuron that carries an electrical signal (action potential) away from the cell body toward a target cell.

axon hillock: Tapering of the neuron cell body that gives rise to the axon.

axon segment: Single stretch of the axon insulated by myelin and bounded by nodes of Ranvier at either end (except for the first, which is after the initial segment, and the last, which is followed by the axon terminal).

axon terminal: End of the axon, where there are usually several branches extending toward the target cell.

axoplasm: Cytoplasm of an axon, which is different in composition than the cytoplasm of the neuronal cell body.

azygos vein: Originates in the lumbar region and passes through the diaphragm into the thoracic cavity on the right side of the vertebral column; drains blood from the intercostal veins, esophageal veins, bronchial veins, and other veins draining the mediastinal region; leads to the superior vena cava.

bacterial flora: Bacteria in the large intestine.

Bainbridge reflex (also called atrial reflex): Autonomic reflex that responds to stretch receptors in the atria that send impulses to the cardioaccelerator area to increase HR when venous flow into the atria increases.

ball-and-socket joint: Synovial joint formed between the spherical end of one bone (the ball) that fits into the depression of a second bone (the socket); found at the hip and shoulder joints; functionally classified as a multiaxial joint.

baroreceptor: Mechanoreceptor that senses the stretch of blood vessels to indicate changes in blood pressure.

baroreceptor reflex: Autonomic reflex in which the cardiac centres monitor signals from the baroreceptor stretch receptors and regulate heart function based on blood flow.

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barrier defences: Antipathogen defences deriving from a barrier that physically prevents pathogens from entering the body to establish an infection.

Bartholin's glands (also greater vestibular glands): Glands that produce a thick mucus that maintains moisture in the vulva area; also referred to as the greater vestibular glands.

basal cell: Type of stem cell found in the stratum basale and in the hair matrix that continually undergoes cell division, producing the keratinocytes of the epidermis.

basal lamina: Thin extracellular layer that lies underneath epithelial cells and separates them from other tissues.

basal metabolic rate (BMR): Amount of energy expended by the body at rest.

basal nuclei: Nuclei of the cerebrum (with a few components in the upper brain stem and diencephalon) that are responsible for assessing cortical movement commands and comparing them with the general state of the individual through broad modulatory activity of dopamine neurons; largely related to motor function.

base: Compound that accepts hydrogen ions (H^+) in solution.

basement membrane: In epithelial tissue, a thin layer of fibrous material that anchors the epithelial tissue to the underlying connective tissue; made up of the basal lamina and reticular lamina.

base of the metatarsal bone: Expanded, proximal end of each metatarsal bone.

basilar membrane: In the ear, the floor of the cochlear duct on which the organ of Corti sits.

basophils: Granulocytes that stain with a basic (alkaline) stain and store histamine and heparin.

B cells: Lymphocytes that act by differentiating into an antibody-secreting plasma cell.

belly: Bulky central body of a muscle.

beta (β)-adrenergic receptor: One of the receptors to which epinephrine and norepinephrine bind, which comes in three subtypes: β_1, β_2, and β_3.

beta (β)-oxidation: Fatty acid oxidation.

beta cell: Pancreatic islet cell type that produces the hormone insulin.

Betz cells: Output cells of the primary motor cortex that cause musculature to move through synapses on cranial and spinal motor neurons.

bi: Two.

biaxial joint: Type of diarthrosis; a joint that allows for movements within two planes (two axes).

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biceps brachii: Two-headed muscle that crosses the shoulder and elbow joints to flex the forearm while assisting in supinating it and flexing the arm at the shoulder.

biceps femoris: Hamstring muscle.

bicuspid valve (also mitral valve or left atrioventricular valve): Valve located between the left atrium and ventricle; consists of two flaps of tissue.

bile: Alkaline solution produced by the liver and important for the emulsification of lipids.

bile canaliculus: Small duct between hepatocytes that collects bile.

bile salts: Salts that are released from the liver in response to lipid ingestion and surround the insoluble triglycerides to aid in their conversion to monoglycerides and free fatty acids.

bilirubin: Yellowish bile pigment produced when iron is removed from heme and is further broken down into waste products.

biliverdin: Green bile pigment produced when the noniron portion of heme is degraded into a waste product; converted to bilirubin in the liver.

binocular vision: Indications of the distance of visual stimuli on the basis of slight differences in the images projected onto either retina.

biogenic amine: Class of neurotransmitters that are enzymatically derived from amino acids but no longer contain a carboxyl group.

biosynthesis reactions: Reactions that create new molecules, also called anabolic reactions.

bipennate: Pennate muscle that has fascicles that are located on both sides of the tendon.

bipolar: Shape of a neuron with two processes extending from the neuron cell body—the axon and one dendrite.

bipolar cell: Cell type in the retina that connects the photoreceptors to the RGCs.

blastocoel: Fluid-filled cavity of the blastocyst.

blastocyst: Term for the conceptus at the developmental stage that consists of about 100 cells shaped into an inner cell mass that is fated to become the embryo and an outer trophoblast that is fated to become the associated fetal membranes and placenta.

blastomere: Daughter cell of a cleavage.

blood: Liquid connective tissue composed of formed elements—erythrocytes, leukocytes, and platelets—and a fluid extracellular matrix called plasma; component of the cardiovascular system.

blood-brain barrier (BBB): Physiological barrier between the circulatory system and the central nervous system that establishes a privileged blood supply, restricting the flow of substances into the CNS.

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blood colloidal osmotic pressure (BCOP): Pressure exerted by colloids suspended in blood within a vessel; a primary determinant is the presence of plasma proteins.

blood flow: Movement of blood through a vessel, tissue, or organ that is usually expressed in terms of volume per unit of time.

blood hydrostatic pressure: Force blood exerts against the walls of a blood vessel or heart chamber.

blood pressure: Force exerted by the blood against the wall of a vessel or heart chamber; can be described with the more generic term *hydrostatic pressure*.

blood-testis barrier: Tight junctions between Sertoli cells that prevent blood-borne pathogens from gaining access to later stages of spermatogenesis and prevent the potential for an autoimmune reaction to haploid sperm.

B lymphocytes (also B cells): Lymphocytes that defend the body against specific pathogens and thereby provide specific immunity.

body: Midportion of the stomach.

body of the rib: Shaft portion of a rib.

body of uterus: Middle section of the uterus.

Bohr effect: Relationship between blood pH and oxygen dissociation from hemoglobin.

bolus: Mass of chewed food.

bond: Electrical force linking atoms.

bone (osseous tissue): Hard, dense connective tissue that forms the structural elements of the skeleton.

bone marrow: Tissue found inside bones; the site of all blood cell differentiation and maturation of B lymphocytes.

bony pelvis: The entire structure formed by the two hip bones, the sacrum, and, attached inferiorly to the sacrum, the coccyx.

Bowman's (glomerular) capsule: Cup-shaped sack lined by a simple squamous epithelium (parietal surface) and specialized cells called podocytes (visceral surface) that participate in the filtration process; receives the filtrate, which then passes on to the PCTs.

Boyle's law: Relationship between volume and pressure as described by the formula $P_1V_1 = P_2V_2$.

brachial artery: Continuation of the axillary artery in the brachium; supplies blood to much of the brachial region; gives off several smaller branches that provide blood to the posterior surface of the arm in the region of the elbow; bifurcates into the radial and ulnar arteries at the coronoid fossa.

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brachialis: Muscle deep to the biceps brachii that provides power in flexing the forearm.

brachial plexus: Nerve plexus associated with the lower cervical spinal nerves and the first thoracic spinal nerve.

brachial vein: A deep vein that flows into the axillary vein in the brachium formed by joining of the radial vein with the ulnar vein.

brachiocephalic artery: Single vessel located on the right side of the body; the first vessel branching from the aortic arch; gives rise to the right subclavian artery and the right common carotid artery; supplies blood to the head, neck, upper limb, and wall of the thoracic region.

brachiocephalic vein: One of a pair of veins that form from a fusion of the external and internal jugular veins and the subclavian vein; subclavian, external and internal jugulars, vertebral, and internal thoracic veins lead to it; drains the upper thoracic region and flows into the superior vena cava.

brachioradialis: Muscle that can flex the forearm quickly or help lift a load slowly.

brain: The large organ of the central nervous system composed of white and grey matter, contained within the cranium, and continuous with the spinal cord.

brain case: Portion of the skull that contains and protects the brain, consisting of the eight bones that form the cranial base and rounded upper skull.

brain stem: Region of the adult brain that includes the midbrain, pons, and medulla oblongata and develops from the mesencephalon, metencephalon, and myelencephalon of the embryonic brain.

Braxton Hicks contractions: Weak and irregular peristaltic contractions that can occur in the second and third trimesters; they do not indicate that childbirth is imminent.

brevis: Short.

bridge: Portion of the external nose that lies in the area of the nasal bones.

broad ligament: Wide ligament that supports the uterus by attaching laterally to both sides of the uterus and pelvic wall.

Broca's area: Region of the frontal lobe associated with the motor commands necessary for speech production and located only in the cerebral hemisphere responsible for language production, which is the left side in approximately 95 percent of the population.

bronchial artery: Systemic branch from the aorta that provides oxygenated blood to the lungs in addition to the pulmonary circuit.

bronchial tree: Collective name for the multiple branches of the bronchi and bronchioles of the respiratory system.

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bronchial vein: Drains the systemic circulation from the lungs and leads to the azygos vein.

bronchiole: Branch of bronchi that are 1 mm or less in diameter and terminate at alveolar sacs.

bronchoconstriction: Decrease in the size of the bronchiole due to relaxation of the muscular wall.

bronchodilation: Increase in the size of the bronchiole due to contraction of the muscular wall.

bronchus: Tube connected to the trachea that branches into many subsidiaries and provides a passageway for air to enter and leave the lungs.

bronchus-associated lymphoid tissue (BALT): Lymphoid nodule associated with the respiratory tract.

brown adipose tissue: Highly vascularized fat tissue packed with mitochondria; these properties confer the ability to oxidize fatty acids to generate heat.

bruise: Localized bleeding under the skin due to damaged blood vessels.

brush border: Formed by microvilli on the surface of certain cuboidal cells; in the kidney, it is found in the PCT; increases surface area for absorption in the kidney.

buccinator: Muscle that compresses the cheek.

buffer: Solution containing a weak acid or a weak base that opposes wide fluctuations in the pH of body fluids.

buffy coat: Thin, pale layer of leukocytes and platelets that separates the erythrocytes from the plasma in a sample of centrifuged blood.

bulbourethral glands (also Cowper's glands): Glands that secrete a lubricating mucus that cleans and lubricates the urethra prior to and during ejaculation.

bulbous (Ruffini) corpuscles: Responsible for the detection of stretching of the skin, known as type II cutaneous mechanoreceptors.

bundle of His (also atrioventricular bundle): Group of specialized myocardial conductile cells that transmit the impulse from the AV node through the interventricular septum; form the left and right atrioventricular bundle branches.

bursa: Connective tissue sac containing lubricating fluid that prevents friction between adjacent structures, such as skin and bone, tendons and bone, or two muscles.

calcaneal tendon (also Achilles tendon): Strong tendon that inserts into the calcaneal bone of the ankle.

calcaneus: Heel bone; posterior, inferior tarsal bone that forms the heel of the foot.

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calcitonin: Peptide hormone produced and secreted by the parafollicular cells (C cells) of the thyroid gland that functions to decrease blood calcium levels.

calmodulin: Regulatory protein that facilitates contraction in smooth muscles.

calorie: Amount of heat it takes to raise 1 kg (1,000 g) of water by 1°C.

calvaria (also skullcap): Rounded top of the skull.

calyces: Cup-like structures receiving urine from the collecting ducts, where it passes on to the renal pelvis and ureter.

canaliculi (singular = canaliculus): Channels within the bone matrix that house one of an osteocyte's many cytoplasmic extensions that it uses to communicate and receive nutrients.

capacitance: Ability of a vein to distend and store blood.

capacitance vessels: Veins; more distensible than arteries.

capacitation: Process that occurs in the female reproductive tract in which sperm are prepared for fertilization; leads to increased motility and changes in their outer membrane that improve their ability to release enzymes capable of digesting an oocyte's outer layers.

capillary: Smallest of blood vessels where physical exchange occurs between the blood and tissue cells surrounded by interstitial fluid.

capillary bed: Network of 10–100 capillaries connecting arterioles to venules.

capillary hydrostatic pressure (CHP): Force blood exerts against a capillary.

capitulum: Knoblike bony structure located anteriorly on the lateral, distal end of the humerus.

carbaminohemoglobin: Compound of carbon dioxide and hemoglobin and one of the ways in which carbon dioxide is carried in the blood.

carbohydrate: Class of organic compounds built from sugar molecules containing carbon, hydrogen, and oxygen in a 1-2-1 ratio.

carbonic anhydrase (CA): Enzyme that catalyzes the reaction that causes carbon dioxide and water to form carbonic acid.

cardia (also cardiac region): Part of the stomach surrounding the cardiac orifice (esophageal hiatus).

cardiac accelerator nerves: Preganglionic sympathetic fibres that cause the heart rate to increase when the cardiovascular centre in the medulla initiates a signal.

cardiac cycle: Period of time between the onset of atrial contraction (atrial systole) and ventricular relaxation (ventricular diastole).

cardiac muscle: Striated muscle found in the heart; joined to one another at intercalated discs and under the regulation of pacemaker cells, which

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contract as one unit to pump blood through the circulatory system. Cardiac muscle is under involuntary control.

cardiac notch: Depression in the medial surface of the inferior lobe of the left lung where the apex of the heart is located.

cardiac output (CO): Amount of blood pumped by each ventricle in 1 minute; equals HR multiplied by SV.

cardiac plexus: Paired complex network of nerve fibres near the base of the heart that receive sympathetic and parasympathetic stimulations to regulate HR.

cardiac reflexes: Series of autonomic reflexes that enable the cardiovascular centres to regulate heart function based on sensory information from a variety of visceral sensors.

cardiac reserve: Difference between maximum and resting CO.

cardiac skeleton (also skeleton of the heart): Reinforced connective tissue located within the atrioventricular septum; includes four rings that surround the openings between the atria and ventricles and the openings to the pulmonary trunk and aorta; the point of attachment for the heart valves.

cardioaccelerator centres: Stimulate cardiac function by regulating heart rate and stroke volume via sympathetic stimulation from the cardiac accelerator nerve.

cardiogenic shock: Type of shock that results from the inability of the heart to maintain cardiac output.

cardioinhibitor centres: Slow cardiac function by decreasing heart rate and stroke volume via parasympathetic stimulation from the vagus nerve.

cardiomyocyte: Muscle cell of the heart.

cardiovascular centre: Region in the medulla that controls the cardiovascular system through cardiac accelerator nerves and vasomotor nerves, which are components of the sympathetic division of the autonomic nervous system.

carotid sinuses: Small pockets near the base of the internal carotid arteries that are the locations of the baroreceptors and chemoreceptors that trigger a reflex that aids in the regulation of vascular homeostasis.

carpal bones: Eight small bones that form the wrist and base of the hand; these are grouped as a proximal row consisting of (from lateral to medial) the scaphoid, lunate, triquetrum, and pisiform bones, and a distal row containing (from lateral to medial) the trapezium, trapezoid, capitate, and hamate bones.

carpal tunnel: Passageway between the anterior forearm and hand formed by the carpal bones and flexor retinaculum.

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cartilage: Semirigid connective tissue found on the skeleton in areas where flexibility and smooth surfaces support movement.

cartilaginous joint: Joint at which the bones are united by hyaline cartilage (synchondrosis) or fibrocartilage (symphysis).

catabolic hormones: Hormones that stimulate the breakdown of larger molecules.

catabolic reactions: Reactions that break down larger molecules into their constituent parts.

catabolism: Breaking down of more complex molecules into simpler molecules.

catalyst: Substance that increases the rate of a chemical reaction without itself being changed in the process.

cation: Atom with a positive charge.

cauda equina: Bundle of spinal nerve roots that descend from the lower spinal cord below the first lumbar vertebra and lie within the vertebral cavity; has the appearance of a horse's tail.

caudal: Describes a position below or lower than another part of the body proper, near or toward the tail (in humans, the coccyx, or lowest part of the spinal column); also referred to as inferior.

cecum: Pouch forming the beginning of the large intestine.

celiac ganglion: One of the collateral ganglia of the sympathetic system that projects to the digestive system.

celiac trunk (also celiac artery): Major branch of the abdominal aorta; gives rise to the left gastric artery, the splenic artery, and the common hepatic artery that forms the hepatic artery to the liver, the right gastric artery to the stomach, and the cystic artery to the gall bladder.

cell: Smallest independently functioning unit of all organisms; in animals, a cell contains cytoplasm, composed of fluid and organelles.

cell cycle: Life cycle of a single cell, from its birth until its division into two new daughter cells.

cell junction: Point of cell-to-cell contact that connects one cell to another in a tissue.

cell membrane: Membrane surrounding all animal cells, composed of a lipid bilayer interspersed with various molecules; also known as plasma membrane.

cellular respiration: Production of ATP from glucose oxidation via glycolysis, the Krebs cycle, and oxidative phosphorylation.

cementum: Bone-like tissue covering the root of a tooth.

central canal (Haversian canal): Longitudinal channel in the centre of each osteon; contains blood vessels, nerves, and lymphatic vessels.

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central chemoreceptor: One of the specialized receptors located in the brain that senses changes in hydrogen ion, oxygen, or carbon dioxide concentrations in the brain.

central nervous system (CNS): Anatomical division of the nervous system located within the cranial and vertebral cavities, namely, the brain and spinal cord.

central neuron: The cell body of a neuron in the autonomic system that is located in the central nervous system, specifically the lateral horn of the spinal cord or a brain stem nucleus.

central sulcus: Surface landmark of the cerebral cortex that marks the boundary between the frontal and parietal lobes.

central tolerance: B cell tolerance induced in immature B cells of the bone marrow.

central vein: Vein that receives blood from hepatic sinusoids.

centriole: Small, self-replicating organelle that provides the origin for microtubule growth and moves DNA during cell division.

centromere: Region of attachment for two sister chromatids.

centrosome: Cellular structure that organizes microtubules during cell division.

cephalic phase (also reflex phase): Initial phase of gastric secretion that occurs before food enters the stomach.

cephalic vein: Superficial vessel in the upper arm; leads to the axillary vein.

cerebellum: Region of the adult brain connected primarily to the pons, which developed from the metencephalon (along with the pons), and is largely responsible for comparing information from the cerebrum with sensory feedback from the periphery through the spinal cord.

cerebral aqueduct: Connection of the ventricular system between the third and fourth ventricles located in the midbrain.

cerebral cortex: Outermost layer of grey matter in the brain, where conscious perception takes place.

cerebral hemisphere: One-half of the bilaterally symmetrical cerebrum.

cerebral peduncles: Segments of the descending motor pathway that make up the white matter of the ventral midbrain.

cerebrospinal fluid (CSF): Circulates throughout and around the CNS; it is produced in special structures to perfuse through the nervous tissue of the CNS to remove metabolic wastes from the interstitial fluids of nervous tissues and return them to the bloodstream.

cerebrovascular accident (CVA): Blockage of blood flow to the brain; also called a stroke.

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cerebrum: Region of the adult brain that develops from the telencephalon and is responsible for higher neurological functions such as memory, emotion, and consciousness.

cervical curve: Posteriorly concave curvature of the cervical vertebral column region; a secondary curve of the vertebral column.

cervical plexus: Nerve plexus associated with the upper cervical spinal nerves.

cervical vertebrae: Seven vertebrae numbered C1–C7 that are located in the neck region of the vertebral column.

cervix: Elongate inferior end of the uterus where it connects to the vagina.

channel protein: Membrane-spanning protein that has an inner pore that allows the passage of one or more substances.

chemical digestion: Enzymatic breakdown of food.

chemical energy: Form of energy that is absorbed as chemical bonds form, stored as they are maintained, and released as they are broken.

chemical synapse: Connection between two neurons, or between a neuron and its target, where a neurotransmitter diffuses across a very short distance.

chemokine: Soluble, long-range, cell-to-cell communication molecule.

chemoreceptor: Sensory receptor cell that is sensitive to chemical stimuli, such as in taste, smell, or pain.

chief cell: Gastric gland cell that secretes pepsinogen.

chloride shift: Facilitated diffusion that exchanges bicarbonate (HCO_3^-) with chloride (Cl^-) ions.

cholecystokinin (CCK): Hormone that stimulates the release of pancreatic lipase and the contraction of the gallbladder to release bile salts.

cholinergic: Synapse at which acetylcholine is released and binds to the nicotinic or muscarinic receptor.

cholinergic system: Neurotransmitter system of acetylcholine, which includes its receptors and the enzyme acetylcholinesterase.

chondrocytes: Cells of the cartilage.

chordae tendineae: String-like extensions of tough connective tissue that extend from the flaps of the atrioventricular valves to the papillary muscles.

chorion: Membrane that develops from the syncytiotrophoblast, cytotrophoblast, and mesoderm; surrounds the embryo and forms the fetal portion of the placenta through the chorionic villi.

chorionic membrane: Precursor to the chorion; forms from extraembryonic mesoderm cells.

chorionic villi: Projections of the chorionic membrane that burrow into the endometrium and develop into the placenta.

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choroid: Highly vascular tissue in the wall of the eye that supplies the outer retina with blood.

choroid plexus: Specialized structure containing ependymal cells lining blood capillaries that filter blood to produce CSF in the four ventricles of the brain.

chromaffin: Neuroendocrine cells of the adrenal medulla that release epinephrine and norepinephrine into the bloodstream as part of sympathetic system activity.

chromatin: Substance consisting of DNA and associated proteins.

chromosome: Condensed version of chromatin.

chronic inflammation: Inflammation occurring for long periods of time.

chyle: Lipid-rich lymph inside the lymphatic capillaries of the small intestine.

chylomicron: Large lipid-transport compound made up of triglycerides, phospholipids, cholesterol, and proteins.

chylomicrons: Vesicles containing cholesterol and triglycerides that transport lipids out of the intestinal cells and into the lymphatic and circulatory systems.

chyme: Soupy liquid created when food is mixed with digestive juices.

chymotrypsin: Pancreatic enzyme that digests protein.

chymotrypsinogen: Proenzyme that is activated by trypsin into chymotrypsin.

cilia: Small appendage on certain cells formed by microtubules and modified for movement of materials across the cellular surface.

ciliary body: Smooth muscle structure on the interior surface of the iris that controls the shape of the lens through the zonule fibres.

ciliated columnar epithelium: Tissue composed of simple columnar epithelial cells with cilia on their apical surfaces.

circadian rhythm: Internal perception of the daily cycle of light and dark based on retinal activity related to sunlight.

circle of Willis: Unique anatomical arrangement of blood vessels around the base of the brain that maintains perfusion of blood into the brain, even if one component of the structure is blocked or narrowed.

circular (also sphincter): Fascicles that are concentrically arranged around an opening.

circular fold (also plica circulare): Deep fold in the mucosa and submucosa of the small intestine.

circulatory shock: Also simply called shock; a life-threatening medical condition in which the circulatory system is unable to supply enough blood flow to provide adequate oxygen and other nutrients to the tissues to maintain cellular metabolism.

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circumduction: Circular motion of the arm, thigh, hand, thumb, or finger that is produced by the sequential combination of flexion, abduction, extension, and adduction.

circumflex artery: Branch of the left coronary artery that follows the coronary sulcus.

cisterna chyli: Bag-like vessel that forms the beginning of the thoracic duct.

citric acid cycle: Also called the Krebs cycle or the tricarboxylic acid cycle; converts pyruvate into CO_2 and high-energy $FADH_2$, NADH, and ATP molecules.

class II MHC: Molecules expressed only on the cells of the immune system, specifically cells that affect other arms of the immune response.

class switching: Ability of B cells to change the class of antibody they produce without altering the specificity for antigen.

clavicle: Collarbone; elongated bone that articulates with the manubrium of the sternum medially and the acromion of the scapula laterally.

clavicular notch: Paired notches located on the superior-lateral sides of the sternal manubrium, for articulation with the clavicle.

cleavage: Form of mitotic cell division in which the cell divides but the total volume remains unchanged; this process serves to produce smaller and smaller cells.

cleavage furrow: Contractile ring that forms around a cell during cytokinesis and pinches the cell into two halves.

clitoris (also glans clitoris): Nerve-rich area of the vulva that contributes to sexual sensation during intercourse.

clonal anergy: Process whereby B cells that react to soluble antigens in bone marrow are made nonfunctional.

clonal deletion: Removal of self-reactive B cells by inducing apoptosis.

clonal expansion: Growth of a clone of selected lymphocytes.

clonal selection: Stimulating growth of lymphocytes that have specific receptors.

clone: Group of lymphocytes sharing the same antigen receptor.

closed reduction: Manual manipulation of a broken bone to set it into its natural position without surgery.

clotting factors: Group of 12 identified substances active in coagulation.

coagulation: Formation of a blood clot; part of the process of hemostasis.

coccyx: Small bone located at the inferior end of the adult vertebral column that is formed by the fusion of four coccygeal vertebrae; also referred to as the tailbone.

cochlea: Auditory portion of the inner ear containing structures to transduce sound stimuli.

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cochlear duct: Space within the auditory portion of the inner ear that contains the organ of Corti and is adjacent to the scala tympani and scala vestibuli on either side.

codon: Consecutive sequence of three nucleotides on an mRNA molecule that corresponds to a specific amino acid.

collagen fibre: Flexible fibrous proteins that give connective tissue tensile strength.

collateral ganglia: Ganglia outside of the sympathetic chain that are targets of sympathetic preganglionic fibres, which are the celiac, inferior mesenteric, and superior mesenteric ganglia.

colloid: Liquid mixture in which the solute particles consist of clumps of molecules large enough to scatter light.

colon: Part of the large intestine between the cecum and the rectum.

colony-stimulating factors (CSFs): Glycoproteins that trigger the proliferation and differentiation of myeloblasts into granular leukocytes (basophils, neutrophils, and eosinophils).

colostrum: Thick, yellowish substance secreted from a mother's breasts in the first postpartum days; rich in immunoglobulins.

common bile duct: Structure formed by the union of the common hepatic duct and the gallbladder's cystic duct.

common carotid artery: Blood vessel that branches off the aorta (or the brachiocephalic artery on the right) and supplies blood to the head and neck.

common hepatic artery: Branch of the celiac trunk that forms the hepatic artery, the right gastric artery, and the cystic artery.

common hepatic duct: Duct formed by the merger of the two hepatic ducts.

common iliac artery: Branch of the aorta that leads to the internal and external iliac arteries.

common iliac vein: One of a pair of veins that flows into the inferior vena cava at the level of L5; the left common iliac vein drains the sacral region; divides into external and internal iliac veins near the inferior portion of the sacroiliac joint.

common pathway: Final coagulation pathway activated by either the intrinsic or the extrinsic pathway and ending in the formation of a blood clot.

compact bone: Dense osseous tissue that can withstand compressive forces.

complement: Enzymatic cascade of constitutive blood proteins that have antipathogen effects, including the direct killing of bacteria.

compliance: Degree to which a blood vessel can stretch as opposed to being rigid.

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compound: Substance composed of two or more different elements joined by chemical bonds.

concentration gradient: Difference in the concentration of a substance between two regions.

concentric contraction: Muscle contraction that shortens the muscle to move a load.

conceptus: Preimplantation stage of a fertilized egg and its associated membranes.

conducting zone: Region of the respiratory system that includes the organs and structures that provide passageways for air and are not directly involved in gas exchange.

conduction: Transfer of heat through physical contact.

condylar process of the mandible: Thickened upward projection from the posterior margin of the mandibular ramus.

condyle: Oval-shaped process located at the top of the condylar process of the mandible.

condyloid joint: Synovial joint in which the shallow depression at the end of one bone receives a rounded end from a second bone or a rounded structure formed by two bones; found at the metacarpophalangeal joints of the fingers or the radiocarpal joint of the wrist; functionally classified as a biaxial joint.

cone photoreceptor: One of the two types of retinal receptor cell that is specialized for colour vision through the use of three photopigments distributed through three separate populations of cells.

connective tissue: Type of tissue that serves to hold in place, connect, and integrate the body's organs and systems.

connective tissue membrane: Connective tissue that encapsulates organs and lines movable joints.

connective tissue proper: Connective tissue containing a viscous matrix, fibres, and cells.

continuous capillary: Most common type of capillary, found in virtually all tissues except epithelia and cartilage; contains very small gaps in the endothelial lining that permit exchange.

continuous conduction: Slow propagation of an action potential along an unmyelinated axon owing to voltage-gated Na^+ channels located along the entire length of the cell membrane.

contractility: Ability to shorten (contract) forcibly.

contraction phase: Twitch contraction phase when tension increases.

contralateral: Word meaning "on the opposite side," as in axons that cross the midline in a fibre tract.

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control centre: Compares values to their normal range; deviations cause the activation of an effector.

convection: Transfer of heat between the skin and air or water.

convergent: Fascicles that extend over a broad area and converge on a common attachment site.

coracoid process: Short, hooklike process that projects anteriorly and laterally from the superior margin of the scapula.

cornea: Fibrous covering of the anterior region of the eye that is transparent so that light can pass through it.

corneal reflex: Protective response to stimulation of the cornea that causes contraction of the orbicularis oculi muscle, resulting in blinking of the eye.

coronal plane: Two-dimensional, vertical plane that divides the body or organ into anterior and posterior portions; also referred to as frontal plane.

coronal suture: Joint that unites the frontal bone to the right and left parietal bones across the top of the skull.

corona radiata: In an oocyte, a layer of granulosa cells that surrounds the oocyte and that must be penetrated by sperm before fertilization can occur.

coronary arteries: Branches of the ascending aorta that supply blood to the heart; the left coronary artery feeds the left side of the heart, the left atrium and ventricle, and the interventricular septum; the right coronary artery feeds the right atrium, portions of both ventricles, and the heart conduction system.

coronary sinus: Large, thin-walled vein on the posterior surface of the heart that lies within the atrioventricular sulcus and drains the heart myocardium directly into the right atrium.

coronary sulcus: Sulcus that marks the boundary between the atria and ventricles.

coronary veins: Vessels that drain the heart and generally parallel the large surface arteries.

coronoid process of the ulna: Projecting bony lip located on the anterior, proximal ulna; forms the inferior margin of the trochlear notch.

corpus albicans: Nonfunctional structure remaining in the ovarian stroma following structural and functional regression of the corpus luteum.

corpus callosum: Large white matter structure that connects the right and left cerebral hemispheres.

corpus cavernosum: Either of two columns of erectile tissue in the penis that fill with blood during an erection.

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corpus luteum: Transformed follicle after ovulation that secretes progesterone.

corpus spongiosum (plural = corpora cavernosa): Column of erectile tissue in the penis that fills with blood during an erection and surrounds the penile urethra on the ventral portion of the penis.

cortex: In hair, the second or middle layer of keratinocytes originating from the hair matrix, as seen in a cross-section of the hair bulb.

cortical nephrons: Nephrons with loops of Henle that do not extend into the renal medulla.

cortical reaction: Following fertilization, the release of cortical granules from the oocyte's plasma membrane into the zona pellucida, creating a fertilization membrane that prevents any further attachment or penetration of sperm; part of the slow block to polyspermy.

corticobulbar tract: Connection between the cortex and the brain stem responsible for generating movement.

corticospinal tract: Connection between the cortex and the spinal cord responsible for generating movement.

cortisol: Glucocorticoid important in gluconeogenesis, the catabolism of glycogen, and downregulation of the immune system.

costal cartilage: Hyaline cartilage structure attached to the anterior end of each rib that provides for either direct or indirect attachment of most ribs to the sternum.

costal facet: Site on the lateral sides of a thoracic vertebra for articulation with the head of a rib.

costal groove: Shallow groove along the inferior margin of a rib that provides passage for blood vessels and a nerve.

countercurrent multiplier system: Involves the descending and ascending loops of Henle directing forming urine in opposing directions to create a concentration gradient when combined with variable permeability and sodium pumping.

covalent bond: Chemical bond in which two atoms share electrons, thereby completing their valence shells.

coxal bone: Hip bone.

cranial: Describes a position above or higher than another part of the body proper; also referred to as superior.

cranial cavity: Division of the posterior (dorsal) cavity that houses the brain.

cranial nerve: One of twelve nerves connected to the brain that are responsible for sensory or motor functions of the head and neck.

cranial nerve ganglion: Sensory ganglion of cranial nerves.

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craniosacral system: Alternate name for the parasympathetic division of the autonomic nervous system that is based on the anatomical location of central neurons in brain stem nuclei and the lateral horn of the sacral spinal cord; also referred to as craniosacral outflow.

cranium: Skull.

creatine phosphate: Phosphagen used to store energy from ATP and transfer it to muscle.

cricoid cartilage: Portion of the larynx composed of a ring of cartilage with a wide posterior region and a thinner anterior region; attached to the esophagus.

crown: Portion of tooth visible superior to the gum line.

cuboid: Tarsal bone that articulates posteriorly with the calcaneus bone, medially with the lateral cuneiform bone, and anteriorly with the fourth and fifth metatarsal bones.

cupula: Specialized structure within the base of a semicircular canal that bends the stereocilia of hair cells when the head rotates by way of the relative movement of the enclosed fluid.

cuspid (also canine): Pointed tooth used for tearing and shredding food.

cutaneous membrane: Skin; epithelial tissue made up of a stratified squamous epithelial cells that cover the outside of the body.

cuticle: In hair, the outermost layer of keratinocytes originating from the hair matrix, as seen in a cross-section of the hair bulb.

cyclic adenosine monophosphate (cAMP): Second messenger that, in response to adenylyl cyclase activation, triggers a phosphorylation cascade.

cystic duct: Duct through which bile drains and enters the gallbladder.

cytokines: Class of proteins that act as autocrine or paracrine signalling molecules; in the cardiovascular system, they stimulate the proliferation of progenitor cells and help stimulate both nonspecific and specific resistance to disease.

cytokinesis: Final stage in cell division, where the cytoplasm divides to form two separate daughter cells.

cytoplasm: Internal material between the cell membrane and nucleus of a cell, mainly consisting of a water-based fluid called cytosol, within which are all the other organelles, cellular solutes, and suspended materials.

cytoskeleton: "skeleton" of a cell; formed by rodlike proteins that support the cell's shape and provide, among other functions, locomotive abilities.

cytosol: Clear, semifluid medium of the cytoplasm, made up mostly of water.

cytotoxic T cells (Tc): T lymphocytes with the ability to induce apoptosis in target cells.

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Dalton's law: Statement of the principle that a specific gas type in a mixture exerts its own pressure as if that specific gas type was not part of a mixture of gases.

deciduous tooth: One of 20 "baby teeth."

decomposition reaction: Type of catabolic reaction in which one or more bonds within a larger molecule are broken, resulting in the release of smaller molecules or atoms.

deep: Describes a position farther from the surface of the body.

defecation: Elimination of undigested substances from the body in the form of feces.

defensins: Antimicrobial proteins released from neutrophils and macrophages that create openings in the plasma membranes to kill cells.

deglutition: Three-stage process of swallowing.

dehydration: State of containing insufficient water in blood and other tissues.

delta cell: Minor cell type in the pancreas that secretes the hormone somatostatin.

deltoid: Shoulder muscle that abducts the arm as well as flexes and medially rotates it and extends and laterally rotates it.

deltoid tuberosity: Roughened, V-shaped region located laterally on the midshaft of the humerus.

denaturation: Change in the structure of a molecule through physical or chemical means.

dendrite: One of many branchlike processes that extends from the neuron cell body and functions as a contact for incoming signals (synapses) from other neurons or sensory cells.

dendrites: Branches off the neuron cell body and appear as thin extensions.

dendritic cells: Two types of phagocytic cells in the thymus that are derived from monocytes.

dens: Bony projection (odontoid process) that extends upward from the body of the C2 (axis) vertebra.

dense body: Sarcoplasmic structure that attaches to the sarcolemma and shortens the muscle as thin filaments slide past thick filaments.

dense connective tissue: Connective tissue proper that contains many fibres that provide both elasticity and protection.

dentes: Teeth.

dentin: Bone-like tissue immediately deep to the enamel of the crown or cementum of the root of a tooth.

dentition: Set of teeth.

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deoxyhemoglobin: Molecule of hemoglobin without an oxygen molecule bound to it.

deoxyribonuclease: Pancreatic enzyme that digests DNA.

deoxyribonucleic acid (DNA): Deoxyribose-containing nucleotide that stores genetic information.

depolarization: Change in a cell membrane potential from rest toward zero.

depolarize: Process where the membrane potential of muscle fibre becomes less negative (closer to zero).

depression: Downward (inferior) motion of the scapula or mandible.

dermal papilla (plural = dermal papillae): Extension of the papillary layer of the dermis that increases surface contact between the epidermis and dermis.

dermis: Layer of skin between the epidermis and hypodermis, composed mainly of connective tissue and containing blood vessels, hair follicles, sweat glands, and other structures.

descending aorta: Portion of the aorta that continues downward past the end of the aortic arch; subdivided into the thoracic aorta and the abdominal aorta.

descending colon: Part of the colon between the transverse colon and the sigmoid colon.

descending tract: Central nervous system fibres carrying motor commands from the brain to the spinal cord or periphery.

desmosome: Type of cell junction that anchors cells together by linking adhesion molecules across their membranes.

detrusor muscle: Smooth muscle in the bladder wall; fibres run in all directions to reduce the size of the organ when emptying it of urine.

development: Changes an organism goes through during its life.

diapedesis (also emigration): Process by which leukocytes squeeze through adjacent cells in a blood vessel wall to enter tissues.

diaphragm: Skeletal muscle that separates the thoracic and abdominal cavities and is dome-shaped at rest.

diaphysis: Tubular shaft that runs between the proximal and distal ends of a long bone.

diarthrosis: Freely mobile joint.

diastole: Period of time when the heart muscle is relaxed and the chambers fill with blood.

diastolic pressure: Lower number recorded when measuring arterial blood pressure; represents the minimal value corresponding to the pressure that remains during ventricular relaxation.

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diencephalon: Region of the adult brain that retains its name from embryonic development and includes the thalamus and hypothalamus.

differentiation: Process in which a cell may undertake major changes in its size, shape, metabolic activity, and overall function.

diffusion: Movement of a substance from an area of higher concentration to one of lower concentration.

digastric: Muscle that has anterior and posterior bellies and elevates the hyoid bone and larynx when one swallows; it also depresses the mandible.

digital veins: Drain the digits and feed into the palmar arches of the hand and dorsal venous arch of the foot.

dihydroxyvitamin D (calcitriol): Active form of vitamin D required by the intestinal epithelial cells for the absorption of calcium.

dilation: First stage of childbirth, involving an increase in cervical diameter.

dipeptidase: Brush border enzyme that acts on proteins.

diploid: Condition marked by the presence of a double complement of genetic material (two sets of chromosomes, one set inherited from each of two parents).

direct pathway: Connections within the basal nuclei from the striatum to the globus pallidus internal segment and substantia nigra pars reticulata that disinhibit the thalamus to increase cortical control of movement.

disaccharide: Pair of carbohydrate monomers bonded by dehydration synthesis via a glycosidic bond.

distal: Describes a position farther from the point of attachment or the trunk of the body.

distal convoluted tubules (DCT): Portions of the nephron distal to the loop of Henle that receive hyposmotic filtrate from the loop of Henle and empty into collecting ducts.

diuresis: Excess production of urine.

diuretic: Compound that increases urine output, leading to decreased water conservation.

DNA polymerase: Enzyme that functions in adding new nucleotides to a growing strand of DNA during DNA replication.

DNA replication: Process of duplicating a molecule of DNA.

dorsal: Describes the back or direction toward the back of the body; also referred to as posterior.

dorsal (posterior) root ganglion: Sensory ganglion attached to the posterior nerve root of a spinal nerve.

dorsal cavity: Posterior body cavity that houses the brain and spinal cord; also referred to as the posterior body cavity.

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dorsal column system: Ascending tract of the spinal cord associated with fine touch and proprioceptive sensations.

dorsal respiratory group (DRG): Region of the medulla oblongata that stimulates the contraction of the diaphragm and intercostal muscles to induce inspiration.

dorsal stream: Connections between cortical areas from the occipital to parietal lobes that are responsible for the perception of visual motion and guiding movement of the body in relation to that motion.

dorsiflexion: Movement at the ankle that brings the top of the foot toward the anterior leg.

dorsum nasi: Intermediate portion of the external nose that connects the bridge to the apex and is supported by the nasal bone.

double helix: Characteristic of DNA where two strands attach via hydrogen bonds between the bases of the component nucleotides.

downregulation: Decrease in the number of hormone receptors, typically in response to chronically excessive levels of a hormone.

ductus arteriosus: Shunt in the fetal pulmonary trunk that diverts oxygenated blood back to the aorta.

ductus deferens (also vas deferens): Duct that transports sperm from the epididymis through the spermatic cord and into the ejaculatory duct; also referred to as the vas deferens.

ductus venosus: Shunt that causes oxygenated blood to bypass the fetal liver on its way to the inferior vena cava.

duodenal gland (also Brunner's gland): Mucous-secreting gland in the duodenal submucosa.

duodenum: First part of the small intestine, which starts at the pyloric sphincter and ends at the jejunum.

dural sinus: Any of the venous structures surrounding the brain, enclosed within the dura mater, which drain blood from the CNS to the common venous return of the jugular veins.

dura mater: Tough, fibrous, outer layer of the meninges that is attached to the inner surface of the cranium and vertebral column and surrounds the entire CNS.

ear ossicles: Three small bones located in the middle ear cavity that serve to transmit sound vibrations to the inner ear.

eccentric contraction: Muscle contraction that lengthens the muscle as the tension is diminished.

eccrine sweat gland: Type of sweat gland that is common throughout the skin surface; it produces a hypotonic sweat for thermoregulation.

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ectoderm: Primary germ layer that develops into the central and peripheral nervous systems, sensory organs, epidermis, hair, and nails.

ectopic pregnancy: Implantation of an embryo outside of the uterus.

effector: Organ that can cause a change in a value.

effector protein: Enzyme that catalyzes the generation of a new molecule, which acts as the intracellular mediator of the signal that binds to the receptor.

effector T cells: Immune cells with a direct, adverse effect on a pathogen.

efferent arteriole: Arteriole carrying blood from the glomerulus to the capillary beds around the convoluted tubules and loop of Henle; portion of the portal system.

efferent branch: Component of a reflex arc that represents the output, with the target being an effector, such as muscle or glandular tissue.

efferent lymphatic vessels: Vessels that lead out of a lymph node.

effort: Force applied to the handle of a lever.

ejaculatory duct: Duct that connects the ampulla of the ductus deferens with the duct of the seminal vesicle at the prostatic urethra.

ejection fraction: Portion of the blood that is pumped or ejected from the heart with each contraction; mathematically represented by SV divided by EDV.

elastic artery (also conducting artery): Artery with abundant elastic fibres located closer to the heart, which maintains the pressure gradient and conducts blood to smaller branches.

elastic cartilage: Type of cartilage, with elastin as the major protein, characterized by rigid support as well as elasticity.

elastic fibre: Fibrous protein within connective tissue that contains a high percentage of the protein elastin, which allows the fibres to stretch and return to their original size.

elasticity: Ability to stretch and rebound.

elbow joint: Joint located between the upper arm and forearm regions of the upper limb; formed by the articulations between the trochlea of the humerus and the trochlear notch of the ulna, and the capitulum of the humerus and the head of the radius.

electrical gradient: Difference in the electrical charge (potential) between two regions.

electrical synapse: Connection between two neurons, or any two electrically active cells, where ions flow directly through channels spanning their adjacent cell membranes.

electrocardiogram (ECG): Surface recording of the electrical activity of the heart that can be used for diagnosis of irregular heart function; also abbreviated as EKG.

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electron: Subatomic particle having a negative charge and nearly no mass; found orbiting the atom's nucleus.

electron shell: Area of space a given distance from an atom's nucleus in which electrons are grouped.

electron transport chain (ETC): ATP production pathway in which electrons are passed through a series of oxidation-reduction reactions that forms water and produces a proton gradient.

element: Substance that cannot be created or broken down by ordinary chemical means.

elevation: Upward (superior) motion of the scapula or mandible.

embryo: Developing human during weeks 3–8.

embryonic disc: Composed of embryonic cells and the amniotic cavity.

embryonic folding: Process by which an embryo develops from a flat disc of cells to a three-dimensional shape resembling a cylinder.

emigration (also diapedesis): Process by which leukocytes squeeze through adjacent cells in a blood vessel wall to enter tissues.

enamel: Covering of the dentin of the crown of a tooth.

encapsulated corpuscle ending: Configuration of a sensory receptor neuron with dendrites surrounded by specialized structures to aid in transduction of a particular type of sensation, such as the lamellated corpuscles in the deep dermis and subcutaneous tissue.

end diastolic volume (EDV; also preload): The amount of blood in the ventricles at the end of atrial systole just prior to ventricular contraction.

endocardium: Innermost layer of the heart lining the heart chambers and heart valves; composed of endothelium reinforced with a thin layer of connective tissue that binds to the myocardium.

endochondral ossification: Process in which bone forms by replacing hyaline cartilage.

endocrine gland: Tissue or organ that secretes hormones into the blood and lymph without ducts such that they may be transported to organs distant from the site of secretion.

endocrine system: Cells, tissues, and organs that secrete hormones as a primary or secondary function and play an integral role in normal bodily processes.

endocytosis: Import of material into the cell by formation of a membrane-bound vesicle.

endoderm: Innermost embryonic germ layer from which most of the digestive system and lower respiratory system derive.

endogenous: Describes a substance made in the human body.

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endometrium: Inner lining of the uterus, part of which builds up during the secretory phase of the menstrual cycle and then sheds with menses.
endomysium: Loose, well-hydrated connective tissue covering each muscle fibre in a skeletal muscle.
endoneurium: Innermost layer of connective tissue that surrounds individual axons within a nerve.
endoplasmic reticulum (ER): Cellular organelle that consists of interconnected membrane-bound tubules, which may or may not be associated with ribosomes (rough type or smooth type, respectively).
endosteum: Delicate membranous lining of a bone's medullary cavity.
endothelins: Group of vasoconstrictive, 21-amino acid peptides; produced by endothelial cells of the renal blood vessels, mesangial cells, and cells of the DCT.
endothelium: Layer of smooth, simple squamous epithelium that lines the endocardium and blood vessels.
end systolic volume (ESV): Amount of blood remaining in each ventricle following systole.
energy-consuming phase: First phase of glycolysis, in which two molecules of ATP are necessary to start the reaction.
energy-yielding phase: Second phase of glycolysis, during which energy is produced.
enteric nervous system (ENS): Neural tissue associated with the digestive system that is responsible for nervous control through autonomic connections.
enteric plexus: Neuronal plexus in the wall of the intestines, which is part of the enteric nervous system.
enteroendocrine cell: Gastric gland cell that releases hormones.
enterohepatic circulation: Recycling mechanism that conserves bile salts.
enterokinase: Enzyme located in the wall of the small intestine that activates trypsin.
enteropeptidase (enterokinase): Intestinal brush border enzyme that activates trypsinogen to trypsin.
enzyme: Protein or RNA that catalyzes chemical reactions.
eosinophils: Granulocytes that stain with eosin; they release antihistamines and are especially active against parasitic worms.
ependymal cell: Glial cell type in the CNS responsible for producing cerebrospinal fluid.
epicardial coronary arteries: Surface arteries of the heart that generally follow the sulci.

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epicardium: Innermost layer of the serous pericardium and the outermost layer of the heart wall.
epidermis: Outermost tissue layer of the skin.
epididymis (plural = epididymides): Coiled tubular structure in which sperm start to mature and are stored until ejaculation.
epiglottis: Leaf-shaped piece of elastic cartilage that is a portion of the larynx that swings to close the trachea during swallowing.
epimysium: Outer layer of connective tissue around a skeletal muscle.
epinephrine: Primary and most potent catecholamine hormone secreted by the adrenal medulla in response to short-term stress; also called adrenaline.
epineurium: Outermost layer of connective tissue that surrounds an entire nerve.
epiphyseal line: Completely ossified remnant of the epiphyseal plate.
epiphyseal plate (also growth plate): Sheet of hyaline cartilage in the metaphysis of an immature bone; replaced by bone tissue as the organ grows in length.
epiphysis: Wide section at each end of a long bone; filled with spongy bone and red marrow.
epiploic appendage: Small sac of fat-filled visceral peritoneum attached to teniae coli.
epithalamus: Region of the diencephalon containing the pineal gland.
epithelial membrane: Epithelium attached to a layer of connective tissue.
epithelial tissue: Type of tissue that serves primarily as a covering or lining of body parts, protecting the body; it also functions in absorption, transport, and secretion.
equilibrium: Sense of balance that includes sensations of position and movement of the head.
erectile tissue: Located in the shaft of the penis and composed of three column-like chambers.
erector spinae group: Large muscle mass of the back; primary extensor of the vertebral column.
erythrocyte (also red blood cell): Mature myeloid blood cell that is composed mostly of hemoglobin and functions primarily in the transportation of oxygen and carbon dioxide.
erythropoietin (EPO): Glycoprotein that triggers the bone marrow to produce RBCs; secreted by the kidney in response to low oxygen levels.
esophageal plexus: Neuronal plexus in the wall of the esophagus that is part of the enteric nervous system.
esophagus: Muscular tube that runs from the pharynx to the stomach.

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estrogens: Class of predominantly female sex hormones important for the development and growth of the female reproductive tract, secondary sex characteristics, the female reproductive cycle, and the maintenance of pregnancy.

ethmoid air cell: One of several small, air-filled spaces located within the lateral sides of the ethmoid bone, between the orbit and upper nasal cavity.

ethmoid bone: Unpaired bone that forms the roof and upper lateral walls of the nasal cavity, portions of the floor of the anterior cranial fossa and the medial wall of the orbit, and the upper portion of the nasal septum.

Eustachian tube: Tube connecting the pharynx with the middle ear, which helps equilibrate air pressure across the tympanic membrane; it is normally closed but will pop open when the muscles of the pharynx contract during swallowing or yawning.

evaporation: Transfer of heat that occurs when water changes from a liquid to a gas.

eversion: Foot movement involving the intertarsal joints of the foot in which the bottom of the foot is turned laterally, away from the midline.

exchange reaction: Type of chemical reaction in which bonds are both formed and broken, resulting in the transfer of components.

excitability: Ability to undergo neural stimulation.

excitable membrane: Cell membrane that regulates the movement of ions so that an electrical signal can be generated.

excitation-contraction coupling: Sequence of events from motor neuron signalling to a skeletal muscle fibre to contraction of the fibre's sarcomeres.

excitatory postsynaptic potential (EPSP): Graded potential in the postsynaptic membrane that is the result of depolarization and makes an action potential more likely to occur.

executive functions: Cognitive processes of the prefrontal cortex that lead to directing goal-directed behaviour, which is a precursor to executing motor commands.

exocrine gland: Group of epithelial cells that secrete substances through ducts that open to the skin or to internal body surfaces that lead to the exterior of the body.

exocrine system: Cells, tissues, and organs that secrete substances directly to target tissues via glandular ducts.

exocytosis: Export of a substance out of a cell by formation of a membrane-bound vesicle.

exogenous: Describes a substance made outside of the human body.

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expiration (also exhalation): Process that causes the air to leave the lungs.
expiratory reserve volume (ERV): Amount of air that can be forcefully exhaled after a normal tidal exhalation.
expulsion: Second stage of childbirth, during which the mother bears down with contractions; this stage ends in birth.
extensibility: Ability to lengthen (extend).
extension: Movement in the sagittal plane that increases the angle of a joint (straightens the joint); motion involving posterior bending of the vertebral column or returning to the upright position from a flexed position.
extensor: Muscle that increases the angle at the joint.
extensor digitorum longus: Muscle that is lateral to the tibialis anterior.
extensor hallucis longus: Muscle that is partly deep to the tibialis anterior and extensor digitorum longus.
extensor radialis longus: Muscle that extends and abducts the hand at the wrist.
external acoustic meatus: Ear canal opening located on the lateral side of the skull.
external anal sphincter: Voluntary skeletal muscle sphincter in the anal canal.
external callus: Collar of hyaline cartilage and bone that forms around the outside of a fracture.
external carotid artery: Arises from the common carotid artery; supplies blood to numerous structures within the face, lower jaw, neck, esophagus, and larynx.
external ear: Structures on the lateral surface of the head, including the auricle and the ear canal up to the tympanic membrane.
external elastic membrane: Membrane composed of elastic fibres that separates the tunica media from the tunica externa; seen in larger arteries.
external iliac artery: Branch of the common iliac artery that leaves the body cavity and becomes a femoral artery; supplies blood to the lower limbs.
external iliac vein: Formed when the femoral vein passes into the body cavity; drains the legs and leads to the common iliac vein.
external intercostal: Superficial intercostal muscles that raise the rib cage.
external jugular vein: One of a pair of major veins located in the superficial neck region that drains blood from the more superficial portions of the head, scalp, and cranial regions and leads to the subclavian vein.
external nose: Region of the nose that is easily visible to others.
external oblique: Superficial abdominal muscle with fascicles that extend inferiorly and medially.

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external occipital protuberance: Small bump located at the midline on the posterior skull.

external respiration: Gas exchange that occurs in the alveoli.

external root sheath: Outer layer of the hair follicle that is an extension of the epidermis, which encloses the hair root.

external urinary (urethral) sphincter: Skeletal muscle; must be relaxed consciously to void urine.

exteroceptor: Sensory receptor that is positioned to interpret stimuli from the external environment, such as photoreceptors in the eye or somatosensory receptors in the skin.

extracellular fluid (ECF): Fluid exterior to cells; includes the interstitial fluid, blood plasma, and fluid found in other reservoirs in the body.

extraocular muscles: Six skeletal muscles that control eye movement within the orbit.

extrapyramidal system: Pathways between the brain and spinal cord that are separate from the corticospinal tract and are responsible for modulating the movements generated through that primary pathway.

extrinsic ligament: Ligament located outside of the articular capsule of a synovial joint.

extrinsic muscles of the hand: Muscles that move the wrists, hands, and fingers and originate on the arm.

extrinsic pathway: Initial coagulation pathway that begins with tissue damage and results in the activation of the common pathway.

facet: Small, flattened area on a bone for an articulation (joint) with another bone, or for muscle attachment.

facial bones: 14 bones that support the facial structures and form the upper and lower jaws and the hard palate.

facial nerve: Seventh cranial nerve; responsible for contraction of the facial muscles and for part of the sense of taste, as well as causing saliva production.

facilitated diffusion: Diffusion of a substance with the aid of a membrane protein.

false ribs: Vertebrochondral ribs 8–12 whose costal cartilage either attaches indirectly to the sternum via the costal cartilage of the next higher rib or does not attach to the sternum at all.

fascicle: Small bundles of nerve or muscle fibres enclosed by connective tissue.

fast glycolytic (FG): Muscle fibre that primarily uses anaerobic glycolysis.

fast oxidative (FO): Intermediate muscle fibre that is between slow oxidative and fast glycolytic fibres.

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fatty acid oxidation: Breakdown of fatty acids into smaller-chain fatty acids and acetyl CoA.

fauces: Portion of the posterior oral cavity that connects the oral cavity to the oropharynx.

Fc region: In an antibody molecule, the site where the two termini of the heavy chains come together; many cells have receptors for this portion of the antibody, adding functionality to these molecules.

feces: Semisolid waste product of digestion.

femoral artery: Continuation of the external iliac artery after it passes through the body cavity; divides into several smaller branches, the lateral deep femoral artery, and the genicular artery; becomes the popliteal artery as it passes posterior to the knee.

femoral nerve: Systemic nerve of the anterior leg that arises from the lumbar plexus.

femoral vein: Drains the upper leg; receives blood from the great saphenous vein, the deep femoral vein, and the femoral circumflex vein; becomes the external iliac vein when it crosses the body wall.

femoropatellar joint: Portion of the knee joint consisting of the articulation between the distal femur and the patella.

femur: Thigh bone; the single bone of the thigh.

fenestrated capillary: Type of capillary with pores or fenestrations in the endothelium that allow for rapid passage of certain small materials.

fenestrations: Small windows through a cell allowing rapid filtration based on size; formed in such a way as to allow substances to cross through a cell without mixing with cell contents.

ferritin: Protein-containing storage form of iron found in the bone marrow, liver, and spleen.

fertilization: Unification of genetic material from male and female haploid gametes.

fertilization membrane: Impenetrable barrier that coats a nascent zygote; part of the slow block to polyspermy.

fetus: Developing human during the time from the end of the embryonic period (week 9) to birth.

fibrin: Insoluble, filamentous protein that forms the structure of a blood clot.

fibrinogen: Plasma protein produced in the liver and involved in blood clotting.

fibrinolysis: Gradual degradation of a blood clot.

fibroblast: Most abundant cell type in connective tissue, secretes protein fibres and matrix into the extracellular space.

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fibrocartilage: Tough form of cartilage, made of thick bundles of collagen fibres embedded in chondroitin sulfate ground substance.
fibrocyte: Less active form of fibroblast.
fibroelastic membrane: Specialized membrane that connects the ends of the C-shape cartilage in the trachea; contains smooth muscle fibres.
fibrous joint: Joint where the articulating areas of the adjacent bones are connected by fibrous connective tissue.
fibrous pericardium: Sturdy outer layer made of tough, dense connective tissue that protects the heart and maintains its position in the thorax.
fibrous tunic: Outer layer of the eye primarily composed of connective tissue known as the sclera and cornea.
fibula: Thin, non-weight-bearing bone found on the lateral side of the leg.
fibular collateral ligament: The second extrinsic ligaments of the knee.
fibularis brevis (also peroneus brevis): Muscle that plantar flexes the foot at the ankle and everts it at the intertarsal joints.
fibularis longus (also peroneus longus): Muscle that plantar flexes the foot at the ankle and everts it at the intertarsal joints.
fibular nerve: Systemic nerve of the posterior leg that begins as part of the sciatic nerve.
fibular notch: Wide groove on the lateral side of the distal tibia for articulation with the fibula at the distal tibiofibular joint.
fight-or-flight response: Set of responses induced by sympathetic activity that lead to either fleeing a threat or standing up to it, which in the modern world is often associated with anxious feelings.
filling time: Duration of ventricular diastole during which filling occurs.
filtration: In the cardiovascular system, the movement of material from a capillary into the interstitial fluid, moving from an area of higher pressure to lower pressure.
filtration slits: Formed by pedicels of podocytes; substances filter between the pedicels based on size.
fimbriae: Fingerlike projections on the distal uterine tubes.
first messenger: Hormone that binds to a cell membrane hormone receptor and triggers activation of a second messenger system.
fissures: Separate the lobes of the lungs from each other.
fixator: Synergist that assists an agonist by preventing or reducing movement at another joint, thereby stabilizing the origin of the agonist.
flagellum: Appendage on certain cells formed by microtubules and modified for movement.
flat bone: Thin and curved bone; serves as a point of attachment for muscles and protects internal organs.

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flatus: Gas in the intestine.

flexion: Movement in the sagittal plane that decreases the angle of a joint (bends the joint); motion involving anterior bending of the vertebral column.

flexor: Muscle that decreases the angle at the joint.

flexor carpi radialis: Muscle that flexes and abducts the hand at the wrist.

flexor carpi ulnaris: Muscle that flexes and adducts the hand at the wrist.

flexor digitorum superficialis: Muscle that flexes the hand and the digits.

flexor retinaculum: Strong band of connective tissue at the anterior wrist that spans the top of the U-shaped grouping of the carpal bones to form the roof of the carpal tunnel.

floating ribs: Vertebral ribs 11–12 that do not attach to the sternum or to the costal cartilage of another rib.

fluid compartment: Fluid inside all cells of the body constitutes a compartment system that is largely segregated from other systems.

fluid connective tissue: Specialized cells that circulate in a watery fluid containing salts, nutrients, and dissolved proteins.

follicle: Ovarian structure of one oocyte and surrounding granulosa (and later theca) cells.

follicle-stimulating hormone (FSH): Anterior pituitary hormone that stimulates the production and maturation of sex cells.

follicular phase: Phase of the ovarian cycle when the tertiary follicles are growing and secreting estrogen.

folliculogenesis: Development of ovarian follicles from primordial to tertiary under the stimulation of gonadotropins.

fontanelle: Expanded area of fibrous connective tissue that separates the brain case bones of the skull prior to birth and during the first year after birth.

fontanelles: Expanded areas of fibrous connective tissue that separate the braincase bones of the skull prior to birth and during the first year after birth.

foot: Portion of the lower limb located distal to the ankle joint.

foramen magnum: Large opening in the occipital bone of the skull through which the spinal cord emerges and the vertebral arteries enter the cranium.

foramen ovale: Opening in the fetal heart that allows blood to flow directly from the right atrium to the left atrium, bypassing the fetal pulmonary circuit.

forced breathing (also hyperpnea): Mode of breathing that occurs during exercise or by active thought that requires muscle contraction for both inspiration and expiration.

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forearm: Region of the upper limb located between the elbow and wrist joints; contains the radius and ulna bones.

forebrain: Anterior region of the adult brain that develops from the prosencephalon and includes the cerebrum and diencephalon.

formed elements: Cellular components of blood (erythrocytes, leukocytes, and platelets).

forming urine: Filtrate undergoing modifications through secretion and reabsorption before true urine is produced.

fossa (plural = fossae): Shallow depression on the surface of a bone.

fossa ovalis: Oval-shaped depression in the interatrial septum that marks the former location of the foramen ovale.

fourth ventricle: The portion of the ventricular system that is in the region of the brain stem and opens into the subarachnoid space through the median and lateral apertures.

fovea: Exact centre of the retina at which visual stimuli are focused for maximal acuity, where the retina is thinnest and there is nothing but photoreceptors.

fovea capitis: Minor indentation on the head of the femur that serves as the site of attachment for the ligament to the head of the femur.

fracture: Broken bone.

fracture hematoma: Blood clot that forms at the site of a broken bone.

Frank-Starling mechanism: Relationship between ventricular stretch and contraction in which the force of heart contraction is directly proportional to the initial length of the muscle fibre.

free nerve ending: Configuration of a sensory receptor neuron with dendrites in the connective tissue of the organ, such as in the dermis of the skin, that are most often sensitive to chemical, thermal, and mechanical stimuli.

frontal bone: Unpaired bone that forms the forehead, roof of the orbit, and floor of the anterior cranial fossa.

frontal eye field: Region of the frontal lobe associated with motor commands to orient the eyes toward an object of visual attention.

frontalis: Front part of the occipitofrontalis muscle.

frontal lobe: Region of the cerebral cortex directly beneath the frontal bone of the cranium.

frontal plane: Two-dimensional, vertical plane that divides the body or organ into anterior and posterior portions; also referred to as coronal plane.

frontal sinus: Air-filled space within the frontal bone; most anterior of the paranasal sinuses.

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fulcrum: Fixed point that a force is applied to on the handle of a lever.
functional residual capacity (FRC): Sum of ERV and RV, which is the amount of air that remains in the lungs after a tidal expiration.
fundus: Dome-shaped region of the stomach above and to the left of the cardia.
fundus (of the uterus): Domed portion of the uterus that is superior to the uterine tubes.
fusiform: Muscle that has fascicles that are spindle-shaped to create large bellies.
G_0 phase: Phase of the cell cycle usually entered from the G_1 phase; characterized by long or permanent periods where the cell does not move forward into the DNA synthesis phase.
G_1 phase: First phase of the cell cycle, after a new cell is born.
G_2 phase: Third phase of the cell cycle, after the DNA synthesis phase.
gallbladder: Accessory digestive organ that stores and concentrates bile.
gamete: Haploid reproductive cell that contributes genetic material to form an offspring.
ganglion: Localized collection of neuron cell bodies in the peripheral nervous system.
ganglionic neuron: Specifically refers to the cell body of a neuron in the autonomic system that is located in a ganglion.
gap junction: Channels between adjacent cardiac muscle fibres that allow the depolarizing current produced by cations to flow from one cardiac muscle cell to the next.
gastric emptying: Process by which mixing waves gradually cause the release of chyme into the duodenum.
gastric gland: Gland in the stomach mucosal epithelium that produces gastric juice.
gastric juice: Complex digestive fluid.
gastric lipase: Secreted by the chief cells in the stomach and responsible for lipid digestion.
gastric phase: Phase of gastric secretion that begins when food enters the stomach.
gastric pit: Narrow channel formed by the epithelial lining of the stomach mucosa.
gastric plexuses: Neuronal networks in the wall of the stomach that are part of the enteric nervous system.
gastrin: Peptide hormone that stimulates secretion of hydrochloric acid and gut motility.
gastrocnemius: Most superficial muscle of the calf.

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gastrocolic reflex: Propulsive movement in the colon activated by the presence of food in the stomach.

gastroileal reflex: Long reflex that increases the strength of segmentation in the ileum.

gastrulation: Process of cell migration and differentiation into three primary germ layers following cleavage and implantation.

gated: Property of a channel that determines how it opens under specific conditions, such as voltage change or physical deformation.

G cell: Gastrin-secreting enteroendocrine cell.

gene: Functional length of DNA that provides the genetic information necessary to build a protein.

gene expression: Active interpretation of the information coded in a gene to produce a functional gene product.

general adaptation syndrome (GAS): The human body's three-stage response pattern to short- and long-term stress.

general sense: Any sensory system that is distributed throughout the body and incorporated into organs of multiple other systems, such as the walls of the digestive organs or the skin.

generator potential: Graded potential from dendrites of a unipolar cell that generates the action potential in the initial segment of that cell's axon.

genome: Entire complement of an organism's DNA; found within virtually every cell.

germinal centres: Clusters of rapidly proliferating B cells found in secondary lymphoid tissues.

gestation: In human development, the period required for embryonic and fetal development in utero; pregnancy.

gigantism: Disorder in children caused when abnormally high levels of GH prompt excessive growth.

gingiva: Gum.

glabella: Slight depression of frontal bone, located at the midline between the eyebrows.

gland: Structure made up of one or more cells modified to synthesize and secrete chemical substances.

glans penis: Bulbous end of the penis that contains a large number of nerve endings.

glassy membrane: Layer of connective tissue that surrounds the base of the hair follicle, connecting it to the dermis.

glenohumeral joint: Shoulder joint; articulation between the glenoid cavity of the scapula and head of the humerus; multiaxial ball-and-socket joint

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that allows for flexion/extension, abduction/adduction, circumduction, and medial/lateral rotation of the humerus.

glenoid cavity (also glenoid fossa): Shallow depression located on the lateral scapula, between the superior and lateral borders.

glenoid labrum: Lip of fibrocartilage located around the outside margin of the glenoid cavity of the scapula.

glial cell: One of the various types of neural tissue cells responsible for maintenance of the tissue and largely responsible for supporting neurons.

globin: Heme-containing globular protein that is a constituent of hemoglobin.

globulins: Heterogeneous group of plasma proteins that includes transport proteins, clotting factors, immune proteins, and others.

glomerular filtration rate (GFR): Rate of renal filtration.

glomerulus: Tuft of capillaries surrounded by Bowman's capsule; filters the blood based on size.

glossopharyngeal nerve: Ninth cranial nerve; responsible for the contraction of muscles in the tongue and throat and for part of the sense of taste as well as causing saliva production.

glottis: Opening between the vocal folds through which air passes when producing speech.

glucagon: Pancreatic hormone that stimulates the catabolism of glycogen to glucose, thereby increasing blood glucose levels.

glucocorticoids: Hormones produced by the zona fasciculata of the adrenal cortex that influence glucose metabolism.

gluconeogenesis: Process of glucose synthesis from pyruvate or other molecules.

gluteal group: Muscle group that extends, flexes, rotates, adducts, and abducts the femur.

gluteal tuberosity: Roughened area on the posterior side of the proximal femur, extending inferiorly from the base of the greater trochanter.

gluteus maximus: Largest of the gluteus muscles that extends the femur.

gluteus medius: Muscle deep to the gluteus maximus that abducts the femur at the hip.

gluteus minimus: Smallest of the gluteal muscles; deep to the gluteus medius.

glycocalyx: Coating of sugar molecules that surrounds the cell membrane.

glycogen: Form that glucose assumes when it is stored.

glycolysis: Series of metabolic reactions that breaks down glucose into pyruvate and produces ATP.

glycoprotein: Protein that has one or more carbohydrates attached.

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glycosuria: Presence of glucose in the urine; caused by high blood glucose levels that exceed the ability of the kidneys to reabsorb the glucose; usually the result of untreated or poorly controlled diabetes mellitus.

goblet cell: Unicellular gland found in columnar epithelium that secretes mucous.

Golgi apparatus: Cellular organelle formed by a series of flattened, membrane-bound sacs that functions in protein modification, tagging, packaging, and transport.

gomphosis: Type of fibrous joint in which the root of a tooth is anchored into its bony jaw socket by strong periodontal ligaments.

gonadal artery: Branch of the abdominal aorta; supplies blood to the gonads or reproductive organs; also described as ovarian arteries or testicular arteries, depending on the sex of the individual.

gonadal vein: Generic term for a vein draining a reproductive organ; may be either an ovarian vein or a testicular vein, depending on the sex of the individual.

gonadotropin-releasing hormone (GnRH): Hormone released by the hypothalamus that regulates the production of follicle-stimulating hormone and luteinizing hormone from the pituitary gland.

gonadotropins: Hormones that regulate the function of the gonads.

gonads: Reproductive organs (testes and ovaries) that produce gametes and reproductive hormones.

G protein: Protein associated with a cell membrane hormone receptor that initiates the next step in a second messenger system upon activation by hormone-receptor binding.

gracilis: Muscle that adducts the thigh and flexes the leg at the knee.

graded muscle response: Modification of contraction strength.

graded potential: Change in the membrane potential that varies in size, depending on the size of the stimulus that elicits it.

granular leukocytes: Leukocytes with abundant granules in their cytoplasm; specifically, neutrophils, eosinophils, and basophils.

granulosa cells: Supportive cells in the ovarian follicle that produce estrogen.

granzyme: Apoptosis-inducing substance contained in granules of NK cells and cytotoxic T cells.

great cardiac vein: Vessel that follows the interventricular sulcus on the anterior surface of the heart and flows along the coronary sulcus into the coronary sinus on the posterior surface; parallels the anterior interventricular artery and drains the areas supplied by this vessel.

great cerebral vein: Receives most of the smaller vessels from the inferior cerebral veins and leads to the straight sinus.

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greater curvature: The convex lateral surface of the stomach.

greater pelvis (also greater pelvic cavity or false pelvis): Broad space above the pelvic brim defined laterally by the fanlike portion of the upper ilium.

greater sciatic notch: Large, U-shaped indentation located on the posterior margin of the ilium, superior to the ischial spine.

greater splanchnic nerve: Nerve that contains fibres of the central sympathetic neurons that do not synapse in the chain ganglia but project onto the celiac ganglion.

greater trochanter: Large, bony expansion of the femur that projects superiorly from the base of the femoral neck.

greater tubercle: Enlarged prominence located on the lateral side of the proximal humerus.

great saphenous vein: Prominent surface vessel located on the medial surface of the leg and thigh; drains the superficial portions of these areas and leads to the femoral vein.

grey matter: Regions of the nervous system containing cell bodies of neurons with few or no myelinated axons; actually may be more pink or tan in colour but called grey in contrast to white matter.

grey rami communicantes (singular = ramus communicans): Unmyelinated structures that provide a short connection from a sympathetic chain ganglion to the spinal nerve that contains the postganglionic sympathetic fibre.

gross anatomy: Study of the larger structures of the body, typically with the unaided eye; also referred to as macroscopic anatomy.

ground substance: Fluid or semifluid portion of the matrix.

growth: Process of increasing in size.

growth hormone (GH): Anterior pituitary hormone that promotes tissue building and influences nutrient metabolism (also called somatotropin).

gustation: Sense of taste.

gustatory receptor cells: Sensory cells in the taste bud that transduce the chemical stimuli of gustation.

gyrus: Ridge formed by convolutions on the surface of the cerebrum or cerebellum.

hair: Keratinous filament growing out of the epidermis.

hair bulb: Structure at the base of the hair root that surrounds the dermal papilla.

hair cells: Mechanoreceptor cells found in the inner ear that transduce stimuli for the senses of hearing and balance.

hair follicle: Cavity or sac from which hair originates.

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hair follicle plexus: Follicles are also wrapped in a plexus of nerve endings—detect the movement of hair at the surface of the skin, such as when an insect may be walking along the skin.

hair matrix: Layer of basal cells from which a strand of hair grows.

hair papilla: Mass of connective tissue, blood capillaries, and nerve endings at the base of the hair follicle.

hair root: Part of hair that is below the epidermis anchored to the follicle.

hair shaft: Part of hair that is above the epidermis but is not anchored to the follicle.

Haldane effect: Relationship between the partial pressure of oxygen and the affinity of hemoglobin for carbon dioxide.

hallux: Big toe; digit 1 of the foot.

hamstring group: Three long muscles on the back of the leg.

hand: Region of the upper limb distal to the wrist joint.

haploid: Contain only half the DNA of a diploid cell; examples are ova and sperm cells.

hard palate: Bony structure that forms the roof of the mouth and floor of the nasal cavity, formed by the palatine process of the maxillary bones and the horizontal plate of the palatine bones.

haustral contraction: Slow segmentation in the large intestine.

haustrum: Small pouch in the colon created by tonic contractions of teniae coli.

head of the femur: Rounded, proximal end of the femur that articulates with the acetabulum of the hip bone to form the hip joint.

head of the fibula: Small, knoblike, proximal end of the fibula; articulates with the inferior aspect of the lateral condyle of the tibia.

head of the humerus: Smooth, rounded region on the medial side of the proximal humerus; articulates with the glenoid fossa of the scapula to form the glenohumeral (shoulder) joint.

head of the metatarsal bone: Expanded, distal end of each metatarsal bone.

head of the radius: Disc-shaped structure that forms the proximal end of the radius; articulates with the capitulum of the humerus as part of the elbow joint, and with the radial notch of the ulna as part of the proximal radioulnar joint.

head of the rib: Posterior end of a rib that articulates with the bodies of thoracic vertebrae.

head of the ulna: Small, rounded distal end of the ulna; articulates with the ulnar notch of the distal radius, forming the distal radioulnar joint.

heart rate (HR): Number of times the heart contracts (beats) per minute.

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heart sounds: Sounds heard via auscultation with a stethoscope of the closing of the atrioventricular valves ("lub") and semilunar valves ("dub").
heavy chain: Larger protein chain of an antibody.
helper T cells (Th): T cells that secrete cytokines to enhance other immune responses, involved in activation of both B and T cell lymphocytes.
hematocrit (also packed cell volume): Volume percentage of erythrocytes in a sample of centrifuged blood.
hematopoiesis: Production of blood cells, which occurs in the red marrow of the bones.
hematopoietic stem cell: Type of pluripotent stem cell that gives rise to the formed elements of blood (hemocytoblast).
heme: Red, iron-containing pigment to which oxygen binds in hemoglobin.
hemidesmosomes: Type of cell junction that links cells to the extracellular matrix.
hemocytoblast: Hematopoietic stem cell that gives rise to the formed elements of blood.
hemoglobin: Oxygen-carrying compound in erythrocytes.
hemolysis: Destruction (lysis) of erythrocytes and the release of their hemoglobin into circulation.
hemopoiesis: Production of the formed elements of blood.
hemopoietic growth factors: Chemical signals including erythropoietin, thrombopoietin, colony-stimulating factors, and interleukins that regulate the differentiation and proliferation of particular blood progenitor cells.
hemorrhage: Excessive bleeding.
hemosiderin: Protein-containing storage form of iron found in the bone marrow, liver, and spleen.
hemostasis: Physiological process by which bleeding ceases.
Henry's law: Statement of the principle that the concentration of gas in a liquid is directly proportional to the solubility and partial pressure of that gas.
heparin: Short-acting anticoagulant stored in mast cells and released when tissues are injured; opposes prothrombin.
hepatic artery: Artery that supplies oxygenated blood to the liver.
hepatic lobule: Hexagonal-shaped structure composed of hepatocytes that radiate outward from a central vein.
hepatic portal system: Specialized circulatory pathway that carries blood from digestive organs to the liver for processing before being sent to the systemic circulation.

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hepatic portal vein: Vein that supplies deoxygenated nutrient-rich blood to the liver.

hepatic sinusoid: Blood capillaries between rows of hepatocytes that receive blood from the hepatic portal vein and the branches of the hepatic artery.

hepatic vein: Drains systemic blood from the liver and flows into the inferior vena cava.

hepatocytes: Major functional cells of the liver.

hepatopancreatic ampulla (also ampulla of Vater): Bulb-like point in the wall of the duodenum where the bile duct and main pancreatic duct unite.

hepatopancreatic sphincter (also sphincter of Oddi): Sphincter regulating the flow of bile and pancreatic juice into the duodenum.

hilum: Concave structure on the mediastinal surface of the lungs where blood vessels, lymphatic vessels, nerves, and a bronchus enter the lung.

hindbrain: Posterior region of the adult brain that develops from the rhombencephalon and includes the pons, medulla oblongata, and cerebellum.

hinge joint: Synovial joint at which the convex surface of one bone articulates with the concave surface of a second bone; includes the elbow, knee, ankle, and interphalangeal joints; functionally classified as a uniaxial joint.

hip bone: Coxal bone; one of two paired bones that form the pelvic girdle; each consists of three areas: the ilium, ischium, and pubis.

hip joint: Joint located at the proximal end of the lower limb; formed by the articulation between the acetabulum of the hip bone and the head of the femur.

hippocampus: Grey matter deep in the temporal lobe that is very important for long-term memory formation.

histamine: Vasoactive mediator in granules of mast cells; the primary cause of allergies and anaphylactic shock.

histone: Family of proteins that associate with DNA in the nucleus to form chromatin.

hole: Opening or depression in a bone.

holocrine secretion: Release of a substance caused by the rupture of a gland cell, which becomes part of the secretion.

homeostasis: Steady state of body systems that living organisms maintain.

homologous: Describes two copies of the same chromosome (not identical), one inherited from each parent.

hormone: Secretion of an endocrine organ that travels via the bloodstream or lymphatics to induce a response in target cells or tissues in another part of the body.

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hormone receptor: Protein within a cell or on the cell membrane that binds a hormone, initiating the target cell response.

human chorionic gonadotropin (hCG): Hormone that directs the corpus luteum to survive, enlarge, and continue producing progesterone and estrogen to suppress menses and secure an environment suitable for the developing embryo.

humeroulnar joint: Articulation between the trochlea of humerus and the trochlear notch of the ulna; uniaxial hinge joint that allows for flexion/extension of the forearm.

humerus: Single bone of the upper arm.

hyaline cartilage: Most common type of cartilage, smooth and made of short collagen fibres embedded in a chondroitin sulfate ground substance.

hydrochloric acid (HCl): Digestive acid secreted by parietal cells in the stomach.

hydrogen bond: Very weak bond between molecules or between parts of large polar molecules like water.

hydrophilic: Describes a substance or structure attracted to water.

hydrophobic: Describes a substance or structure repelled by water.

hydrostatic pressure: Pressure exerted by a fluid against a wall, caused by its own weight or pumping force.

hymen: Membrane that covers part of the opening of the vagina.

hyoid bone: Small, U-shaped bone located in the upper neck that does not contact any other bone.

hypercalcemia: Condition characterized by abnormally high levels of calcium.

hypercapnia: Abnormally elevated blood levels of CO_2.

hyperchloremia: Higher-than-normal blood chloride levels.

hyperextension: Excessive extension of a joint, beyond the normal range of movement.

hyperflexion: Excessive flexion of a joint, beyond the normal range of movement.

hyperkalemia: Higher-than-normal blood potassium levels.

hypernatremia: Abnormal increase in blood sodium levels.

hyperparathyroidism: Disorder caused by overproduction of PTH that results in abnormally elevated blood calcium.

hyperphosphatemia: Abnormally increased blood phosphate levels.

hyperplasia: Process in which one cell splits to produce new cells.

hyperpolarization: Period of the action potential when the membrane voltage is below −70 mV with K^+ channels open and potassium ions reach equilibrium.

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hypertension: Chronic and persistent blood pressure measurements of 140/90 mm Hg or above.
hypertonia: Abnormally high muscle tone.
hypertonic: Describes a solution concentration that is higher than a reference concentration.
hypertrophic cardiomyopathy: Pathological enlargement of the heart, generally for no known reason.
hypertrophy: Addition of structural proteins to muscle fibres.
hypervolemia: Abnormally high levels of fluid and blood within the body.
hypocalcemia: Condition characterized by abnormally low levels of calcium.
hypocapnia: Abnormally low blood levels of CO_2.
hypochloremia: Lower-than-normal blood chloride levels.
hypodermis: Connective tissue connecting the integument to the underlying bone and muscle.
hypoglossal nerve: 12th cranial nerve; responsible for the contraction of muscles of the tongue.
hypokalemia: Abnormally decreased blood levels of potassium.
hyponatremia: Lower-than-normal levels of sodium in the blood.
hyponychium: Thickened layer of stratum corneum that lies below the free edge of the nail.
hypoparathyroidism: Disorder caused by underproduction of PTH that results in abnormally low blood calcium.
hypophosphatemia: Abnormally low blood phosphate levels.
hypophyseal (pituitary) fossa: Shallow depression on top of the sella turcica that houses the pituitary (hypophyseal) gland.
hypophyseal portal system: Network of blood vessels that enables hypothalamic hormones to travel into the anterior lobe of the pituitary without entering the systemic circulation.
hypothalamus: Major region of the diencephalon that is responsible for coordinating autonomic and endocrine control of homeostasis.
hypotonia: Abnormally low muscle tone caused by the absence of low-level contractions.
hypotonic: Describes a solution concentration that is lower than a reference concentration.
hypovolemia: Abnormally low levels of fluid and blood within the body.
hypovolemic shock: Type of circulatory shock caused by excessive loss of blood volume due to hemorrhage or possibly dehydration.
hypoxia: Lack of oxygen supply to the tissues.

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IgA: Antibody whose dimer is secreted by exocrine glands, is especially effective against digestive and respiratory pathogens, and can pass immunity to an infant through breastfeeding.

IgD: Class of antibody whose only known function is as a receptor on naive B cells; important in B cell activation.

IgE: Antibody that binds to mast cells and causes antigen-specific degranulation during an allergic response.

IgG: Main blood antibody of late primary and early secondary responses; passed from carrier to unborn child via placenta.

IgM: Antibody whose monomer is a surface receptor of naive B cells; the pentamer is the first antibody made during primary responses.

ileocecal sphincter: Sphincter located where the small intestine joins with the large intestine.

ileum: End of the small intestine between the jejunum and the large intestine.

iliac crest: Curved, superior margin of the ilium.

iliac fossa: Shallow depression found on the anterior and medial surfaces of the upper ilium.

iliacus: Muscle that, along with the psoas major, makes up the iliopsoas.

iliocostalis cervicis: Muscle of the iliocostalis group associated with the cervical region.

iliocostalis group: Laterally placed muscles of the erector spinae.

iliocostalis lumborum: Muscle of the iliocostalis group associated with the lumbar region.

iliocostalis thoracis: Muscle of the iliocostalis group associated with the thoracic region.

iliopsoas group: Muscle group consisting of iliacus and psoas major muscles; flexes the thigh at the hip, rotates it laterally, and flexes the trunk of the body onto the hip.

ilium: Superior portion of the hip bone.

immune system: Series of barriers, cells, and soluble mediators that combine in response to infections of the body by pathogenic organisms.

immunoglobulin (Ig, also antibody or gamma globulin): Antigen-specific proteins produced by specialized B lymphocytes that protect the body by binding to foreign objects such as bacteria and viruses.

immunological memory: Ability of the adaptive immune response to mount a stronger and faster immune response upon reexposure to a pathogen.

implantation: When the developing zygote lodges into the uterus for development.

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inactivation gate: Part of a voltage-gated Na^+ channel that closes when the membrane potential reaches +30 mV.

inactive proenzymes: Forms in which proteases are stored and released to prevent the inappropriate digestion of the native proteins of the stomach, pancreas, and small intestine.

incisor: Midline, chisel-shaped tooth used for cutting into food.

incontinence: Loss of ability to control micturition.

incus (also anvil): Ossicle of the middle ear that connects the malleus to the stapes.

indirect pathway: Connections within the basal nuclei from the striatum through the globus pallidus external segment and subthalamic nucleus to the globus pallidus internal segment/substantia nigra pars compacta that result in inhibition of the thalamus to decrease cortical control of movement.

inferior: Describes a position below or lower than another part of the body proper, near or toward the tail (in humans, the coccyx, or lowest part of the spinal column); also referred to as caudal.

inferior angle of scapula: The most inferior portion of the scapula, particularly important because it serves as the attachment point for several powerful muscles involved in shoulder and upper limb movements.

inferior articular process: Bony process that extends downward from the vertebral arch of a vertebra that articulates with the superior articular process of the next lower vertebra.

inferior colliculus: Half of the midbrain tectum that is part of the brain stem auditory pathway.

inferior mesenteric ganglion: One of the collateral ganglia of the sympathetic system that projects to the digestive system.

inferior nasal concha: One of the paired bones that project from the lateral walls of the nasal cavity to form the largest and most inferior of the nasal conchae.

inferior pubic ramus: Narrow segment of bone that passes inferiorly and laterally from the pubic body; joins with the ischial ramus to form the ischiopubic ramus.

inferior rotation: Movement of the scapula during upper limb adduction in which the glenoid cavity of the scapula moves in a downward direction as the medial end of the scapular spine moves in an upward direction.

inferior vena cava: Large systemic vein that drains blood from areas largely inferior to the diaphragm; empties into the right atrium.

inflammation: Basic innate immune response characterized by heat, redness, pain, and swelling.

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infrahyoid muscles: Anterior neck muscles that are attached to, and inferior to, the hyoid bone.

infraspinatus: Muscle that laterally rotates the arm.

infraspinous fossa: Broad depression located on the posterior scapula, inferior to the spine.

infundibulum: Stalk containing vasculature and neural tissue that connects the pituitary gland to the hypothalamus (also called the pituitary stalk).

ingestion: Taking food into the GI tract through the mouth.

inguinal canal: Opening in abdominal wall that connects the testes to the abdominal cavity.

inhibin: Hormone secreted by the male and female gonads that inhibits FSH production by the anterior pituitary.

inhibiting hormones: Hormones that inhibit secretion from the anterior pituitary.

inhibitory postsynaptic potential (IPSP): Graded potential in the postsynaptic membrane that is the result of hyperpolarization and makes an action potential less likely to occur.

initial segment: First part of the axon as it emerges from the axon hillock, where the electrical signals known as action potentials are generated.

innate immune response: Rapid but relatively nonspecific immune response.

inner cell mass: Cluster of cells within the blastocyst that is fated to become the embryo.

inner ear: Structure within the temporal bone that contains the sensory apparati of hearing and balance.

innermost intercostal: The deepest intercostal muscles that draw the ribs together.

inner segment: In the eye, the section of a photoreceptor that contains the nucleus and other major organelles for normal cellular functions.

inorganic compound: Substance that does not contain both carbon and hydrogen.

insertion: End of a skeletal muscle that is attached to the structure (usually a bone) that is moved when the muscle contracts.

inspiration (also inhalation): Process that causes air to enter the lungs.

inspiratory capacity (IC): Sum of the TV and IRV, which is the amount of air that can maximally be inhaled past a tidal expiration.

inspiratory reserve volume (IRV): Amount of air that enters the lungs due to deep inhalation past the tidal volume.

insulin: Pancreatic hormone that enhances the cellular uptake and utilization of glucose, thereby decreasing blood glucose levels.

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insulin-like growth factors (IGF): Protein that enhances cellular proliferation, inhibits apoptosis, and stimulates the cellular uptake of amino acids for protein synthesis.

integral protein: Membrane-associated protein that spans the entire width of the lipid bilayer.

integration (association areas): Nervous system function that combines sensory perceptions and higher cognitive functions (memories, learning, emotion, etc.) to produce a response.

integumentary system: Skin and its accessory structures.

interatrial septum: Cardiac septum located between the two atria; contains the fossa ovalis after birth.

intercalated cell: Specialized cell of the collecting ducts that secrete or absorb acid or bicarbonate; important in acid-base balance.

intercalated disc: Physical junction between adjacent cardiac muscle cells; consisting of desmosomes, specialized linking proteoglycans, and gap junctions that allow passage of ions between the two cells.

intercondylar eminence: Irregular elevation on the superior end of the tibia, between the articulating surfaces of the medial and lateral condyles.

intercondylar fossa: Deep depression on the posterior side of the distal femur that separates the medial and lateral condyles.

intercostal artery: Branch of the thoracic aorta; supplies blood to the muscles of the thoracic cavity and vertebral column.

intercostal muscles: Muscles that span the spaces between the ribs.

intercostal nerve: Systemic nerve in the thoracic cavity that is found between two ribs.

interferons: Early induced proteins made in virally infected cells that cause nearby cells to make antiviral proteins.

interleukins: Signalling molecules that may function in hemopoiesis, inflammation, and specific immune responses.

intermediate cuneiform: Middle of the three cuneiform tarsal bones; articulates posteriorly with the navicular bone, medially with the medial cuneiform bone, laterally with the lateral cuneiform bone, and anteriorly with the second metatarsal bone.

intermediate filament: Type of cytoskeletal filament made of keratin, characterized by an intermediate thickness, and playing a role in resisting cellular tension.

internal acoustic meatus: Opening into the petrous ridge, located on the lateral wall of the posterior cranial fossa.

internal anal sphincter: Involuntary smooth muscle sphincter in the anal canal.

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internal callus: Fibrocartilaginous matrix, in the endosteal region, between the two ends of a broken bone.

internal capsule: Segment of the descending motor pathway that passes between the caudate nucleus and the putamen.

internal carotid artery: Arises from the common carotid artery and begins with the carotid sinus; goes through the carotid canal of the temporal bone to the base of the brain; combines with branches of the vertebral artery forming the arterial circle; supplies blood to the brain.

internal elastic membrane: Membrane composed of elastic fibres that separates the tunica intima from the tunica media; seen in larger arteries.

internal iliac artery: Branch from the common iliac arteries; supplies blood to the urinary bladder, walls of the pelvis, external genitalia, and the medial portion of the femoral region; in females, also provides blood to the uterus and vagina.

internal iliac vein: Drains the pelvic organs and integument; formed from several smaller veins in the region; leads to the common iliac vein.

internal intercostal: Intermediate intercostal muscles that draw the ribs together.

internal jugular vein: One of a pair of major veins located in the neck region that passes through the jugular foramen and canal and flows parallel to the common carotid artery that is more or less its counterpart; primarily drains blood from the brain, receives the superficial facial vein, and empties into the subclavian vein.

internal oblique: Flat, intermediate abdominal muscle with fascicles that run perpendicular to those of the external oblique.

internal respiration: Gas exchange that occurs at the level of body tissues.

internal root sheath: Innermost layer of keratinocytes in the hair follicle that surround the hair root up to the hair shaft.

internal thoracic vein (also internal mammary vein): Drains the anterior surface of the chest wall and leads to the brachiocephalic vein.

internal urinary (urethral) sphincter: Smooth muscle at the juncture of the bladder and urethra; relaxes as the bladder fills to allow urine into the urethra.

internodal pathways: Specialized conductile cells within the atria that transmit the impulse from the SA node throughout the myocardial cells of the atrium and to the AV node.

interoceptor: Sensory receptor that is positioned to interpret stimuli from internal organs, such as stretch receptors in the wall of blood vessels.

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interosseous border of the fibula: Small ridge running down the medial side of the fibular shaft for attachment of the interosseous membrane between the fibula and tibia.

interosseous membrane: Wide sheet of fibrous connective tissue that fills the gap between two parallel bones, forming a syndesmosis; found between the radius and ulna of the forearm and between the tibia and fibula of the leg.

interphase: Entire life cycle of a cell, excluding mitosis.

interstitial fluid (IF): Fluid in the small spaces between cells not contained within blood vessels.

interstitial fluid colloidal osmotic pressure (IFCOP): Pressure exerted by the colloids within the interstitial fluid.

interstitial fluid hydrostatic pressure (IFHP): Force exerted by the fluid in the tissue spaces.

intertrochanteric crest: Short, prominent ridge running between the greater and lesser trochanters on the posterior side of the proximal femur.

intertrochanteric line: Small ridge running between the greater and lesser trochanters on the anterior side of the proximal femur.

interventricular foramina: Openings between the lateral ventricles and the third ventricle, allowing for the passage of CSF.

interventricular septum: Cardiac septum located between the two ventricles.

intervertebral disc: Structure located between the bodies of adjacent vertebrae that strongly joins the vertebrae; provides padding, weight-bearing ability, and enables vertebral column movements.

intervertebral foramen: Opening located between adjacent vertebrae for exit of a spinal nerve.

intestinal gland (also crypt of Lieberkühn): Gland in the small intestinal mucosa that secretes intestinal juice.

intestinal juice: Mixture of water and mucus that helps absorb nutrients from chyme.

intestinal phase: Phase of gastric secretion that begins when chyme enters the intestine.

intra-alveolar pressure (intrapulmonary pressure): Pressure of the air within the alveoli.

intracapsular ligament: Ligament that is located within the articular capsule of a synovial joint.

intracellular fluid (ICF): Fluid in the cytosol of cells.

intramembranous ossification: Process by which bone forms directly from mesenchymal tissue.

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intramural ganglia: Terminal ganglia of the parasympathetic system that are found within the walls of the target effector.

intrapleural pressure: Pressure of the air within the pleural cavity.

intrinsic factor: Glycoprotein required for vitamin B_{12} absorption in the small intestine.

intrinsic ligament: Ligament that is fused to or incorporated into the wall of the articular capsule of a synovial joint.

intrinsic pathway: Initial coagulation pathway that begins with vascular damage or contact with foreign substances and results in the activation of the common pathway.

inversion: Foot movement involving the intertarsal joints of the foot in which the bottom of the foot is turned toward the midline.

involution: Postpartum shrinkage of the uterus back to its prepregnancy volume.

ion: Atom with an overall positive or negative charge.

ionic bond: Attraction between an anion and a cation.

ionotropic receptor: Neurotransmitter receptor that acts as an ion channel gate and opens by the binding of the neurotransmitter.

ipsilateral: Word meaning on the same side, as in axons that do not cross the midline in a fibre tract.

iris: Coloured portion of the anterior eye that surrounds the pupil.

irregular bone: Bone of complex shape; protects internal organs from compressive forces.

ischemia: Insufficient blood flow to the tissues.

ischial ramus: Bony extension projecting anteriorly and superiorly from the ischial tuberosity; joins with the inferior pubic ramus to form the ischiopubic ramus.

ischial spine: Pointed, bony projection from the posterior margin of the ischium that separates the greater sciatic notch and lesser sciatic notch.

ischial tuberosity: Large, roughened protuberance that forms the posteroinferior portion of the hip bone; weight-bearing region of the pelvis when sitting.

ischiopubic ramus: Narrow extension of bone that connects the ischial tuberosity to the pubic body; formed by the junction of the ischial ramus and inferior pubic ramus.

ischium: Posteroinferior portion of the hip bone.

isometric contraction: Muscle contraction that occurs with no change in muscle length.

isotonic: Describes a solution concentration that is the same as a reference concentration.

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isotonic contraction: Muscle contraction that involves changes in muscle length.

isovolumic contraction (also isovolumetric contraction): Initial phase of ventricular contraction in which tension and pressure in the ventricle increase but no blood is pumped or ejected from the heart.

isovolumic ventricular relaxation phase: Initial phase of the ventricular diastole when pressure in the ventricles drops below pressure in the two major arteries, the pulmonary trunk and the aorta, and blood attempts to flow back into the ventricles, producing the dicrotic notch of the ECG and closing the two semilunar valves.

isthmus: Narrow, medial portion of the uterine tube that joins the uterus.

jaundice: Yellowing of the skin or whites of the eyes due to excess bilirubin in the blood.

jejunum: Middle part of the small intestine between the duodenum and the ileum.

joint: Site at which two or more bones or bone and cartilage come together (articulate).

joint cavity: Space enclosed by the articular capsule of a synovial joint that is filled with synovial fluid and contains the articulating surfaces of the adjacent bones.

jugular (suprasternal) notch: Shallow notch located on the superior surface of the sternal manubrium.

jugular foramina: Openings located between the temporal bone and occipital bone that allow the internal jugular vein and three cranial nerves to pass through.

jugular veins: Blood vessels that return "used" blood from the head and neck.

juxtaglomerular apparatus (JGA): Located at the juncture of the DCT and the afferent and efferent arterioles of the glomerulus; plays a role in the regulation of renal blood flow and GFR.

juxtaglomerular cell: Modified smooth muscle cells of the afferent arteriole; secretes renin in response to a drop in blood pressure.

juxtamedullary nephrons: Nephrons adjacent to the border of the cortex and medulla with loops of Henle that extend into the renal medulla.

keratin: Type of structural protein that gives skin, hair, and nails its hard, water-resistant properties.

keratinocyte: Cell that produces keratin and is the most predominant type of cell found in the epidermis.

keratohyalin: Granulated protein found in the stratum granulosum.

ketone bodies: Alternative source of energy when glucose is limited, created when too much acetyl CoA is created during fatty acid oxidation.

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kinesthesia: Sense of body movement based on sensations in skeletal muscles, tendons, joints, and the skin.

kinetic energy: Energy that matter possesses because of its motion.

kinetochore: Region of a centromere where microtubules attach to a pair of sister chromatids.

knee joint: Joint that separates the thigh and leg portions of the lower limb; formed by the articulations between the medial and lateral condyles of the femur, and the medial and lateral condyles of the tibia.

Korotkoff sounds: Noises created by turbulent blood flow through the vessels.

Krebs cycle: Also called the citric acid cycle or the tricarboxylic acid cycle, converts pyruvate into CO_2 and high-energy $FADH_2$, NADH, and ATP molecules.

labial frenulum: Midline mucous membrane fold that attaches the inner surface of the lips to the gums.

labia majora: Hair-covered folds of skin located behind the mons pubis.

labia minora: Thin, pigmented, hairless flaps of skin located medial and deep to the labia majora.

labium: Lip.

lacrimal bone: Paired bones that contribute to the anterior-medial wall of each orbit.

lacrimal glands: Are lateral to the orbit that produces tears to wash across the surface of the eye.

lactase: Brush border enzyme that breaks down lactose into glucose and galactose.

lactation: Process by which milk is synthesized and secreted from the mammary glands of the postpartum female breast in response to sucking at the nipple.

lacteals: Lymphatic capillaries in the small intestine critical for the transport of dietary lipids and lipid-soluble vitamins to the blood.

lactic acid: Product of anaerobic glycolysis.

lactiferous ducts: Ducts that connect the mammary glands to the nipple and allow for the transport of milk.

lactiferous sinus: Area of milk collection between alveoli and lactiferous duct.

lacunae (singular = lacuna): Small spaces in bone or cartilage tissue that cells occupy.

lambdoid suture: Inverted V-shaped joint that unites the occipital bone to the right and left parietal bones on the posterior skull.

lamellae: Concentric rings of calcified matrix in the centre of each osteon.

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lamellated (Pacinian) corpuscles: Responsible for the detection of deep pressure and vibration.

lamina: Portion of the vertebral arch on each vertebra that extends between the transverse and spinous process.

lamina propria: Areolar connective tissue underlying a mucous membrane.

Langerhans cell: Specialized dendritic cell found in the stratum spinosum that functions as a macrophage.

lanugo: Silk-like hairs that coat the fetus; shed later in fetal development.

large intestine: Terminal portion of the alimentary canal.

large motor unit: Arrangement where a single motor neuron supplies a large number of muscle fibres in a muscle; concerned with simple, or "gross," movements.

laryngeal prominence: Region where the two lamine of the thyroid cartilage join, forming a protrusion known as the "Adam's apple."

laryngopharynx: Portion of the pharynx bordered by the oropharynx superiorly and esophagus and trachea inferiorly; serves as a route for both air and food.

larynx: Cartilaginous structure that produces the voice, prevents food and beverages from entering the trachea, and regulates the volume of air that enters and leaves the lungs.

latch-bridges: Subset of a cross-bridge in which actin and myosin remain locked together.

latent period: The time when a twitch does not produce contraction.

lateral: Describes the side or direction toward the side of the body.

lateral (external) rotation: Movement of the arm at the shoulder joint or the thigh at the hip joint that moves the anterior surface of the limb away from the midline of the body.

lateral apertures: Pair of openings from the fourth ventricle to the subarachnoid space on either side and between the medulla and cerebellum.

lateral column: White matter of the spinal cord between the posterior horn on one side and the axons from the anterior horn on the same side; composed of many different groups of axons, of both ascending and descending tracts, carrying motor commands to and from the brain.

lateral condyle of the femur: Smooth, articulating surface that forms the distal and posterior sides of the lateral expansion of the distal femur.

lateral condyle of the tibia: Lateral, expanded region of the proximal tibia that includes the smooth surface that articulates with the lateral condyle of the femur as part of the knee joint.

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lateral corticospinal tract: Division of the corticospinal pathway that travels through the lateral column of the spinal cord and controls appendicular musculature through the lateral motor neurons in the ventral (anterior) horn.

lateral cuneiform: Most lateral of the three cuneiform tarsal bones; articulates posteriorly with the navicular bone, medially with the intermediate cuneiform bone, laterally with the cuboid bone, and anteriorly with the third metatarsal bone.

lateral epicondyle of the femur: Roughened area of the femur located on the lateral side of the lateral condyle.

lateral excursion: Side-to-side movement of the mandible away from the midline toward either the right or left side.

lateral flexion: Bending of the neck or body toward the right or left side.

lateral horn: Region of the spinal cord grey matter in the thoracic, upper lumbar, and sacral regions that is the central component of the sympathetic division of the autonomic nervous system.

lateralis: To the outside.

lateral malleolus: Expanded distal end of the fibula.

lateral meniscus: C-shaped fibrocartilage articular disc located at the knee, between the lateral condyle of the femur and the lateral condyle of the tibia.

lateral sulcus: Surface landmark of the cerebral cortex that marks the boundary between the temporal lobe and the frontal and parietal lobes.

lateral tibiofemoral joint: Portion of the knee consisting of the articulation between the lateral condyle of the tibia and the lateral condyle of the femur; allows for flexion/extension at the knee.

lateral ventricles: Portions of the ventricular system that are in the region of the cerebrum.

latissimus dorsi: Broad, triangular axial muscle located on the inferior part of the back.

leakage channel: Ion channel that opens randomly and is not gated to a specific event, also known as a nongated channel.

leaky tight junctions: Tight junctions in which the sealing strands of proteins between the membranes of adjacent cells are fewer in number and incomplete; allows limited intercellular movement of solvent and solutes.

left atrioventricular valve (also mitral valve or bicuspid valve): Valve located between the left atrium and ventricle; consists of two flaps of tissue.

left colic flexure (also splenic flexure): Point where the transverse colon curves below the inferior end of the spleen.

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left gastric artery: Branch of the celiac trunk; supplies blood to the stomach.
leg: Portion of the lower limb located between the knee and ankle joints.
lens: Component of the eye that focuses light on the retina.
leptin: Protein hormone secreted by adipose tissues in response to food consumption that promotes satiety.
lesser curvature: The concave medial border.
lesser pelvis (also lesser pelvic cavity or true pelvis): Narrow space located within the pelvis, defined superiorly by the pelvic brim (pelvic inlet) and inferiorly by the pelvic outlet.
lesser sciatic notch: Shallow indentation along the posterior margin of the ischium, inferior to the ischial spine.
lesser splanchnic nerve: Nerve that contains fibres of the central sympathetic neurons that do not synapse in the chain ganglia but project onto the inferior mesenteric ganglion.
lesser trochanter: Small, bony projection on the medial side of the proximal femur, at the base of the femoral neck.
lesser tubercle: Small, bony prominence located on the anterior side of the proximal humerus.
letdown reflex: Release of milk from the alveoli triggered by infant suckling.
leukemia: Cancer involving leukocytes.
leukocyte (also white blood cell): Colourless, nucleated blood cell, the chief function of which is to protect the body from disease.
leukocytosis: Excessive leukocyte proliferation.
leukopenia: Below-normal production of leukocytes.
Leydig cells: Cells between the seminiferous tubules of the testes that produce testosterone; a type of interstitial cell.
ligament: Strong band of dense connective tissue spanning between bones.
ligament of the head of the femur: Ligament that spans the acetabulum of the hip bone and the fovea capitis of the femoral head.
ligand: Molecule that binds with specificity to a specific receptor molecule.
ligand-gated channels: Another name for an ionotropic receptor for which a neurotransmitter is the ligand.
light chain: Small protein chain of an antibody.
limbic cortex: Collection of structures of the cerebral cortex that are involved in emotion, memory, and behaviour and are part of the larger limbic system.
limbic lobe: Structures arranged around the edges of the cerebrum that are involved in memory and emotion.

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limbic system: Structures at the edge (limit) of the boundary between the forebrain and hindbrain that are most associated with emotional behaviour and memory formation.

linea alba: White, fibrous band that runs along the midline of the trunk.

linea aspera: Longitudinally running bony ridge located in the middle third of the posterior femur.

lingual frenulum: Mucous membrane fold that attaches the bottom of the tongue to the floor of the mouth.

lingual glands: In the lamina propria of the tongue, secrete mucus and a watery serous fluid that contains the enzyme.

lingual lipase: Digestive enzyme from glands in the tongue that acts on triglycerides.

lingual tonsil: Lymphoid tissue located at the base of the tongue.

lipid: Class of nonpolar organic compounds built from hydrocarbons and distinguished by the fact that they are not soluble in water.

lipogenesis: Synthesis of lipids that occurs in the liver or adipose tissues.

lipolysis: Breakdown of triglycerides into glycerol and fatty acids.

lipoprotein lipase: Enzyme that breaks down triglycerides in chylomicrons into fatty acids and monoglycerides.

liver: Largest gland in the body whose main digestive function is the production of bile.

load: Resistance to the movement of the handle in a lever system.

lobe: Glandular tissue in the breast that contains groups of milk-secreting cells.

long bone: Cylinder-shaped bone that is longer than it is wide; functions as a lever.

longitudinal fissure: Large separation along the midline between the two cerebral hemispheres.

long reflex: Reflex arc that includes the central nervous system.

longus: Long.

loop of Henle: Descending and ascending portions between the proximal and distal convoluted tubules; those of cortical nephrons do not extend into the medulla, whereas those of juxtamedullary nephrons do extend into the medulla.

loose connective tissue (also areolar tissue): Type of connective tissue proper that shows little specialization, with cells dispersed in the matrix.

lower esophageal sphincter: Smooth muscle sphincter that regulates food movement from the esophagus to the stomach.

lower motor neuron: Second neuron in the motor command pathway that is directly connected to the skeletal muscle.

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lumbar curve: Posteriorly concave curvature of the lumbar vertebral column region; a secondary curve of the vertebral column.

lumbar plexus: Nerve plexus associated with the lumbar spinal nerves.

lumbar puncture: Procedure used to withdraw CSF from the lower lumbar region of the vertebral column that avoids the risk of damaging CNS tissue because the spinal cord ends at the upper lumbar vertebrae.

lumbar vertebrae: Five vertebrae numbered L1–L5 that are located in the lumbar region (lower back) of the vertebral column.

lumen: Interior of a tubular structure such as a blood vessel or a portion of the alimentary canal through which blood, chyme, or other substances travel.

lung: Organ of the respiratory system that performs gas exchange.

lunula: Basal part of the nail body that consists of a crescent-shaped layer of thick epithelium.

luteal phase: Postovulatory phase in the ovarian cycle of progesterone secretion.

luteinizing hormone (LH): Anterior pituitary hormone that triggers ovulation and the production of ovarian hormones and the production of testosterone.

lymph: Liquid of the lymphatic system that is returned to the blood.

lymphatic capillaries: Smallest of the lymphatic vessels and the origin of lymph flow.

lymphatic system: Network of lymphatic vessels, lymph nodes, and ducts that carries lymph from the tissues and back to the bloodstream.

lymphatic trunks: Large lymphatics that collect lymph from smaller lymphatic vessels and empty into the blood via lymphatic ducts.

lymphatic vessels: Vessels for transporting the cells of the immune system.

lymph node: One of the bean-shaped organs associated with the lymphatic vessels.

lymphocytes: Agranular leukocytes of the lymphoid stem cell line, many of which function in specific immunity.

lymphoid follicles: The sites of the formation of lymphocytes, with specific B cell–rich and T cell–rich areas.

lymphoid nodules: Unencapsulated patches of lymphoid tissue found throughout the body.

lymphoid stem cells: Type of hematopoietic stem cells that gives rise to lymphocytes, including various T cells, B cells, and NK cells, all of which function in immunity.

lymphoma: Form of cancer in which masses of malignant T and/or B lymphocytes collect in lymph nodes, the spleen, the liver, and other tissues.

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lysosome: Membrane-bound cellular organelle originating from the Golgi apparatus and containing digestive enzymes.

lysozyme: Component of saliva that makes it antimicrobial.

macrophage: Amoeboid phagocyte found in several tissues throughout the body.

macula: Enlargement at the base of a semicircular canal at which transduction of equilibrium stimuli takes place within the ampulla.

macula densa: Cells found in the part of the DCT forming the JGA; sense Na^+ concentration in the forming urine.

main pancreatic duct (also duct of Wirsung): Duct through which pancreatic juice drains from the pancreas.

major duodenal papilla: Point at which the hepatopancreatic ampulla opens into the duodenum.

major histocompatibility complex (MHC): Gene cluster whose proteins present antigens to T cells.

malleus (also hammer): Ossicle that is directly attached to the tympanic membrane.

maltase: Brush border enzyme that breaks down maltose and maltotriose into two and three molecules of glucose, respectively.

mammary glands: Glands inside the breast that secrete milk.

mandible: Unpaired bone that forms the lower jawbone; the only movable bone of the skull.

mandibular fossa: Oval depression located on the inferior surface of the skull.

manubrium: Expanded, superior portion of the sternum.

marginal arteries: Branches of the right coronary artery that supply blood to the superficial portions of the right ventricle.

masseter: Main muscle for chewing that elevates the mandible to close the mouth.

mass movement: Long, slow, peristaltic wave in the large intestine.

mass number: Sum of the number of protons and neutrons in the nucleus of an atom.

mast cell: Cell found in the skin and the lining of body cells that contains cytoplasmic granules with vasoactive mediators such as histamine.

mastication: Chewing.

mastoid process: Large bony prominence on the inferior, lateral skull, just behind the earlobe.

matrix: Extracellular material that is produced by the cells embedded in it, containing ground substance and fibres.

matter: Physical substance; that which occupies space and has mass.

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maxilla (also maxillary bone): Paired bones that form the upper jaw and anterior portion of the hard palate.

maxillary sinus: Air-filled space located within each maxillary bone; largest of the paranasal sinuses.

maximus: Largest.

mean arterial pressure (MAP): Average driving force of blood to the tissues; approximated by taking diastolic pressure and adding one-third of pulse pressure.

meatus: One of three recesses (superior, middle, and inferior) in the nasal cavity attached to the conchae that increases the surface area of the nasal cavity.

mechanical digestion: Chewing, mixing, and segmentation that prepares food for chemical digestion.

mechanically gated channel: Ion channel that opens when a physical event directly affects the structure of the protein.

mechanoreceptor: Receptor cell that transduces mechanical stimuli into an electrochemical signal.

meconium: Fetal wastes consisting of ingested amniotic fluid, cellular debris, mucus, and bile.

medial: Describes the middle or direction toward the middle of the body.

medial (internal) rotation: Movement of the arm at the shoulder joint or the thigh at the hip joint that brings the anterior surface of the limb toward the midline of the body.

medial condyle of the femur: Smooth, articulating surface that forms the distal and posterior sides of the medial expansion of the distal femur.

medial condyle of the tibia: Medial, expanded region of the proximal tibia that includes the smooth surface that articulates with the medial condyle of the femur as part of the knee joint.

medial cuneiform: Most medial of the three cuneiform tarsal bones; articulates posteriorly with the navicular bone, laterally with the intermediate cuneiform bone, and anteriorly with the first and second metatarsal bones.

medial epicondyle of the femur: Roughened area of the distal femur located on the medial side of the medial condyle.

medial excursion: Side-to-side movement that returns the mandible to the midline.

medialis: To the inside.

medial malleolus: Bony expansion located on the medial side of the distal tibia.

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medial meniscus: C-shaped fibrocartilage articular disc located at the knee, between the medial condyle of the femur and medial condyle of the tibia.

medial tibiofemoral joint: Portion of the knee consisting of the articulation between the medial condyle of the tibia and the medial condyle of the femur; allows for flexion/extension at the knee.

median aperture: Singular opening from the fourth ventricle into the subarachnoid space at the midline between the medulla and cerebellum.

median nerve: Systemic nerve of the arm, located between the ulnar and radial nerves.

mediastinal artery: Branch of the thoracic aorta; supplies blood to the mediastinum.

medius: Medium.

medulla (hair): In hair, the innermost layer of keratinocytes originating from the hair matrix.

medulla (kidney): Inner region of the kidney containing the renal pyramids.

medulla (medulla oblongata): White matter region in the brain that is continuous with the white matter of the spinal cord.

medullary cavity: Hollow region of the diaphysis; filled with yellow marrow.

megakaryocyte: Bone marrow cell that produces platelets.

Meissner corpuscle (also tactile corpuscle): Receptor in the skin that responds to light touch.

melanin: Pigment that determines the colour of hair and skin.

melanocyte: Cell found in the stratum basale of the epidermis that produces the pigment melanin.

melanosome: Intercellular vesicle that transfers melanin from melanocytes into keratinocytes of the epidermis.

melatonin: Amino acid–derived hormone that is secreted in response to low light and causes drowsiness.

membrane potential: Distribution of charge across the cell membrane, based on the charges of ions.

memory cell: Type of B or T lymphocyte that forms after exposure to a pathogen.

memory T cells: Long-lived immune cell reserved for future exposure to a pathogen.

menarche: First menstruation in a pubertal female.

meninges: Protective outer coverings of the CNS composed of connective tissue.

meniscus: Articular disc.

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menses: Shedding of the inner portion of the endometrium out through the vagina; also referred to as menstruation.

menses phase: Phase of the menstrual cycle in which the endometrial lining is shed.

menstrual cycle: Approximately 28-day cycle of changes in the uterus consisting of a menses phase, a proliferative phase, and a secretory phase.

Merkel cell: Receptor cell in the stratum basale of the epidermis that responds to the sense of touch.

merocrine secretion: Release of a substance from a gland via exocytosis.

mesangial: Contractile cells found in the glomerulus; can contract or relax to regulate filtration rate.

mesenchymal cell: Adult stem cell from which most connective tissue cells are derived.

mesoappendix: Mesentery of the appendix.

mesoderm: Middle primary embryonic germ layer that becomes the skeleton, muscles, connective tissue, heart, blood vessels, and kidneys.

mesothelium: Simple squamous epithelial tissue that covers the major body cavities and is the epithelial portion of serous membranes.

messenger RNA (mRNA): Nucleotide molecule that serves as an intermediate in the genetic code between DNA and protein.

metabolic acidosis: Condition wherein a deficiency of bicarbonate causes the blood to be overly acidic.

metabolic alkalosis: Condition wherein an excess of bicarbonate causes the blood to be overly alkaline.

metabolic rate: Amount of energy consumed minus the amount of energy expended by the body.

metabolism: Sum of all catabolic and anabolic reactions that take place in the body.

metabotropic receptor: Neurotransmitter receptor that involves a complex of proteins that cause metabolic changes in a cell.

metacarpal bone: One of the five long bones that form the palm of the hand; numbered 1–5, starting on the lateral (thumb) side of the hand.

metaphase: Second stage of mitosis (and meiosis), characterized by the linear alignment of sister chromatids in the centre of the cell.

metaphase plate: Linear alignment of sister chromatids in the centre of the cell, which takes place during metaphase.

metarteriole: Short vessel arising from a terminal arteriole that branches to supply a capillary bed.

metatarsal bone: One of the five elongated bones that form the anterior half of the foot; numbered 1–5, starting on the medial side of the foot.

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micelle: Tiny lipid-transport compound composed of bile salts and phospholipids with a fatty acid and monoacylglyceride core.
microcirculation: Blood flow through the capillaries.
microfilament: The thinnest of the cytoskeletal filaments; composed of actin subunits that function in muscle contraction and cellular structural support.
microglia: Glial cells that protect the nervous system against infection but are not nervous tissue because they are related to macrophages.
microscopic anatomy: Study of very small structures of the body using magnification.
microtubule: The thickest of the cytoskeletal filaments, composed of tubulin subunits that function in cellular movement and structural support.
microvillus: Small projection of the plasma membrane of the absorptive cells of the small intestinal mucosa.
micturition: Also called urination or voiding.
midbrain: Middle region of the adult brain that develops from the mesencephalon.
middle cardiac vein: Vessel that parallels and drains the areas supplied by the posterior interventricular artery; drains into the great cardiac vein.
middle ear: Space within the temporal bone between the ear canal and bony labyrinth where the ossicles amplify sound waves from the tympanic membrane to the oval window.
middle nasal concha: Nasal concha formed by the ethmoid bone that is located between the superior and inferior conchae.
midsagittal or median plane: Vertical plane that runs directly down the middle of the body.
migrating motility complex: Form of peristalsis in the small intestine.
mineralocorticoids: Hormones produced by the zona glomerulosa cells of the adrenal cortex that influence fluid and electrolyte balance.
minerals: Inorganic compounds required by the body to ensure proper function of the body.
minimus: Smallest.
mitochondrion: One of the cellular organelles bound by a double lipid bilayer that functions primarily in the production of cellular energy (ATP).
mitosis: Division of genetic material, during which the cell nucleus breaks down and two new, fully functional nuclei are formed.
mitotic phase: Phase of the cell cycle in which a cell undergoes mitosis.
mitotic spindle: Network of microtubules, originating from centrioles, that arranges and pulls apart chromosomes during mitosis.

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mitral valve (also left atrioventricular valve or bicuspid valve): Valve located between the left atrium and ventricle; consists of two flaps of tissue.
mixing wave: Unique type of peristalsis that occurs in the stomach.
modelling: Process, during bone growth, by which bone is resorbed on one surface of a bone and deposited on another.
molar: Tooth used for crushing and grinding food.
molecule: Two or more atoms covalently bonded together.
monocyte: Agranular leukocyte of the myeloid stem cell line that circulates in the bloodstream; tissue monocytes are macrophages.
monoglyceride molecules: Lipid consisting of a single fatty acid chain attached to a glycerol backbone.
monosaccharide: Monomer of carbohydrate; also known as a simple sugar.
mons pubis: Mound of fatty tissue located at the front of the vulva.
morula: Tightly packed sphere of blastomeres that has reached the uterus but has not yet implanted itself.
motilin: Hormone that initiates migrating motility complexes.
motility: Movement of food through the GI tract.
motor end-plate: Sarcolemma of muscle fibre at the neuromuscular junction, with receptors for the neurotransmitter acetylcholine.
motor unit: A motor neuron and the group of muscle fibres it innervates.
movement: Actions at the joints of the body and the motion of individual organs and even of individual cells.
mucosa (mucous membrane): Innermost lining of the alimentary canal.
mucosa-associated lymphoid tissue (MALT): Lymphoid nodule associated with the mucosa.
mucosal barrier: Protective barrier that prevents gastric juice from destroying the stomach itself.
mucous gland: Group of cells that secrete mucous, a thick, slippery substance that keeps tissues moist and acts as a lubricant.
mucous membrane (mucosa): Tissue membrane that is covered by protective mucous and lines tissue exposed to the outside environment.
mucous neck cell: Gastric gland cell that secretes a uniquely acidic mucus.
mucus: Alkaline protective coat secreted by the mucus cells in the epithelium.
multiaxial joint: Type of diarthrosis; a joint that allows for movements within three planes (three axes).
multimodal integration area: Region of the cerebral cortex in which information from more than one sensory modality is processed to arrive at higher-level cortical functions such as memory, learning, or cognition.
multipennate: Pennate muscle that has a tendon branching within it.

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multipolar: Shape of a neuron that has multiple processes—the axon and two or more dendrites.

multipotent: Describes the condition of being able to differentiate into different types of cells within a given cell lineage or a small number of lineages, such as a red blood cell or white blood cell.

murmur: Unusual heart sound detected by auscultation; typically related to septal or valve defects.

muscarinic receptor: Type of acetylcholine receptor protein that is characterized by also binding to muscarine and is a metabotropic receptor.

muscle fatigue: Occurs when a muscle can no longer contract in response to signals from the nervous system.

muscle fibre: Skeletal muscle cells; they are long and cylindrical.

muscle spindles: Stretch receptors in the skeletal muscle tissue.

muscle tension: Force generated by the contraction of the muscle; tension generated during isotonic contractions and isometric contractions.

muscle tissue: Type of tissue that is capable of contracting and generating tension in response to stimulation; produces movement.

muscle tone: Low levels of muscle contraction that occur when a muscle is not producing movement.

muscular artery (also distributing artery): Artery with abundant smooth muscle in the tunica media that branches to distribute blood to the arteriole network.

muscularis: Muscle (skeletal or smooth) layer of the alimentary canal wall.

myelin: Lipid-rich insulating substance surrounding the axons of many neurons, allowing for faster transmission of electrical signals.

myelin sheath: Lipid-rich layer of insulation that surrounds an axon, formed by oligodendrocytes in the CNS and Schwann cells in the PNS; facilitates the transmission of electrical signals.

myeloid stem cells: Type of hematopoietic stem cell that gives rise to some formed elements, including erythrocytes, megakaryocytes that produce platelets, and a myeloblast lineage that gives rise to monocytes and three forms of granular leukocytes (neutrophils, eosinophils, and basophils).

myenteric plexus (plexus of Auerbach): Major nerve supply to alimentary canal wall; controls motility.

myocardial contractile cells: Bulk of the cardiac muscle cells in the atria and ventricles that conduct impulses and contract to propel blood.

myocardium: Thickest layer of the heart composed of cardiac muscle cells built on a framework of primarily collagenous fibres and blood vessels that supply it and the nervous fibres that help regulate it.

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myocyte: Muscle cells.
myofibril: Long, cylindrical organelle that runs parallel within the muscle fibre and contains the sarcomeres.
myofilaments: Highly organized arrangement of the contractile fibres in the sarcomere.
myogenic mechanism: Mechanism by which smooth muscle responds to stretch by contracting; an increase in blood pressure causes vasoconstriction and a decrease in blood pressure causes vasodilation so that blood flow downstream remains steady.
myogenic response: Constriction or dilation in the walls of arterioles in response to pressures related to blood flow; reduces high blood flow or increases low blood flow to help maintain consistent flow to the capillary network.
myogram: Instrument used to measure twitch tension.
myometrium: Smooth muscle layer of the uterus that allows for uterine contractions during labour and expulsion of menstrual blood.
myosin: Protein that makes up most of the thick cylindrical myofilament within a sarcomere muscle fibre.
nail bed: Layer of epidermis upon which the nail body forms.
nail body: Main keratinous plate that forms the nail.
nail cuticle (eponychium): Fold of epithelium that extends over the nail bed, also called the eponychium.
nail fold: Fold of epithelium that extends over the sides of the nail body, holding it in place.
nail root: Part of the nail that is lodged deep in the epidermis from which the nail grows.
naive lymphocyte: Mature B or T cell that has not yet encountered antigen for the first time.
naris (plural = nares): Opening of the nostrils.
nasal bone: Bone of the skull that lies under the root and bridge of the nose and is connected to the frontal and maxillary bones.
nasal cavity: Nares open into this segment of the respiratory system, which is separated into left and right sections by the nasal septum.
nasal conchae (singular = concha): Serve to swirl the incoming air, which helps warm and moisturize it before the air moves into the delicate air sacs of the lungs.
nasal septum: Flat, midline structure that divides the nasal cavity into halves, formed by the perpendicular plate of the ethmoid bone, vomer bone, and septal cartilage.

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nasolacrimal canal: Passage for drainage of tears that extends downward from the medial-anterior orbit to the nasal cavity, terminating behind the inferior nasal conchae.

nasopharynx: The most superior part of the pharynx, which is involved only in breathing and speech.

natural killer (NK) cells: Cytotoxic lymphocytes capable of recognizing cells that do not express "self" proteins on their plasma membrane or that contain foreign or abnormal markers; provide generalized, nonspecific immunity.

navicular: Tarsal bone that articulates posteriorly with the talus bone, laterally with the cuboid bone, and anteriorly with the medial, intermediate, and lateral cuneiform bones.

neck of the femur: Narrowed region located inferior to the head of the femur.

neck of the radius: Narrowed region immediately distal to the head of the radius.

neck of the rib: Narrowed region of a rib, next to the rib head.

negative feedback: Homeostatic mechanism that tends to stabilize an upset in the body's physiological condition by preventing an excessive response to a stimulus, typically as the stimulus is removed.

negative inotropic factors: Factors that negatively impact or lower heart contractility.

nephrons: Functional units of the kidney that carry out all filtration and modification to produce urine; consist of renal corpuscles, proximal and distal convoluted tubules, and descending and ascending loops of Henle; drain into collecting ducts.

nerve: Cordlike bundle of axons located in the peripheral nervous system that transmits sensory input and response output to and from the central nervous system.

nerve plexus: Network of nerves without neuronal cell bodies included.

nervi vasorum: Small nerve fibres found in arteries and veins that trigger contraction of the smooth muscle in their walls.

nervous tissue: Type of tissue that is capable of sending and receiving impulses through electrochemical signals.

net filtration pressure (NFP): Force driving fluid out of the capillary and into the tissue spaces; equal to the difference of the capillary hydrostatic pressure and the blood colloidal osmotic pressure.

neural fold: Elevated edge of the neural groove.

neural plate: Thickened layer of neuroepithelium that runs longitudinally along the dorsal surface of an embryo and gives rise to nervous system tissue.

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neural tube: Precursor to structures of the central nervous system, formed by the invagination and separation of neuroepithelium.
neural tunic: Layer of the eye that contains nervous tissue, namely, the retina.
neurogenic shock: Type of shock that occurs with cranial or high spinal injuries that damage the cardiovascular centres in the medulla oblongata or the nervous fibres originating from this region.
neuroglia (glial cells): Supportive neural cells.
neuromuscular junction (NMJ): Synapse between the axon terminal of a motor neuron and the section of the membrane of a muscle fibre with receptors for the acetylcholine released by the terminal.
neuron: Neural tissue cell that is primarily responsible for generating and propagating electrical signals into, within, and out of the nervous system.
neuropeptide: Neurotransmitter type that includes protein molecules and shorter chains of amino acids.
neurotransmitter: Signalling chemical released by nerve terminals that binds to and activates receptors on target cells.
neurulation: Embryonic process that establishes the central nervous system.
neutron: Heavy subatomic particle having no electrical charge and found in the atom's nucleus.
neutrophils: Granulocytes that stain with a neutral dye and are the most numerous of the leukocytes; especially active against bacteria.
nicotinic receptor: Type of acetylcholine receptor protein that is characterized by also binding to nicotine and is an ionotropic receptor.
nipple: External features of the breast surrounded by a pigmented areola.
nociceptor: Receptor cell that senses pain stimuli.
node of Ranvier: Gap between two myelinated regions of an axon, allowing for the strengthening of the electrical signal as it propagates down the axon.
nonshivering thermogenesis: Process of breaking down brown adipose tissue to produce heat in the absence of a shivering response.
norepinephrine: Secondary catecholamine hormone secreted by the adrenal medulla in response to short-term stress; also called noradrenaline.
normal range: Range of values around the set point that do not cause a reaction by the control centre.
notochord: Rod-shaped, mesoderm-derived structure that provides support for the growing fetus.
nuclear envelope: Membrane that surrounds the nucleus, consisting of a double lipid bilayer.

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nuclear pore: One of the small, protein-lined openings found scattered throughout the nuclear envelope.
nucleolus: Small region of the nucleus that functions in ribosome synthesis.
nucleotide: Class of organic compounds composed of one or more phosphate groups, a pentose sugar, and a nitrogen-containing base.
nucleus (cell): Cell's central organelle; contains the cell's DNA.
nucleus (nervous system): In the nervous system, a localized collection of neuron cell bodies that are functionally related; a "centre" of neural function.
nucleus pulposus: Gel-like central region of an intervertebral disc; provides for padding, weight-bearing, and movement between adjacent vertebrae.
nutrient foramen: Small opening in the middle of the external surface of the diaphysis, through which an artery enters the bone to provide nourishment.
oblique: At an angle.
obstructive shock: Type of shock that occurs when a significant portion of the vascular system is blocked.
obturator foramen: Large opening located in the anterior hip bone, between the pubis and ischium regions.
occipital bone: Unpaired bone that forms the posterior portions of the brain case and base of the skull.
occipital condyle: Paired, oval-shaped bony knobs located on the inferior skull, to either side of the foramen magnum.
occipitalis: Posterior part of the occipitofrontalis muscle.
occipital lobe: Region of the cerebral cortex directly beneath the occipital bone of the cranium.
occipital sinus: Enlarged vein that drains the occipital region near the falx cerebelli and flows into the left and right transverse sinuses and also into the vertebral veins.
occipitofrontalis: Muscle that makes up the scalp with a frontal belly and an occipital belly.
oculomotor nerve: Third cranial nerve; responsible for contraction of four of the extraocular muscles, the muscle in the upper eyelid, and pupillary constriction.
odorant molecules: Volatile chemicals that bind to receptor proteins in olfactory neurons to stimulate the sense of smell.
olecranon process: Expanded posterior and superior portions of the proximal ulna; forms the bony tip of the elbow.
olfaction: Special sense responsible for smell, which has a unique, direct connection to the cerebrum.

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olfactory bulb: Central target of the first cranial nerve; located on the ventral surface of the frontal lobe in the cerebrum.

olfactory cortex: That is located in the inferior and medial areas of the temporal lobe.

olfactory epithelium: Region of the nasal epithelium where olfactory neurons are located.

olfactory hairs: Dendrites of the olfactory sensory neuron located in the apical surface of the epithelium into the mucus lining the cavity with role in detection of odorant molecules dissolved in the mucus.

olfactory nerve: First cranial nerve; responsible for the sense of smell.

olfactory sensory neuron: Receptor cell of the olfactory system, sensitive to the chemical stimuli of smell, the axons of which compose the first cranial nerve.

olfactory tract: Narrow band of nerve fibres in the brain that connects the olfactory bulb to the primary olfactory cortex.

oligodendrocyte: Glial cell type in the CNS that provides the myelin insulation for axons in tracts.

oliguria: Below-normal urine production of 400–500 mL/day.

oocyte: Cell that results from the division of the oogonium and undergoes meiosis I at the LH surge and meiosis II at fertilization to become a haploid ovum.

oogenesis: Process by which oogonia divide by mitosis to primary oocytes, which undergo meiosis to produce the secondary oocyte and, upon fertilization, the ovum.

oogonia: Ovarian stem cells that undergo mitosis during female fetal development to form primary oocytes.

open reduction: Surgical exposure of a bone to reset a fracture.

opposition: Thumb movement that brings the tip of the thumb in contact with the tip of a finger.

opsin: Protein that contains the photosensitive cofactor retinal for phototransduction.

opsonization: Enhancement of phagocytosis by the binding of antibody or antimicrobial protein.

optic canal: Opening spanning between middle cranial fossa and posterior orbit.

optic chiasm: Decussation point in the visual system at which medial retina fibres cross to the other side of the brain.

optic disc: Spot on the retina at which RGC axons leave the eye and blood vessels of the inner retina pass.

optic nerve: Second cranial nerve, which is responsible for visual sensation.

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oral cavity (also buccal cavity): Mouth.
oral vestibule: Part of the mouth bounded externally by the cheeks and lips and internally by the gums and teeth.
orbicularis oculi: Circular muscle that closes the eye.
orbicularis oris: Circular muscle that moves the lips.
orbit: Bony socket that contains the eyeball and associated muscles.
organ: Functionally distinct structure composed of two or more types of tissues.
organelle: Any of several different types of membrane-enclosed specialized structures in the cell that perform specific functions for the cell.
organic compound: Substance that contains both carbon and hydrogen.
organism: Living being that has a cellular structure and that can independently perform all physiologic functions necessary for life.
organ of Corti: Structure in the cochlea in which hair cells transduce movements from sound waves into electrochemical signals.
organogenesis: Development of the rudimentary structures of all of an embryo's organs from the germ layers.
organ system: Group of organs that work together to carry out a particular function.
origin: End of a skeletal muscle that is attached to another structure (usually a bone) in a fixed position.
oropharynx: Portion of the pharynx flanked by the nasopharynx, oral cavity, and laryngopharynx that is a passageway for both air and food.
orthostatic reflex: Sympathetic function that maintains blood pressure when standing to offset the increased effect of gravity.
osmoreceptor: Receptor cell that senses differences in the concentrations of body fluids on the basis of osmotic pressure.
osmosis: Diffusion of water molecules down their concentration gradient across a selectively permeable membrane.
ossicles: Three small bones in the middle ear.
ossification (also osteogenesis): Bone formation.
ossification centre: Cluster of osteoblasts found in the early stages of intramembranous ossification.
osteoblast: Cell responsible for forming new bone.
osteoclast: Cell responsible for resorbing bone.
osteocyte: Bone cell located within lacunae typically arranged in concentric circles around a central canal.
osteogenic cell: Undifferentiated cell with high mitotic activity; the only bone cells that divide; they differentiate and develop into osteoblasts.
osteoid: Uncalcified bone matrix secreted by osteoblasts.

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osteon (also Haversian system): Basic structural unit of compact bone; made of concentric layers of calcified matrix.

otolith: Layer of calcium carbonate crystals located on top of the otolithic membrane.

otolithic membrane: Gelatinous substance in the utricle and saccule of the inner ear that contains calcium carbonate crystals and into which the stereocilia of hair cells are embedded.

outer segment: In the eye, the section of a photoreceptor that contains opsin molecules that transduce light stimuli.

oval window: Membrane at the base of the cochlea where the stapes attaches, marking the beginning of the scala vestibuli.

ovarian cycle: Approximately 28-day cycle of changes in the ovary consisting of a follicular phase and a luteal phase.

ovaries: Female gonads that produce oocytes and sex steroid hormones (notably estrogen and progesterone).

ovulation: Release of a secondary oocyte and associated granulosa cells from an ovary.

ovum: Haploid female gamete resulting from completion of meiosis II at fertilization.

oxidation: Loss of an electron.

oxidation-reduction reaction (also redox reaction): Pair of reactions in which an electron is passed from one molecule to another, oxidizing one and reducing the other.

oxidative phosphorylation: Process that converts high-energy NADH and $FADH_2$ into ATP.

oxygen debt: Amount of oxygen needed to compensate for ATP produced without oxygen during muscle contraction.

oxygen-hemoglobin dissociation curve: Graph that describes the relationship of partial pressure to the binding and disassociation of oxygen to and from heme.

oxyhemoglobin ($Hb–O_2$): Bound form of hemoglobin and oxygen.

oxytocin (OT): Hypothalamic hormone stored in the posterior pituitary gland and important in stimulating uterine contractions in labour, milk ejection during breastfeeding, and feelings of attachment (produced by males and females).

pacemaker: Cluster of specialized myocardial cells known as the SA node that initiates the sinus rhythm.

Pacinian corpuscle (also lamellated corpuscle): Receptor in the skin that responds to vibration.

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packed cell volume (PCV; also hematocrit): Volume percentage of erythrocytes present in a sample of centrifuged blood.

palatine bone: Paired bones that form the posterior quarter of the hard palate and a small area in floor of the orbit.

palatine process: Medial projection from the maxilla bone that forms the anterior three-quarters of the hard palate.

palatine tonsil: One of the paired structures composed of lymphoid tissue located anterior to the uvula at the roof of the isthmus of the fauces.

palatoglossal arch: Muscular fold that extends from the lateral side of the soft palate to the base of the tongue.

palatopharyngeal arch: Muscular fold that extends from the lateral side of the soft palate to the side of the pharynx.

palmaris longus: Muscle that provides weak flexion of the hand at the wrist.

palmar venous arches: Drain the hand and digits and feed into the radial and ulnar veins.

pancreas: Organ with both exocrine and endocrine functions located posterior to the stomach that is important for digestion and the regulation of blood glucose.

pancreatic amylase: Enzyme secreted by the pancreas that completes the chemical digestion of carbohydrates in the small intestine.

pancreatic duct: Duct that fuses with the common bile duct just before entering the duodenum via a common opening.

pancreatic islets: Specialized clusters of pancreatic cells that have endocrine functions; also called islets of Langerhans.

pancreatic juice: Secretion of the pancreas containing digestive enzymes and bicarbonate.

pancreatic lipase: Enzyme secreted by the pancreas that participates in lipid digestion.

pancreatic nuclease: Enzyme secreted by the pancreas that participates in nucleic acid digestion.

papilla: For gustation, a bumplike projection on the surface of the tongue that contains taste buds.

papillae: Extensions of lamina propria of the top and sides of the tongue mucosa.

papillary layer: Superficial layer of the dermis, made of loose, areolar connective tissue.

papillary muscle: Extension of the myocardium in the ventricles to which the chordae tendineae attach.

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paracrine: Chemical signal that elicits a response in neighbouring cells; also called paracrine factor.

parallel: Fascicles that extend in the same direction as the long axis of the muscle.

paranasal sinus: One of the cavities within the skull that is connected to the conchae that serves to warm and humidify incoming air, produce mucus, and lighten the weight of the skull; consists of frontal, maxillary, sphenoidal, and ethmoidal sinuses.

paranasal sinuses: Cavities within the skull that are connected to the conchae that serve to warm and humidify incoming air, produce mucus, and lighten the weight of the skull; consist of frontal, maxillary, sphenoidal, and ethmoidal sinuses.

parasagittal plane (longitudinal section): Divides the body into unequal right and left sides.

parasympathetic division: Division of the autonomic nervous system responsible for restful and digestive functions.

parasympathetic nervous system: Branch of the autonomic nervous system that conserves energy and calms the body after stress.

parathyroid glands: Small, round glands embedded in the posterior thyroid gland that produce parathyroid hormone.

parathyroid hormone (PTH): Peptide hormone produced and secreted by the parathyroid glands in response to low blood calcium levels.

paravertebral ganglia: Autonomic ganglia superior to the sympathetic chain ganglia.

parenchyma: Functional cells of a gland or organ, in contrast with the supportive or connective tissue of a gland or organ.

parietal bone: Paired bones that form the upper, lateral sides of the skull.

parietal branches (also somatic branches): Group of arterial branches of the thoracic aorta; include those that supply blood to the thoracic cavity, the vertebral column, and the superior surface of the diaphragm.

parietal cell: Gastric gland cell that secretes hydrochloric acid and intrinsic factor.

parietal layer: Serous membrane that lines the walls of the body cavity.

parietal lobe: Region of the cerebral cortex directly beneath the parietal bone of the cranium.

parietal pericardium: Layer of serous pericardium that is fused to the fibrous pericardium.

parietal peritoneum: Lines the abdominal wall.

parietal pleura: Outermost layer of the pleura that connects to the thoracic wall, mediastinum, and diaphragm.

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parieto-occipital sulcus: Groove in the cerebral cortex representing the border between the parietal and occipital cortices.
parotid gland: One of a pair of major salivary glands located inferior and anterior to the ears.
partial pressure: Force exerted by each gas in a mixture of gases.
parturition: Childbirth.
passive immunity: Transfer of immunity to a pathogen to an individual that lacks immunity to this pathogen, usually by the injection of antibodies.
passive transport: Form of transport across the cell membrane that does not require input of cellular energy.
patella: Kneecap; the largest sesamoid bone of the body; articulates with the distal femur.
patellar ligament: Ligament spanning from the patella to the anterior tibia; serves as the final attachment for the quadriceps femoris muscle.
patellar surface: Smooth groove located on the anterior side of the distal femur, between the medial and lateral condyles; site of articulation for the patella.
pectinate muscles: Muscular ridges seen on the anterior surface of the right atrium.
pectoral girdle: Shoulder girdle; the set of bones, consisting of the scapula and clavicle, which attaches each upper limb to the axial skeleton.
pectoralis major: Thick, fan-shaped axial muscle that covers much of the superior thorax.
pectoralis minor: Muscle that moves the scapula and assists in inhalation.
pedicels: Fingerlike projections of podocytes surrounding glomerular capillaries; interdigitate to form a filtration membrane.
pedicle: Portion of the vertebral arch that extends from the vertebral body to the transverse process.
pelvic brim: Pelvic inlet; the dividing line between the greater and lesser pelvic regions; formed by the superior margin of the pubic symphysis, the pectineal lines of each pubis, the arcuate lines of each ilium, and the sacral promontory.
pelvic girdle: Hip girdle; consists of a single hip bone, which attaches a lower limb to the sacrum of the axial skeleton.
pelvic inlet: Pelvic brim.
pelvic outlet: Inferior opening of the lesser pelvis; formed by the inferior margin of the pubic symphysis, the right and left ischiopubic rami and sacrotuberous ligaments, and the tip of the coccyx.
pelvis: Ring of bone consisting of the right and left hip bones, the sacrum, and the coccyx.

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penis: Male organ of copulation.

pennate: Fascicles that are arranged differently based on their angles to the tendon.

pepsin: Enzyme that begins to break down proteins in the stomach.

pepsinogen: Inactive form of pepsin.

peptide bond: Covalent bond formed by dehydration synthesis between two amino acids.

perforating canal (also Volkmann's canal): Channel that branches off from the central canal and houses vessels and nerves that extend to the periosteum and endosteum.

perforin: Molecule in NK cell and cytotoxic T cell granules that forms pores in the membrane of a target cell.

perfusion: Distribution of blood into the capillaries so the tissues can be supplied.

pericardial cavity: Cavity surrounding the heart filled with a lubricating serous fluid that reduces friction as the heart contracts.

pericardium (also pericardial sac): Membrane that separates the heart from other mediastinal structures; consists of two distinct, fused sublayers: the fibrous pericardium and the parietal pericardium.

perichondrium: Membrane that covers cartilage.

perimetrium: Outer epithelial layer of the uterine wall.

perimysium: Connective tissue that bundles skeletal muscle fibres into fascicles within a skeletal muscle.

perineurium: Layer of connective tissue surrounding fascicles within a nerve.

periodic table of the elements: Arrangement of the elements in a table according to their atomic number; elements having similar properties because of their electron arrangements compose columns in the table, while elements having the same number of valence shells compose rows in the table.

periodontal ligament: Band of dense connective tissue that anchors the root of a tooth into the bony jaw socket.

periosteum: Fibrous membrane covering the outer surface of bone and continuous with ligaments.

peripheral chemoreceptor: One of the specialized receptors located in the aortic arch and carotid arteries that senses changes in pH, carbon dioxide, or oxygen blood levels.

peripheral nervous system (PNS): Anatomical division of the nervous system that is largely outside the cranial and vertebral cavities, namely, all parts except the brain and spinal cord.

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peripheral protein: Membrane-associated protein that does not span the width of the lipid bilayer, but is attached peripherally to integral proteins, membrane lipids, or other components of the membrane.

peripheral tolerance: Mature B cell made tolerant by lack of T cell help.

peristalsis: Muscular contractions and relaxations that propel food through the GI tract.

peritoneal cavity: The space bounded by the visceral and parietal peritoneal surfaces.

peritoneal fold: Large folds that envelop various abdominal organs, holding them to the dorsal surface of the body wall.

peritoneum: Broad serous membranous sac made up of squamous epithelial tissue surrounded by connective tissue that holds in place the digestive organs within the abdominal cavity.

peritubular capillaries: Second capillary bed of the renal portal system; surround the proximal and distal convoluted tubules; associated with the vasa recta.

permanent tooth: One of 32 adult teeth.

peroxisome: Membrane-bound organelle that contains enzymes primarily responsible for detoxifying harmful substances.

perpendicular plate of the ethmoid bone: Downward, midline extension of the ethmoid bone that forms the superior portion of the nasal septum.

Peyer's patches: A type of MALT in the small intestine important for immune responses against ingested substances.

pH: Negative logarithm of the hydrogen-ion (H^+) concentration of a solution.

phagocytosis: Movement of material from the outside to the inside of the cells via vesicles made from invaginations of the plasma membrane.

phalanx bone (plural = phalanges): One of the 28 bones that form the fingers, thumbs, and toes.

pharyngeal tonsil: Structure composed of lymphoid tissue located in the nasopharynx.

pharynx: Region of the conducting zone that forms a tube of skeletal muscle lined with respiratory epithelium; located between the nasal conchae and the esophagus and trachea.

philtrum: Concave surface of the face that connects the apex of the nose to the top lip.

phospholipid: A lipid compound in which a phosphate group is combined with a diglyceride.

phosphorylation: Addition of one or more phosphate groups to an organic compound.

photoreceptor: Receptor cell specialized to respond to light stimuli.

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phrenic nerve: Systemic nerve from the cervical plexus that innervates the diaphragm.

physiological sphincter: Sphincter consisting of circular smooth muscle indistinguishable from adjacent muscle but possessing differential innervations, permitting its function as a sphincter; structurally weak.

physiology: Science that studies the chemistry, biochemistry, and physics of the body's functions.

pia mater: Thin, innermost membrane of the meninges that directly covers the surface of the CNS.

pineal gland: Endocrine gland that secretes melatonin, which is important in regulating the sleep-wake cycle.

pinealocyte: Cell of the pineal gland that produces and secretes the hormone melatonin.

pinocytosis: Endocytosis of fluid.

pituitary dwarfism: Disorder in children caused when abnormally low levels of GH result in growth retardation.

pituitary gland: Bean-sized organ suspended from the hypothalamus that produces, stores, and secretes hormones in response to hypothalamic stimulation (also called hypophysis).

pivot joint: Synovial joint at which the rounded portion of a bone rotates within a ring formed by a ligament and an articulating bone; functionally classified as uniaxial joint.

placenta: Organ that forms during pregnancy to nourish the developing fetus; also regulates waste and gas exchange between mother and fetus.

placenta previa: Low placement of fetus within the uterus that causes the placenta to partially or completely cover the opening of the cervix as it grows.

placentation: Formation of the placenta; complete by weeks 14–16 of pregnancy.

plane: Imaginary two-dimensional surface that passes through the body.

plane joint: Synovial joint formed between the flattened articulating surfaces of adjacent bones; functionally classified as a multiaxial joint.

plantar flexion: Foot movement at the ankle in which the heel is lifted off the ground.

plasma: In blood, the liquid extracellular matrix composed mostly of water that circulates the formed elements and dissolved materials throughout the cardiovascular system.

plasma cell: One form of B cells that produces the antibodies or immunoglobulins.

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plasma osmolality: Ratio of solutes to a volume of solvent in the plasma; plasma osmolality reflects a person's state of hydration.
plasmin: Blood protein active in fibrinolysis.
plateau phase: Long refractory periods required for the cardiac muscle cells to pump blood effectively before they are capable of firing for a second time.
platelet plug: Accumulation and adhesion of platelets at the site of blood vessel injury.
platelets (also thrombocytes): One of the formed elements of blood that consists of cell fragments broken off from megakaryocytes.
pleura: Serous membrane that lines the pleural cavity and covers the lungs.
pleural cavity: Cavity in the thoracic cavity that surrounds the lungs.
pleural fluid: Substance that acts as a lubricant for the visceral and parietal layers of the pleura during the movement of breathing.
plexus: Network of nerves or nervous tissue.
pluripotent: Describes the condition of being able to differentiate into a large variety of cell types.
pluripotent stem cell: Stem cell that derives from totipotent stem cells and is capable of differentiating into many, but not all, cell types.
pneumotaxic centre: Network of neurons within the pons that inhibits the activity of the neurons in the dorsal respiratory group; controls rate of breathing.
podocytes: Cells forming fingerlike processes; form the visceral layer of Bowman's capsule; pedicels of the podocytes interdigitate to form a filtration membrane.
polar body: Smaller cell produced during the process of meiosis in oogenesis.
polar molecule: Molecule covalently bonded where one atom is more electronegative and draws electrons toward its nucleus, resulting in slight negative and positive charges.
pollex: Thumb; digit 1 of the hand.
polyclonal response: Response by multiple clones to a complex antigen with many determinants.
polymorphonuclear neutrophil: White blood cells with a lobed nucleus.
polypeptide: Chain of amino acids linked by peptide bonds.
polyribosome: Simultaneous translation of a single mRNA transcript by multiple ribosomes.
polysaccharides: Complex carbohydrates made up of many monosaccharides.
polyspermy: Penetration of an oocyte by more than one sperm.

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polyuria: Urine production in excess of 2.5 L/day; may be caused by diabetes insipidus, diabetes mellitus, or excessive use of diuretics.

popliteal fossa: Diamond-shaped space at the back of the knee.

popliteus: Muscle that flexes the leg at the knee and creates the floor of the popliteal fossa.

porta hepatis: "gateway to the liver" where the hepatic artery and hepatic portal vein enter the liver.

portal triad: Bile duct, hepatic artery branch, and hepatic portal vein branch.

positive chemotaxis: Process in which a cell is attracted to move in the direction of chemical stimuli.

positive feedback: Mechanism that intensifies a change in the body's physiological condition in response to a stimulus.

positive inotropic factors: Factors that positively impact or increase heart contractility.

postabsorptive state: Also called the fasting state; the metabolic state occurring after digestion, when food is no longer the body's source of energy and it must rely on stored glycogen.

postcentral gyrus: Primary motor cortex located in the frontal lobe of the cerebral cortex.

posterior: Describes the back or direction toward the back of the body; also referred to as dorsal.

posterior arch: Posterior portion of the ringlike C1 (atlas) vertebra.

posterior cardiac vein: Vessel that parallels and drains the areas supplied by the marginal artery branch of the circumflex artery; drains into the great cardiac vein.

posterior cavity: Posterior body cavity that houses the brain and spinal cord; also referred to as dorsal cavity.

posterior columns: White matter of the spinal cord that lies between the posterior horns of the grey matter, sometimes referred to as the dorsal column; composed of axons of ascending tracts that carry sensory information up to the brain.

posterior cruciate ligament: Intracapsular ligament of the knee; extends from the posterior, superior surface of the tibia to the inner aspect of the medial condyle of the femur; prevents anterior displacement of the femur when the knee is flexed and weight-bearing.

posterior horn: Grey matter region of the spinal cord in which sensory input arrives, sometimes referred to as the dorsal horn.

posterior interventricular artery (also posterior descending artery): Branch of the right coronary artery that runs along the posterior portion

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of the interventricular sulcus toward the apex of the heart and gives rise to branches that supply the interventricular septum and portions of both ventricles.

posterior interventricular sulcus: Sulcus located between the left and right ventricles on the posterior surface of the heart.

posterior median sulcus: Midline feature of the posterior spinal cord, marking the separation between right and left sides of the cord.

posterior pituitary (neurohypophysis): Extension of the neurons of the paraventricular and supraoptic nuclei of the hypothalamus.

postganglionic fibre: Axon from a ganglionic neuron in the autonomic nervous system that projects to and synapses with the target effector; sometimes referred to as a postganglionic neuron.

postsynaptic potential (PSP): Graded potential in the postsynaptic membrane caused by the binding of neurotransmitter to protein receptors.

potential energy: Stored energy matter possesses because of the positioning or structure of its components.

power stroke: Action of myosin pulling actin inward (toward the M line).

PP cell: Minor cell type in the pancreas that secretes the hormone pancreatic polypeptide.

precapillary sphincters: Circular rings of smooth muscle that surround the entrance to a capillary and regulate blood flow into that capillary.

precentral gyrus: Ridge just posterior to the central sulcus, in the parietal lobe, where somatosensory processing initially takes place in the cerebrum.

prefrontal lobe: Specific region of the frontal lobe anterior to the more specific motor function areas, which can be related to the early planning of movements and intentions to the point of being personality-type functions.

preganglionic fibre: Axon from a central neuron in the autonomic nervous system that projects to and synapses with a ganglionic neuron; sometimes referred to as a preganglionic neuron.

preload (also end diastolic volume): Amount of blood in the ventricles at the end of atrial systole just prior to ventricular contraction.

premolar (also bicuspid): Transitional tooth used for mastication, crushing, and grinding food.

premotor area: Region of the frontal lobe responsible for planning movements that will be executed through the primary motor cortex.

premotor cortex: Cortical area anterior to the primary motor cortex that is responsible for planning movements.

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prepotential depolarization (also spontaneous depolarization): Mechanism that accounts for the autorhythmic property of cardiac muscle; the membrane potential increases as sodium ions diffuse through the always-open sodium ion channels and causes the electrical potential to rise.

prepuce (also foreskin): Flap of skin that forms a collar around, and thus protects and lubricates, the glans penis; also referred to as the foreskin.

prevertebral ganglia: Autonomic ganglia that are anterior to the vertebral column and functionally related to the sympathetic chain ganglia.

primary adaptive response: Immune system's response to the first exposure to a pathogen.

primary bronchi: Bronchi that enter the lungs at the hilum.

primary curve: Anteriorly concave curvatures of the thoracic and sacrococcygeal regions that are retained from the original fetal curvature of the vertebral column.

primary follicles: Ovarian follicles with a primary oocyte and one layer of cuboidal granulosa cells.

primary germ layers: The endoderm, mesoderm, and ectoderm.

primary lymphoid organ: Site where lymphocytes mature and proliferate; red bone marrow and thymus gland.

primary oocytes: Formed from ogonia in the fetal ovary prior to birth.

primary ossification centre: Region, deep in the periosteal collar, where bone development starts during endochondral ossification.

primary sensory cortex: Region of the cerebral cortex that initially receives sensory input from an ascending pathway from the thalamus and begins the processing that will result in conscious perception of that modality.

primary spermatocyte: Cell that results from the division of spermatogonium and undergoes meiosis I and meiosis II to form spermatids.

prime mover (also agonist): Principal muscle involved in an action.

primitive streak: Indentation along the dorsal surface of the epiblast through which cells migrate to form the endoderm and mesoderm during gastrulation.

primordial follicles: Least-developed ovarian follicles that consist of a single oocyte and a single layer of flat (squamous) granulosa cells.

principal cells: Found in collecting ducts and possess channels for the recovery or loss of sodium and potassium; under the control of aldosterone; also have aquaporin channels under ADH control to regulate recovery of water.

process: In cells, an extension of a cell body; in the case of neurons, this includes the axon and dendrites.

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product: One or more substances produced by a chemical reaction.
progesterone: Predominantly female sex hormone important in regulating the female reproductive cycle and the maintenance of pregnancy.
projection: Bone markings where part of the surface sticks out above the rest of the surface, where tendons and ligaments attach.
prolactin (PRL): Anterior pituitary hormone that promotes development of the mammary glands and the production of breast milk.
proliferative phase: Phase of the menstrual cycle in which the endometrium proliferates.
promoter: Region of DNA that signals transcription to begin at that site within the gene.
pronated position: Forearm position in which the palm faces backward.
pronation: Forearm motion that moves the palm of the hand from the palm forward to the palm backward position.
pronator quadratus: Pronator that originates on the ulna and inserts on the radius.
pronator teres: Pronator that originates on the humerus and inserts on the radius.
prone: Face down.
propagation: Movement of an action potential along the length of an axon.
prophase: First stage of mitosis (and meiosis), characterized by breakdown of the nuclear envelope and condensing of the chromatin to form chromosomes.
proprioception: General sensory perceptions providing information about the location and movement of body parts; the "sense of the self."
proprioceptor: Receptor cell that senses changes in the position and kinesthetic aspects of the body.
propulsion: Voluntary process of swallowing and the involuntary process of peristalsis that moves food through the digestive tract.
prostaglandin: Lipid compound derived from fatty acid chains; important in regulating several body processes.
prostate gland, or prostate: Doughnut-shaped gland at the base of the bladder surrounding the urethra and contributing fluid to semen during ejaculation.
protein: Class of organic compounds that are composed of many amino acids linked together by peptide bonds.
protein kinase: Enzyme that initiates a phosphorylation cascade upon activation.
proteolysis: Process of breaking proteins into smaller peptides.
proton: Heavy subatomic particle having a positive charge and found in the atom's nucleus.

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protraction: Anterior motion of the scapula or mandible.

proximal: Describes a position nearer to the point of attachment or the trunk of the body.

proximal convoluted tubules (PCTs): Tortuous tubules receiving filtrate from Bowman's capsule; most active part of the nephron in reabsorption and secretion.

proximal radioulnar joint: Articulation between head of radius and radial notch of ulna; uniaxial pivot joint that allows for rotation of radius during pronation/supination of the forearm.

pseudostratified columnar epithelium: Tissue that consists of a single layer of irregularly shaped and sized cells that give the appearance of multiple layers; found in ducts of certain glands and the upper respiratory tract.

psoas major: Muscle that, along with the iliacus, makes up the iliopsoas.

pubic arch: Bony structure formed by the pubic symphysis and the bodies and inferior pubic rami of the adjacent pubic bones.

pubic body: Enlarged, medial portion of the pubis region of the hip bone.

pubic symphysis: Joint formed by the articulation between the pubic bodies of the right and left hip bones.

pubis: Anterior portion of the hip bone.

pulmonary artery: One of two branches, left and right, that divides off from the pulmonary trunk and leads to smaller arterioles and eventually to the pulmonary capillaries.

pulmonary capillaries: Capillaries surrounding the alveoli of the lungs where gas exchange occurs: Carbon dioxide exits the blood and oxygen enters.

pulmonary circuit: System of blood vessels that provides gas exchange via a network of arteries, veins, and capillaries that run from the heart, through the body, and back to the lungs.

pulmonary surfactant: Substance composed of phospholipids and proteins that reduces the surface tension of the alveoli; made by type II alveolar cells.

pulmonary trunk: Large arterial vessel that carries blood ejected from the right ventricle; divides into the left and right pulmonary arteries.

pulmonary valve (also pulmonary semilunar valve, pulmonic valve, or right semilunar valve): Valve at the base of the pulmonary trunk that prevents backflow of blood into the right ventricle; consists of three flaps.

pulmonary veins: Veins that carry highly oxygenated blood into the left atrium, which pumps the blood into the left ventricle, which in turn pumps oxygenated blood into the aorta and to the many branches of the systemic circuit.

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pulmonary ventilation: Exchange of gases between the lungs and the atmosphere; breathing.

pulp cavity: Deepest portion of a tooth, containing nerve endings and blood vessels.

pulse: Alternating expansion and recoil of an artery as blood moves through the vessel; an indicator of heart rate.

pulse pressure: Difference between the systolic and diastolic pressures.

pupil: Open hole at the centre of the iris that light passes through into the eye.

Purkinje cell: A multipolar neuron that has a very important role to play in the cerebellum.

Purkinje fibres: Specialized myocardial conduction fibres that arise from the bundle branches and spread the impulse to the myocardial contraction fibres of the ventricles.

P wave: Component of the electrocardiogram that represents the depolarization of the atria.

pyloric antrum: Wider, more superior part of the pylorus.

pyloric canal: Narrow, more inferior part of the pylorus.

pyloric sphincter: Sphincter that controls stomach emptying.

pylorus: Lower, funnel-shaped part of the stomach that is continuous with the duodenum.

pyramidal decussation: Location at which corticospinal tract fibres cross the midline and segregate into the anterior and lateral divisions of the pathway.

pyramids: Segment of the descending motor pathway that travels in the anterior position of the medulla.

pyruvate: Three-carbon end product of glycolysis and starting material that is converted into acetyl CoA that enters the Krebs cycle.

pyruvic acid: Product of glycolysis that can be used in aerobic respiration or converted to lactic acid.

QRS complex: Component of the electrocardiogram that represents the depolarization of the ventricles and includes, as a component, the repolarization of the atria.

quadriceps femoris group: Four muscles that extend and stabilize the knee.

quadriceps tendon (also patellar tendon): Tendon common to all four quadriceps muscles, inserts into the patella.

quickening: Fetal movements that are strong enough to be felt by the mother.

quiet breathing (also eupnea): Mode of breathing that occurs at rest and does not require the cognitive thought of the individual.

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radial artery: Formed at the bifurcation of the brachial artery; parallels the radius; gives off smaller branches until it reaches the carpal region, where it fuses with the ulnar artery to form the superficial and deep palmar arches; supplies blood to the lower arm and carpal region.

radial collateral ligament: Intrinsic ligament on the lateral side of the elbow joint; runs from the lateral epicondyle of humerus to merge with the annular ligament.

radial nerve: Systemic nerve of the arm, the distal component of which is located near the radial bone.

radial tuberosity: Oval-shaped, roughened protuberance located on the medial side of the proximal radius.

radial vein: Parallels the radius and radial artery; arises from the palmar venous arches and leads to the brachial vein.

radiation: Transfer of heat via infrared waves.

radiocarpal joint: Wrist joint; located between the forearm and hand regions of the upper limb; articulation formed proximally by the distal end of the radius and the fibrocartilaginous pad that unites the distal radius and ulna bone, and distally by the scaphoid, lunate, and triquetrum carpal bones.

radius: Bone located on the lateral side of the forearm.

ramus of the mandible: Vertical portion of the mandible.

reabsorption: In the cardiovascular system, the movement of material from the interstitial fluid into the capillaries.

reactant: One or more substances that enter into the reaction.

receptor: Protein molecule that contains a binding site for another specific molecule (called a ligand).

receptor-mediated endocytosis: Endocytosis of ligands attached to membrane-bound receptors.

receptor potential: Graded potential in a specialized sensory cell that directly causes the release of neurotransmitter without an intervening action potential.

recruitment: Increase in the number of motor units involved in contraction.

rectal valve: One of three transverse folds in the rectum where feces are separated from flatus.

rectum: Part of the large intestine between the sigmoid colon and anal canal.

rectus: Straight.

rectus abdominis: Long, linear muscle that extends along the middle of the trunk.

rectus femoris: Quadricep muscle on the anterior aspect of the thigh.

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rectus sheaths: Tissue that makes up the linea alba.

red blood cells (RBCs; also erythrocytes): One of the formed elements of blood that transports oxygen.

red marrow: Connective tissue within the spaces of spongy (cancellous) bone tissue; site of hematopoiesis.

red nucleus: Midbrain nucleus that sends corrective commands to the spinal cord along the rubrospinal tract, based on the disparity between an original command and the sensory feedback from movement.

red pulp: Splenic nodule area consisting of mostly red blood cells.

reduction: Gaining of an electron.

referred pain: The conscious perception of visceral sensation projected to a different region of the body, such as the left shoulder and arm pain as a sign of a heart attack.

reflex arc: Circuit of a reflex that involves a sensory input and motor output, or an afferent branch and an efferent branch, and an integrating centre to connect the two branches.

refractory period: Time after the initiation of an action potential when another action potential cannot be generated.

regional anatomy: Study of the structures that contribute to specific body regions.

regulatory T cells (Treg; also suppressor T cells): Class of CD4 T cells that regulates other T cell responses.

relative refractory period: Time during the refractory period when a new action potential can only be initiated by a stronger stimulus than the current action potential because voltage-gated K^+ channels are not closed.

relaxation phase: Period after twitch contraction when tension decreases.

releasing hormones: Hormones that stimulate the secretion of hormones from the anterior pituitary.

remodelling: Process by which osteoclasts resorb old or damaged bone at the same time as and on the same surface where osteoblasts form new bone to replace that which is resorbed.

renal artery: Branch of the abdominal aorta; supplies each kidney.

renal columns: Extensions of the renal cortex into the renal medulla; separate the renal pyramids; contain blood vessels and connective tissues.

renal corpuscle: Consists of the glomerulus and Bowman's capsule.

renal cortex: Outer part of the kidney containing all of the nephrons; some nephrons have loops of Henle extending into the medulla.

renal hilum: Recessed medial area of the kidney through which the renal artery, renal vein, ureters, lymphatics, and nerves pass.

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renal papillae: Medullary area of the renal pyramids where collecting ducts empty urine into the minor calyces.

renal pyramids: Six to eight cone-shaped tissues in the medulla of the kidney containing collecting ducts and the loops of Henle of juxtamedullary nephrons.

renal vein: Largest vein entering the inferior vena cava; drains the kidneys and leads to the inferior vena cava.

renin: Enzyme produced by juxtaglomerular cells in response to decreased blood pressure or sympathetic nervous activity; catalyzes the conversion of angiotensinogen into angiotensin I.

renin-angiotensin-aldosterone system (RAAS): Hormone system that has specialized cells of the kidneys secrete the enzyme renin in response to low blood volume or low blood pressure.

repolarization: Return of the membrane potential to its normally negative voltage at the end of the action potential.

reposition: Movement of the thumb from opposition back to the anatomical position (next to index finger).

reproduction: Process by which new organisms are generated.

residual volume (RV): Amount of air that remains in the lungs after maximum exhalation.

resistance: Property of an axon that relates to the ability of particles to diffuse through the cytoplasm; this is inversely proportional to the fibre diameter.

respiratory acidosis: Condition wherein an excess of carbonic acid or CO_2 causes the blood to be overly acidic.

respiratory alkalosis: Condition wherein a deficiency of carbonic acid/CO_2 levels causes the blood to be overly alkaline.

respiratory bronchiole: Specific type of bronchiole that leads to alveolar sacs.

respiratory cycle: One sequence of inspiration and expiration.

respiratory epithelium: Ciliated lining of much of the conducting zone that is specialized to remove debris and pathogens and produce mucus.

respiratory membrane: Alveolar and capillary wall together, which form an air-blood barrier that facilitates the simple diffusion of gases.

respiratory pump: Increase in the volume of the thorax during inhalation that decreases air pressure, enabling venous blood to flow into the thoracic region; then exhalation increases pressure, moving blood into the atria.

respiratory rate: Total number of breaths taken each minute.

respiratory volume: Varying amounts of air within the lung at a given time.

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respiratory zone: Includes structures of the respiratory system that are directly involved in gas exchange.

response: Nervous system function that causes a target tissue (muscle or gland) to produce an event as a consequence to stimuli.

responsiveness: Ability of an organism or a system to adjust to changes in conditions.

rest and digest: Set of functions associated with the parasympathetic system that lead to restful actions and digestion.

resting membrane potential: The difference in voltage measured across a cell membrane under steady-state conditions, typically −70 mV.

reticular fibre: Fine fibrous protein, made of collagen subunits, which cross-link to form supporting "nets" within connective tissue.

reticular formation: Diffuse region of grey matter throughout the brain stem that regulates sleep, wakefulness, and states of consciousness.

reticular lamina: Matrix containing collagen and elastin secreted by connective tissue; a component of the basement membrane.

reticular layer: Deeper layer of the dermis; it has a reticulated appearance due to the presence of abundant collagen and elastin fibres.

reticular tissue: Type of loose connective tissue that provides a supportive framework to soft organs, such as the lymphatic tissue, spleen, and liver.

reticulocyte: Immature erythrocyte that may still contain fragments of organelles.

reticuloendothelial cell (also Kupffer cell): Phagocyte in hepatic sinusoids that filters out material from venous blood from the alimentary canal.

reticulospinal tract: Extrapyramidal connections between the brain stem and spinal cord that modulate movement, contribute to posture, and regulate muscle tone.

retina: Nervous tissue of the eye at which phototransduction takes place.

retinal ganglion cell (RGC): Neuron of the retina that projects along the second cranial nerve.

retraction: Posterior motion of the scapula or mandible.

retroperitoneal: Behind the peritoneum; in the case of the kidney and ureters, between the parietal peritoneum and the abdominal wall.

Rh blood group: Blood-type classification based on the presence or absence of the antigen Rh on the erythrocyte membrane surface.

rhodopsin: Photopigment molecule found in the rod photoreceptors.

rhomboid major: Muscle that attaches the vertebral border of the scapula to the spinous process of the thoracic vertebrae.

rhomboid minor: Muscle that attaches the vertebral border of the scapula to the spinous process of the thoracic vertebrae.

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ribonuclease: Pancreatic enzyme that digests RNA.
ribonucleic acid (RNA): Ribose-containing nucleotide that helps manifest the genetic code as protein.
ribosomal RNA (rRNA): RNA that makes up the subunits of a ribosome.
ribosome: Cellular organelle that functions in protein synthesis.
ribs: Thin, curved bones of the chest wall.
right atrioventricular valve (also tricuspid valve): Valve located between the right atrium and ventricle; consists of three flaps of tissue.
right colic flexure (also hepatic flexure): Point at the inferior surface of the liver where the ascending colon turns abruptly to the left.
right lymphatic duct: Drains lymph fluid from the upper right side of the body into the right subclavian vein.
RNA polymerase: Enzyme that unwinds DNA and then adds new nucleotides to a growing strand of RNA for the transcription phase of protein synthesis.
rod photoreceptor: One of the two types of retinal receptor cell that is specialized for low-light vision.
root (nose): Region of the external nose between the eyebrows.
root (tooth): Portion of a tooth embedded in the alveolar processes beneath the gum line.
rotation: Movement of a bone around a central axis (atlantoaxial joint) or around its long axis (proximal radioulnar joint; shoulder or hip joint); twisting of the vertebral column resulting from the summation of small motions between adjacent vertebrae.
rotator cuff: Strong connective tissue structure formed by the fusion of four rotator cuff muscle tendons to the articular capsule of the shoulder joint; surrounds and supports superior, anterior, lateral, and posterior sides of the humeral head.
rough ER (RER): Organelle that function as the site for protein synthesis; many ribosomes attach to the ER giving it the studded appearance of rough ER.
round window: Membrane that marks the end of the scala tympani.
rubrospinal tract: Descending motor control pathway, originating in the red nucleus, that mediates control of the limbs on the basis of cerebellar processing.
rugae: Folds of alimentary canal mucosa and submucosa in the empty stomach and other organs.
rugae (of the vagina): Folds of skin in the vagina that allow it to stretch during intercourse and childbirth.
saccule: Structure of the inner ear responsible for transducing linear acceleration in the vertical plane.

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sacral canal: Bony tunnel that runs through the sacrum.
sacral foramina: Series of paired openings for nerve exit located on both the anterior (ventral) and posterior (dorsal) aspects of the sacrum.
sacral hiatus: Inferior opening and termination of the sacral canal.
sacral plexus: Nerve plexus associated with the lower lumbar and sacral spinal nerves.
sacral promontory: Anterior lip of the base (superior end) of the sacrum.
sacrococcygeal curve: Anteriorly concave curvature formed by the sacrum and coccyx; a primary curve of the vertebral column.
sacroiliac joint: Joint formed by the articulation between the auricular surfaces of the sacrum and ilium.
sacrum: Single bone located near the inferior end of the adult vertebral column that is formed by the fusion of five sacral vertebrae; forms the posterior portion of the pelvis.
saddle joint: Synovial joint in which the articulating ends of both bones are convex and concave in shape, such as the first carpometacarpal joint at the base of the thumb; functionally classified as a biaxial joint.
sagittal plane: Two-dimensional, vertical plane that divides the body or organ into right and left sides.
sagittal suture: Joint that unites the right and left parietal bones at the midline along the top of the skull.
saliva: Aqueous solution of proteins and ions secreted into the mouth by the salivary glands.
salivary amylase: Digestive enzyme that is found in the saliva and begins the digestion of carbohydrates in the mouth.
salivary gland: Exocrine gland that secretes a digestive fluid called saliva.
salivation: Secretion of saliva.
saltatory conduction: Quick propagation of the action potential along a myelinated axon owing to voltage-gated Na^+ channels being present only at the nodes of Ranvier.
saphenous nerve: Systemic nerve of the lower anterior leg that is a branch from the femoral nerve.
sarcolemma: Plasma membrane of a skeletal muscle fibre.
sarcomere: Longitudinally repeating functional unit of skeletal muscle, with all the contractile and associated proteins involved in contraction.
sarcoplasm: Cytoplasm of a muscle cell.
sarcoplasmic reticulum (SR): Specialized smooth endoplasmic reticulum, which stores, releases, and retrieves Ca^{++}.
sartorius: Bandlike muscle that flexes, abducts, and laterally rotates the leg at the hip.

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satellite cell: Glial cell type in the PNS that provides support for neurons in the ganglia.

scala tympani: Portion of the cochlea that extends from the apex to the round window.

scala vestibuli: Portion of the cochlea that extends from the oval window to the apex.

scalene muscles: Flex, laterally flex, and rotate the head; contribute to deep inhalation.

scapula: Shoulder blade bone located on the posterior side of the shoulder.

Schwann cell: Glial cell type in the PNS that provides the myelin insulation for axons in nerves.

sciatic nerve: Systemic nerve from the sacral plexus that is a combination of the tibial and fibular nerves and extends across the hip joint and gluteal region into the upper posterior leg.

sclera: White of the eye.

scrotum: External pouch of skin and muscle that houses the testes.

sebaceous gland: Type of oil gland found in the dermis all over the body and helps lubricate and waterproof the skin and hair by secreting sebum.

sebum: Oily substance that is composed of a mixture of lipids that lubricates the skin and hair.

secondary active transport: Process harnessing an electrochemical gradient established by primary active transport to drive the transport of a second molecule.

secondary adaptive response: Immune response observed upon reexposure to a pathogen, which is stronger and faster than a primary response.

secondary curve: Posteriorly concave curvatures of the cervical and lumbar regions of the vertebral column that develop after the time of birth.

secondary follicles: Ovarian follicles with a primary oocyte and multiple layers of granulosa cells.

secondary lymphoid organs: Sites where lymphocytes mount adaptive immune responses; examples include lymph nodes and spleen.

secondary oocyte: Daughter oocyte resulting from meiosis in a primary oocyte; leaves the ovary during ovulation.

secondary ossification centre: Region of bone development in the epiphyses.

secondary spermatocytes: Products of meiosis I in primary spermatocytes, where each of the 23 pairs of chromosomes separates resulting in two cells, each with only half the number of chromosomes.

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second messenger: Molecule that initiates a signalling cascade in response to hormone binding on a cell membrane receptor and activation of a G protein.

secretin: Hormone released in the small intestine to aid in digestion.

secretory phase: Phase of the menstrual cycle in which the endometrium secretes a nutrient-rich fluid in preparation for implantation of an embryo.

section: A single flat surface of a three-dimensional structure that has been cut through.

segmentation: Alternating contractions and relaxations of nonadjacent segments of the intestine that move food forward and backward, breaking it apart and mixing it with digestive juices.

selective permeability: Feature of any barrier that allows certain substances to cross but excludes others.

sella turcica: Elevated area of sphenoid bone located at the midline of the middle cranial fossa.

semen: Ejaculatory fluid composed of sperm and secretions from the seminal vesicles, prostate, and bulbourethral glands.

semicircular canals: Structures within the inner ear responsible for transducing rotational movement information.

semilunar valves: Valves located at the base of the pulmonary trunk and at the base of the aorta.

semimembranosus: Hamstring muscle.

seminal vesicle: Gland that produces seminal fluid, which contributes to semen.

seminiferous tubules: Tube structures within the testes where spermatogenesis occurs.

semitendinosus: Hamstring muscle.

sensation: Nervous system function that receives information from the environment and translates it into the electrical signals of nervous tissue.

sensor (also receptor): Reports a monitored physiological value to the control centre.

sensory ganglia: Clusters of nerve cell bodies located outside the central nervous system that relay sensory information.

sensory homunculus: Topographic representation of the body within the somatosensory cortex demonstrating the correspondence between neurons processing stimuli and sensitivity.

sensory modality: A particular system for interpreting and perceiving environmental stimuli by the nervous system.

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sensory receptor: Nervous structures specialized for detection of temperature, touch, pain, and so on.
sepsis (also septicemia): Organismal-level inflammatory response to a massive infection.
septal cartilage: Flat cartilage structure that forms the anterior portion of the nasal septum.
septic shock (also blood poisoning): Type of shock that follows a massive infection resulting in organism-wide inflammation.
septum (plural = septa): Walls or partitions that divide the heart into chambers.
serosa: Outermost layer of the alimentary canal wall present in regions within the abdominal cavity.
serous gland: Group of cells within the serous membrane that secrete a lubricating substance onto the surface.
serous membrane (serosa): Type of tissue membrane that lines body cavities and lubricates them with serous fluid.
serous pericardium: Delicate layer that also consists of two layers: the parietal pericardium and the visceral pericardium (epicardium).
serratus anterior: Large and flat muscle that originates on the ribs and inserts onto the scapula.
Sertoli cells: Cells that support germ cells through the process of spermatogenesis; a type of sustentacular cell.
serum: Blood plasma that does not contain clotting factors.
sesamoid bone: Small, round bone embedded in a tendon; protects the tendon from compressive forces.
set point: Ideal value for a physiological parameter; the level or small range within which a physiological parameter, such as blood pressure, is stable and optimally healthful—that is, within its parameters of homeostasis.
shaft of the clavicle: Body of the clavicle bone.
shaft of the femur: Cylindrically shaped region that forms the central portion of the femur.
shaft of the fibula: Elongated, slender portion located between the expanded ends of the fibula.
shaft of the humerus: Narrow, elongated, central region of the humerus.
shaft of the radius: Narrow, elongated, central region of the radius.
shaft of the tibia: Triangular, central portion of the tibia.
shaft of the ulna: Narrow, elongated, central region of the ulna.
short bone: Cube-shaped bone that is approximately equal in length, width, and thickness; provides limited motion.

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short reflex: Reflex arc that does not include any components of the central nervous system.

shunt: Circulatory shortcut that diverts the flow of blood from one region to another.

sigmoid colon: End portion of the colon, which terminates at the rectum.

simple columnar epithelium: Tissue that consists of a single layer of columnlike cells; promotes secretion and absorption in tissues and organs.

simple cuboidal epithelium: Tissue that consists of a single layer of cube-shaped cells; promotes secretion and absorption in ducts and tubules.

simple squamous epithelium: Tissue that consists of a single layer of flat, scalelike cells; promotes diffusion and filtration across surfaces.

sinoatrial (SA) node: Known as the pacemaker, a specialized clump of myocardial conducting cells located in the superior portion of the right atrium that has the highest inherent rate of depolarization that then spreads throughout the heart.

sinusoid capillary: Rarest type of capillary, which has extremely large intercellular gaps in the basement membrane in addition to clefts and fenestrations; found in areas such as the bone marrow and liver, where passage of large molecules occurs.

sinus rhythm: Normal electrical pattern followed by contraction of the heart.

sister chromatid: One of a pair of identical chromosomes, formed during DNA replication.

skeletal muscle: Striated, multinucleated muscle that requires signalling from the nervous system to trigger contraction; most skeletal muscles are referred to as voluntary muscles that move bones and produce movement.

skeletal muscle pump: Effect on increasing blood pressure within veins by compression of the vessel caused by the contraction of nearby skeletal muscle.

skeletal system: Organ system composed of bones and cartilage that provides for movement, support, and protection.

skeleton: Bones of the body.

skull: Bony structure that forms the head, face, and jaws, and protects the brain; consists of 22 bones.

sliding filament model of muscle contraction: Skeletal muscle fibre contracts as the thin filaments are pulled and then slide past the thick filaments within the fibre's sarcomeres.

slow oxidative (SO): Muscle fibre that primarily uses aerobic respiration.

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small cardiac vein: Parallels the right coronary artery and drains blood from the posterior surfaces of the right atrium and ventricle; drains into the coronary sinus, middle cardiac vein, or right atrium.

small intestine: Section of the alimentary canal where most digestion and absorption occurs.

small motor unit: Arrangement where a single motor neuron supplies a small number of muscle fibres; permits very fine motor control of the muscle.

smooth ER (SER): Organelle lacking attached ribosomes that are specialized for lipid synthesis, detoxification, carbohydrate metabolism, and calcium ion storage.

smooth muscle: Nonstriated, mononucleated muscle in the skin that is associated with hair follicles; assists in moving materials in the walls of internal organs, blood vessels, and internal passageways.

sodium bicarbonate: Anion released into the small intestine to neutralize the pH of the food from the stomach.

sodium-potassium pump (ATPase): Cell membrane proteins specialized in moving sodium ions (Na^+) out of a cell and potassium ions (K^+) into a cell, thus regulating ion concentration on both sides of the cell membrane.

soft palate: Posterior region of the bottom portion of the nasal cavity that consists of skeletal muscle.

soleus: Wide, flat muscle deep to the gastrocnemius.

solitary nucleus: Medullar nucleus that receives taste information from the facial and glossopharyngeal nerves.

solution: Homogeneous liquid mixture in which a solute is dissolved into molecules within a solvent.

soma (cell body): In neurons, that portion of the cell that contains the nucleus; the cell body, as opposed to the cell processes (axons and dendrites).

somatic cell: All cells of the body excluding gamete cells.

somatic nervous system (SNS): Functional division of the nervous system that is concerned with conscious perception, voluntary movement, and skeletal muscle reflexes.

somatic reflex: Reflex involving skeletal muscle as the effector, under the control of the somatic nervous system.

somatosensation: General senses related to the body, usually thought of as the senses of touch, which would include pain, temperature, and proprioception.

somite: One of the paired, repeating blocks of tissue located on either side of the notochord in the early embryo.

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spatial summation: Combination of graded potentials across the neuronal cell membrane caused by signals from separate presynaptic elements that add up to initiate an action potential.

specialized receptor cell: Cell that transduces environmental stimuli into neural signals.

special sense: Any sensory system associated with a specific organ structure, namely, smell, taste, sight, hearing, and balance.

sperm (also spermatozoon): Male gamete.

spermatic cord: Bundle of nerves and blood vessels that supplies the testes; contains ductus deferens.

spermatid: Immature sperm cells produced by meiosis II of secondary spermatocytes.

spermatogenesis: Formation of new sperm; occurs in the seminiferous tubules of the testes.

spermatogonia (singular = spermatogonium): Diploid precursor cells that become sperm.

spermatozoa: Formed sperm that are the end result of spermiogenesis.

spermiogenesis: Transformation of spermatids to spermatozoa during spermatogenesis.

S phase: Stage of the cell cycle during which DNA replication occurs.

sphenoid bone: Unpaired bone that forms the central base of the skull.

sphenoid sinus: Air-filled space located within the sphenoid bone; most posterior of the paranasal sinuses.

sphygmomanometer: Blood pressure cuff attached to a device that measures blood pressure.

spinal accessory nerve: 11th cranial nerve; responsible for contraction of neck muscles.

spinal cavity (vertebral cavity): Division of the dorsal cavity that houses the spinal cord; also referred to as the vertebral cavity.

spinal cord: Organ of the central nervous system found within the vertebral cavity and connected with the periphery through spinal nerves; mediates reflex behaviours.

spinal nerve: One of 31 nerves connected to the spinal cord.

spine of the scapula: Prominent ridge passing mediolaterally across the upper portion of the posterior scapular surface.

spinothalamic tract: Ascending tract of the spinal cord associated with pain and temperature sensations.

spinous process: Unpaired bony process that extends posteriorly from the vertebral arch of a vertebra.

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spiral ganglion: Location of neuronal cell bodies that transmit auditory information along the eighth cranial nerve.

spleen: Secondary lymphoid organ that filters pathogens from the blood (white pulp) and removes degenerating or damaged blood cells (red pulp).

splenic artery: Branch of the celiac trunk; supplies blood to the spleen.

splenius: Posterior neck muscles.

spongy bone (also cancellous bone): Trabeculated osseous tissue that supports shifts in weight distribution.

spontaneous depolarization (also prepotential depolarization): The mechanism that accounts for the autorhythmic property of cardiac muscle; the membrane potential increases as sodium ions diffuse through the always-open sodium ion channels and causes the electrical potential to rise.

squamous suture: Joint that unites the parietal bone to the squamous portion of the temporal bone on the lateral side of the skull.

stage of exhaustion: Stage three of the general adaptation syndrome; the body's long-term response to stress mediated by the hormones of the adrenal cortex.

stage of resistance: Stage two of the general adaptation syndrome; the body's continued response to stress after stage one diminishes.

stapes (also stirrup): Ossicle of the middle ear that is attached to the inner ear.

stem cell: Cell that is oligo-, multi-, or pluripotent and has the ability to produce additional stem cells rather than becoming further specialized.

stereocilia: Array of apical membrane extensions in a hair cell that transduce movements when they are bent.

sternal (medial) end of the clavicle: Medial end of the clavicle that articulates with the manubrium of the sternum.

sternal angle: Junction line between manubrium and body of the sternum; the site for attachment of the second rib to the sternum.

sternal body: The elongated, central portion of the sternum.

sternoclavicular joint: Articulation between the manubrium of the sternum and the sternal end of the clavicle; forms the only bony attachment between the pectoral girdle of the upper limb and the axial skeleton.

sternocleidomastoid: Major muscle that laterally flexes and rotates the head.

sternum: Flattened bone located at the centre of the anterior chest.

steroid (also sterol): Lipid compound composed of four hydrocarbon rings bonded to a variety of other atoms and molecules.

stimulus: An event in the external or internal environment that registers as activity in a sensory neuron.

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stomach: Alimentary canal organ that contributes to chemical and mechanical digestion of food from the esophagus before releasing it, as chyme, to the small intestine.

straight sinus: Enlarged vein that drains blood from the brain; receives most of the blood from the great cerebral vein and flows into the left or right transverse sinus.

stratified columnar epithelium: Tissue that consists of two or more layers of columnlike cells, contains glands, and is found in some ducts.

stratified cuboidal epithelium: Tissue that consists of two or more layers of cube-shaped cells, found in some ducts.

stratified squamous epithelium: Tissue that consists of multiple layers of cells, with the most apical being flat scalelike cells; protects surfaces from abrasion.

stratum basale: Deepest layer of the epidermis, made of epidermal stem cells.

stratum basalis: Part of the lamina propria adjacent to the myometrium; does not shed during menses.

stratum corneum: Most superficial layer of the epidermis.

stratum functionalis: Contains the glandular portion of the lamina propria and the endothelial tissue that lines the uterine lumen.

stratum granulosum: Layer of the epidermis superficial to the stratum spinosum.

stratum lucidum: Layer of the epidermis between the stratum granulosum and stratum corneum, found only in thick skin covering the palms, soles of the feet, and digits.

stratum spinosum: Layer of the epidermis superficial to the stratum basale, characterized by the presence of desmosomes.

stress-relaxation response: Relaxation of smooth muscle tissue after being stretched.

stretch receptors: Monitor the stretching of tendons, muscles, and the components of joints.

stretch reflex: Response to activation of the muscle spindle stretch receptor that causes contraction of the muscle to maintain a constant length.

striation: Alignment of parallel actin and myosin filaments, which form a banded pattern.

stroke volume (SV): Amount of blood pumped by each ventricle per contraction; also the difference between EDV and ESV.

styloid process: Downward projecting, elongated bony process located on the inferior aspect of the skull.

styloid process of the radius: Pointed projection located on the lateral end of the distal radius.

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styloid process of the ulna: Short, bony projection located on the medial end of the distal ulna.

subarachnoid space: Space between the arachnoid mater and pia mater that contains CSF and the fibrous connections of the arachnoid trabeculae.

subclavian artery: Right subclavian arises from the brachiocephalic artery, whereas the left subclavian artery arises from the aortic arch; gives rise to the internal thoracic, vertebral, and thyrocervical arteries; supplies blood to the arms, chest, shoulders, back, and central nervous system.

subclavian vein: Located deep in the thoracic cavity; becomes the axillary vein as it enters the axillary region; drains the axillary and smaller local veins near the scapular region; leads to the brachiocephalic vein.

subclavius: Muscle that stabilizes the clavicle during movement.

subcortical nucleus: All the nuclei beneath the cerebral cortex, including the basal nuclei and the basal forebrain.

sublingual gland: One of a pair of major salivary glands located beneath the tongue.

submandibular gland: One of a pair of major salivary glands located in the floor of the mouth.

submodality: Specific sense within a broader major sense, such as sweet as a part of the sense of taste or colour as a part of vision.

submucosa: Layer of dense connective tissue in the alimentary canal wall that binds the overlying mucosa to the underlying muscularis.

submucosal plexus (plexus of Meissner): Nerve supply that regulates activity of glands and smooth muscle.

subpubic angle: Inverted V-shape formed by the convergence of the right and left ischiopubic rami; this angle is greater than 80 degrees in females and less than 70 degrees in males.

subscapular fossa: Broad depression located on the anterior (deep) surface of the scapula.

subscapularis: Muscle that originates on the anterior scapula and medially rotates the arm.

subscapular vein: Drains blood from the subscapular region and leads to the axillary vein.

substantia nigra pars reticulata: Nuclei within the basal nuclei that serve as an output centre of the nuclei; part of the motor pathway.

substrate: Reactant in an enzymatic reaction.

subthalamus: Nucleus within the basal nuclei that is part of the indirect pathway.

sucrase: Brush border enzyme that breaks down sucrose into glucose and fructose.

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sudoriferous gland: Sweat gland.
sulcus (plural = sulci): Fat-filled groove visible on the surface of the heart; coronary vessels are also located in these areas.
summate: To add together, as in the cumulative change in postsynaptic potentials toward reaching threshold in the membrane, either across a span of the membrane or over a certain amount of time.
superficial: Describes a position nearer to the surface of the body.
superior: Describes a position above or higher than another part of the body proper; also referred to as cranial.
superior articular process: Bony process that extends upward from the vertebral arch of a vertebra and articulates with the inferior articular process of the next higher vertebra.
superior articular process of the sacrum: Paired processes that extend upward from the sacrum to articulate (join) with the inferior articular processes from the L5 vertebra.
superior cervical ganglion: One of the paravertebral ganglia of the sympathetic system that projects to the head.
superior colliculus: Structure in the midbrain that combines visual, auditory, and somatosensory input to coordinate spatial and topographic representations of the three sensory systems.
superior mesenteric ganglion: One of the collateral ganglia of the sympathetic system that projects to the digestive system.
superior nasal concha: Smallest and most superiorly located of the nasal conchae; formed by the ethmoid bone.
superior orbital fissure: Irregularly shaped opening between the middle cranial fossa and the posterior orbit.
superior pubic ramus: Narrow segment of bone that passes laterally from the pubic body to join the ilium.
superior rotation: Movement of the scapula during upper limb abduction in which the glenoid cavity of the scapula moves in an upward direction as the medial end of the scapular spine moves in a downward direction.
superior sagittal sinus: Enlarged vein located midsagittally between the meningeal and periosteal layers of the dura mater within the falx cerebri; receives most of the blood drained from the superior surface of the cerebrum and leads to the inferior jugular vein and the vertebral vein.
superior vena cava: Large systemic vein that returns blood to the heart from the superior portion of the body.
supinated position: Forearm position in which the palm faces anteriorly (anatomical position).

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supination: Forearm motion that moves the palm of the hand from the palm backward to the palm forward position.
supinator: Muscle that moves the palm and forearm anteriorly.
supine: Face-up.
supplemental motor area: Cortical area anterior to the primary motor cortex that is responsible for planning movements.
supportive connective tissue: Type of connective tissue that provides strength to the body and protects soft tissue.
suprahyoid muscles: Neck muscles that are superior to the hyoid bone.
supraorbital foramen: Opening located on the anterior skull, at the superior margin of the orbit.
suprascapular notch: Small notch located along the superior border of the scapula, medial to the coracoid process.
supraspinatus: Muscle that abducts the arm.
supraspinous fossa: Narrow depression located on the posterior scapula, superior to the spine.
surgical neck: Region of the humerus where the expanded, proximal end joins with the narrower shaft.
suspension: Liquid mixture in which particles distributed in the liquid settle out over time.
suspensory ligaments: Bands of connective tissue that suspend the breast onto the chest wall by attachment to the overlying dermis.
suture: Fibrous joint that connects the bones of the skull (except the mandible); an immobile joint (synarthrosis).
sweat gland: Type of gland found in the dermis that secretes sweat through a duct to cool the body.
sympathetic chain ganglia: Autonomic ganglia in a chain along the anterolateral aspect of the vertebral column that are responsible for contributing to homeostatic mechanisms of the autonomic nervous system.
sympathetic division: Division of the autonomic nervous system associated with the fight-or-flight response.
sympathetic nervous system: Branch of the autonomic nervous system that mediates the body's involuntary response to stress, danger, or intense physical activity.
symphysis: Type of cartilaginous joint where the bones are joined by fibrocartilage.
symporters: Secondary active transporters that move two substances in the same direction.
synapse: Narrow junction across which a chemical signal passes from one neuron to the next, initiating a new electrical signal in the target cell.

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synaptic cleft: Small gap between cells in a chemical synapse where a neurotransmitter diffuses from the presynaptic element to the postsynaptic element.

synaptic end bulb: Swelling at the end of an axon where neurotransmitter molecules are released onto a target cell across a synapse.

synarthrosis: Immobile or nearly immobile joint.

synchondrosis: Type of cartilaginous joint where the bones are joined by hyaline cartilage.

syncytiotrophoblast: Superficial cells of the trophoblast that fuse to form a multinucleated body that digests endometrial cells to firmly secure the blastocyst to the uterine wall.

syndesmosis: Type of fibrous joint in which two separated, parallel bones are connected by an interosseous membrane.

synergist: Muscle whose contraction helps a prime mover in an action.

synostosis: Site at which adjacent bones or bony components have fused together.

synovial fluid: Thick, lubricating fluid that fills the interior of a synovial joint.

synovial joint: Joint at which the articulating surfaces of the bones are located within a joint cavity formed by an articular capsule.

synovial membrane: Connective tissue membrane that lines the cavities of freely movable joints, producing synovial fluid for lubrication.

synthesis reaction: Type of anabolic reaction in which two or more atoms or molecules bond, resulting in the formation of a larger molecule.

systemic anatomy: Study of the structures that contribute to specific body systems.

systemic circuit: Provides blood rich in oxygen to the body's tissues, then returns the less oxygenated blood to the heart.

systemic edema: Increased fluid retention in the interstitial spaces and cells of the body; can be seen as swelling over large areas of the body, particularly the lower extremities.

systemic nerve: Nerve in the periphery distal to a nerve plexus or spinal nerve.

systole: Period of time when the heart muscle is contracting.

systolic pressure: Larger number recorded when measuring arterial blood pressure; represents the maximum value following ventricular contraction.

talus: Tarsal bone that articulates superiorly with the tibia and fibula at the ankle joint; also articulates inferiorly with the calcaneus bone and anteriorly with the navicular bone.

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target effector: Organ, tissue, or gland that will respond to the control of an autonomic or somatic or endocrine signal.

target heart rate: Range in which both the heart and the lungs receive the maximum benefit from an aerobic workout.

tarsal bone: One of the seven bones that make up the posterior foot; includes the calcaneus, talus, navicular, cuboid, medial cuneiform, intermediate cuneiform, and lateral cuneiform bones.

taste buds: Structures within a papilla on the tongue that contain gustatory receptor cells.

T cell: Lymphocyte that acts by secreting molecules that regulate the immune system or by causing the destruction of foreign cells, viruses, and cancer cells.

T cell–dependent antigen: Antigen that binds to B cells, which requires signals from T cells to make antibody.

T cell–independent antigen: Binds to B cells, which do not require signals from T cells to make antibody.

tectorial membrane: Component of the organ of Corti that lies over the hair cells, into which the stereocilia are embedded.

tectospinal tract: Extrapyramidal connections between the superior colliculus and spinal cord.

telophase: Final stage of mitosis (and meiosis), preceding cytokinesis, characterized by the formation of two new daughter nuclei.

temporal bone: Paired bones that form the lateral, inferior portions of the skull, with squamous, mastoid, and petrous portions.

temporal fossa: Shallow space on the lateral side of the skull, above the level of the zygomatic arch.

temporalis: Muscle that retracts the mandible.

temporal lobe: Region of the cerebral cortex directly beneath the temporal bone of the cranium.

temporal summation: Combination of graded potentials at the same location on a neuron, resulting in a strong signal from one input.

tendon: Dense connective tissue structure that anchors a muscle to bone.

tendon (Golgi) stretch organs: Transduce the stretch levels of tendons.

tendon sheath: Connective tissue that surrounds a tendon at places where the tendon crosses a joint; contains a lubricating fluid to prevent friction and allow smooth movements of the tendon.

tenia coli: One of three smooth muscle bands that make up the longitudinal muscle layer of the muscularis in all of the large intestine except the terminal end.

tensor fascia lata: Muscle that flexes and abducts the thigh.

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teres major: Muscle that extends the arm and assists in adduction and medial rotation of it.

teres minor: Muscle that laterally rotates and extends the arm.

terminal bronchioles: Smallest airways that lead to the structures of gas exchange.

terminal ganglia: Ganglia of the parasympathetic division of the autonomic system, which are located near or within the target effector, the latter also known as intramural ganglia.

terminal ganglion: Autonomic ganglia that are near or within the walls of organs and are responsible for contributing to homeostatic mechanisms of the autonomic nervous system.

tertiary follicles (also antral follicles): Ovarian follicles with a primary or secondary oocyte, multiple layers of granulosa cells, and a fully formed antrum.

testes (singular = testis): Male gonads.

testosterone: Steroid hormone secreted by the testes and important in the maturation of sperm cells, growth and development of the reproductive system, and development of secondary sex characteristics.

tetanus: A continuous fused contraction.

Th1 cells: Cells that secrete cytokines that enhance the activity of macrophages and other cells.

Th2 cells: Cells that secrete cytokines that induce B cells to differentiate into antibody-secreting plasma cells.

thalamus: Major region of the diencephalon that is responsible for relaying information between the cerebrum and the hindbrain, spinal cord, and periphery.

theca cells: Estrogen-producing cells in a maturing ovarian follicle.

thermoneutral: External temperature at which the body does not expend any energy for thermoregulation, about 29°C.

thermoreceptor: Type of sensory receptor capable of transducing temperature stimuli into neural action potentials.

thermoregulation: Process of regulating the temperature of the body.

thick filament: The thick myosin strands and their multiple heads projecting from the centre of the sarcomere toward, but not all the way to, the Z discs.

thigh: Portion of the lower limb located between the hip and knee joints.

thin filament: Thin strands of actin and its troponin-tropomyosin complex projecting from the Z discs toward the centre of the sarcomere.

third ventricle: Portion of the ventricular system that is in the region of the diencephalon.

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thoracic aorta: Portion of the descending aorta superior to the aortic hiatus.
thoracic cage: Consists of 12 pairs of ribs and the sternum.
thoracic cavity: Division of the anterior (ventral) cavity that houses the heart, lungs, esophagus, and trachea.
thoracic curve: Anteriorly concave curvature of the thoracic vertebral column region; a primary curve of the vertebral column.
thoracic duct: Large duct that drains lymph from the lower limbs, left thorax, left upper limb, and the left side of the head.
thoracic vertebrae: 12 vertebrae numbered T1–T12 that are located in the thoracic region (upper back) of the vertebral column.
thoracic wall compliance: Ability of the thoracic wall to stretch while under pressure.
thoracolumbar system: Alternate name for the sympathetic division of the autonomic nervous system that is based on the anatomical location of central neurons in the lateral horn of the thoracic.
thoroughfare channel: Continuation of the metarteriole that enables blood to bypass a capillary bed and flow directly into a venule, creating a vascular shunt.
threshold: Membrane voltage at which an action potential is initiated.
thrombin: Enzyme essential for the final steps in formation of a fibrin clot.
thrombocytes: Platelets, one of the formed elements of blood that consists of cell fragments broken off from megakaryocytes.
thrombocytopenia: Condition in which there are too few platelets, resulting in abnormal bleeding (hemophilia).
thrombocytosis: Condition in which there are too many platelets, resulting in abnormal clotting (thrombosis).
thrombopoietin: Hormone secreted by the liver and kidneys that prompts the development of megakaryocytes into thrombocytes (platelets).
thymocyte: Immature T cell found in the thymus.
thymosins: Hormones produced and secreted by the thymus that play an important role in the development and differentiation of T cells.
thymus: Organ involved in the development and maturation of T cells; particularly active during infancy and childhood.
thyroid cartilage: Largest piece of cartilage that makes up the larynx and consists of two lamine.
thyroid gland: Large endocrine gland responsible for the synthesis of thyroid hormones.
thyroid-stimulating hormone (TSH): Anterior pituitary hormone that triggers secretion of thyroid hormones by the thyroid gland (also called thyrotropin).

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thyroxine (also tetraiodothyronine, T4): Amino acid–derived thyroid hormone that is more abundant but less potent than T_3 and often converted to T_3 by target cells.

tibia: Shin bone; the large, weight-bearing bone located on the medial side of the leg.

tibial collateral ligament: Extrinsic ligament of knee joint that spans from the medial epicondyle of the femur to the medial tibia; resists hyperextension and rotation of extended knee.

tibialis anterior: Muscle located on the lateral surface of the tibia.

tibial nerve: Systemic nerve of the posterior leg that begins as part of the sciatic nerve.

tibial tuberosity: Elevated area on the anterior surface of the proximal tibia.

tidal volume (TV): Amount of air that normally enters the lungs during quiet breathing.

tight junction: Forms an impermeable barrier between cells that blocks hydrophilic ions or molecules.

tissue: Group of similar or closely related cells that act together to perform a specific function.

tissue factor: Protein thromboplastin, which initiates the extrinsic pathway when released in response to tissue damage.

tissue membrane: Thin layer or sheet of cells that covers the outside of the body, organs, internal passageways, and the lining of joint cavities.

T lymphocytes (also T cells): Lymphocytes that provide cellular-level immunity by physically attacking foreign or diseased cells.

tongue: Accessory digestive organ of the mouth, the bulk of which is composed of skeletal muscle.

tonicity: A measure of a solution's ability to change the volume of cells by altering their water content.

tonsils (palatine, pharyngeal, and lingual): Lymphoid nodules associated with the nasopharynx.

topographical: Relating to positional information.

total dead space: Sum of the anatomical dead space and alveolar dead space.

total lung capacity (TLC): Total amount of air that can be held in the lungs; sum of TV, ERV, IRV, and RV.

total pressure: Sum of all the partial pressures of a gaseous mixture.

totipotent stem cell: Embryonic stem cell that is capable of differentiating into any and all cells of the body, enabling the full development of an organism.

trabeculae (singular = trabecula): Spikes or sections of the latticelike matrix in spongy bone.

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trabeculae carneae: Ridges of muscle covered by endocardium located in the ventricles.

trachea: Tube composed of cartilaginous rings and supporting tissue that connects the lung bronchi and the larynx; provides a route for air to enter and exit the lung.

trachealis muscle: Smooth muscle located in the fibroelastic membrane of the trachea.

tract: Bundle of axons in the central nervous system having the same function and point of origin.

transcription: Process of producing an mRNA molecule that is complementary to a particular gene of DNA.

transduction: Process of changing an environmental stimulus into the electrochemical signals of the nervous system.

transferrin: Plasma protein that binds reversibly to iron and distributes it throughout the body.

transfer RNA (tRNA): Molecules of RNA that serve to bring amino acids to a growing polypeptide strand and properly place them into the sequence.

transient ischemic attack (TIA): Temporary loss of neurological function caused by a brief interruption in blood flow; also known as a ministroke.

transitional epithelium: Form of stratified epithelium found in the urinary tract, characterized by an apical layer of cells that change shape in response to the presence of urine.

translation: Process of producing a protein from the nucleotide sequence code of an mRNA transcript.

transpulmonary pressure: Pressure difference between the intrapleural and intra-alveolar pressures.

transverse colon: Part of the colon between the ascending colon and the descending colon.

transverse foramen: Opening found only in the transverse processes of cervical vertebrae.

transverse plane: Two-dimensional, horizontal plane that divides the body or organ into superior and inferior portions.

transverse process: Paired bony process that extends laterally from the vertebral arch of a vertebra.

transversus abdominis: Deep layer of the abdomen that has fascicles arranged transversely around the abdomen.

trapezius: Muscle that stabilizes the upper part of the back.

treppe: Stepwise increase in contraction tension.

tri: Three.

triad: A grouping of one T-tubule and two terminal cisternae.

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tricarboxylic acid cycle (TCA): Also called the Krebs cycle or the citric acid cycle; converts pyruvate into CO_2 and high-energy $FADH_2$, NADH, and ATP molecules.

triceps brachii: Three-headed muscle that extends the forearm.

tricuspid valve: Term used most often in clinical settings for the right atrioventricular valve.

trigeminal nerve: Fifth cranial nerve; responsible for cutaneous sensation of the face and contraction of the muscles of mastication.

triglyceride: Lipid compound composed of a glycerol molecule bonded with three fatty acid chains.

trigone: Area at the base of the bladder marked by the two ureters in the posterior-lateral aspect and the urethral orifice in the anterior aspect oriented like points on a triangle.

triiodothyronine (also T3): Amino acid–derived thyroid hormone that is less abundant but more potent than T_4.

trimester: Division of the duration of a pregnancy into three 3-month terms.

trochlea: Pulley-shaped region located medially at the distal end of the humerus; articulates at the elbow with the trochlear notch of the ulna.

trochlear nerve: Fourth cranial nerve; responsible for contraction of one of the extraocular muscles.

trochlear notch: Large, C-shaped depression located on the anterior side of the proximal ulna; articulates at the elbow with the trochlea of the humerus.

trophoblast: Fluid-filled shell of squamous cells destined to become the chorionic villi, placenta, and associated fetal membranes.

tropomyosin: Regulatory protein that covers myosin-binding sites to prevent actin from binding to myosin.

troponin: Regulatory protein that binds to actin, tropomyosin, and calcium.

true labour: Regular contractions that immediately precede childbirth; they do not abate with hydration or rest, and they become more frequent and powerful with time.

true ribs: Vertebrosternal ribs 1–7, which attach via their costal cartilage directly to the sternum.

true vocal cord: One of the pair of folded, white membranes that have a free inner edge that oscillates as air passes through to produce sound.

trunk: Large vessel that gives rise to smaller vessels.

trypsin: Pancreatic enzyme that activates chymotrypsin and digests protein.

trypsinogen: Proenzyme form of trypsin.

T-tubule: Projection of the sarcolemma into the interior of the cell.

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tubercle of the rib: Small bump on the posterior side of a rib for articulation with the transverse process of a thoracic vertebra.

tubuloglomerular feedback: Feedback mechanism involving the JGA; macula densa cells monitor Na^+ concentration in the terminal portion of the ascending loop of Henle and act to cause vasoconstriction or vasodilation of afferent and efferent arterioles to alter GFR.

tunica externa (also tunica adventitia): Outermost layer or tunic of a vessel (except capillaries).

tunica intima (also tunica interna): Innermost lining or tunic of a vessel.

tunica media: Middle layer or tunic of a vessel (except capillaries).

T wave: Component of the electrocardiogram that represents the repolarization of the ventricles.

twitch: Single contraction produced by one action potential.

tympanic membrane: Ear drum.

type I alveolar cell: Squamous epithelial cells that are the major cell type in the alveolar wall; highly permeable to gases.

type II alveolar cell: Cuboidal epithelial cells that are the minor cell type in the alveolar wall; secrete pulmonary surfactant.

ulna: Bone located on the medial side of the forearm.

ulnar artery: Formed at the bifurcation of the brachial artery; parallels the ulna; gives off smaller branches until it reaches the carpal region, where it fuses with the radial artery to form the superficial and deep palmar arches; supplies blood to the lower arm and carpal region.

ulnar collateral ligament: Intrinsic ligament on the medial side of the elbow joint; spans from the medial epicondyle of the humerus to the medial ulna.

ulnar nerve: Systemic nerve of the arm located close to the ulna, a bone of the forearm.

ulnar tuberosity: Roughened area located on the anterior, proximal ulna inferior to the coronoid process.

ulnar vein: Parallels the ulna and ulnar artery; arises from the palmar venous arches and leads to the brachial vein.

umbilical arteries: Pair of vessels that runs within the umbilical cord and carries fetal blood low in oxygen and high in waste to the placenta for exchange with maternal blood.

umbilical cord: Connection between the developing conceptus and the placenta; carries deoxygenated blood and waste from the fetus and returns nutrients and oxygen from the mother.

umbilical vein: Single vessel that originates in the placenta and runs within the umbilical cord, carrying oxygen- and nutrient-rich blood to the fetal heart.

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uniaxial joint: Type of diarthrosis; joint that allows for motion within only one plane (one axis).

unipennate: Pennate muscle that has fascicles located on one side of the tendon.

unipolar: Shape of a neuron that has only one process that includes both the axon and dendrite.

universal donor: Individual with type O^- blood.

universal recipient: Individual with type AB^+ blood.

upper esophageal sphincter: Skeletal muscle sphincter that regulates food movement from the pharynx to the esophagus.

upper motor neuron: First neuron in the motor command pathway with its cell body in the cerebral cortex; synapses on the lower motor neuron in the spinal cord.

upregulation: Increase in the number of hormone receptors, typically in response to chronically reduced levels of a hormone.

urea cycle: Process that converts potentially toxic nitrogen waste into urea that can be eliminated through the kidneys.

urethra: Transports urine from the bladder to the outside environment.

urinalysis: Analysis of urine to diagnose disease.

uterine tubes (also fallopian tubes or oviducts): Ducts that facilitate transport of an ovulated oocyte to the uterus.

uterus: Muscular hollow organ in which a fertilized egg develops into a fetus.

utricle: Structure of the inner ear responsible for transducing linear acceleration in the horizontal plane.

uvula: Fleshy bead of tissue that drops down from the centre of the posterior edge of the soft palate.

vagina: Tunnel-like organ that provides access to the uterus for the insertion of semen and from the uterus for the birth of a baby.

vagus nerve: 10th cranial nerve; responsible for the autonomic control of organs in the thoracic and upper abdominal cavities.

valence shell: Outermost electron shell of an atom.

Valsalva's maneuver: Voluntary contraction of the diaphragm and abdominal wall muscles and closing of the glottis, which increases intra-abdominal pressure and facilitates defecation.

valve: In the cardiovascular system, a specialized structure located within the heart or vessels that ensures one-way flow of blood.

varicosity: Structure of some autonomic connections that is not a typical synaptic end bulb, but a string of swellings along the length of a fibre that makes a network of connections with the target effector.

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vasa recta: Branches of the efferent arterioles that parallel the course of the loops of Henle and are continuous with the peritubular capillaries; with the glomerulus, form a portal system.

vasa vasorum: Small blood vessels located within the walls or tunics of larger vessels that supply nourishment to and remove wastes from the cells of the vessels.

vascular shock: Type of shock that occurs when arterioles lose their normal muscular tone and dilate dramatically.

vascular shunt: Continuation of the metarteriole and thoroughfare channel that allows blood to bypass the capillary beds to flow directly from the arterial to the venous circulation.

vascular spasm: Initial step in hemostasis, in which the smooth muscle in the walls of the ruptured or damaged blood vessel contracts.

vascular tone: Contractile state of smooth muscle in a blood vessel.

vascular tunic: Middle layer of the eye primarily composed of connective tissue with a rich blood supply.

vasoconstriction: Constriction of the smooth muscle of a blood vessel, resulting in a decreased vascular diameter.

vasodilation: Relaxation of the smooth muscle in the wall of a blood vessel, resulting in an increased vascular diameter.

vasomotion: Irregular, pulsating flow of blood through capillaries and related structures.

vasomotor centres: Control vessel tone or contraction of the smooth muscle in the tunica media.

vasomotor nerves: Preganglionic sympathetic fibres that cause the constriction of blood vessels in response to signals from the cardiovascular centre.

vastus intermedius: Quadricep muscle that is between the vastus lateralis and vastus medialis and is deep to the rectus femoris.

vastus lateralis: Quadricep muscle on the lateral aspect of the thigh.

vastus medialis: Quadricep muscle on the medial aspect of the thigh.

vein: Blood vessel that conducts blood toward the heart.

vein valves: Assist the unidirectional flow of blood toward the heart; particularly those of the limbs.

venous reserve: Volume of blood contained within systemic veins in the integument, bone marrow, and liver that can be returned to the heart for circulation if needed.

ventilation: Movement of air into and out of the lungs; consists of inspiration and expiration.

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ventral: Describes the front or direction toward the front of the body; also referred to as anterior.

ventral cavity: Larger body cavity located anterior to the posterior (dorsal) body cavity; includes the serous membrane-lined pleural cavities for the lungs, pericardial cavity for the heart, and peritoneal cavity for the abdominal and pelvic organs; also referred to as the anterior body cavity.

ventral respiratory group (VRG): Region of the medulla oblongata that stimulates the contraction of the accessory muscles involved in respiration to induce forced inspiration and expiration.

ventral stream: Connections between cortical areas from the occipital lobe to the temporal lobe that are responsible for the identification of visual stimuli.

ventricle (brain): Central cavity within the brain where CSF is produced and circulates.

ventricle (heart): One of the primary pumping chambers of the heart located in the lower portion of the heart; the left ventricle is the major pumping chamber on the lower left side of the heart that ejects blood into the systemic circuit via the aorta and receives blood from the left atrium; the right ventricle is the major pumping chamber on the lower right side of the heart that ejects blood into the pulmonary circuit via the pulmonary trunk and receives blood from the right atrium.

ventricular ejection phase: Second phase of ventricular systole during which blood is pumped from the ventricle.

venule: Small vessel leading from the capillaries to veins.

vernix caseosa: Waxy, cheese-like substance that protects the delicate fetal skin until birth.

vertebra: Individual bone in the neck and back regions of the vertebral column.

vertebral (spinal) canal: Bony passageway within the vertebral column for the spinal cord that is formed by a series of individual vertebral foramina.

vertebral arch: Bony arch formed by the posterior portion of each vertebra that surrounds and protects the spinal cord.

vertebral arteries: Arteries that ascend along either side of the vertebral column through the transverse foramina of the cervical vertebrae and enter the cranium through the foramen magnum.

vertebral body: The anterior portion of each vertebra; the part that supports body weight.

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vertebral column: Entire sequence of bones that extend from the skull to the tailbone.

vertebral foramen: Opening associated with each vertebra, defined by the vertebral arch that provides passage for the spinal cord.

vesicle: Membrane-bound structure that contains materials within or outside of the cell.

vestibular apparatus: Component of the vestibular system that contains the hair cell with stereocilia responsible for senses, head position, head movement, and whether our bodies are in motion.

vestibular fold: Part of the folded region of the glottis composed of mucous membrane; supports the epiglottis during swallowing.

vestibular ganglion: Location of neuronal cell bodies that transmit equilibrium information along the eighth cranial nerve.

vestibular nuclei: Targets of the vestibular component of the eighth cranial nerve.

vestibule: In the ear, the portion of the inner ear responsible for the sense of equilibrium.

vestibulocochlear nerve (auditory): Eighth cranial nerve; responsible for the sensations of hearing and balance.

vestibulo-ocular reflex (VOR): Reflex based on connections between the vestibular system and the cranial nerves of eye movements that ensures images are stabilized on the retina as the head and body move.

vestibulospinal tract: Extrapyramidal connections between the vestibular nuclei in the brain stem and spinal cord that modulate movement and contribute to balance on the basis of the sense of equilibrium.

villus: Projection of the mucosa of the small intestine.

visceral branches: Branches of the descending aorta that supply blood to the viscera.

visceral layer: Serous membrane that covers the organs (the viscera).

visceral muscle: Smooth muscle found in the walls of visceral organs.

visceral pericardium (epicardium): Layer of serous pericardium that is fused to the heart and is part of the heart wall.

visceral peritoneum: Envelopes the abdominal organs.

visceral pleura: Innermost layer of the pleura that is superficial to the lungs and extends into the lung fissures.

visceral reflex: Reflex involving an internal organ as the effector, under the control of the autonomic nervous system.

visceral sense: Sense associated with the internal organs.

vision: Special sense of sight based on the transduction of light stimuli.

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visual acuity: Property of vision related to the sharpness of focus, which varies in relation to retinal position.

vital capacity (VC): Sum of TV, ERV, and IRV, which is all the volumes that participate in gas exchange.

vitamin D: Compound that aids absorption of calcium and phosphates in the intestine to improve bone health.

vitamins: Organic compounds required by the body to perform biochemical reactions like metabolism and bone, cell, and tissue growth.

vitreous humour: Viscous fluid that fills the posterior chamber of the eye.

voltage-gated channel: Ion channel that opens because of a change in the charge distributed across the membrane where it is located.

voltage-gated sodium channels: Membrane proteins that open sodium channels in response to a sufficient voltage change and initiate and transmit the action potential as Na^+ enters through the channel.

voluntary phase: Initial phase of deglutition, in which the bolus moves from the mouth to the oropharynx.

vomer bone: Unpaired bone that forms the inferior and posterior portions of the nasal septum.

vulva: External female genitalia.

wave summation: Addition of successive neural stimuli to produce greater contraction.

white blood cells (WBCs; also leukocytes): One of the formed elements of blood that provides defence against disease agents and foreign materials.

white matter: Regions of the nervous system containing mostly myelinated axons, making the tissue appear white because of the high lipid content of myelin.

white pulp: Splenic nodule area that resembles the lymphoid follicles of the lymph nodes.

white rami communicantes (singular = ramus communicans): Myelinated structures that provide a short connection from a sympathetic chain ganglion to the spinal nerve that contains the preganglionic sympathetic fibre.

withdrawal reflex: From a painful stimulus only requires the sensory fibre that enters the spinal cord and the motor neuron that projects to a muscle.

working memory: Function of the prefrontal cortex to maintain a representation of information that is not in the immediate environment.

xiphoid process: Small process that forms the inferior tip of the sternum.

yellow marrow: Connective tissue in the interior cavity of a bone where fat is stored.

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yolk sac: Membrane associated with primitive circulation to the developing embryo; source of the first blood cells and germ cells and contributes to the umbilical cord structure.

Z discs: Three-dimensional cylinder-like arrangement of sarcomere.

zona fasciculata: Intermediate region of the adrenal cortex that produces hormones called glucocorticoids.

zona glomerulosa: Most superficial region of the adrenal cortex; produces the hormones collectively referred to as mineralocorticoids.

zona pellucida: Thick, gel-like glycoprotein membrane that coats the oocyte and must be penetrated by sperm before fertilization can occur.

zona reticularis: Deepest region of the adrenal cortex; produces the steroid sex hormones called androgens.

zonule fibres: Fibrous connections between the ciliary body and the lens.

zygomatic arch: Elongated, freestanding arch on the lateral skull, formed anteriorly by the temporal process of the zygomatic bone.

zygomatic bone: Cheekbone; paired bones that contribute to the lateral orbit and anterior zygomatic arch.

zygote: Fertilized egg; a diploid cell resulting from the fertilization of haploid gametes from the male and female lines.

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Figure Descriptions

Figure 1.1

This illustration shows the biological organization of the human body as a pyramid with six main levels. The chemical level is at the apex of the pyramid, where atoms bond to form molecules with three-dimensional structures. The molecular sublevel is presented as an example with two white hydrogen atoms bonding to a red oxygen atom to create water. The next level down on the pyramid is the cellular level, as illustrated with a long, tapered, smooth muscle cell; at this level, a variety of molecules combine to form the interior fluid and organelles of a body cell. The next level down is the tissue level, a community of similar cells that forms body tissue; the example given here is a section of smooth muscle tissue, which contains many smooth muscle cells closely bound side by side. The next level down is the organ level, as illustrated with the urinary bladder and urethra. The urinary bladder contains smooth muscle, while the urethra contains skeletal muscle; these are both examples of muscle tissues. The next level down is the organ system level, as illustrated by the entire urinary system, containing the kidneys, ureters, bladder, and urethra; at this level, two or more organs work closely together to perform the functions of a body system. At the base of the pyramid is the organismal level, as illustrated with a woman drinking water; at this level, many organ systems work harmoniously together to perform the functions of an independent organism.

Figure 1.2

This illustration shows six silhouettes of a human body, male and female, each showing the components of a different organ system. The integumentary system encloses internal body structures and is the site of many sensory receptors; it includes the hair, skin, and nails. The skeletal system supports the body and, along with the muscular system, enables movement; it includes cartilage, such as that at the tip of the nose, as well as the bones and joints. The muscular system enables movement, along with the skeletal system, but also helps maintain body temperature; it includes skeletal muscles as well as tendons that connect skeletal muscles to bones. The nervous system detects and processes sensory information and activates bodily responses; it includes the brain, spinal cord, and peripheral nerves, such as those located in the limbs. The endocrine system secretes hormones and regulates physiological processes; it includes the pituitary gland in the brain, the thyroid gland in the throat, the pancreas in the abdomen, the adrenal glands on top of the kidneys, and the testes in the scrotum of males as well as the ovaries in the pelvic region of females. The cardiovascular system delivers oxygen and nutrients to the tissues, equalizes temperature in the body, and performs many other functions; it includes the heart and blood vessels.

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Figure 1.3

This illustration shows six silhouettes of a human body, male and female, each showing the components of a different organ system. The lymphatic system returns fluid to the blood and defends against pathogens; it includes the thymus in the chest, the spleen in the abdomen, the lymphatic vessels that spread throughout the body, and the lymph nodes distributed along the lymphatic vessels. The respiratory system removes carbon dioxide from the body and delivers oxygen to the blood; it includes the nasal passages, the trachea, and the lungs. The digestive system processes food for use by the body and removes wastes from undigested food; it includes the stomach, the liver, the gall bladder (connected to the liver), the large intestine, and the small intestine. The urinary system controls water balance in the body and removes and excretes waste from the blood; it includes the kidneys and the urinary bladder. The reproductive systems of males and females produce sex hormones and gametes; the male reproductive system is specialized to deliver gametes to the female, while the female reproductive system is specialized to support the embryo and fetus until birth and produce milk for the infant after birth. The male reproductive system includes the two testes within the scrotum as well as the epididymis, which wraps around each testis; the female reproductive system includes the mammary glands within the breasts and the ovaries and uterus within the pelvic cavity.

Figure 1.5

This figure shows two flowcharts labelled A and B. Chart A shows a general negative feedback loop. The loop starts with a stimulus perceived by a sensor, which sends that information to a control centre. The control centre sends a processed response as a signal to an effector, which creates a response to correct the condition; once this is corrected, it feeds back to the stimulus to inhibit the sensor from receiving more signal from the stimulus, which was already corrected by this process. Chart B shows body temperature regulation as an example of a negative feedback system. Here, the stimulus is body temperature exceeding 37°C. The sensor is a set of nerve cells in the skin and brain, and the control centre is the temperature regulatory centre in the brain; the effectors are sweat glands throughout the body that increase their secretion, which leads to heat loss to inhibit the rising body temperature, which then feeds back to the signal to inhibit the nerve cells in the skin and brain from responding, as the stimulus was eliminated.

Figure 1.6

This diagram shows the steps of a positive feedback loop as a series of stepwise arrows looping around a diagram of an infant within the uterus of a pregnant woman. The stimulus is the physical pressure by the head of the fetus against the cervix, transmitting nerve impulses from the cervix to the brain. Next, the brain stimulates the pituitary gland to secrete oxytocin, which is carried in the bloodstream to the uterus. Finally, the oxytocin stimulates uterine contractions and pushes the fetus harder into the cervix, combined with the relaxation of the cervix. As the head of the fetus pushes against the cervix with increasing force, the uterine contractions grow stronger and more frequent. This mechanism is a positive feedback loop.

Figure 1.7

This diagram shows anterior and posterior views of the human body with all regional labels. In the anterior view, labels identify the frons or forehead (frontal), cranium or skull (cranial), facies or face (facial), oris or mouth (oral), mentis or chin (mental), oculus or eye (orbital or ocular), bucca or cheek (buccal), auris or ear (otic), nasus or nose (nasal), cervicis or neck (cervical),

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thorcis or thorax or chest (thoracic), mamma or breast (mammary), abdomen (abdominal), umbilicus or navel (umbilical), hip (coxal), pelvis (pelvic), inguen or groin (inguinal), pubis (pubic), axilla or armpit (axillary), brachium or arm (brachial), antecubitis or front of elbow (antecubital), antebrachium or forearm (antebrachial), carpus or wrist (carpal), pollex or thumb, palma or palm (palmar), digits (phalanges) or fingers (digital or phalangeal), patella or kneecap (patellar), crus or leg (crural), tarsus or ankle (tarsal), digits (phalanges) or toes (digital or phalangeal), femur or thigh (femoral), pes or foot (pedal), and hallux or great toe. The posterior view labels the cephalon or head (cephalic), cervicis or neck (cervical), shoulder (acromial), dorsum or back (dorsal), brachium or arm (brachial), olecranon or back of elbow (olecranal), lumbus or loin (lumbar), sacrum (sacral), antebrachium or forearm (antebrachial), manus or hand (manual), gluteus or buttock (gluteal), femur or thigh (femoral), popliteus or back of knee (popliteal), sura or calf (sural), calcaneus or heel of foot (calcaneal), and planta or sole of foot (plantar). Both diagrams mark the upper limb and lower limb.

Figure 1.8

This illustration shows two diagrams: one of a side view of a female and the other of an anterior view of a female. Each diagram shows directional terms using double-sided arrows. On the left diagram, which is the lateral view, the cranial-caudal arrow runs vertically behind the torso and lower abdomen; the cranial arrow is pointing toward the back of the head, while the caudal arrow is pointing toward the tailbone. The posterior-anterior arrow is running horizontally through the back and chest; the posterior or dorsal arrow is pointing toward the back, while the anterior or ventral arrow is pointing toward the chest. On the right diagram, which is the anterior view, the proximal-distal arrow is on the left arm ("left" refers to the left side of the woman's body from her perspective, while "right" refers to the right side of the woman's body from her perspective); the proximal arrow is pointing up toward the left shoulder, while the distal arrow is pointing down toward the left hand. The same example is given for the right leg; the proximal arrow is pointing up toward the right hip, while the distal arrow is pointing down toward the right foot. The lateral-medial arrow is running horizontally on the abdomen; the medial arrow is pointing toward the navel (umbilicus), while the lateral arrow is pointing away from the body to the right. The illustration also describes the terms "superior," which refers to the orientation toward the head, and "inferior," which describes the orientation toward the feet.

Figure 1.10

This illustration shows lateral (right) and anterior (front) views of the body and highlights the body cavities with different colours. The cranial cavity is a large, bean-shaped cavity filling most of the upper skull, where the brain is located. The vertebral cavity is a very narrow, threadlike cavity running from the cranial cavity down the entire length of the spinal cord. Together, the cranial cavity and vertebral cavity can be referred to as the dorsal body cavity. The thoracic cavity consists of three cavities (detailed on the anterior view) that fill the interior area of the chest. The two pleural cavities are situated on both sides of the body, anterior to the spine and lateral to the breastbone. The superior mediastinum is a wedge-shaped cavity located between the superior regions of the two thoracic cavities. The pericardial cavity within the mediastinum is located at the centre of the chest below the superior mediastinum—it roughly outlines the shape of the heart. The diaphragm divides the thoracic and the abdominal cavities. The abdominal cavity occupies the entire lower half of the trunk, anterior to the spine. Just under the abdominal cavity, anterior to the buttocks, is the pelvic cavity. The pelvic cavity is funnel-shaped and is located inferior and anterior to the abdominal cavity. There is no anatomical structure between these two body cavities, so together, the abdominal and

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pelvic cavities can be referred to as the abdominopelvic cavity. The thoracic, abdominal, and pelvic cavities together can be referred to as the ventral body cavity.

Figure 1.11

This illustration has two parts. Part A (left) shows the nine abdominopelvic regions named based on their anatomical positions. For example, the right hypochondriac region is located on the left in the illustration, but anatomically, it is on the right side of the body. It contains the base of the right ribs, part of the liver, and part of the gall bladder. The upper right square is the left hypochondriac region and contains the base of the left ribs, part of the liver, and part of the stomach. The epigastric region is the upper central square and contains the bottom edge of the liver, the gall bladder, and the upper areas of the stomach. The diaphragm curves like an upside-down U over these three regions. The central left square is called the right lumbar region and contains the right part of the colon and the right part of the small intestines. The central middle square is the umbilical region and contains part of the stomach, part of the liver, the central part of the colon, and the central part of the small intestines. The central right square is called the left lumbar region and contains the left part of the colon, cecum, and small intestines. The lower left square is the right iliac region and contains the right pelvic bone and part of the colon. The lower central square is the hypogastric region and contains the bottom of the pubic bones, the upper regions of the bladder, and the lower region of the small intestine. The lower right square is the left iliac region and contains the left pelvic bone and the lower left regions of the small intestine. Part B shows four abdominopelvic quadrants. The upper left square is the right upper quadrant (RUQ) and includes the lower right ribs, the right side of the liver, the gall bladder, part of the stomach, and part of the colon. The upper right square is the left upper quadrant (LUQ) and includes the lower left ribs, part of the stomach, part of the liver, and part of the colon. The lower left square is the right lower quadrant (RLQ) and includes the right half of the small intestines, part of the colon, the right pelvic bone, and the upper right area of the bladder. The lower right square is the left lower quadrant (LLQ) and contains the left half of the small intestine, the left pelvic bone, and the upper left area of the bladder.

Figure 1.12

This diagram shows the pericardium on the left next to an analogy of a hand punching a balloon on the right. The pericardium is a two-layered sac that surrounds the entire heart except where the blood vessels emerge on the heart's superior side. The pericardium has two layers because it folds over itself in the shape of the letter U. The inner layer that borders the heart is the visceral pericardium (in contact with the hand on the analogy), while the outer layer is the parietal pericardium (the outer balloon layer on the analogy). The space between the two layers is called the pericardial cavity (the air space on the analogy) and is filled with fluid. The heart sits in the cavity much like a fist punching into a balloon. The balloon surrounds the lower part of the fist with a two-layered sac, with the top of the balloon, where it contacts the fist, being analogous to the visceral pericardium. The bottom of the balloon, where it is tied off, is analogous to the parietal pericardium. The air within the balloon is analogous to the pericardial cavity, which in reality is filled with fluid.

Figure 2.6

The top panel in this figure shows two hydrogen atoms sharing two electrons, which is a single covalent bond. The hydrogen atoms each share their solitary electron. The middle panel in this figure shows a molecule of oxygen gas with two oxygen atoms sharing four electrons, which is a double covalent bond. An atom of oxygen has six electrons in its valence shell and achieves stability by sharing two pairs of electrons. The bottom panel in this figure shows

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two oxygen atoms and one carbon atom sharing two pairs of electrons, which is two double covalent bonds. An atom of carbon and two atoms of oxygen achieve stability by sharing two electron pairs each.

Figure 2.7

This figure shows three different models for diagraming the structure of a water molecule. The top panel uses the planetary model and shows two hydrogen atoms and one oxygen atom with electrons in orbit. The unshared electrons in the outer shell of the oxygen atom are weakly negative, while the outer shells of the hydrogen atoms are weakly positive. The lower left panel shows a three-dimensional model of a water molecule, where spheres representing the three atoms are pressed up against each other. The lower right panel shows the structural formula for a water molecule, where the three spheres are separated and the bonds between them are indicated by a line.

Figure 3.8

This diagram shows four sodium-potassium pumps embedded in the plasma membrane. Potassium is pumped from the extracellular space, where it is highly concentrated, into the cytoplasm. Sodium is pumped out of the cytoplasm, where it is highly concentrated, into the extracellular space. An ATP molecule is shown bonding to the potassium pump from the cytoplasm side of the membrane. This molecule detaches from the potassium pump and becomes an ADP molecule, leaving a phosphate molecule behind. This phosphate molecule is released back into the cytoplasm, along with potassium ions transported through the membrane via the pump.

Figure 3.9

This image shows the three different types of endocytosis. The left panel shows phagocytosis, where a large particle is seen to be engulfed by the membrane and released into the intracellular fluid as a vacuole. In the middle panel, pinocytosis is shown, where a small particle is engulfed by the membrane and released into the intracellular fluid as a vesicle. In the right panel, receptor-mediated endocytosis is shown, where the ligand binds to a receptor on the exterior of the cell membrane. It is then engulfed by the membrane and released into the intracellular fluid as a coated vesicle.

Figure 3.13

This figure shows the structure of the Golgi apparatus. The diagram in the left panel shows the location and structure of the Golgi apparatus between the plasma membrane and the rough endoplasmic reticulum and nucleus. Transport vesicles bring material from the rough endoplasmic reticulum to the cisternae of the Golgi apparatus. Secretory vesicles bring material from the Golgi apparatus to the plasma membrane, where it is transmitted into the extracellular fluid. The right panel presents a micrograph showing the folds of the Golgi in detail. The trans and cis faces of the organelle are labelled.

Figure 3.15

This figure shows the different cytoskeletal components in a cell. The left panel shows the microtubules with the structure of the column formed by tubulin dimers. The tubulin dimer looks like two strings of pearls coiled into a tubular column approximately 25 nanometres in diameter. The middle panel shows the actin filaments and the helical structure formed by the filaments. The filaments are composed of individual actin subunits, and the helical

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structure is approximately 7 nanometres across. The right panel shows the fibrous structure of the intermediate filaments with different keratins coiled together. It has a rope-like coiled structure that is approximately 8 to 12 nanometres across.

Figure 3.20

This figure shows the DNA double helix in the top left panel. The different nucleotides are colour-coded and combine with the sugar-phosphate backbone to form a twisted ladderlike structure. In the top right panel, the interaction between the nucleotide molecules through hydrogen bonds and the location of the sugar-phosphate backbone is shown. Thymine and adenine molecules form two hydrogen bonds between them, while guanine and cytosine form three. Opposite their hydrogen bonds, each nitrogenous base is bonded to a sugar molecule, which in turn is bonded to a phosphate molecule. These latter two molecules compose the sugar-phosphate backbone of DNA. In the bottom panel, the molecular structure of a nucleotide is described in detail, showing where the nitrogenous base joins the sugar molecule and where the sugar joins the phosphate.

Figure 3.26

This tabular image shows the different stages of mitosis and cytokinesis using both drawings and text. The top panel is a series of schematics for each step, followed by text listing the important aspects of that step. The bottom panel shows fluorescent micrographs for the corresponding stage. The first five stages illustrate mitosis, and the last stage illustrates cytokinesis. In prophase, chromosomes condense and become visible, spindle fibres emerge from the centrosomes, the nuclear envelope breaks down, and centrosomes move toward opposite poles of the cell. In prometaphase, chromosomes continue to condense, kinetochores appear at the centromeres, and mitotic spindle microtubules attach to kinetochores. In metaphase, chromosomes are lined up at the metaphase plate, and each sister chromatid is attached to a spindle fibre originating from opposite poles. In anaphase, centromeres split in two, sister chromatids (now called chromosomes) are pulled toward opposite poles, and certain spindle fibres begin to elongate the cell. Mitosis concludes with telophase, wherein chromosomes arrive at opposite poles and begin to decondense, the nuclear envelope material surrounds each set of chromosomes, the mitotic spindle breaks down, and spindle fibres continue to push poles apart. Finally, in cytokinesis for animal cells, a cleavage furrow separates the daughter cells, while for plant cells, a cell plate, the precursor to a new cell wall, separates the daughter cells.

Figure 4.1

This diagram shows the silhouette of a female surrounded by four micrographs of tissue. Each micrograph has arrows pointing to the organs where that tissue is found. The upper left micrograph shows nervous tissue that is whitish with several large, purple, irregularly shaped neurons embedded throughout. Nervous tissue is found in the brain, spinal cord, and nerves. The upper right micrograph shows muscle tissue that is red with elongated cells and prominent, purple nuclei. Cardiac muscle is found in the heart. Smooth muscle is found in internal organs, such as the stomach. Skeletal muscle is found in parts that are moved voluntarily, such as the arms. The lower left micrograph shows epithelial tissue. This tissue is purple with many round, purple cells with dark-purple nuclei. Epithelial tissue is found in the lining of GI tract organs and other hollow organs, such as the small intestine. Epithelial tissue also composes the outer layer of the skin, known as the epidermis. Finally, the lower right micrograph shows connective tissue, which is composed of very loosely packed purple cells and fibres. There are large open spaces between clumps of cells and fibres. Connective tissue is found in the leg within fat and other soft padding tissue as well as bones and tendons.

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Figure 4.2

This illustration shows the silhouette of a female from an anterior view. Several organs are showing in her neck, thorax, abdomen, left arm, and right leg. Text boxes point out and describe the mucous membranes in several different organs. The topmost box points to the mouth and trachea. It states that mucous membranes line the digestive, respiratory, urinary, and reproductive tracts. They are coated with the secretions of mucous glands. The second box points to the outside edge of the lungs as well as the large intestine. It states that serous membranes line body cavities that are closed to the exterior of the body, including the peritoneal, pleural, and pericardial cavities. The third box points to the skin of the hand. It states that the cutaneous membrane, also known as the skin, covers the body surface. The fourth box points to the right knee. It states that synovial membranes line joint cavities and produce the fluid within the joint.

Figure 4.3

These three illustrations each show the edges of two vertical cell membranes. The cell membranes are viewed partially from the side so that the inside edge of the right cell membrane is visible. The upper left image shows a tight junction. The two cell membranes are bound by transmembrane protein strands. The proteins travel the inside edge of the right cell membrane and cross over to the left cell membrane, cinching the two membranes together. The cell membranes are still somewhat separated in between neighbouring strands, creating intercellular spaces. The upper right diagram shows a gap junction. Gap junctions are composed of two interlocking connexins, which are round, hollow tubes that extend through the cell membranes. Two connexins, one from the left cell membrane and the other from the right cell membrane, meet between the two cells, forming a connexon. Even at the site of the connexon, there is a small gap between the cell membranes. On the inside edge of the right cell membrane, the gap junction appears as a depression. Three connexins are embedded in the membranes like buttons on a shirt. The bottom images show the three types of anchoring junctions. The left image shows a desmosome. Here, the inside edges of both the right and left cell membranes have brown, round plaques. Each plaque has tentacle-like intermediate filaments (keratin) that extend into each cell's cytoplasm. The two plaques are connected across the intercellular space by several interlocking transmembrane glycoproteins (cadherin). The connected glycoproteins look similar to a zipped-up zipper between the right and left cell membranes. The right image shows an example of adherens. These are similar to desmosomes, with two plaques on the inside edge of each cell membrane connected across the intercellular space by glycoproteins. However, the plaques do not contain the tentacle-like intermediate filaments branching into the cytoplasm. Instead, the plaques are ribbed with green actin filaments. The filaments are neatly arranged in parallel, horizontal strands on the surface of the plaque facing the cytoplasm. The bottom image shows a hemidesmosome. Rather than being located between two neighbouring cells, the hemidesmosome is located between the bottom of a cell and the basement membrane. A hemidesmosome contains a single plaque on the inside edge of the cell membrane. Like the desmosome, intermediate filaments project from the plaque into the cytoplasm. The opposite side of the plaque has purple, knob-shaped integrins extending out to the basal lamina of the basement membrane.

Figure 4.4

This figure is a table showing the appearance of squamous, cuboidal, and columnar epithelial tissues. Simple and stratified forms are shown for each tissue type. In a simple squamous epithelium, the cells are flattened and single layered. In a simple cuboidal epithelium, the cells are cube-shaped and single layered. In a simple columnar epithelium, the cells are rectangular

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and attached to the basement membrane on one of their narrow sides so that each cell is standing up like a column. There is only one layer of cells. In a pseudostratified columnar epithelium, the cells are column-like in appearance, but they vary in height. The taller cells bend over the tops of the shorter cells so that the top of the epithelial tissue is continuous. There is only one layer of cells. A stratified squamous epithelium contains many layers of flattened cells. A stratified cuboidal epithelium contains many layers of cube-shaped cells. A stratified columnar epithelium contains many layers of rectangular, column-shaped cells.

Figure 4.5

This illustration shows a diagram of a goblet cell. The goblet cell is shaped roughly like an upside-down vase. The enlarged end at the top contains seven finger-like projections labelled microvilli. Below the microvilli, secretory vesicles containing mucin are moving from the upper half of the cell toward the microvilli. Below the secretory vesicles are several rough endoplasmic reticula and an irregularly shaped Golgi apparatus with secretory vesicles budding off of it. The narrow, lower half of the cell contains the oval-shaped nucleus as well as a few mitochondria and segments of the endoplasmic reticulum.

Figure 4.6

This figure is a table with three columns and nine rows. The leftmost column is titled "Cells" and contains a drawing in each row showing how epithelial cells are arranged above a basement membrane. The middle column is titled "Location," while the rightmost column is titled "Function." In a simple squamous epithelium, the cells are flattened and single layered. Simple squamous cells are found in the air sacs of the lungs and in the lining of the heart, blood vessels, and lymphatic vessels. Their function is to allow materials to pass through by diffusion and filtration as well as to secrete lubricating substances. In a simple cuboidal epithelium, the cells are cube-shaped, single layered, and located in ducts and secretory portions of small glands as well as in the kidney tubules. The function of a simple cuboidal epithelium is to secrete and absorb. In a simple columnar epithelium, the cells are rectangular and attached to the basement membrane on one of their narrow sides so that each cell is standing up like a column. There is only one layer of cells. A simple columnar epithelium is found in ciliated tissues, including the larger bronchioles, uterine tubes, and uterus, as well as in smooth, nonciliated tissues, such as the digestive tract and bladder. The function of a simple columnar epithelium is to absorb substances but also to secrete mucus and enzymes. In a pseudostratified columnar epithelium, the cells are column-like in appearance, but they vary in height. The taller cells bend over the tops of the shorter cells so that the top of the epithelial tissue is continuous. There is only one layer of cells. A pseudostratified columnar epithelium lines the bronchi, the trachea, and much of the upper respiratory tract. The function of a pseudostratified columnar epithelium is to secrete mucus and also move that mucus using the hairlike cilia projecting from the top of each cell. A stratified squamous epithelium contains many layers of flattened cells. A stratified squamous epithelium lines the esophagus, mouth, and vagina. The function of a stratified squamous epithelium is to protect against abrasion. A stratified cuboidal epithelium contains many layers of cube-shaped cells. A stratified cuboidal epithelium is found in the sweat glands, salivary glands, and mammary glands. The function of a stratified cuboidal epithelium is to protect other tissues of the body. A stratified columnar epithelium contains many layers of rectangular, column-shaped cells. A stratified columnar epithelium is located in the male and female urethrae and the ducts of some glands. The function of a stratified columnar epithelium is to secrete and protect. A transitional epithelium consists of many layers of irregularly shaped cells of diverse sizes. A transitional epithelium is found lining the urinary bladder, urethra, and ureters. The function of a transitional epithelium is to allow the urinary organs to expand and stretch.

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Figure 4.7

These three diagrams show the three modes of secretion. All three diagrams show three orange cells in a line attached to a basement membrane. Each cell has a large nucleus in its lower half. The upper half of each cell contains a Golgi apparatus, which appears like an upside-down jellyfish. Yellow secretory vesicles are budding from the top end of the Golgi apparatus. Each vesicle contains several orange circles, which are the secreted substance. In merocrine secretion, the secretory vesicles travel to the top edge of the cell and release the secretion from the cell by melding with the cell membrane. In apocrine secretion, the top third of the cell, which contains the secretory vesicles, pinches in at the sides and then completely disconnects above the Golgi complex. The pinched-off portion of the cell is the secretion, as it contains the majority of the secretory vesicles. In holocrine secretion, the upper third of the cell, just above the Golgi complex, forms many finger-like projections. Each projection contains several vesicles. The tips of the projections that contain secretory vesicles bud off from the cell. In this method of secretion, the mature cell eventually dies and becomes the secretory product.

Figure 4.9

The left image shows a diagram of connective tissue. As a whole, the connective tissue appears somewhat disorganized, with fibres and cells mixed together heterogeneously. There are many open spaces between the embedded elements, suggesting that the connective tissue is somewhat loosely packed. The thickest fibres are collagen fibres; the thinner fibres are elastic fibres. Both the collagen fibres and the elastic fibres crisscross randomly throughout the tissue. In addition, a net of reticular fibres appears in the upper part of the diagram. Two yellow and oval-shaped adipocytes are embedded below the reticular fibre net, with a small dark nucleus squeezed into one corner of the cell. A mesenchymal cell is next to one of the adipocytes. The cell is rectangular and has four projections stemming from each corner of the cell. The projections appear to attach to the nearby collagen fibres. A fibroblast is located at the centre of the diagram. The fibroblast appears similar to the mesenchymal cell, except that it is larger and has more projections. Finally, a macrophage is in the lower right of the diagram. The macrophage is a white, oval-shaped disc with a prominent nucleus. The right diagram is a micrograph of connective tissue. The tissue is mostly stained pink; however, the thick collagen fibres crisscrossing the tissue are white. Five adipocytes also appear white, except for their cell membrane and nucleus, which stained dark. A mesenchymal cell occupies the space between two adipocytes. It stains a very deep purple, but its shape is unclear in the micrograph. A fibrocyte is also visible as an oval-shaped cell with a deep-purple nucleus.

Figure 4.12

Part A shows a diagram of regular dense connective tissue alongside a micrograph. The tissue is composed of parallel, threadlike collagen fibres running vertically through the diagram. Between the vertical fibres, several dark, oval-shaped fibroblast nuclei are visible. In the micrograph, the whitish collagen strands run horizontally. Several dark-purple fibroblast nuclei are embedded in the lightly stained matrix. Part B shows a diagram of irregular dense connective tissue on the left and a micrograph on the right. In the diagram, the collagen fibres are arranged in bundles that curve and loop throughout the tissue. The fibres within a bundle run parallel to each other, but separate bundles crisscross throughout the tissue. Because of this, the irregular dense connective tissue appears less organized than the regular dense connective tissue. This is also evident in the micrograph, where the white collagen bundles radiate throughout the micrograph in all directions. The fibroblasts are visible as red-stained cells with dark-purple nuclei.

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Figure 4.13

The first row of this diagram is a drawing and a micrograph of hyaline cartilage. The cartilage contains chondrocytes encapsulated in lacunae. Several of the lacunae are joined into groups or small stacks and embedded in the surrounding matrix. The micrograph shows the lacunae as white rings surrounding the purple-stained chondrocytes. Some occur as joined pairs, while others are embedded singly within the pink-stained matrix. The middle row shows a diagram and a micrograph of fibrocartilage that contains many fine collagen fibres embedded in the matrix. The collagen fibres are roughly parallel to each other but run through the matrix in a wavy fashion. There are also four round chondrocyte cells embedded within the matrix. In the micrograph, the matrix is shaded red and the collagen fibres are visible in white. The lacunae are clearly visible as a faint purple ring containing several dark-purple chondrocytes. The bottom row shows a diagram and micrograph of elastic cartilage. In the diagram, fine elastic fibres are seen crisscrossing the matrix. Many of the elastic fibres branch off from each other, unlike the collagen fibres depicted in the previous two rows. The lacunae are clearly visible as white rings containing stained chondrocytes. The fibres stain deeply in this micrograph and can be seen crisscrossing through the tissue.

Figure 4.15

This figure shows three micrographs, each depicting one of the three muscle tissues. Picture A shows skeletal muscle tissue, which is dense strips of pink tissue. Many small nuclei are dispersed throughout the tissue. The nuclei are flat and elongated, with multiple nuclei clustered into each cell. Picture B shows smooth muscle, which is densely packed and looks similar to skeletal muscle except that each cell only has one oval-shaped nucleus. Picture C shows cardiac muscle. Unlike skeletal and smooth muscle cells, cardiac muscle cells are not densely packed. The cardiac cells are branched, creating a large amount of space between each muscle cell.

Figure 4.16

This figure shows a diagram of a neuron and a micrograph showing two neuron cells. The body of the neuron contains a single purple nucleus. The cell is irregularly shaped, having many projections emerging from its surface. Six sets of dendrites project from the top, right, and bottom edges of the cell. The dendrites are yellow and branch many times after leaving the cell, taking on the appearance of tiny trees. The axon projects from the left edge of the cell. The axon is a long cable-like structure that branches into several finger-like projections at its end. This is where the neuron makes contact with other cells. The area where the axon emerges from the cell body contains microfibrils and microtubules. The micrograph is considerably less magnified than the diagram. The neurons stain darkly, and their nuclei are clearly visible. Their irregular cell body is also visible, along with the beginning of the axons.

Figure 4.17

The left side of this diagram shows various types of nerve cells. The largest cell is a neuron. The central body of the neuron contains a single nucleus. Six sets of dendrites project from the top, left, and right edges of the neuron. The dendrites are yellow and branch many times after leaving the cell, taking on the appearance of tiny trees. The axon projects from the bottom edge of the cell and is covered with purple sheaths labelled as the myelin sheath. The sheath is not continuous but instead is a series of equally spaced segments along the axon. Another cell, called an oligodendrocyte, is spiderlike in appearance, with its leglike projections each connecting to a segment of the neuron's myelin sheath. Above the

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neuron are three astrocytes. They are much smaller than the neuron, have no axons, and are also irregularly shaped cells with many dendrites projecting from the central body. Finally, a microglial cell is shown above the neuron. It is the smallest of the cells in this figure and is an elongated cell with many fine, tentacle-like projections. The projections are concentrated at the two ends of the cell, with the middle area lacking any projections. The right side of the micrograph of the neural tissue shows that this tissue is very heterogeneous, with both large and small cells embedded in the matrix. Much of the space between the cells is occupied by threadlike nerve fibres.

Figure 5.1

This illustration shows a cross-section of skin tissue. The outermost layer is called the epidermis and occupies one-fifth of the cross-section. Several hairs are emerging from the surface. The epidermis dives around one of the hairs, forming a follicle. The middle layer is called the dermis, which occupies four-fifths of the cross-section. The dermis contains an arrector pili muscle connected to one of the follicles. The dermis also contains an eccrine sweat gland, composed of a bunch of tubules. One tubule travels up from the bunch, through the epidermis, opening onto the surface of a pore. There are two string-like nerves travelling vertically through the dermis. The right nerve is attached to a Pacinian corpuscle, which is a yellow structure consisting of concentric ovals similar to an onion. The lowest level of the skin, the hypodermis, contains fatty tissue, arteries, and veins. Blood vessels travel from the hypodermis and connect to hair follicles and the arrector pili muscle in the dermis.

Figure 5.2

Part A is a micrograph showing a cross-section of thin skin. The topmost layer is a thin, translucent layer with irregular texture and areas where cells are sloughing off. The deepest layer is dark purple and extends into the third layer with finger-like projections. The third light purple layer contains thin bands of fibres and small, dark cells. The fourth and deepest layer is darker than the third layer but is still light purple. It contains thick fibre bands that are loosely packed. Part B is a magnified view of the epidermis of thick skin. It shows the topmost layer is five times thicker than the topmost layer of thin skin. The topmost layer of thick skin is also denser and less translucent than the topmost layer of thin skin.

Figure 5.4

This illustration shows a cross-section of the epidermis. The cells of the innermost layer, the stratum basale, are large and have a purple nucleus. The stratum basale curls around the dermis, which projects into the epidermis. The stratum basale transitions from the dermis and contains four layers of large, triangle-shaped keratinocytes. Fibres are visible within the spaces between keratinocytes in the stratum basale. A melanocyte is also present in this layer. The melanocyte possesses finger-like projections extending from its main cell body. The projections branch through the extracellular spaces between nearby keratinocytes. Above the stratum basale is the stratum spinosum, which consists of 8 to 10 layers of oval-shaped keratinocytes. The nucleus is present in these keratinocytes but has faded to a lighter purple. The stratum granulosum contains 3 to 5 layers of keratinocytes, each containing granules marked as red dots in its cytoplasm, labelled the lamellar granules. The stratum lucidum contains 4 layers of diamond-shaped cells with no nucleus, found only in the epithelium of thick skin. The stratum corneum contains 15 to 30 layers of keratinocytes with no nucleus or cytoplasm. A few of the cells in the topmost layer of the stratum corneum are flaking off from the skin.

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Figure 5.5

This figure is an electron micrograph of skin tissue showing the layered structure of the epidermis above the dermis. The outermost layer is the stratum corneum, appearing as a dark, dense surface layer. Beneath it is the stratum granulosum, followed by the thicker stratum spinosum and the deepest epidermal layer, the stratum basale or germinativum, where new epidermal cells form. Below the epidermis lies the dermis, containing connective tissue and small blood vessels, including a labelled capillary. In the middle-right region of the image are remnants of a cross-sectioned shed hair and its follicle within the dermal tissue.

Figure 5.7

This figure consists of two diagrams side by side. The right diagram shows the development of light-coloured skin; the left shows the development of dark-coloured skin. In both, a brown melanocyte sits at the border between the dermis and epidermis. The melanocyte has a large nucleus and six finger-like extensions. These reach between cells of the stratum basalis. Sections of the extensions detach and travel through the skin. These are melanosomes. In the left diagram, both the melanocyte and melanosomes contain melanin particles, shown as dark dots. Melanosomes travel upward to outer skin layers, releasing melanin. As a result, keratinocytes in the left diagram contain several melanin particles that darken skin colour. In light-coloured skin, the melanocyte contains no melanin. It still releases melanosomes into upper layers of the skin; however, these melanosomes contain no melanin. Therefore, the skin does not darken and remains light.

Figure 5.8

This diagram shows a cross-section of the skin containing a hair follicle. The follicle is teardrop-shaped. Its enlarged base, labelled the hair bulb, is embedded in the hypodermis. The outermost layer of the follicle is the epidermis, which invaginates from the skin surface to envelope the follicle. Within the epidermis is the outer root sheath, which is only present on the hair bulb. It does not extend up the shaft of the hair. Within the outer root sheath is the inner root sheath. The inner root sheath extends about half of the way up the hair shaft, ending midway through the dermis. The hair matrix is the innermost layer. The hair matrix surrounds the bottom of the hair shaft, where it is embedded within the hair bulb. The hair shaft itself contains three layers: the outermost cuticle, a middle layer called the cortex, and an innermost layer called the medulla.

Figure 5.10

These two images show the anatomy of the fingernail region. The left image shows a dorsal view of a finger. The proximal nail fold is the part underneath where the skin of the finger connects with the edge of the nail. The eponychium is a thin, pink layer between the white proximal edge of the nail (the lunula) and the edge of the finger skin. The lunula appears as a crescent-shaped white area at the proximal edge of the pink-shaded nail. The lateral nail folds are where the sides of the nail contact the finger skin. The distal edge of the nail is white and is called the free edge. The nail grows distally out from the proximal nail fold. The right image shows a lateral view of the nail bed anatomy. In this view, one can see how the edge of the nail is located just proximal to the nail fold. This end of the nail, from which the nail grows, is called the nail root.

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Figure 5.13

Part A is a photo of a man skiing with several snow-covered trees in the background. Part B is a diagram with a right and left half. The left half is titled "Heat is retained by your body," while the right half is titled "Heat through radiation and convection." Both show blood flowing from an artery through three capillary beds within the skin. The capillary beds are arranged vertically, with the topmost bed located along the boundary of the dermis and epidermis. The bottommost bed is located deep in the hypodermis. The middle bed is evenly spaced between the topmost and bottommost beds. In each capillary bed, oxygenated blood (red) enters the bed on the left and deoxygenated blood (blue) leaves the bed on the right. The left diagram shows a picture of snowflakes above the capillary beds, indicating that the weather is cold. Blood is only flowing through the deepest of the three capillary beds, as the upper beds are closed off to reduce heat loss from the outer layers of the skin. The right diagram shows a picture of the sun above the capillary beds, indicating that the weather is hot. Blood is flowing through all three capillary beds, allowing heat to radiate out of the blood, increasing heat loss, as demonstrated in part C with a photo of a man running through a forested trail on a summer day.

Figure 6.3

This illustration depicts an anterior view of the right femur, or thigh bone. The inferior end that connects to the knee is at the bottom of the diagram, and the superior end that connects to the hip is at the top of the diagram. The bottom end of the bone contains a smaller lateral bulge and a larger medial bulge. A blue articular cartilage covers the inner half of each bulge as well as the small trench that runs between the bulges. This area of the inferior end of the bone is labelled the distal epiphysis. Above the distal epiphysis is the metaphysis, where the bone tapers from the wide epiphysis into the relatively thin shaft. The entire length of the shaft is the diaphysis. The superior half of the femur is cut away to show its internal contents. The bone is covered with an outer translucent sheet called the periosteum. At the midpoint of the diaphysis, a nutrient artery travels through the periosteum and into the inner layers of the bone. The periosteum surrounds a white cylinder of solid bone labelled compact bone. The cavity at the centre of the compact bone is called the medullary cavity. The inner layer of the compact bone that lines the medullary cavity is called the endosteum. Within the diaphysis, the medullary cavity contains a cylinder of yellow bone marrow that is penetrated by the nutrient artery. The superior end of the femur is also connected to the diaphysis by a metaphysis. In this upper metaphysis, the bone gradually widens between the diaphysis and the proximal epiphysis. The proximal epiphysis of the femur is roughly hexagonal in shape. However, the upper right side of the hexagon has a large, protruding knob. The femur connects and rotates within the hip socket at this knob. The knob is covered with a blue-coloured articular cartilage. The internal anatomy of the upper metaphysis and proximal epiphysis is revealed. The medullary cavity in these regions is filled with the meshlike spongy bone. Red bone marrow occupies the many cavities within the spongy bone. There is a clear, white line separating the spongy bone of the upper metaphysis from that of the proximal epiphysis. This line is the epiphyseal line.

Figure 6.4

The top of this illustration shows an anterior view of the proximal end of the femur. The top image has two zoomed-in boxes. The left box is situated on the border between the diaphysis and the metaphysis. Its callout magnifies the periosteum on the right side of the femur. The view shows that the periosteum contains an outer fibrous layer composed of yellow fibres. The inner layer of the periosteum is called the cellular layer, which is composed of irregularly shaped cells. The cellular layer gradually shrinks in width as it transitions from the metaphysis

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to the diaphysis. A small blood vessel runs through both layers and enters the bone. The right zoomed-in box magnifies the endosteum on the left side of the bone. The box is situated just inferior to the border between the diaphysis and the metaphysic. It calls out the inner edge of the compact bone layer. The magnified view shows concentric circles of dark-coloured bone matrix. Between the circles are small cavities containing orange, diamond-shaped cells labelled osteocytes. The left edge of the bone matrix is lined with a single layer of flattened cells called the endosteum. There is a large cell, labelled an osteoclast, between two of the endosteum cells. The osteoclast is cutting a depression into the bony matrix under the endosteum. At another part of the endosteum, three smaller osteoblasts are secreting a blue substance that builds up the outermost layer of the bony matrix.

Figure 6.6

This illustration contains three diagrams. The left diagram is titled "Examples of processes formed where tendons or ligaments attach." The image shows an anterior view of the femur and an anterior view of the humerus. For the femur, the distal epiphysis contains a smaller lateral bulge and a larger medial bulge. These are examples of condyles. The inner halves of the two condyles and the groove between them compose a facet. An oval-shaped ridge on the medial surface of the distal metaphysis is an example of a tubercle. On the proximal epiphysis of the femur, the large knob that attaches to the hip socket is an example of a head. The tip of the head contains a small depression that is an example of a fovea called the fovea capitis. On the humerus, the distal epiphysis contains a central depression that is an example of a fossa. Two condyles are located on the right and left sides of the fossa. The diaphysis of the humerus contains a small ridge running up the shaft that is an example of a tuberosity. The proximal epiphysis of the humerus contains a lateral and a medial bulge that are both examples of tubercles. Finally, a narrow groove runs from the centre of the proximal metaphysis to in between the medial and lateral condyles. This is an example of a sulcus. The right image is entitled "Examples of an elevation or depression." It shows an anterior view of the hip bones. The hip bones are shaped like two wings that join at the bottom. The crest along the upper edge of each hip bone, at the tip of each "wing," is an example of an elevation. A depression on the inner surface of both hip bones just under the crest is called a fossa. The lower right image is entitled "Examples of openings" and shows an anterior view of the skull. The bone underlying the chin is an example of a protuberance, while two small holes above each eye socket are examples of foramina. Five green sinuses surround the nose cavity. These are sinuses because they are hollowed-out cavities within the skull bones. A small channel leads into the corner of each eye, where the tear ducts occur. These two channels are both examples of a canal. Finally, the bones that form the posterior wall of the eye socket have a small crack running diagonally away from the nose. These are examples of fissures.

Figure 6.7

The top of this diagram shows the cross-section of a generic bone with three marked areas: the periosteum, the middle of the compact bone layer, and the inner edge of the compact bone where it transitions into the spongy bone. The periosteum points to two zoomed-in images. In one image, four osteoblast cells are sitting end to end on the periosteum. The osteoblasts are roughly square-shaped, except for one of the cells that is developing small, finger-like projections. Osteoblasts form the matrix of the bone. The other image called out from the periosteum shows a large, amorphous osteogenic cell sitting on the periosteum. The osteogenic cell is surrounded on both sides by a row of much smaller osteoblasts. The cell is shaped like a mushroom cap and also has finger-like projections. The cell is a stem

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cell that develops into other bone cells. The middle of the compact bone layer points to an osteocyte. The osteocyte is a thin cell and roughly diamond-shaped, with many branching, finger-like projections. Osteocytes maintain bone tissue. The inner edge of the compact bone points to an osteoclast. The osteoclast is a large, round cell with multiple nuclei. It also has rows of fine finger-like projections on its lower surface, where it is sitting on the compact bone. Osteoclasts reabsorb bone.

Figure 6.8

A generic long bone is shown at the top of this illustration. The bone is split in half lengthwise to show its internal anatomy. The outer gray covering of the bone is the periosteum. Within the periosteum is a thin layer of compact bone. The compact bone surrounds a central cavity called the medullary cavity. The medullary cavity is filled with spongy bone at the two epiphyses. A callout box shows that the main image is zooming in on the compact bone on the left side of the bone. In the main image, the periosteum is being peeled back to show its two layers. The outer layer of the periosteum is the outer fibrous layer. This layer has a periosteal artery and a periosteal vein running along its outside edge. The inner layer of the periosteum is the inner osteogenic layer. The compact bone lies to the right of the periosteum and occupies the majority of the main image. Two flat layers of compact bone line the inner surface of the osteogenic periosteum. These sheets of compact bone are called the circumferential lamellae. The majority of the compact bone has lamellae running perpendicular to that of the circumferential lamellae. These concentric lamellae are arranged in a series of concentric tubes. There are small cavities between the layers of concentric lamellae called lacunae. The centremost concentric lamella surrounds a hollow central canal. A blue vein, a red artery, a yellow nerve, and a green lymph vessel run vertically through the central canal. A set of concentric lamellae, its associated lacunae, and the vessels and nerves of the central canal are collectively called an osteon. The front edge of the diagram shows a longitudinal cross-section of one of the osteons. The vessels and nerves are visible running through the centre of the osteon throughout its length. In addition, blood vessels can run from the periosteum through the sides of the osteons and connect with the vessels of the central canal. The blood vessels travel through the sides of the osteons via a perforating canal. The open areas between neighbouring osteons are also filled with compact bone. This “filler” bone is referred to as the interstitial lamellae. At the far right of the compact bone, the edge of the spongy bone is visible. The spongy bone is a series of crisscrossing bony arches called trabeculae. There are many open spaces between the trabeculae, giving the spongy bone its spongelike appearance.

Figure 6.9

This illustration shows the spongy bone within the proximal epiphysis of the femur in two successively magnified images. The lower-magnification image shows two layers of crisscrossing trabeculae. The surface of each is dotted with small black holes, which are the openings of the canaliculi. One of the trabeculae is in a cross-section to show its internal layers. The outermost covering of the lamellae is called the endosteum. This endosteum surrounds several layers of concentric lamellae. The higher-magnification image shows the cross-section of the trabeculae more clearly. Three concentric lamellae are shown in this view, each possessing perpendicular black lines. These lines are the canaliculi and are oriented on the round lamellae, similar to the spokes of a wheel. In between the lamellae are small cavities called lacunae, which house cells called osteocytes. In addition, two large osteoclasts are seated on the outer edge of the outermost lamellae. The outermost lamellae are also surrounded by groups of small, white osteoblasts.

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Figure 6.10

This illustration shows an anterior view of the right femur. The femur is split in half lengthwise to show its internal anatomy. The outer covering of the femur is the periosteum. Within it is a thin layer of compact bone that surrounds a central cavity called the medullary or marrow cavity. This cavity is filled with spongy bone at both epiphyses. A nutrient artery and vein travel through the periosteum and compact bone at the centre of the diaphysis. After entering the bone, the nutrient arteries and veins spread throughout the marrow cavity in both directions. Some of the arteries and veins in the marrow cavity also spread into the spongy bone within the distal and proximal epiphyses. However, additional blood vessels called the metaphyseal arteries and the metaphyseal veins enter into the metaphysis from outside of the bone.

Figure 6.11

Image A shows seven osteoblasts, which are cells with small, finger-like projections. They are surrounded by granules of osteoid. Both the cells and the osteoid are contained within a blue, circular, ossification centre that is surrounded by a "socket" of dark, string-like collagen fibres and gray mesenchymal cells. The cells are generally amorphous, similar in appearance to an amoeba. In image B, the ossification centre is no longer surrounded by a ring of osteoblasts. The osteoblasts have secreted bone into the ossification centre, creating a new bone matrix. There are also five osteocytes embedded in the new bone matrix. The osteocytes are thin, oval-shaped cells with many finger-like projections. Osteoid particles are still embedded in the bony matrix in image B. In image C, the ring of osteoblasts surrounding the ossification centre has separated, forming an upper and lower layer of osteoblasts sandwiched between the two layers of mesenchyme cells. The mesenchyme cells and the surrounding collagen fibres form the periosteum. The osteoblasts secrete spongy bone into the space between the two osteoblast rows. Therefore, the accumulating spongy bone pushes the upper and lower rows of osteoblasts away from each other. In this image, most of the spongy bone has been secreted by the osteoblasts, as the trabeculae are visible. In addition, an artery has already broken through the periosteum and invaded the spongy bone. Image D looks similar to image C, except that the rows of osteoblasts are now secreting layers of compact bone between the spongy bone and the periosteum. The artery has now branched and spread throughout the spongy bone. The cavities between the trabeculae now contain red bone marrow.

Figure 6.12

Image A shows a small piece of hyaline cartilage that looks like a bone but without the characteristic enlarged ends. The hyaline cartilage is surrounded by a thin perichondrium. In image B, the hyaline cartilage has increased in size, and the ends have begun to bulge outward. A group of dark granules forms at the centre of the cartilage. This is the calcified matrix, as opposed to the rest of the cartilage, which is uncalcified matrix. In image C, the hyaline cartilage has again increased in size, and spongy bone has formed at the calcified matrix. This is now called the primary ossification centre. A nutrient artery has invaded the ossification centre and is growing through the cavities of the new spongy bone. In image D, the cartilage now looks like a bone, as it has greatly increased in size and each end has two bulges. Only the proximal half of the bone is shown in all the remaining images. Spongy bone has completely developed in the medullary cavity, which is surrounded, on both sides, by compact bone. Now, the calcified matrix is located at the border between the proximal metaphysis and the proximal epiphysis. The epiphysis is still composed of uncalcified matrix. In image E, arteries and veins have now invaded the epiphysis, forming a calcified matrix at its centre. This is called a secondary ossification centre. In image F, the interior of the epiphysis

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is now completely calcified into bone. The outer edge of the epiphysis remains as cartilage, forming the articular cartilage at the joint. In addition, the border between the epiphysis and the metaphysis remains uncalcified, forming the epiphyseal plate.

Figure 6.13

This illustration shows a left-to-right progression of bone repair. The break is shown in the leftmost image, where the femur has an oblique, closed fracture in the middle of its shaft. The next image magnifies the break, showing that blood has filled the area between the broken bones. Blood has also filled in around the lateral and medial sides of the break. The influx of blood causes the broken area to swell, creating a hematoma. In the next image, the hematoma has been replaced with an external callus between the two broken ends. Within the internal callus, the blood vessels have reconnected, and some spongy bone has regenerated in the gap between the two bone halves. In the next image, spongy bone has completely regenerated, connecting the two broken ends, referred to as the bony callus. The external callus still remains on the lateral and medial sides of the break, as the compact bone has not yet regenerated. In the next image, the compact bone has fully regenerated, encapsulating the bony callus and completely reconnecting the two bone halves. The bone has a slight bulge at the location of the healed fracture, which is clearly shown in the final image, which shows a zoomed-out image of the completely healed femur.

Figure 6.14

This illustration resembles a flowchart. It begins with the sun shining on a silhouette of a man. One arrow leads from the sun to the man's skin, stating that vitamin D is synthesized in the skin after the absorption of sunlight. Another arrow points into the man's mouth and states that vitamin D is ingested through food and supplements, absorbed by the intestines, and carried to the liver via the bloodstream. A callout on the liver states that in the liver, vitamin D turns into 25 (OH) D, also known as calcidiol, the primary form of circulating vitamin D. Another callout on the right kidney states that in the kidneys, vitamin D is transformed into 1,25 (OH) D2. This is also known as calcitriol, a biologically active form of vitamin D. The synthesis of vitamin D facilitates calcium absorption from the small intestine, calcium reabsorption from the kidneys, and the rebuilding of bone tissue.

Figure 7.1

The figure shows the anterior (front) and posterior (back) views of the human skeleton. The axial skeleton is beige; the appendicular skeleton is green. The bones are grouped into major regions of the body as follows: The skull is the cranial portion and facial portion; the pectoral (shoulder) girdle is the clavicle and scapula; the thoracic cage is the sternum and ribs; the spine/core is the vertebral column and pelvic girdle (hip bones); the upper limbs are the humerus, ulna, radius, carpals, metacarpals, and phalanges; and the lower limbs are the femur, patella, tibia, fibula, tarsals, metatarsals, and phalanges.

Figure 7.3

The figure shows the anterior (front) view of the skull with labelled bones and openings. The bones and features are grouped as follows: The cranial bones are the frontal bone, parietal bone, sphenoid bone, temporal bone, and ethmoid bone; the sutures and landmarks are the coronal suture and glabella; the orbital region is the orbit, optic canal, superior orbital fissure, inferior orbital fissure, supraorbital foramen, supraorbital margin, and lacrimal bone; the nasal region is the nasal bone, palatine bone, perpendicular plate of ethmoid bone, vomer bone, middle

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nasal concha, and inferior nasal concha; and the facial bones are the zygomatic bone, maxilla, alveolar process of maxilla, mental foramen, alveolar process of mandible, and mandible.

Figure 7.4

The figure shows the right lateral (side) view of the skull with labelled bones, sutures, and landmarks. The bones and features are grouped as follows: The cranial bones are the frontal bone, parietal bone, temporal bone, occipital bone, sphenoid bone (greater wing), and ethmoid bone; the sutures are the coronal suture, squamous suture, and lambdoid suture; the temporal bone features are the squamous temporal, zygomatic process, external acoustic meatus, mastoid portion, styloid process, mastoid process, articular tubercle, and mandibular fossa; the facial bones and features are the lacrimal bone, lacrimal fossa, nasal bone, zygomatic bone, temporal process, maxilla, mandible, and mental protuberance of the mandible; and additional landmarks are the zygomatic arch and pterion.

Figure 7.7

The figure shows the inferior (bottom-up) and superior (top-down) views of the base of the skull, with inset diagrams of a skull indicating the viewing angles. The upper panel is the inferior view and labels the following bones and structures: maxilla (palatine process), zygomatic bone, palatine bone (horizontal plate), vomer, medial and lateral pterygoid plates, zygomatic arch, sphenoid bone, articular tubercle, mandibular fossa, external auditory meatus, mastoid process, styloid process, stylomastoid foramen, entrance to carotid canal, foramen ovale, foramen spinosum, foramen lacerum, jugular foramen, temporal bone, occipital condyle, foramen magnum, occipital bone, superior nuchal line, and external occipital protuberance. The lower panel is the superior view and labels the following bones and structures: frontal bone, ethmoid bone (crista galli and cribriform plate), sphenoid bone (lesser wing and hypophyseal fossa—sella turcica), superior orbital fissure, foramen rotundum, foramen ovale, foramen spinosum, foramen lacerum and exit of carotid canal, internal acoustic meatus, jugular foramen, hypoglossal canal, temporal bone (petrous portion / petrous ridge), occipital bone, foramen magnum, and parietal bone.

Figure 7.9

The figure shows the superior (top-down) and posterior (back) views of the sphenoid bone with an inset image of a skull highlighting the sphenoid bone in yellow to indicate its location. The upper panel is the superior view and labels the following bones and structures: greater wing, lesser wing, body of sphenoid, hypophyseal fossa of sella turcica, optic canal, superior orbital fissure, foramen rotundum, foramen ovale, and foramen spinosum. The lower panel is the posterior view and labels the following bones and structures: greater wing, lesser wing, body of sphenoid, superior orbital fissure, and pterygoid plates.

Figure 7.10

The figure shows a midsagittal section of the skull with labelled bones and structures. The following bones and features are indicated: parietal bone, temporal bone, internal acoustic meatus, hypoglossal canal, occipital bone, styloid process, medial and lateral pterygoid plates, mandibular foramen, lingula, mylohyoid line, mandible, hyoid bone, palatine bone, maxilla, vomer, inferior nasal concha, sphenoid bone, sphenoid sinus, nasal bone, perpendicular plate, cribriform plate, crista galli, frontal sinus, and sella turcica (hypophyseal fossa).

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Figure 7.20

The figure shows the superior view of a single vertebra and the left posterolateral view of articulated vertebrae with labelled features. The superior view labels the following structures: spinal cord, vertebral foramen, facet of superior articular process, facet for head of rib, spinous process, transverse process, vertebral arch (lamina and pedicle), and body. The left posterolateral view labels the following structures: spinal cord, facet of superior articular process, facet for head of rib, inferior articular process, spinous process, transverse process, intervertebral disc, body, vertebral arch (lamina and pedicle), and spinal nerve exiting through intervertebral foramen.

Figure 7.22

The figure shows multiple views of the cervical vertebrae with an inset image highlighting the cervical region of the spine in green. The upper left panel shows the structure of a typical cervical vertebra, labelling the spinous process (bifid), vertebral foramen, lamina, pedicle, superior articular process, transverse process, transverse foramen, body, and groove for spinal nerve. The upper right panel shows a lateral view of the cervical spine, labelling the dens of axis, transverse ligament, C1 (atlas), C2 (axis), C3, C7 (vertebra prominens), inferior articular process, bifid spinous process, and transverse process. The lower left panel shows a superior view of the atlas, labelling the dens, superior articular facet, transverse foramen, transverse process, ligament, anterior arch, and posterior arch. The lower middle panel shows a superior view of the axis, labelling the dens, superior articular facet, transverse foramen, transverse process, lamina, and spinous process. The lower right panel shows an anterior view of the axis, labelling the dens, transverse process, inferior articular process, and body.

Figure 7.27

The figure shows the anterior views of the sternum and the skeleton of the thorax. The left panel shows the sternum with the following structures labelled: clavicular notch, jugular notch, manubrium, sternal angle, body, and xiphoid process. The right panel shows the anterior skeleton of the thorax with the following structures labelled: clavicular notch, clavicle, scapula, jugular notch, sternum (manubrium, body, and xiphoid process), sternal angle, costal cartilages, intercostal space, and thoracic vertebrae T11 and T12, with ribs numbered, from top to bottom, 1 to 12.

Figure 8.1

The figure shows the anterior (front) and posterior (back) views of the human skeleton. The axial skeleton is beige; the appendicular skeleton is green. The bones are grouped into major regions of the body as follows: The skull is the cranial portion and facial portion; the pectoral (shoulder) girdle is the clavicle and scapula; the thoracic cage is the sternum and ribs; the spine/core is the vertebral column and pelvic girdle (hip bones); the upper limbs are the humerus, ulna, radius, carpals, metacarpals, and phalanges; and the lower limbs are the femur, patella, tibia, fibula, tarsals, metatarsals, and phalanges.

Figure 8.2

The figure shows multiple views of the pectoral girdle and clavicle. The top left panel shows an anterior view of the pectoral girdle, labelling the coracoclavicular ligament, acromioclavicular joint, glenohumeral joint, scapula, clavicle, and costoclavicular ligament. The top right panel shows a posterior view of the pectoral girdle, labelling the clavicle, scapula, ribs, and vertebrae. The bottom panels show the clavicle, with the superior view labelling the acromial end

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(lateral) and sternal end (medial) and the inferior view showing the same ends with anterior and posterior orientation indicated.

Figure 8.3

The figure shows the anterior and posterior aspects of the right scapula with an inset image indicating its location in the pectoral girdle. The anterior aspect labels the following structures: acromion, coracoid process, glenoid cavity, suprascapular notch, superior border, superior angle, lateral border, medial border, and inferior angle. The posterior aspect labels the following structures: acromion, coracoid process, glenoid cavity, suprascapular notch, spine, supraspinous fossa, infraspinous fossa, subscapular fossa, lateral border, medial border, and inferior angle.

Figure 8.4

The figure shows the anterior and posterior views of the right humerus with an inset image indicating its location in the skeleton. The anterior view labels the following structures: humerus, head, anatomical neck, surgical neck, greater tubercle, lesser tubercle, intertubercular groove (sulcus), deltoid tuberosity, body (shaft), lateral supracondylar ridge, radial fossa, capitulum, head of radius, medial epicondyle, trochlea, and coronoid process of ulna. The posterior view labels the following structures: greater tubercle, anatomical neck, deltoid tuberosity, body (shaft), lateral epicondyle, olecranon fossa, coronoid fossa, medial epicondyle, olecranon of ulna, and head of radius.

Figure 8.5

The figure shows the anterior and posterior views of the right forearm with an inset image indicating its location in the skeleton. The anterior view labels the following structures: radius, ulna, radial notch of the ulna, head of radius, neck of radius, radial tuberosity, olecranon process, trochlear notch, coronoid process, proximal radioulnar joint, interosseous membrane, ulnar notch of the radius, distal radioulnar joint, head of ulna, styloid process of ulna, and styloid process of radius. The posterior view labels the following structures: radius, ulna, head of radius, neck of radius, and olecranon process.

Figure 8.6

The figure shows the anterior and posterior views of the left hand with an inset image indicating the location of carpals, metacarpals, and phalanges in the right hand. The anterior view labels the following structures: thumb (pollex), index finger, middle finger, ring finger, little finger, phalanges (distal and proximal), metacarpals (1 to 5), carpals (trapezium, trapezoid, scaphoid, hamate, capitate, pisiform, triquetrum, and lunate), radius, and ulna. The posterior view labels the following structures: phalanges (proximal, middle, and distal), metacarpals (1 to 5; with head, shaft, and base), carpals (trapezium, trapezoid, scaphoid, hamate, capitate, pisiform, triquetrum, and lunate), radius, and ulna.

Figure 8.9

The figure shows the lateral and medial views of the right hip bone with an inset image indicating the location of the pelvic girdle. The lateral view labels the following structures: ilium, iliac crest, posterior superior iliac spine, posterior inferior iliac spine, greater sciatic notch, ischial body, ischial spine, lesser sciatic notch, ischium, obturator foramen, ischial tuberosity, ischial ramus, ischiopubic ramus, anterior superior iliac spine, anterior inferior iliac spine, acetabulum, arcuate line, superior ramus of pubis, pubic tubercle, pubic body, and

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articular surface of pubis (at pubic symphysis). The medial view labels the following structures: ilium, iliac fossa, posterior superior iliac spine, posterior inferior iliac spine, auricular surface, greater sciatic notch, ischial spine, lesser sciatic notch, obturator foramen, ischium, ischial ramus, ischiopubic ramus, and pubis.

Figure 8.12

The figure shows the anterior and posterior views of the right femur with an inset image indicating its location in the skeleton. The anterior view labels the following structures: hip bone, femur, head, neck, greater trochanter, intertrochanteric line, lesser trochanter, body (shaft), lateral epicondyle, medial epicondyle, adductor tubercle, patella, tibia, and fibula. The posterior view labels the following structures: hip bone, femur, head, neck, greater trochanter, intertrochanteric crest, gluteal tuberosity, linea aspera, body (shaft), lateral epicondyle, medial epicondyle, intercondylar fossa, lateral condyle, tibia, and fibula.

Figure 8.13

The figure shows the anterior and posterior views of the right leg with an inset image indicating the location of the tibia and fibula. The anterior view labels the following structures: lateral condyle, medial condyle, tibial tuberosity, anterior border, interosseous membrane, tibia, fibula, medial malleolus, lateral malleolus, and articular surface. The posterior view labels the following structures: articular surface of medial condyle, articular surface of lateral condyle, head of fibula, soleal line, tibia, fibula, medial malleolus, and lateral malleolus.

Figure 8.14

The figure shows the superior, medial, and lateral views of the right foot with an inset image indicating the locations of tarsals, metatarsals, and phalanges. The superior view labels the following: distal phalanges, middle phalanges, proximal phalanges, metatarsals (1 to 5), medial cuneiform, intermediate cuneiform, lateral cuneiform, navicular, cuboid, talus, trochlea of talus, and calcaneus. The medial view labels the following: first metatarsal, medial cuneiform, intermediate cuneiform, navicular, talus, facet for medial malleolus, sustentaculum tali (talar shelf), calcaneus, and calcaneal tuberosity. The lateral view labels the following: fifth metatarsal, lateral cuneiform, intermediate cuneiform, navicular, cuboid, calcaneus, facet for lateral malleolus, and talus.

Figure 9.8

The figure shows a sagittal section of the knee joint highlighting key internal structures. The femur (upper bone) and tibia (lower bone) are shown with the patella (kneecap) anteriorly. The anterior cruciate ligament (ACL) and posterior cruciate ligament (PCL) cross within the joint, stabilizing it. The synovial cavity is visible between the articular surfaces. Surrounding structures include the tendon of quadriceps femoris, patellar ligament, and infrapatellar fat pad. Three bursae are labelled: suprapatellar bursa, prepatellar bursa, and infrapatellar bursa, which reduce friction during movement.

Figure 9.9

The figure shows the six major types of synovial joints, each paired with its location in the human skeleton. The pivot joint, shown between the C1 and C2 vertebrae, allows rotational movement around a single axis. The hinge joint, shown at the elbow, permits flexion and extension. The saddle joint, located between the trapezium carpal bone and the first metacarpal bone, enables biaxial movement, including opposition of the thumb. The plane joint, located

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between tarsal bones, allows gliding movements. The condyloid joint, shown between the radius and carpal bones of the wrist, allows movement but no rotation. The ball-and-socket joint, shown at the hip, allows movement in multiple planes, including rotation. Each joint type is illustrated with an inset diagram showing its articular surfaces and permitted motions with arrows.

Figure 9.10

This figure highlights angular and rotational movements across major body regions. Two side-view male figures demonstrate flexion (bending) and extension (straightening) at the shoulder and knee joints, with arrows indicating the direction of movement. A head in profile shows flexion (chin toward chest) and extension (head tilting back), while a male torso bends forward and backward to show flexion and extension of the vertebral column. A frontal view shows abduction (arms moving away from the midline), adduction (arms moving toward the midline), and circumduction (arms moving in a circular path). Rotation is shown with arrows around the head and leg, indicating the head turning left and right and medial (inward) and lateral (outward) rotation of the thigh using the foot as a reference point.

Figure 9.11

Illustration showing additional types of body movements with arrows indicating the direction of movement for each action. A pair of forearms demonstrates pronation (palm facing downward as the radius crosses over the ulna) and supination (palm facing upward with the radius and ulna parallel). Feet illustrate dorsiflexion (toes pointing upward) and plantar flexion (toes pointing downward) as well as inversion (sole turning medially) and eversion (sole turning laterally). A side view of a male head and shoulders demonstrates protraction (jutting the mandible forward) and retraction (pulling the mandible backward) as well as elevation (closing the jaw) and depression (opening the jaw). A hand demonstrates opposition, with the thumb touching the tip of another finger.

Figure 9.13

Detailed cross-sectional illustration of the shoulder joint showing the articulation between the head of the humerus and the glenoid cavity of the scapula. The articular cartilage covering the joint surfaces and the glenoid labrum deepening the cavity are highlighted. The articular capsule is labelled with its synovial and fibrous membranes. Surrounding structures include the clavicle, acromion of the scapula, acromioclavicular and coracoacromial ligaments, and the subacromial bursa. The tendon of the supraspinatus muscle passes superiorly over the joint, and the tendon of the long head of the biceps brachii runs through the joint space within a tendon sheath.

Figure 9.14

Labelled diagrams of the elbow joint showing three views. Panel A, a medial sagittal section through the right elbow in lateral view, labels the humerus, fat pad, tendon of triceps muscle, bursa, trochlea, articular cartilage of the trochlear notch, olecranon bursa, articular capsule, synovial membrane, synovial cavity, articular cartilage of trochlea, tendon of brachialis muscle, ulna, and coronoid process. Panel B, a lateral view of the right elbow joint, labels the humerus, lateral epicondyle, radius, annular ligament, radial collateral ligament, ulna, olecranon process, and articular capsule. Panel C, a medial view of the left elbow joint, labels the articular capsule, annular ligament, ulnar collateral ligament, radius, ulna, and coronoid process.

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Figure 9.15

Sagittal section and anterior views of the knee joint showing bones, ligaments, and cartilage that stabilize the joint; also, the superior view of the right tibia joint surface details the menisci and the cruciate ligaments. The sagittal view highlights the quadriceps tendon attaching to the patella, the patellar ligament connecting the patella to the tibial tuberosity, and the medial and lateral menisci between the femoral and tibial condyles. Collateral ligaments are labelled on both sides: the fibular (lateral) collateral ligament and the tibial (medial) collateral ligament. The superior view details with a light-gray colour the anterior cruciate ligament and posterior ligament and with a light-blue colour the articular cartilage on both medial and lateral condyles and medial and lateral menisci. The anterior view shows the muscles (quadriceps femoris), tendons (tendon of quadriceps femoris and lateral and medial patellar retinaculum), and ligaments (fibular and tibial collateral and patellar) that surround the knee joint.

Figure 10.1

This figure shows three micrographs, each depicting one of the three muscle tissues. Picture A shows skeletal muscle tissue, which is dense strips of pink tissue. Many small nuclei are dispersed throughout the tissue. The nuclei are flat and elongated, with multiple nuclei clustered into each cell. Picture B shows smooth muscle, which is densely packed and looks similar to skeletal muscle except that each cell only has one oval-shaped nucleus. Picture C shows cardiac muscle. Unlike skeletal and smooth muscle cells, cardiac muscle cells are not densely packed. The cardiac cells are branched, creating a large amount of space between each muscle cell.

Figure 10.2

Diagram showing the structural organization of skeletal muscle from the largest to the smallest components. The whole skeletal muscle is surrounded by the epimysium and is composed of multiple bundles called fascicles. Each fascicle is encased in perimysium and contains multiple muscle fibres (cells) surrounded by endomysium. A muscle fibre is a long cylindrical cell with a sarcolemma (cell membrane) and contains many myofibrils, which are the contractile elements. A satellite cell is shown on the periphery of the muscle fibre, associated with repair and growth. Arrows indicate the progressive magnification from the whole muscle to the myofibril level.

Figure 10.3

Diagram showing the microscopic anatomy of a skeletal muscle fibre and its myofibrils. The top portion depicts a cylindrical muscle fibre with multiple nuclei at the periphery, a sarcolemma (cell membrane), mitochondria, and parallel myofibrils. Light I bands and dark A bands are visible, giving the fibre a striated appearance. The bottom portion magnifies a single myofibril, showing repeating sarcomeres as the functional contractile units. Each sarcomere is bounded by Z discs and contains thin actin filaments and thick myosin filaments. The I band corresponds to regions with only thin filaments, the A band spans the length of the thick filaments, the H zone is the central region with only thick filaments, and the M line runs down the centre. The sarcoplasmic reticulum is shown surrounding the myofibril, storing and releasing calcium for contraction.

Figure 10.4

Detailed diagram of a sarcomere, the contractile unit of a muscle fibre, showing its structural components and molecular arrangement. The central image displays a sarcomere bounded by Z lines, with thin actin filaments extending from the Z lines and thick myosin filaments

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positioned centrally. The lighter I bands flank the sarcomere edges, while the darker A band spans the length of the thick filaments. The H zone, in the centre, contains only thick filaments, with the M line running through the middle anchoring them. Insets highlight molecular details: On the left, a portion of a thick filament is shown with projecting myosin heads; below it, a myosin molecule is illustrated with its twisted tail, flexible hinge region, heads, ATP-binding sites, and actin-binding sites. On the right, a portion of a thin filament is shown, made of actin subunits with binding sites for myosin, tropomyosin strands covering these sites, and troponin complexes positioned along the filament.

Figure 10.5

Diagram of a neuromuscular junction showing how a motor neuron stimulates a muscle fibre. At the top, a motor neuron with a myelin sheath surrounding the axon branches into axon terminals that form synaptic end bulbs at the neuromuscular junction on a skeletal muscle fibre. The muscle fibre is labelled with sarcolemma, sarcoplasm, and myofibrils. A zoomed view shows the synaptic end bulb above the muscle cell membrane, with synaptic vesicles containing acetylcholine. A nerve impulse or action potential reaches the synaptic end bulb, causing vesicles to release acetylcholine by exocytosis into the synaptic cleft. In the lower magnified view, acetylcholine diffuses across the synaptic cleft and binds to acetylcholine receptors on the motor end-plate of the sarcolemma. Binding opens ion channels, allowing sodium ions to enter the muscle cell, initiating muscle fibre activation.

Figure 10.7

Diagram illustrating the sequence of events in excitation-contraction coupling. At the top, a motor neuron delivers an action potential to the neuromuscular junction, causing a release of acetylcholine (ACh) into the synaptic cleft. ACh binds to receptors on the muscle fibre's sarcolemma, opening sodium ion channels and triggering a new action potential that propagates along the sarcolemma and down the T-tubules. This leads to calcium release from the sarcoplasmic reticulum into the sarcoplasm. Calcium binds to troponin on the thin filaments, shifting tropomyosin and exposing actin's myosin-binding sites. This allows myosin heads to form cross-bridges with actin, powered by ATP hydrolysis, leading to filament sliding and muscle fibre shortening. The diagram concludes with a depiction of the whole muscle contracting and generating tension.

Figure 10.10

Diagram illustrating the cross-bridge cycle of muscle contraction in five steps. First, calcium ions bind to troponin, exposing actin's myosin-binding sites. Second, the myosin head, carrying ADP and Pi, forms a cross-bridge with actin. Third, the myosin head pivots, pulling the thin filament toward the M line as ADP and Pi are released. This is called the power stroke. Fourth, ATP binds to the myosin head, causing it to detach from actin. Fifth, ATP is hydrolyzed to ADP and Pi, recocking the myosin head to its high-energy position, ready for another cycle.

Figure 10.12

Graph showing the relationship between sarcomere length (x-axis, as a percentage of resting length) and muscle tension (y-axis, as a percentage of maximum). Tension rises steeply from near zero at about 60% sarcomere length, reaching a plateau at maximum tension between about 100% and 120% length, then declines as sarcomere length increases, falling back to zero near 170%. Illustrations below the x-axis depict sarcomeres at different lengths: Short sarcomeres show overlapping filaments (decreased length), optimal length shows

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ideal cross-bridge overlap, and very stretched sarcomeres show minimal overlap and no cross-bridges.

Figure 11.2

Composite diagram of skeletal muscle fascicle arrangements, each panel naming the pattern and an example muscle. Circular (sphincter) fibres encircle an opening; an inset highlights orbicularis oris around the mouth, which constricts the oral opening when it contracts. Parallel non-fusiform fibres run along the long axis (sartorius). Parallel-fusiform has a thick belly and tapered ends (biceps brachii). Convergent has a broad origin that fans into a single tendon (pectoralis major). Unipennate fibres attach to one side of a central tendon (extensor digitorum). Bipennate fibres attach to both sides of a central tendon (rectus femoris). Multipennate consists of several tendons in bundles (deltoid).

Figure 11.3

Anterior and posterior views of the human body showing major skeletal muscles, with the right side of each view showing superficial muscles and the left side showing deeper muscles. In the anterior superficial view, labelled muscles include frontalis, orbicularis oculi, zygomaticus, orbicularis oris, sternocleidomastoid, deltoid, pectoralis major, biceps brachii, brachialis, brachioradialis, flexor carpi radialis, sartorius, quadriceps femoris group (rectus femoris, vastus lateralis, and vastus medialis), tibialis anterior, and fibularis longus. In the anterior deep view, labelled muscles include temporalis, masseter, platysma, pectoralis minor, serratus anterior, external oblique, transversus abdominis, flexor digitorum superficialis, adductor longus, gracilis, and gastrocnemius. In the posterior superficial view, labelled muscles include trapezius, deltoid, triceps brachii, latissimus dorsi, gluteus medius, gluteus maximus, hamstrings (biceps femoris and semitendinosus), gastrocnemius, soleus, and calcaneal (Achilles) tendon. In the posterior deep view, labelled muscles include splenius capitis, levator scapulae, rhomboid major, infraspinatus, teres major, teres minor, external oblique, gluteus minimus, adductor magnus, and fibularis longus.

Figure 11.6

The image shows a labelled anterior view of the neck with muscles, bones, and other structures identified. At the top, the inferior edge of the mandible is labelled. The suprahyoid muscles are listed on the right and include the geniohyoid, digastric, mylohyoid, and stylohyoid. The styloglossus muscle is labelled near the upper neck. The hyoid bone is labelled in the mid-neck region. The infrahyoid muscles are listed on the right and include the thyrohyoid, omohyoid, sternohyoid, and sternothyroid. The thyroid cartilage of the larynx, thyroid gland, and trachea are labelled along the midline of the neck. At the base of the neck, the right and left clavicles, sternum, and scapula are labelled.

Figure 11.7

The image shows three labelled views of the neck muscles. The left panel shows a left lateral view with the splenius capitis, sternocleidomastoid, levator scapulae, trapezius, acromion process of scapula, and scalenes labelled. The middle panel shows a posterior view of the superficial neck muscles with the right trapezius removed, labelling the levator scapulae and multifidus muscles as well as the first thoracic vertebrae. A boxed region highlights the location of the suboccipital muscles. The right panel shows a posterior view of the deep neck muscles with the left semispinalis capitis removed, labelling the suboccipital muscles, splenius capitis (cut), longissimus capitis, and semispinalis capitis.

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Figure 11.8

The image shows four labelled views of the muscles of the neck and back. The top left panel shows a left lateral view of the neck with the levator scapulae, sternocleidomastoid, splenius, trapezius, medial scalene, anterior scalene, and clavicle labelled. The top right panel shows a posterior view with the superficial left-side and deep right-side muscles of the neck and upper back labelled, including the trapezius, splenius capitis, splenius cervicis, rhomboides minor, and rhomboides major. The bottom left panel shows a posterior view of the deep muscles of the back, labelling the semispinalis capitis (joined with deep spinalis capitis), semispinalis cervicis, longissimus cervicis, spinalis thoracis, semispinalis thoracis, multifidus, longissimus capitis, iliocostalis cervicis, iliocostalis thoracis, longissimus thoracis, and iliocostalis lumborum. The bottom right inset shows the deep spinal muscles with the multifidus removed, labelling the transverse processes of the vertebrae, rotator brevis, rotator longus, interspinales, short rotator, and intertransversarii.

Figure 11.9

The image shows two labelled views of the abdominal muscles. Panel A shows an anterior lateral view of the superficial and deep abdominal muscles. The labelled superficial structures include the pectoralis major, latissimus dorsi, anterior serratus muscles, external oblique, linea alba of the rectus sheath, rectus abdominis (enclosed within the rectus sheath), and tendinous intersections between the anterior segments of the rectus abdominis. A magnified inset highlights the deep abdominal muscles and connective tissue, labelling the rectus sheath, transversus abdominis, internal oblique, aponeurosis of the internal oblique, and external oblique. Panel B shows an anterior view of the posterior abdominal muscles, labelling the quadratus lumborum, sacrum, ilia of the hip bones, iliacus, and psoas major.

Figure 11.10

The image shows an inferior view of the diaphragm with labelled anatomical structures. The central tendon of the diaphragm is shown in the middle. The diaphragm itself is labelled along the periphery. The sternum is labelled at the top, and the vertebrae are labelled at the bottom. Openings through the diaphragm are labelled, including the vena cava passing through the caval opening, the esophagus passing through the esophageal hiatus, and the aorta passing through the aortic hiatus. The 12th (floating) ribs are labelled on each side. The left psoas major and left quadratus lumborum muscles are labelled along the lower lateral edge of the figure.

Figure 11.11

The image shows two labelled views of the thoracic wall and intercostal muscles. The left panel shows the anterior thoracic wall with the pectoralis major dissected to reveal underlying structures. Labelled features include the clavicle, ribs, sternum, pectoralis minor, serratus anterior, internal intercostals, and external intercostals. A boxed region highlights the intercostal space. The right panel is an enlarged view of the intercostal space, showing the layering of the external intercostal, internal intercostal, and innermost intercostal muscles between two ribs.

Figure 11.13

The image shows four labelled views of the muscles of the left shoulder. Panel A shows a left anterior lateral view with the pectoralis major and latissimus dorsi labelled. Panel B shows a posterior view with the left deltoid and left latissimus dorsi labelled. Panel C shows

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an anterior lateral view of the deep muscles of the left shoulder, labelling the pectoralis major (cut), deltoid (cut), coracoid process of the scapula, subscapularis, teres major, and serratus anterior. Panel D shows a posterior view of the deep muscles of the left shoulder, labelling the teres minor, supraspinatus, spine of the scapula, deltoid (cut), infraspinatus, teres major, latissimus dorsi near its origin, humerus, triceps brachii long head, and triceps brachii lateral head.

Figure 11.14

The image shows six labelled views of the muscles of the left upper arm and forearm. The top left panel shows an anterior lateral view of the left upper arm, labelling the biceps brachii short head, biceps brachii long head, and brachialis. The top right panel shows a posterior view of the left upper arm, labelling the triceps brachii lateral head and triceps brachii long head. The middle left panel shows the superficial muscles of the left forearm in palmar view, labelling the biceps brachii, brachioradialis, pronator teres, flexor carpi radialis, palmaris longus, flexor carpi ulnaris, and flexor digitorum superficialis. The middle right panel shows the superficial muscles of the left forearm in dorsal view, labelling the triceps brachii, brachioradialis, extensor carpi radialis longus, extensor carpi radialis brevis, abductor pollicis longus, extensor pollicis brevis, extensor pollicis longus, anconeus, extensor carpi ulnaris, extensor digitorum, and extensor digiti minimi, along with the lateral epicondyle of the humerus. The bottom left panel shows the deep muscles of the left forearm in palmar view, labelling the brachialis (cut), flexor digitorum profundus, flexor retinaculum (cut), flexor pollicis longus, pronator quadratus, and medial and lateral epicondyles of the humerus. The bottom right panel shows the deep muscles of the left forearm in dorsal view, labelling the abductor pollicis longus, extensor pollicis longus, extensor pollicis brevis, extensor indicis, flexor digitorum profundus, extensor retinaculum, flexor carpi ulnaris, and medial epicondyle of the humerus.

Figure 11.15

The image shows three labelled views of the pelvic and thigh muscles of the right leg. The top panel shows an anterior view of the superficial pelvic and thigh muscles, labelling the quadratus lumborum, iliacus, crest of ilium, tensor fascia latae, rectus femoris, vastus lateralis, vastus medialis, quadriceps tendon (or patellar tendon), patellar ligament, psoas major, pectineus, sacrum, adductor longus, gracilis, adductor magnus, and sartorius. The bottom left panel shows an anterior view of the deep pelvic and thigh muscles, labelling the iliac crest, pubis, femur, pectineus, obturator externus, adductor brevis, adductor longus, and adductor magnus. The bottom right panel shows a posterior view of the pelvic and thigh muscles, labelling the crest of ilium, sacrum, gluteus medius (cut), gluteus minimus, piriformis, superior gemellus, inferior gemellus, obturator internus, obturator externus, quadratus femoris, biceps femoris, gluteus maximus (cut), adductor group, gracilis, semimembranosus, and semitendinosus.

Figure 11.16

The image shows three labelled views of the muscles of the right lower leg. The left panel shows an anterior view of the superficial muscles, labelling the tibialis anterior, fibularis longus, extensor digitorum longus, fibularis brevis, extensor hallucis longus, fibularis tertius, superior extensor retinaculum, and inferior extensor retinaculum. The middle panel shows a posterior view of the superficial muscles, labelling the gastrocnemius lateral head, gastrocnemius medial head, plantaris, soleus, calcaneal (Achilles) tendon, and calcaneus (heel). The right panel shows a posterior view of the deep muscles, labelling the popliteus, soleus (cut), fibularis longus, tibialis posterior, flexor digitorum longus, flexor hallucis longus, and fibularis brevis.

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Figure 12.4

This illustration shows a superior view of a cross-section of the brain. The anterior side of the brain is at the top of the diagram, with the two eyes clearly visible. Each eye contains a left nerve tract and a right nerve tract. In the left eye, the left nerve tract travels straight back to the right side of the thalamus. It then enters the left occipital lobe. Conversely, the right nerve tract crosses to the right side of the brain through the optic chiasma. It travels through the right side of the thalamus and enters the right occipital lobe. In the right eye, the opposite is true. The left nerve tract crosses over to the left side of the brain at the optic chiasma, travelling into the left side of the thalamus and the left side of the occipital lobe. However, the right nerve tract leads straight back to the right side of the thalamus and the right occipital lobe. Therefore, the optic chiasma is where the right nerve tract from the right eye crosses over the left nerve tract from the left eye.

Figure 12.5

This illustration shows a silhouette of a human with only the brain, spinal cord, PNS ganglia, nerves, and a section of the digestive tract visible. The brain, which is part of the CNS, is the area of perception and processing of sensory stimuli (somatic/autonomic), the execution of voluntary motor responses (somatic), and the regulation of homeostatic mechanisms (autonomic). The spinal cord, which is part of the CNS, is the area where reflexes are initiated. The gray matter of the ventral horn initiates somatic reflexes, while the gray matter of the lateral horn initiates autonomic reflexes. The spinal cord is also the somatic and autonomic pathway for sensory and motor functions between the PNS and the brain. The nerves, which are part of the PNS, are the fibres of sensory and motor neurons, which can be either somatic or autonomic. The ganglia, which are part of the PNS, are the areas for the reception of somatic and autonomic sensory stimuli. These are received by the dorsal root ganglia and cranial ganglia. The autonomic ganglia are also the relay for visceral motor responses. The digestive tract is part of the enteric nervous system, the ENS, which is located in the digestive tract and is responsible for autonomous function. The ENS can operate independently of the brain and spinal cord.

Figure 12.6

This illustration shows the anatomy of a neuron. The neuron has a very irregular cell body (soma) containing a purple nucleus. There are six projections protruding from the top, bottom, and left side of the cell body. Each of the projections branches many times, forming small, tree-shaped structures protruding from the cell body. The right side of the cell body tapers into a long cord called the axon. The axon is insulated by segments of myelin sheath, which resemble a semitransparent toilet paper roll wound around the axon. The myelin sheath is not continuous but is separated into equally spaced segments. The bare axon segments between the sheath segments are called nodes of Ranvier. An oligodendrocyte is reaching its two armlike projections onto two myelin sheath segments. The axon branches many times at its end, where it connects to the dendrites of another neuron. Each connection between an axon branch and a dendrite is called a synapse. The cell membrane completely surrounds the cell body, dendrites, and axon. The axon of another nerve is seen in the upper left of the diagram, connecting with the dendrites of the central neuron.

Figure 12.7

Three illustrations show some of the possible shapes that neurons can take. In the unipolar neuron, the dendrite enters from the left and merges with the axon into a common pathway,

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which is connected to the cell body. The axon leaves the cell body through the common pathway, then branches off to the right, in the opposite direction as the dendrite. Therefore, this neuron is T-shaped. In the bipolar neuron, the dendrite enters the left side of the cell body, while the axon emerges from the opposite (right) side. In a multipolar neuron, multiple dendrites enter the cell body. The only part of the cell body that does not have dendrites is the part that elongates into the axon.

Figure 12.8

This diagram contains three black-and-white drawings of more specialized nerve cells. Part A shows a pyramidal cell of the cerebral cortex, which has two long nerve tracts attached to the top and bottom of the cell body. However, the cell body also has many shorter dendrites projecting out a short distance from the cell body. Part B shows a Purkinje cell of the cerebellar cortex. This cell has a single long nerve tract entering the bottom of the cell body. Two large nerve tracts leave the top of the cell body but immediately branch many times to form a large web of nerve fibres. Therefore, the Purkinje cell somewhat resembles a shrub or coral in shape. Part C shows the olfactory cells in the olfactory epithelium and olfactory bulbs. It contains several cell groups linked together. At the bottom, there is a row of olfactory epithelial cells that are tightly packed side by side, somewhat resembling the slats of a fence. There are six neurons embedded in this epithelium. Each neuron connects to the epithelium through branching nerve fibres projecting from the bottom of its cell body. A single nerve fibre projects from the top of each neuron and synapses with nerve fibres from the neurons above. These upper neurons are cross-shaped, with one nerve fibre projecting from the bottom, top, right, and left sides. The upper cells synapse with the epithelial nerve cells using the nerve tract projecting from the bottom of their cell bodies. The nerve tract projecting from the top continues the pathway, making a ninety-degree turn to the right and continuing to the right border of the image.

Figure 12.9

This diagram shows several types of nervous system cells associated with two multipolar neurons. Astrocytes are star-shaped cells with many dendrite-like projections but no axon. They are connected with the multipolar neurons and other cells in the diagram through their dendrite-like projections. Ependymal cells have a teardrop-shaped cell body and a long tail that branches several times before connecting with astrocytes and the multipolar neuron. Microglial cells are small cells with rectangular bodies and many dendrite-like projections stemming from their shorter sides. The projections are so extensive that they give the microglial cell a fuzzy appearance. The oligodendrocytes have circular cell bodies with four dendrite-like projections. Each projection is connected to a segment of myelin sheath on the axons of the multipolar neurons. The oligodendrocytes are the same colour as the myelin sheath segment and add layers to the sheath using their projections.

Figure 12.10

This diagram shows a collection of peripheral nervous system glial cells. The largest cell is a unipolar peripheral ganglionic neuron, which has a common nerve tract projecting from the bottom of its cell body. The common nerve tract then splits into the axon, going off to the left, and the dendrite, going off to the right. The cell body of the neuron is covered with several satellite cells that are irregular and flattened. Schwann cells wrap around each myelin sheath segment on the axon, with their nucleus creating a small bump on each segment.

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Figure 12.11

This two-part diagram shows the process of myelination represented by three images and a micrograph. In the left image, the cell membrane of a cylindrical Schwann cell, which has a blue nucleus, is indented around an axon. The upper and lower lip of the cell membrane is visible where the membrane indents around the axon. In the middle image, the lower lip of the cell membrane dives under the upper lip and wraps around the axon. In the right image, the process in part B has continued, forming many layers of myelin that wrap around the axon. The nucleus of the Schwann cell is still visible in the outermost layer, just to the left of the upper lip. The area of the axon next to the Schwann cell, which has no myelin, is labelled as a node of Ranvier. The micrograph shows details of the inset on the right, representing a section through the axon labelling the axolemma, myelin sheet, external lamina, and endonerium (collagen).

Figure 12.12

This diagram shows the complete pathway a nerve impulse takes when a person tests the temperature of shower water with their hand. First, a sensory nerve ending in the index finger sends a nerve impulse to the spinal cord. A cross-section of one segment of the spinal cord is shown from a superior view. The sensory nerve connected to the nerve ending is located in the dorsal root ganglion. The nerve ending is a dendrite of the sensory neuron, as it also has an axon that synapses with an interneuron. The interneuron then synapses with a second interneuron in the thalamus. This second interneuron synapses with brain tissue in the cerebral cortex, allowing conscious perception of the water temperature. The brain then initiates a motor command by stimulating an upper motor neuron in the cerebral cortex. The axon of the upper motor neuron extends all the way to the spinal cord, where it synapses with a lower motor neuron in the gray matter of the spinal cord. The impulse then travels down the lower motor neuron back to the hand, where it synapses with the skeletal muscles of the hand. This triggers the muscle contractions that turn the dials of the shower to adjust the water temperature.

Figure 12.15

This diagram shows a cross-section of a cell membrane. The cell membrane proteins are large, blocky objects. Peripheral proteins are not embedded in the phospholipid bilayer. The peripheral protein shown here is attached to the outside surface of another protein on the extracellular fluid side. Integral proteins are embedded between the phospholipids of the cell membrane. The transmembrane integral protein extends through both phospholipid layers. The opposite ends of this protein project into the cytosol and the extracellular fluid. A second, smaller integral protein only extends into the inner phospholipid layer. Its opposite end projects into the cytosol. This second protein is, therefore, not a transmembrane protein. The channel protein is cylinder-shaped with a hollow internal tube labelled the pore. The sides of the channel protein can bulge inward to close the pore.

Figure 12.16

These two diagrams each show a channel protein embedded in the cell membrane. In the left diagram, there is a large number of sodium ions (Na plus) and calcium ions (Ca2 plus) in the extracellular fluid. Within the cytosol, there is a large number of potassium ions (K plus) but only a few sodium ions. In this diagram, the channel is closed. Two ACh molecules are floating in the extracellular fluid. Their label indicates that a neurotransmitter, a ligand, is required to open the ion channel. The neurotransmitter receptor site on the extracellular fluid side of the channel protein matches the shape of the ACh molecules. In the right diagram,

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the two ACh molecules attach to the neurotransmitter receptor sites on the channel protein. This opens the channel, and the sodium and calcium ions diffuse through the channel and into the cytosol, down their concentration gradient. The potassium ions also diffuse through the channel in the opposite direction down their concentration gradient (out of the cell and into the extracellular fluid).

Figure 12.17

These two diagrams each show a channel protein embedded in the cell membrane. In the left diagram, there is a large number of sodium ions in the extracellular fluid but only a few sodium ions in the cytosol. There is a large number of calcium ions in the cytosol but only a few calcium ions in the extracellular fluid. In this diagram, the channel is closed, as the extracellular side has a lid, somewhat resembling that on a trash can, that is closed over the channel opening. In the right diagram, the mechanically gated channel is open. This allows the sodium ions to flow from the extracellular fluid into the cell, down their concentration gradient. At the same time, the calcium ions are moving from the cytosol into the extracellular fluid, down their concentration gradient.

Figure 12.18

This is a two-part diagram. Both diagrams show a voltage-gated channel embedded in the lipid membrane bilayer. The channel contains a sphere-shaped gate that is attached to a filament. In the first diagram, there are several ions in the cytosol but only one ion in the extracellular fluid. The voltage across the membrane is currently negative 70 millivolts, and the voltage-gated channel is closed. In the second diagram, the voltage in the cytosol is negative 50 millivolts. This voltage change has caused the voltage-gated channel to open, as the small sphere is no longer occluding the channel. One of the ions is moving through the channel, down its concentration gradient, and out into the extracellular fluid.

Figure 12.19

This is a two-part diagram. Both diagrams show a leakage channel embedded in the lipid membrane bilayer. The leakage channel is cylindrical with a large, central opening. In the first diagram, there are several ions in the cytosol but only one ion in the extracellular fluid. No ions are moving through the leakage channel because the channel is closed. In the second diagram, the leakage channel randomly opens, allowing two ions to travel through the channel, down their concentration gradient, and out into the extracellular fluid.

Figure 12.22

This graph has membrane potential in millivolts on the y-axis, ranging from negative 70 to positive 30. Time is on the x-axis. In step one, which is labelled “at rest,” the plot line is steady at negative 70 millivolts. In step two, a stimulus is applied, causing the plot line to increase to positive 30 millivolts. The curve sharply increases at step three, labelled “voltage rises.” After peaking at positive 30, the plot line then quickly drops back to negative 70. This is the fourth step, labelled “voltage falls.” The plot line continues to drop below negative 70, and this is step five, labelled “end of action potential.” Finally, the plot line gradually increases back to negative 70 millivolts, which is step six, labelled “return to rest.”

Figure 12.23

The graph has membrane potential in millivolts on the y-axis, ranging from negative 90 millivolts to negative 40 millivolts. Time is on the x-axis. The left half of the plot line is

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labelled "depolarizing graded potential." The plot has four progressively larger peaks, with each starting at the resting membrane potential of negative 70 millivolts. The lowest peak reaches about negative 65 millivolts and is narrow in width, as this represents a small stimulus that causes a small depolarization of the cell membrane. The second peak reaches about negative 60 millivolts but is still narrow. This represents a larger stimulus causing more depolarization. The third peak also reaches about negative 62 millivolts but is about twice as wide as the other two peaks. This represents a stimulus of longer duration, which causes a longer-lasting depolarization. However, this stimulus is not greater in strength than the previous stimulus. The rightmost peak among the depolarizing graded potentials reaches above the threshold line to about negative 52 millivolts. This represents a stimulus of sufficient strength to trigger an action potential (at negative 55 millivolts). The right half of the plot is labelled "hyperpolarizing graded potential." The plot line in this half begins at the resting potential of negative 70 millivolts, then drops to more negative membrane potentials. The first peak drops to negative 75 millivolts, the second peak drops to negative 78 millivolts, and the third peak drops to negative 87 millivolts. These peaks represent a stimulus that results in hyperpolarization, which is triggered by the activation of specific ion channels in the cell membrane.

Figure 12.24

This graph has membrane potential in millivolts on the y-axis, ranging from negative 90 to positive 30. Time is on the x-axis. The plot line is moving up and down between the resting membrane potential of negative 70 millivolts and the threshold potential of negative 55 millivolts. An EPSP causes the plot line to move higher, closer to the threshold potential. An IPSP causes the plot line to move lower, farther away from the threshold potential. Toward the right side of the graph, the neuron receives an EPSP that pushes the membrane potential above the threshold, triggering an action potential that causes the plot line to quickly rise above positive 30 millivolts. The plot line then quickly drops back below negative 80 millivolts but then gradually increases back to negative 70 millivolts. A picture of a neuron indicates that excitatory postsynaptic potentials are commonly provided by synapses on the neuron's dendrites. Inhibitory postsynaptic potentials are commonly provided by synapses near the neuron's axon hillock.

Figure 12.25

This diagram shows a postsynaptic neuron. An axon from a presynaptic neuron is synapsing with the dendrites on the postsynaptic neuron. The axon of the presynaptic neuron branches into several club-shaped axon terminals. A magnified view of one of the synapses reveals that the axon terminal does not contact the dendrite of the postsynaptic neuron. Instead, there is a small space between the two structures, called the synaptic cleft. The axon terminal of the presynaptic neuron contains several synaptic vesicles, each holding about a dozen neurotransmitter particles. The synaptic vesicles travel to the edge of the axon terminal and release their neurotransmitters into the synaptic clefts. The neurotransmitters travel through the synaptic cleft and bind to carrier proteins on the postsynaptic neuron that contain receptors for neurotransmitters.

Figure 12.26

This diagram contains two images, labelled A and B. Both images show a cross-section of a postsynaptic membrane. There are two proteins embedded in each of the two membrane cross-sections. In diagram A, direct activation brings about an immediate response. Here, both of the membrane proteins are ion channels. Several hexagonal neurotransmitters

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bind to ionotropic receptors on the extracellular fluid side of the channels. The binding of neurotransmitters causes the channels to open, allowing ions to flow from the extracellular fluid into the cytosol. Image B shows indirect activation, which involves a prolonged response, amplified over time. Here, one of the cell membrane proteins is solid, while the other is a channel. Neurotransmitters bind to metabotropic receptors on the extracellular side of the solid protein. This triggers the solid protein to activate a G protein in the cytoplasm. The G protein binds to an effector protein in the cytoplasm, which results in the production of several second messenger particles. The second messenger activates enzymes that open the channel protein, allowing ions to enter the cytoplasm.

Figure 13.6

The image shows two views of the spinal cord in cross-section. The top panel is a labelled diagram showing gray matter and white matter regions. The gray matter is arranged in an H-shaped pattern, with the posterior (dorsal) horn, lateral horn, and anterior (ventral) horn labelled. The central canal is labelled at the centre. Surrounding the grey matter, the white matter is divided into posterior (dorsal) columns, lateral columns, and anterior (ventral) columns. The bottom panel shows a histological cross-section of the spinal cord, with the grey matter visible as a butterfly- or H-shaped region in the centre, surrounded by lighter-stained white matter.

Figure 13.7

The image shows a labelled diagram of the arteries of the brain, focusing on the circle of Willis and associated vessels. At the top, the anterior communicating artery connects the two anterior cerebral arteries. Branching laterally from the internal carotid artery are the middle cerebral artery, ophthalmic artery, and anterior choroidal artery. Posteriorly, the posterior communicating arteries connect to the posterior cerebral arteries. The basilar artery runs along the midline, giving off pontine arteries and the superior cerebellar arteries and continuing upward to join the posterior cerebral arteries. Inferiorly, the basilar artery is formed by the merging of the vertebral arteries, which also give off the anterior inferior cerebellar arteries and posterior inferior cerebellar arteries. The anterior spinal artery descends from the vertebral arteries along the midline.

Figure 13.8

The image shows a sagittal section of the head with the dural venous sinuses and cerebral veins labelled. The cranium and dura mater are labelled at the top. The superior sagittal sinus runs along the top midline, with cerebral veins draining into it. The inferior sagittal sinus runs below it and connects to the straight sinus, which continues posteriorly to the confluence of sinuses. The transverse sinus extends laterally from the confluence, and the occipital sinus descends toward the base of the skull. The great cerebral vein is shown draining into the straight sinus. The diagram also notes that blood returns to the jugular vein via the sigmoid sinus.

Figure 13.9

The image shows a cross-section of the meninges and superior sagittal sinus. The outermost layer is bone, followed by the dura mater. Beneath the dura is the subdural space and the arachnoid mater, with arachnoid granulation villi projecting into the superior sagittal sinus to allow cerebrospinal fluid drainage. The subarachnoid space lies below the arachnoid mater and contains arachnoid trabeculae. The pia mater closely follows the surface of the

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cerebral cortex. Cerebral veins drain blood into the superior sagittal sinus, which runs along the longitudinal fissure at the midline.

Figure 13.10

The image shows a sagittal section of the brain with the ventricular system and cerebrospinal fluid flow pathway labelled. The right lateral ventricle is shown connecting to the third ventricle via the interventricular foramen. The choroid plexus is labelled within the ventricles as the site of cerebrospinal fluid production. From the third ventricle, fluid passes through the cerebral aqueduct into the fourth ventricle. The fourth ventricle has a median aperture and lateral apertures through which fluid flows into the subarachnoid space. The central canal is labelled, showing the path of fluid into the spinal cord. The subarachnoid space surrounds the brain, and arachnoid granulations drain cerebrospinal fluid into the superior sagittal sinus, which is labelled at the top. The meningeal dura mater is also labelled, showing the outer protective covering of the brain.

Figure 13.11

The image shows two views of a spinal nerve and its connective tissue coverings. Panel A is a diagram illustrating the structure of a spinal nerve. It shows the entire spinal nerve surrounded by the epineurium, with blood vessels running through it. Inside the nerve, bundles of axons called fascicles are each surrounded by perineurium, while individual axons are wrapped in endoneurium. An enlarged cross-section highlights the arrangement of fascicles, perineurium, and axons. Panel B is a histological section of a spinal nerve stained pink, showing fascicles surrounded by perineurium and the entire nerve encased in epineurium.

Figure 13.13

The image shows the inferior view of the brain with all twelve cranial nerves labelled. The olfactory nerve (I) is seen at the most anterior end, followed by the optic nerve (II). The oculomotor nerve (III) and trochlear nerve (IV) are positioned slightly posterior to the optic chiasm. The trigeminal nerve (V) is shown branching laterally. The abducens nerve (VI), facial nerve (VII), and vestibulocochlear nerve (VIII) are arranged in sequence along the brain stem. Further posteriorly, the glossopharyngeal nerve (IX), vagus nerve (X), accessory nerve (XI), and hypoglossal nerve (XII) are labelled near the medulla and spinal cord region.

Figure 13.14

This image shows the major nerve plexuses and named peripheral nerves along the human torso and pelvis in an anterior view. The cervical plexus, arising from spinal nerves C1 to C5, is labelled at the top, along with the phrenic nerve. The brachial plexus, arising from C5 to T1, is shown branching into the axillary, median, radial, and ulnar nerves. Lower down, the lumbar plexus from L1 to L4 is labelled, with the femoral and obturator nerves indicated. The sacral plexus from L4 to S4 is shown giving rise to the sciatic nerve, which divides into the common fibular nerve and tibial nerve. The vertebral column is drawn in the centre for reference, with spinal nerve roots indicated along its length.

Figure 14.1

Diagram showing three types of sensory neurons and receptor structures. The first neuron has free nerve endings at the dendrites on one end, a long axon with myelin sheaths, and a cell body along the axon. It is labelled "Neuron (receptor) with free nerve endings." The second neuron has dendrites enclosed in a capsule labelled "encapsulated nerve ending," connected

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to an axon with myelin segments and a cell body along it. It is labelled "Neuron (receptor) with encapsulated nerve endings." The third panel shows a rod photoreceptor cell connected to a bipolar cell. It has an elongated, cylindrical outer segment labelled "rod," and the bipolar cell is shown receiving its signal.

Figure 14.3

Illustration showing the olfactory system and nasal cavity. The first panel depicts the nasal cavity with air entering through the nose and passing the nasal conchae toward the olfactory epithelium beneath the olfactory bulb. The second panel magnifies the olfactory region, showing olfactory neurons extending through the ethmoid bone to the olfactory bulb, where they connect with mitral cells in the olfactory tract. It also labels olfactory receptors, glands, cilia, and mucus, where odour molecules dissolve. A histological image at the bottom shows the layered olfactory epithelium in pink and purple staining.

Figure 14.4

Illustration showing the anatomy of the human ear in cross-section, divided into external, middle, and inner regions. The external ear includes the auricle and ear canal leading to the tympanic membrane (eardrum). The middle ear contains the ossicles—the malleus, incus, and stapes (attached to the oval window)—within the tympanic cavity. The inner ear features the cochlea, vestibule, and semicircular canals, connected to the vestibular and cochlear nerves. The round window and Eustachian tube are also labelled.

Figure 14.5

Diagram illustrating how sound waves are transmitted through the ear. A tuning fork generates waves representing alternating areas of high and low pressure. The tympanic membrane vibrates in response, and these vibrations are amplified by the ossicles in the middle ear. The stapes transmits vibrations through the oval window, creating standing waves in the vestibular fluid of the cochlea. Within the cochlea, the basilar membrane vibrates at frequency-specific points, stimulating hair cells in the organ of Corti. Insets show wave frequency and amplitude relationships.

Figure 14.9

Diagram illustrating how different sound frequencies are detected along the cochlea. The image shows the ear from the outer to the inner sections, with the cochlea expanded to display the basilar and tectorial membranes. High-frequency sounds (20,000 Hz) stimulate the base near the oval window, midrange frequencies (1,500 Hz) affect the middle, and low frequencies (20 Hz) reach the apex. A graph below shows that fibre length in the basilar membrane increases toward the apex, corresponding to lower frequencies.

Figure 14.10

Diagram showing how the maculae in the utricle and saccule detect head position and linear acceleration. The left side illustrates their location within the inner ear with an inset showing a close-up view of the endolymph, macula, otoliths, otolithic membrane, hair cells, and vestibular division of the vestibulocochlear nerve. On the right, two panels show a person's head upright and tilted forward. When upright, otoliths rest evenly on the otolithic membrane above hair cells. When the head tilts, gravity shifts the otoliths, bending the hair cells and signalling a change in head position to the vestibular nerve.

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Figure 14.13

Cross-sectional diagram of the human eye labelled with structures organized by region: External and outer structures include the lateral rectus muscle, medial rectus muscle, sclera, and cornea. Middle and vascular layers include the choroid, ciliary body, ciliary muscle, ciliary process, suspensory ligaments, iris, and pupil. Internal and neural layers include the retina, fovea centralis, optic disc (blind spot), optic (II) nerve, and central retinal artery and vein. Cavities and chambers include the anterior cavity, anterior chamber, posterior chamber, posterior cavity, vitreous chamber, and scleral venous sinus (canal of Schlemm).

Figure 14.14

Diagram and micrograph of the retina showing its layered structure and cell types. The diagram depicts photoreceptor cells, including rods and cones, with labelled parts such as pigment epithelium, melanin granules, connecting stalks, discs, mitochondria, Golgi apparatus, nuclei, bipolar cells, and ganglion cells, with light entering from below. The micrograph shows the corresponding histological layers: choroid, pigment epithelium, rods and cones, bipolar cells, ganglion cells, and optic nerve axons, with light passing through the layers toward the photoreceptors.

Figure 14.15

Diagram comparing the dorsal column system and spinothalamic tract pathways for sensory transmission. On the left, the dorsal column system carries fine touch and proprioception sensations from the right side of the body, showing first-order neurons travelling from the dorsal root ganglion through the fasciculus gracilis and fasciculus cuneatus to the nucleus gracilis and nucleus cuneatus in the medulla, second-order neurons crossing via the medial lemniscus to the thalamus, and third-order neurons projecting to the postcentral gyrus. On the right, the spinothalamic tract carries pain and temperature sensations from the right side of the body, with first-order neurons in the dorsal root ganglion synapsing in the spinal cord, second-order neurons ascending via the lateral spinothalamic tract to the thalamus, and third-order neurons ending in the postcentral gyrus.

Figure 14.16

Diagram illustrating the vestibulo-ocular reflex showing how head rotation triggers compensating eye movement. The semicircular canals, utricle, and saccule detect rotation, sending signals to the vestibular nuclei in the pons. These connect to the abducens nucleus and oculomotor nucleus, coordinating excitation (shown in magenta) and inhibition (shown in green) of extraocular muscles. During rightward head rotation, excitation occurs in the left lateral rectus and right medial rectus muscles to produce compensating leftward eye movement, while inhibition affects the opposite eye muscles to maintain stable vision.

Figure 14.17

Diagram showing the visual pathways from both eyes to the brain, viewed from below (inferior view). It illustrates how the left and right visual fields overlap to form a binocular field. The optic nerves from each eye meet at the optic chiasm, where fibres from the nasal halves cross to the opposite side, while temporal fibres remain uncrossed. The optic tracts then carry visual information to the lateral geniculate nucleus of the thalamus and onward to the visual cortices of the opposite hemispheres. Additional structures labelled include the pituitary gland and the suprachiasmatic nucleus of the hypothalamus.

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Figure 14.18

Diagram of the sensory homunculus, representing the body map on the primary somatosensory cortex. It shows exaggerated body parts corresponding to the amount of cortical area devoted to sensory input from each region. Labels include hip, leg, foot, toes, genitals, trunk, neck, head, shoulder, arm, elbow, forearm, wrist, hand, fingers (little, ring, middle, index, and thumb), eye, nose, face, lips, teeth, gums, jaw, tongue, and pharynx. The hands, lips, and tongue are disproportionately large, reflecting their high sensory sensitivity.

Figure 14.21

Diagram showing the corticospinal (pyramidal) motor pathway from the brain to skeletal muscles. Labels include the precentral gyrus, cerebral peduncle, midbrain, medulla, pyramids, decussation of pyramids, spinal cord, lateral corticospinal tract, anterior corticospinal tract, upper motor neuron, lower motor neuron, and connection to skeletal muscles. A key identifies upper motor neurons in orange and lower motor neurons in green, illustrating how motor commands travel from the cerebral cortex through the brain stem, cross at the medulla, and descend to activate muscle movement.

Figure 15.1

Diagram showing the sympathetic division of the autonomic nervous system, including spinal cord regions, sympathetic chain ganglia, associated nerves, and target organs. The spinal cord extends from the medulla through the thoracic (T1 to T12), lumbar (L1 to L3), sacral (S1 to S5), and coccygeal regions. Labelled structures include the right and left chain ganglia, superior cervical ganglion, greater and lesser splanchnic nerves, celiac ganglion, superior and inferior mesenteric ganglia, and coccygeal ganglia fused together (ganglion impar). Target organs connected by dashed red lines include the eye, lacrimal and salivary glands, heart, lungs, esophagus, stomach, abdominal blood vessels, liver, pancreas, adrenal glands, intestines, rectum, kidneys, bladder, gonads, and external genitalia.

Figure 15.2

Figure illustrating three pathways of sympathetic preganglionic neurons in the autonomic nervous system. Panel A shows a central neuron synapsing at the same spinal level within the sympathetic chain ganglion. Panel B depicts a central neuron synapsing at a superior or inferior ganglion within the chain. Panel C shows a neuron passing through the white ramus without synapsing in the chain ganglion, instead continuing via a splanchnic nerve to a prevertebral ganglion. Labelled structures include the spinal cord, dorsal root ganglion, spinal nerve, white and gray rami communicantes, sympathetic chain ganglion, splanchnic nerve, prevertebral ganglion, and target effectors. A key identifies the axons and cell bodies of central and ganglionic neurons as well as synapses.

Figure 15.3

Diagram illustrating the parasympathetic division of the autonomic nervous system, showing cranial and sacral origins, associated ganglia, and target organs. The spinal cord is labelled with parasympathetic nuclei in the brain stem: Edinger-Westphal nucleus, superior and inferior salivatory nuclei, and dorsal nucleus of the vagus with nucleus ambiguus. Cranial nerves III, VII, IX, and X connect to terminal ganglia—ciliary, pterygopalatine, submandibular, and otic ganglia. Labelled target organs include the eye, lacrimal and salivary glands, mucous membranes, heart, lungs, esophagus, stomach, abdominal blood vessels, liver, pancreas, adrenal glands,

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intestines, rectum, kidneys, bladder, gonads, and external genitalia. Sympathetic fibres are shown in red and parasympathetic fibres in blue.

Figure 15.4

Diagram showing the structure and function of postganglionic varicosities in autonomic neurotransmission. The left portion depicts a postganglionic axon running along smooth muscle, with multiple swellings labelled as postganglionic varicosities. The magnified view shows a single varicosity containing synaptic vesicles that release neurotransmitters across the gap to bind with neurotransmitter receptors on the sarcolemma (muscle cell membrane). Labelled components include the postganglionic axon, smooth muscle, synaptic vesicles, neurotransmitter, receptors, and sarcolemma.

Figure 15.5

Diagram comparing the autonomic and somatic efferent pathways. The top section illustrates the autonomic efferent pathway, where a central neuron in the spinal cord sends a myelinated autonomic presynaptic axon to a ganglionic neuron, which then connects via an unmyelinated autonomic postsynaptic axon to a smooth muscle target effector. A magnified inset shows a postganglionic varicosity releasing neurotransmitters onto the smooth muscle membrane. The bottom section shows the somatic efferent pathway, where a single myelinated somatic motor neuron extends directly from the spinal cord to a skeletal muscle target effector. The inset depicts a synaptic terminal forming a neuromuscular junction.

Figure 15.7

Diagram comparing long and short reflex pathways in the autonomic nervous system. The upper panel illustrates a long reflex, where a sensory receptor cell sends a signal through a sensory neuron to the spinal cord or brain, synapsing in the central nervous system before continuing through a peripheral ganglion to the target effector. The lower panel shows a short reflex, in which the sensory receptor cell synapses directly within a peripheral ganglion without central nervous system involvement. Both pathways include labelled structures such as the sensory receptor cell, peripheral ganglion, sensory cell synapse, and target effector.

Figure 15.8

Diagram illustrating the neural control of pupil dilation and constriction. At the top, light enters the retina, where ganglion cell bodies send signals via the optic nerve to the brain. The lower half depicts two pathways: In dim light, sympathetic neurons in the cervical vertebra are activated, synapsing in the superior cervical ganglion, and postganglionic neurons release norepinephrine to contract radial iris muscles, dilating the pupils; in bright light, parasympathetic neurons from the Edinger-Westphal nucleus synapse in the ciliary ganglion, and postganglionic neurons release acetylcholine to contract circular iris muscles, constricting the pupils. Colour-coded axons distinguish sympathetic, parasympathetic, and sensory nerves.

Figure 15.9

Diagram illustrating the pupillary light reflex pathway. In step one, light is shone into the right eye. In step two, action potentials from the right eye travel to both right and left pretectal nuclei. In step three, these nuclei stimulate both sides of the Edinger-Westphal nucleus in the midbrain, even though light enters only the right eye. In step four, both Edinger-Westphal nuclei send action potentials through the right and left oculomotor nerves (cranial nerve III)

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to the ciliary ganglia, causing constriction of both pupils. Key structures labelled include the pretectal nucleus, oculomotor nerves, and ciliary ganglia.

Figure 16.1

This diagram shows the endocrine glands and cells that are located throughout the body. The endocrine system organs include the pineal gland and pituitary gland in the brain. The pituitary is located on the anterior side of the hypothalamus, while the pineal gland is located on the posterior side of the hypothalamus. The thyroid gland is a butterfly-shaped gland that wraps around the trachea within the neck. Four small, disc-shaped parathyroid glands are embedded in the posterior side of the thyroid. The adrenal glands are located on top of the kidneys. The pancreas is located at the centre of the abdomen. In females, the two ovaries are connected to the uterus by two long, curved tubes in the pelvic region. In males, the two testes are located in the scrotum below the penis.

Figure 16.2

This table shows the chemical structure of amine hormones, peptide hormones, protein hormones, and steroid hormones. Amine hormones are amino acids with modified side groups. The example given is norepinephrine, which contains the NH2 group typical of an amino acid, along with a hydroxyl (OH) group. The carboxyl group typical of most amino acids is replaced with a benzene ring, depicted as a hexagon of carbons that are connected by alternating single and double bonds. Peptide hormones are composed of short chains of amino acids. The example given is oxytocin, which has a chain of the following amino acids: Gly, Leu, and Pro. Pro is at the bottom of the chain, which connects to a ring of the following amino acids: Cys, Cys, Tyr, Ile, Glu, and Asp. Protein hormones are composed of long chains of linked amino acids. The example given is human growth hormone, which is composed of a bundle of amino acid strands, some threadlike, some coiled, and some in flat, folded sheets. Finally, steroid hormones are derived from the lipid cholesterol. Testosterone and progesterone are given as examples, which each contain several hexagonal and pentagonal carbon rings linked together.

Figure 16.3

This illustration shows the steps involved with the binding of lipid-soluble hormones. Lipid-soluble hormones, such as steroid hormones, easily diffuse through the cell membrane. The hormone binds to its receptor in the cytosol, forming a receptor-hormone complex. The receptor-hormone complex then enters the nucleus and binds to the target gene on the cell's DNA. Transcription of the gene creates a messenger RNA that is translated into the desired protein within the cytoplasm. It is these proteins that alter the cell's activity.

Figure 16.4

This illustration shows the binding of water-soluble hormones. Water-soluble hormones cannot diffuse through the cell membrane. These hormones must bind to a receptor on the outer surface of the cell membrane. The receptor then activates a G protein in the cytoplasm, which travels to and activates adenylyl cyclase. Adenylyl cyclase catalyzes the conversion of ATP to cAMP, the secondary messenger in this pathway. CAMP, in turn, activates protein kinases, which phosphorylate proteins in the cytoplasm. This phosphorylation, shown as a P being added to a polypeptide chain, activates the proteins, allowing them to alter cell activity.

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Figure 16.5

This diagram shows a negative feedback loop using the example of glucocorticoid regulation in the blood. Step one in the cycle is when an imbalance occurs. The hypothalamus perceives low blood concentrations of glucocorticoids in the blood. This is illustrated by there being only five glucocorticoids floating in a cross-section of an artery. Step two in the cycle is hormone release, where the hypothalamus releases the corticotropin-releasing hormone (CRH). Step three is labelled "correction." Here, the CRH release starts a hormone cascade that triggers the adrenal gland to release glucocorticoid into the blood. This allows the blood concentration of glucocorticoid to increase, as illustrated by eight glucocorticoid molecules now being present in the cross-section of the artery. Step four is labelled "negative feedback." Here, the hypothalamus perceives normal concentrations of glucocorticoids in the blood and stops releasing CRH. This brings blood glucocorticoid levels back to homeostasis.

Figure 16.7

This illustration zooms in on the hypothalamus and the attached pituitary gland. The posterior pituitary is highlighted. Two nuclei in the hypothalamus contain neurosecretory cells that release different hormones. The neurosecretory cells of the paraventricular nucleus release oxytocin (OT), while the neurosecretory cells of the supraoptic nucleus release antidiuretic hormone (ADH). The neurosecretory cells stretch down the infundibulum into the posterior pituitary. The tubelike extensions of the neurosecretory cells within the infundibulum are the hypothalamophypophyseal tracts. These tracts connect with a weblike network of blood vessels in the posterior pituitary called the capillary plexus. From the capillary plexus, the posterior pituitary secretes the OT or ADH into a single vein that exits the pituitary.

Figure 16.8

This illustration zooms in on the hypothalamus and the attached pituitary gland. The anterior pituitary is highlighted. Three neurosecretory cells are secreting hormones into a weblike network of arteries within the infundibulum. The artery net is the primary capillary plexus of the hypophyseal portal system. The superior hypophyseal artery enters the primary capillary plexus from outside of the infundibulum. The hypophyseal portal vein runs down from the primary capillary plexus, through the infundibulum, and connects to the secondary capillary plexus of the hypophyseal portal system. The secondary capillary plexus is located within the anterior pituitary. The hormones released from the neurosecretory cells of the hypothalamus travel through the primary capillary plexus, down the hypophyseal portal vein, and into the secondary capillary plexus. There, the hypothalamus hormones stimulate the anterior pituitary to release its hormones. The anterior pituitary hormones leave the primary capillary plexus from a single vein at the bottom of the anterior lobe.

Figure 16.9

This flowchart illustrates the hormone cascade that stimulates human growth. In step one, the hypothalamus releases growth hormone-releasing hormone (GHRH). GHRH travels into the primary capillary plexus of the anterior pituitary, where it stimulates the anterior pituitary to release growth hormone (GH). The release of GH causes three types of effects. In the glucose-sparing effect, GH stimulates adipose cells to break down stored fat, fueling the growth effects (discussed next). The target cells for the glucose-sparing effects are adipose cells. In the growth effects, GH increases the uptake of amino acids from the blood and enhances cellular proliferation while also reducing apoptosis. The target cells for the growth effects are bone cells, muscle cells, nervous system cells, and immune system cells.

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In the diabetogenic effect, GH stimulates the liver to break down glycogen into glucose, fueling the growth effects. The liver also releases IGF in response to GH. The IGF further stimulates the growth effects but also negatively feeds back to the hypothalamus. When high IGF-1 levels are perceived by the hypothalamus, it releases growth hormone-inhibiting hormone (GHIH). GHIH inhibits GH release by the anterior pituitary.

Figure 16.10

These two diagrammatic tables show the major pituitary hormones, their releasing hormone from the hypothalamus, their target organs, and their effects. The top part of the diagram shows the posterior pituitary hormones. ADH is produced by the hypothalamus and stored in the posterior pituitary. The targets of ADH are the kidneys, sweat glands, and circulatory system, as this hormone affects water balance. OT is produced by the posterior pituitary and has no releasing hormone. Its target is the female reproductive system, as this hormone triggers uterine contractions during childbirth. The anterior pituitary hormones are listed in the lower diagram. The release of LH by the anterior pituitary is triggered by the release of GnRH from the hypothalamus. The target of LH is the reproductive system, as this hormone stimulates the production of sex hormones by the gonads. The release of FSH by the anterior pituitary is triggered by the release of GnRH from the hypothalamus. The target of FSH is the reproductive system, as this hormone stimulates the production of sperm and eggs. The release of TSH by the anterior pituitary is triggered by the release of TRH from the hypothalamus. The target of TSH is the thyroid gland, as this hormone stimulates the release of thyroid hormone (TH). TH regulates metabolism. The release of PRL by the anterior pituitary is triggered by the release of PRH and inhibited by the release of PIH from the hypothalamus. The target of PRL is the mammary glands, as this hormone promotes milk production. The release of GH by the anterior pituitary is triggered by the release of GHRH and inhibited by the release of GHIH from the hypothalamus. The targets of GH are the liver, bones, and muscles, as it induces its targets to produce insulin-like growth factors (IGF), as this hormone stimulates body growth and a higher metabolic rate. The release of ACTH by the anterior pituitary is triggered by the release of CRH from the hypothalamus. The targets of ACTH are the adrenal glands, as this hormone induces its targets to produce glucocorticoids, which regulate metabolism and the stress response.

Figure 16.11

Part A of this figure is a diagram of the anterior view of the thyroid gland. The thyroid gland is a butterfly-shaped gland wrapping around the trachea. It narrows at its centre, just under the thyroid cartilage of the larynx. This narrow area is called the isthmus of the thyroid. Two large arteries, the common carotid arteries, run parallel to the trachea on the outer border of the thyroid. A small artery enters the superior edge of the thyroid, near the isthmus, and branches throughout the two "wings" of the thyroid. Part B of this figure is a posterior view of the thyroid. The posterior view shows that the thyroid does not completely wrap around the posterior of the trachea. The posterior sides of the thyroid wings can be seen protruding from under the cricoid cartilage of the larynx. The posterior sides of the thyroid "wings" each contain two small, disc-shaped parathyroid glands embedded in the thyroid tissue. Within each wing, one disc is located superior to the other. These are labelled the left and right parathyroid glands. Just under the inferior parathyroid glands are two arteries that bring blood to the thyroid from the left and right subclavian arteries. Part C of this figure is a micrograph of thyroid tissue. The thyroid follicle cells are cuboidal epithelial cells. These cells form a ring around irregular-shaped cavities called follicles. The follicles contain light-coloured colloid. A larger parafollicular cell is embedded between two of the follicular cells near the edge of a follicle.

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Figure 16.12

This diagram illustrates a negative feedback loop. It shows the general steps of a negative feedback loop at the centre (imbalance, hormone release, correction, and negative feedback) using the example of the hormone cascade that regulates metabolic rate. The hypothalamus releases TRH in response to low metabolic rate and/or low T3 and T4 concentrations in the blood (imbalance). This triggers TSH release by the pituitary (hormone release). The TSH travels to the thyroid, where it triggers T3 and T4 release by the thyroid cells. T3 and T4 increase basal metabolic rate of the body cells and cause a rise in body temperature (the calorigenic effect). T3 and T4 then feed back to the hypothalamus and inhibit TRH and TSH release. If metabolic rate is high and/or T3 and T4 concentrations are low, then the hypothalamus stops releasing TRH (negative feedback). As a result, the anterior pituitary will not release TSH, and no T3 or T4 will be produced by the thyroid.

Figure 16.13

Illustration showing the thyroid and parathyroid glands with a corresponding histological micrograph. The left panel shows a posterior view of the neck with labelled structures, including the hyoid bone, thyroid cartilage, cricoid cartilage, thyroid gland, and paired left and right parathyroid glands. The right panel presents a micrograph of parathyroid tissue, identifying oxyphil cells, parathyroid (chief) cells, and a blood vessel.

Figure 16.14

This diagram shows the role of parathyroid hormone (PTH) in maintaining blood calcium homeostasis. When blood calcium concentration drops, chief cells of the parathyroid gland release PTH. PTH affects bone, the kidneys, and the intestines. In regard to bone, PTH inhibits osteoblasts and stimulates osteoclasts. This results in compact bone being broken down, as illustrated by an osteoclast burrowing into the surface of a bone. The breakdown releases calcium ions into a nearby blood vessel. The osteoblasts are inactive in this stage. In regard to the kidneys, PTH stimulates kidney tubule cells to recover waste calcium from the urine. PTH also stimulates kidney tubule cells to release calcitriol. This is illustrated with a cross-section of a kidney tubule, showing the cells of the tubule wall. Urine is running to the left of the tubule wall cells, while an artery is to the right. The right edge of the tubule wall cells and the left edge of the artery are separated by a small region of interstitial space. The cells are removing calcium from the urine and pumping it into the interstitial fluid, after which the calcium enters the artery. The cells are also pumping calcitriol into the blood vessel. In regard to the intestine, PTH stimulates the intestines to absorb calcium from digesting food. A cross-section of an intestinal cell is shown, which is cube-shaped but with finger-like projections on the intestinal lumen side (top). Beneath the intestinal cell is an artery. Calcitriol is leaving the artery and entering the intestinal cell, stimulating it to absorb calcium from food in the intestinal lumen. The effects of PTH on bone, the kidneys, and the intestines all cause blood calcium levels to increase. High calcium concentrations in the blood stimulate the parafollicular cells in the thyroid to release calcitonin. Calcitonin reverses the effects of PTH by stimulating osteoblasts and inhibiting osteoclasts in bone tissue. This is illustrated by calcium ions leaving a blood vessel and travelling to osteoblasts on a section of compact bone. The osteoblasts are thickening the compact bone layer, while, in this stage, the osteoclasts are inactive.

Figure 16.15

This diagram shows the left adrenal gland located atop the left kidney. The gland is composed of an outer cortex and an inner medulla, all surrounded by a connective tissue capsule.

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The cortex can be subdivided into additional zones, all of which produce different types of hormones. The outermost layer is the zona glomerulosa, which releases mineralocorticoids, such as aldosterone, that regulate mineral balance. Underneath this layer is the zona fasciculate, which releases glucocorticoids, such as cortisol, corticosterone, and cortisone, that regulate glucose metabolism. Underneath this layer is the zona reticularis, which releases androgens, such as dehydroepiandrosterone, that stimulate masculinization. Below this layer is the adrenal medulla, which releases stress hormones, such as epinephrine and norepinephrine, that stimulate the sympathetic ANS.

Figure 16.16

This diagram shows the anatomy of the pancreas. The left, larger side of the pancreas is seated within the curve of the duodenum of the small intestine. The smaller, rightmost tip of the pancreas is located near the spleen. The splenic artery is seen travelling to the spleen; however, it has several branches connecting to the pancreas. An interior view of the pancreas shows that the pancreatic duct is a large tube running through the centre of the pancreas. It branches throughout its length into several horseshoe-shaped pockets of acinar cells. These cells secrete digestive enzymes, which travel down the bile duct and into the small intestine. There are also small pancreatic islets scattered throughout the pancreas. The pancreatic islets secrete the pancreatic hormones insulin and glucagon into the splenic artery. An inset micrograph shows that the pancreatic islets are small discs of tissue consisting of a thin, outer ring called the exocrine acinus, a thicker, inner ring of beta cells, and a central circle of alpha cells.

Figure 16.17

This diagram shows the homeostatic regulation of blood glucose levels. Blood glucose concentration is tightly maintained between 70 milligrams per deciliter and 110 milligrams per deciliter. If blood glucose concentration rises above this range (hyperglycemia), insulin is released from the pancreas. Insulin triggers body cells to take up glucose from the blood and utilize it in cellular respiration. Insulin also inhibits glycogenolysis, in that glucose is removed from the blood and stored as glycogen in the liver. Insulin also inhibits gluconeogenesis, in that amino acids and free glycerol are not converted to glucose in the ER. If blood glucose concentration drops below this range, glucagon is released, which stimulates body cells to release glucose into the blood. All these actions cause blood glucose concentration to decrease. When blood glucose concentration is low (hypoglycemia), alpha cells of the pancreas release glucagon. Glucagon inhibits body cells from taking up glucose from the blood and utilizing it in cellular respiration. Glucagon also stimulates glycogenolysis, in that glycogen in the liver is broken down into glucose and released into the blood. Glucagon also stimulates gluconeogenesis, in that amino acids and free glycerol are converted to glucose in the ER and released into the blood. All these actions cause blood glucose concentrations to increase.

Figure 17.1

Illustration comparing hematocrit levels in three test tubes representing different blood conditions. The left tube shows normal blood, with plasma (top yellow layer), buffy coat (thin white layer of white blood cells and platelets), and hematocrit (red blood cell layer) at typical levels—approximately 37 to 47% for females and 42 to 52% for males. The middle tube depicts anemia, with a depressed hematocrit percentage, indicating fewer red blood cells. The right tube shows polycythemia, with an elevated hematocrit percentage, indicating an excess of red blood cells.

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Figure 17.2

Diagram showing the process of hematopoiesis, the formation of blood cells from multipotent hematopoietic stem cells. The stem cell divides, with some remaining as stem cells and others differentiating based on chemical signals. The myeloid stem cell line gives rise to megakaryoblasts (then megakaryocytes, then platelets), proerythroblasts (then reticulocytes, then erythrocytes), myeloblasts (then basophils, neutrophils, and eosinophils), and monoblasts (then monocytes). The lymphoid stem cell line forms lymphoblasts, which differentiate into natural killer cells (large granular lymphocytes) and small lymphocytes that become T lymphocytes and B lymphocytes.

Figure 17.5

Diagram showing the life cycle and recycling of red blood cells. In step one, hemopoiesis of erythrocytes begins in hemopoietic bone marrow from stem cells that develop into erythroblasts and reticulocytes. In step two, reticulocytes enter the bloodstream and mature into erythrocytes, which circulate for about 120 days. In step three, aged or damaged erythrocytes are phagocytosed by macrophages in the bone marrow, liver, and spleen. In step four, the globin portion of hemoglobin is broken down into amino acids for reuse in protein synthesis. In step five, the heme portion is degraded into biliverdin, then bilirubin, while iron ions bind to transferrin for transport. In step six, iron is stored as ferritin in the liver or reused in hemopoiesis, while bilirubin contributes to bile formation. The diagram traces heme, iron, and globin recycling pathways, emphasizing the liver's role in processing and storage.

Figure 17.6

Diagram illustrating leukocyte migration and immune response during infection or injury. In step one, leukocytes—eosinophils, monocytes, and neutrophils—detect chemical attractants released by pathogens and nearby damaged cells in the bloodstream. In step two, leukocytes move toward higher concentrations of these signals (positive chemotaxis) and squeeze between capillary epithelial cells to reach the affected tissue. In step three, in the tissue, monocytes differentiate into macrophages that engulf pathogens, while eosinophils and neutrophils release cytotoxic granules and enzymes to destroy microbes. The process shows leukocyte activation, movement, and phagocytic action at the site of infection.

Figure 17.10

The image illustrates the process of blood clotting, or hemostasis. When a blood vessel is injured, blood components such as erythrocytes, leukocytes, and platelets leak out. Smooth muscle in the vessel wall contracts to reduce blood loss, and platelets adhere to exposed collagen, releasing chemical signals that make them spiked and sticky, forming a platelet plug. During coagulation, fibrinogen is converted to fibrin, creating a mesh that traps blood cells and strengthens the clot. The fibrin synthesis cascade involves intrinsic and extrinsic pathways that converge into a final common pathway. Both pathways activate factor X, which converts prothrombin to thrombin; thrombin then transforms fibrinogen into fibrin, which stabilizes into a cross-linked fibrin clot with the help of factor XIIIa.

Figure 17.11

This image illustrates how maternal sensitization to the Rh factor can lead to hemolytic disease of the newborn. The placenta normally separates maternal and fetal blood, with fetal circulation passing through the umbilical vessels and the embryonic chorion isolating fetal blood from maternal blood pools. During the birth of a first Rh-positive infant, Rh-positive fetal

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erythrocytes can leak into the Rh-negative mother's blood when the embryonic chorion ruptures. The maternal immune system recognizes the Rh antigen as foreign, causing B cells to produce anti-Rh antibodies. In a subsequent pregnancy with another Rh-positive fetus, these maternal anti-Rh antibodies, which are small enough to cross the embryonic chorion, enter the fetal circulation and attack the Rh-positive erythrocytes, potentially leading to hemolytic disease in the fetus.

Figure 17.12

This image shows a blood typing test used to determine an individual's ABO and Rh (D) blood group. Three test wells are labelled "Anti-A," "Anti-B," and "Anti-D," each containing specific antibodies that react with their corresponding antigens on red blood cells. In the sample, agglutination—visible clumping of red blood cells—is observed in the Anti-A and Anti-D wells but not in the Anti-B well. The presence of agglutination indicates that the corresponding antigen is present on the red blood cells. Therefore, this sample is identified as blood type A positive (A plus), meaning the cells have A and Rh (D) antigens but lack the B antigen.

Figure 18.1

This image shows the anatomical position of the heart within the thoracic cavity. The large colour diagram depicts a frontal section through the chest, showing the heart centred between the lungs within the mediastinum, bordered laterally by the right and left lungs and inferiorly by the diaphragm. The superior and inferior venae cavae deliver deoxygenated blood to the right atrium, while the pulmonary trunk and arch of the aorta emerge from the superior aspect of the heart. The right and left auricles and ventricles are visible, and the pericardial cavity surrounds the heart. The smaller sagittal view illustrates the heart's position relative to the trachea, thymus, aortic arch, esophagus, diaphragm, and thoracic aorta, emphasizing its location behind the sternum and slightly to the left of the midline.

Figure 18.2

This image illustrates the flow of blood through the pulmonary and systemic circuits of the cardiovascular system. The upper diagram shows the internal structure of the heart with labelled chambers, valves, and major vessels. Deoxygenated blood enters the right atrium through the superior and inferior venae cavae, passes through the tricuspid valve into the right ventricle, and is pumped through the pulmonary semilunar valve into the pulmonary trunk, which branches into the right and left pulmonary arteries leading to the lungs. Oxygenated blood returns to the left atrium via the pulmonary veins, flows through the mitral valve into the left ventricle, and exits through the aortic semilunar valve into the aorta for distribution to the body. The lower diagram shows the complete circulation through the human body: Blue vessels represent the pulmonary circuit carrying deoxygenated blood to the lungs, while red vessels represent the systemic circuit delivering oxygenated blood to tissues throughout the upper and lower body before returning to the heart.

Figure 18.4

The image shows anterior and posterior views of the heart with labelled vessels, arteries, and veins. In the anterior view, the labelled parts include the brachiocephalic trunk, left common carotid artery, left subclavian artery, aortic arch, ascending aorta, pulmonary trunk, right and left pulmonary arteries, right and left pulmonary veins, superior vena cava, and inferior vena cava. On the right side of the heart are the right atrium, right auricle, right ventricle, right coronary artery, right marginal artery, small cardiac vein, and anterior cardiac vein. On the left side are

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the left atrium, auricle of the left atrium, left ventricle, left coronary artery, circumflex artery, great cardiac vein, and anterior interventricular artery. Additional structures shown include the ligamentum arteriosum and the apex of the heart. In the posterior view, the labelled parts include the aorta, superior and inferior venae cavae, right and left pulmonary arteries, and right and left pulmonary veins. On the right side are the right atrium, right ventricle, right coronary artery, posterior interventricular artery, small cardiac vein, and middle cardiac vein. On the left side are the left atrium, auricle of the left atrium, left ventricle, circumflex branch of the left coronary artery, great cardiac vein, posterior vein of the left ventricle, and coronary sinus, with the apex also visible.

Figure 18.7

The image shows an anterior view of the heart, labelled with external and internal anatomical structures. At the top are the aorta, superior vena cava, and pulmonary trunk branching into the right and left pulmonary arteries. The right side includes the right pulmonary veins, right atrium, fossa ovalis, tricuspid valve, right ventricle, chordae tendineae, trabeculae carneae, moderator band, and inferior vena cava. The left side shows the left pulmonary veins, left atrium, mitral (bicuspid) valve, left ventricle, papillary muscle, and interventricular septum. The pulmonary valve and aortic valve are positioned near the centre. The heart wall layers—epicardium, myocardium, and endocardium—are also labelled.

Figure 18.12

The image shows the coronary circulation of the heart in anterior and posterior views. In the anterior view, labelled structures include the aortic arch, ascending aorta, right and left coronary arteries, pulmonary trunk, circumflex artery, anterior interventricular artery, great cardiac vein, right atrium, atrial arteries, anterior cardiac veins, small cardiac vein, and marginal artery. In the posterior view, labelled parts include the coronary sinus, small cardiac vein, circumflex artery, great cardiac vein, marginal artery, posterior interventricular artery, posterior cardiac vein, left ventricle, middle cardiac vein, and right coronary artery.

Figure 18.13

The image shows the structure of cardiac muscle cells and their interconnections. Panel A depicts cardiac muscle fibres with labelled intercalated discs, nuclei, mitochondria, and gap junctions connecting adjacent cells. Panel B presents a micrograph highlighting intercalated discs between striated muscle fibres. Panel C provides a close-up view of the intercalated disc region, showing desmosomes that anchor cells, gap junctions that facilitate electrical connectivity, and A and I bands representing striated sarcomere regions.

Figure 18.14

The image shows the conduction system of the heart in a frontal section. Labelled structures include the sinoatrial (SA) node; the anterior, middle, and posterior internodal pathways; and the atrioventricular (AV) node within the right atrium. The AV bundle (bundle of His) extends into the interventricular septum, dividing into right and left bundle branches that lead to the Purkinje fibres along the ventricular walls. The diagram also labels the arch of the aorta, Bachman's bundle connecting to the left atrium, the right atrium, the right ventricle, and the left ventricle.

Figure 18.15

The graph shows the pacemaker action potential of cardiac autorhythmic cells, with membrane potential (in millivolts) on the y-axis and time (in seconds) on the x-axis. The trace includes

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three labelled phases: the slow influx of sodium ions (Na plus) during the prepotential phase, the rapid influx of calcium ions (Ca2 plus) causing depolarization, and the outflux of potassium ions (K plus) leading to repolarization. A dashed line indicates the threshold potential around negative 40 millivolts, and the membrane potential oscillates between approximately negative 60 millivolts and positive 20 millivolts.

Figure 18.16

The image illustrates the cardiac muscle cell action potential and compares it with skeletal muscle. Panel A shows the phases of the cardiac action potential: rapid depolarization caused by sodium (Na plus) influx, a plateau phase from slow calcium (Ca2 plus) influx while Na plus channels close, and repolarization as Ca2 plus channels close and potassium (K plus) channels open. The graph also indicates absolute and relative refractory periods. Panel B compares skeletal and cardiac muscle, showing that skeletal muscle has a short action potential and contraction, whereas cardiac muscle has a longer action potential and contraction due to the extended plateau phase.

Figure 18.17

The image shows a standard electrocardiogram (ECG) trace with labelled waves, intervals, and segments. The top section displays repeating ECG cycles over a one-second interval, while the enlarged lower section highlights individual components: the P wave representing atrial depolarization, the QRS complex representing ventricular depolarization, and the T wave representing ventricular repolarization. Labelled intervals include the PR interval between the P and Q waves and the QT interval from Q to T, while the PR and ST segments indicate periods between depolarization and repolarization events. The y-axis shows voltage in millivolts, and the x-axis represents time.

Figure 18.18

The diagram illustrates the cardiac conduction cycle through six stages, each linked to an electrocardiogram (ECG) waveform segment. Stage one shows the resting heart before depolarization. In stage two, the sinoatrial (SA) node fires, initiating atrial depolarization, represented by the P wave. Stage three shows full atrial depolarization as impulses reach the atrioventricular (AV) node. In stage four, depolarization spreads through the AV bundle and bundle branches, producing the QRS complex as ventricles depolarize. Stage five depicts complete ventricular depolarization, and stage six shows ventricular repolarization associated with the T wave, completing one heartbeat before returning to rest. Red arrows indicate the sequence of electrical activation through the heart.

Figure 18.19

The diagram shows the cardiac cycle, linking mechanical heart activity with electrical signals on an ECG. The cycle begins with ventricular filling during late ventricular diastole, followed by atrial contraction marking atrial systole, associated with the P wave. Next is isovolumic contraction at the start of ventricular systole, leading to ventricular contraction and ejection phases corresponding to the QRS complex as blood is pumped out of the ventricles. The cycle concludes with isovolumic relaxation during early ventricular diastole, associated with the T wave as the ventricles repolarize. Purple arrows indicate the sequence of events through atrial and ventricular systole and diastole.

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Figure 18.20

The diagram illustrates one cardiac cycle, showing the relationship between the electrocardiogram (ECG) waveform and the mechanical phases of atrial and ventricular activity. The P wave corresponds to atrial systole, during which the atria contract. The QRS complex represents ventricular systole, or contraction, as the ventricles depolarize and pump blood. The T wave marks ventricular diastole, or relaxation, as the ventricles repolarize. Below the ECG, colour-coded bars indicate alternating periods of atrial systole and diastole (orange) and ventricular systole and diastole (green), demonstrating how the chambers contract and relax in a coordinated sequence to complete one full cardiac cycle.

Figure 18.21

The diagram shows the relationship between pressure changes in the atria, ventricles, and aorta during one cardiac cycle, along with corresponding heart sounds. Atrial pressure (orange) remains low, ventricular pressure (green) rises sharply during systole, and aortic pressure (red) increases as the semilunar valves open. The first heart sound, "lub," occurs when the atrioventricular (AV) valves close at the start of ventricular systole. The second sound, "dub," occurs when the semilunar valves close, marking the onset of ventricular diastole. The brief third sound is linked to ventricular filling. Valve opening and closing events are indicated along the curves, showing how pressure dynamics coordinate with the heart's rhythmic sounds.

Figure 18.23

The diagram summarizes the factors that influence cardiac output (CO), which equals heart rate (HR) multiplied by stroke volume (SV). Factors affecting heart rate include autonomic innervation, hormones, fitness levels, and age. Factors affecting stroke volume include heart size, fitness levels, gender, contractility, duration of contraction, preload (end-diastolic volume, EDV), and afterload (resistance). Stroke volume is calculated as the difference between EDV and end-systolic volume (ESV). Together, HR and SV determine overall cardiac output, representing the volume of blood pumped by the heart per minute.

Figure 18.25

The diagram shows how autonomic stimulation affects cardiac pacemaker activity through changes in membrane potential over time. In the normal (resting) state, spontaneous depolarization, or prepotential, triggers regular action potentials. During parasympathetic stimulation, hyperpolarization and slower depolarization occur, decreasing heart rate. Under sympathetic stimulation, reduced repolarization and faster depolarization lead to more frequent action potentials, increasing heart rate. The graphs illustrate how autonomic control adjusts heart rhythm by modulating the rate of depolarization in pacemaker cells.

Figure 18.26

The diagram illustrates the interconnected factors that regulate cardiac output (CO), defined as heart rate (HR) multiplied by stroke volume (SV). Heart rate is influenced by autonomic innervation, hormones, and the atrial reflex. Stroke volume is determined by three main factors—preload, contractility, and afterload. Preload is affected by venous return and filling time, while contractility depends on autonomic innervation and hormones. Afterload is influenced by vasodilation or vasoconstriction. Preload contributes to end-diastolic volume (EDV), and both contractility and afterload affect end-systolic volume (ESV). Stroke volume is calculated as EDV minus ESV, and together with heart rate, these mechanisms determine total cardiac output.

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Figure 19.1

The diagram illustrates the pathways of pulmonary and systemic circulation. In pulmonary circulation, deoxygenated blood flows from the heart through the pulmonary artery to the lungs, where gas exchange occurs, and oxygenated blood returns via the pulmonary veins. In systemic circulation, oxygenated blood is pumped from the heart through the aorta to the upper body, liver, stomach, intestines, kidneys, and lower body. Blood passes through arteries, capillaries, and veins—shown in red for oxygenated, blue for deoxygenated, and purple for gas exchange vessels—before returning via the vena cava. Key labelled structures include the pulmonary artery and vein, aorta, vena cava, hepatic artery and vein, hepatic portal vein, renal artery and vein, and organs such as the lungs, liver, kidneys, and digestive tract.

Figure 19.2

The image compares the structure of arteries and veins in both diagrams and a histological view. The artery wall shows three layers: the tunica intima, tunica media, and tunica externa. It includes an endothelium, elastic fibres, internal and external elastic membranes, smooth muscle, vasa vasorum, and nervi vasorum, indicating a thick, elastic, and muscular structure. The vein wall also consists of the same three layers but has a thinner tunica media, less smooth muscle and elastic tissue, and a larger lumen. The vasa vasorum and endothelium are visible, but the elastic membranes are less distinct. The histological section shows the artery with a thick, circular wall and narrow lumen, while the vein appears thinner-walled and irregular, demonstrating structural differences suited to their functions in blood transport.

Figure 19.3

The diagram compares the wall structures of an elastic artery, muscular artery, and arteriole. All three have three layers: tunica intima, tunica media, and tunica externa. The elastic artery has a thick tunica media rich in elastic fibres that allow it to stretch and recoil with blood pressure changes. The muscular artery has a smaller proportion of elastic fibres and a thicker tunica media composed mainly of smooth muscle for regulating blood flow through vasoconstriction and vasodilation. The arteriole has the thinnest wall, with only a few layers of smooth muscle in the tunica media and a thin tunica externa, allowing fine control of blood flow into capillary networks.

Figure 19.7

The image is a line graph showing changes in blood pressure throughout the circulatory system. The y-axis represents pressure in millimetres of mercury from 0 to 120, and the x-axis shows vessel types from left to right: aorta, elastic arteries, muscular arteries, arterioles, capillaries, venules, medium and large veins, and venae cavae. The graph includes three labelled curves: systolic pressure (upper line), mean arterial pressure (middle line), and diastolic pressure (lower line). Pulse pressure is indicated on the left side, and the oscillations of the systolic and diastolic lines gradually decrease as blood moves from the arteries through the veins.

Figure 19.9

The image is a graph showing how blood pressure is measured using Korotkoff sounds. The y-axis represents pressure in millimetres of mercury from 60 to 140, and the x-axis represents time. A red line shows oscillating blood pressure waves, while a gray line indicates cuff pressure decreasing over time. Two dashed vertical lines mark key points: The first sound heard corresponds to systolic blood pressure, and the last sound heard corresponds to

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diastolic blood pressure. Below the graph, a series of black spikes labelled “Korotkoff sounds in stethoscope” align with the period between the systolic and diastolic pressure markers.

Figure 19.10

The image contains four line graphs comparing properties of blood vessels across different types. Graph A shows vessel diameter, which decreases from elastic arteries to capillaries and then increases through veins to the venae cavae. Graph B shows total cross-sectional area, which remains low through arteries, peaks sharply at capillaries, and decreases again toward the veins. Graph C shows average blood pressure, starting high in elastic arteries and steadily declining through veins. Graph D shows velocity of blood flow, which is high in arteries, slows significantly at capillaries, and increases again in veins.

Figure 19.12

The image illustrates capillary fluid exchange along three regions of a capillary: the arterial end, mid-capillary, and venous end. On the left, labelled “Filtration,” a large red upward arrow shows fluid exiting the capillary. The arterial end has a net filtration pressure of positive 10 millimetres of mercury because capillary hydrostatic pressure (35 millimetres of mercury) exceeds blood colloidal osmotic pressure (25 millimetres of mercury). In the centre, labelled “No net movement,” a purple upward arrow indicates equilibrium, with net filtration pressure at 0 millimetres of mercury as both pressures equal 25 millimetres of mercury. On the right, labelled “Reabsorption,” a large blue downward arrow shows fluid reentering the capillary. The venous end has a net filtration pressure of negative 7 millimetres of mercury because capillary hydrostatic pressure (18 millimetres of mercury) is less than blood colloidal osmotic pressure (25 millimetres of mercury).

Figure 19.13

The image is a flowchart showing the mechanisms regulating blood flow and pressure through autoregulation, neural mechanisms, and endocrine control. The top section, labelled “Autoregulation,” begins with normal resting conditions, where changes to blood flow detected by local receptors lead to either vasodilation or vasoconstriction. Vasodilators, such as decreased O2, increased CO2, metabolic acids, nitric oxide, potassium, hydrogen ions, inflammation, and increased body temperature, relax precapillary sphincters to increase blood flow, while vasoconstrictors, like prostaglandins and products from activated platelets, leukocytes, and endothelins, constrict sphincters to decrease flow. Both lead to restored homeostasis. The middle section, “Neural and endocrine mechanisms,” divides into neural and endocrine pathways. The neural mechanism influences blood pressure and blood chemistry through cardiac and vasomotor centres. Sympathetic stimulation increases cardiac output and blood flow, parasympathetic stimulation decreases them, and specific neurotransmitters cause vasoconstriction or vasodilation, leading to homeostasis restoration. The endocrine control section shows renal, adrenal, brain, and heart inputs producing hormones such as erythropoietin, renin, angiotensin, aldosterone, catecholamines, antidiuretic hormone, and atrial natriuretic hormone, which regulate blood volume, pressure, and vessel tone via vasoconstriction or vasodilation.

Figure 19.14

The image is a flowchart showing how baroreceptor reflexes regulate blood pressure to maintain homeostasis. The top half illustrates the response to increased blood pressure: Elevated blood pressure increases baroreceptor firing, which stimulates cardiac inhibitor

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centres while inhibiting cardiac accelerator and vasomotor centres. This decreases cardiac output (heart rate and stroke volume) and causes vasodilation, resulting in a drop in blood pressure and the restoration of homeostasis. The bottom half shows the response to decreased blood pressure: Reduced blood pressure lowers baroreceptor firing, decreasing activity in cardiac inhibitor centres and increasing activity in cardiac accelerator and vasomotor centres. This raises cardiac output and causes vasoconstriction, which increases blood pressure and restores homeostasis.

Figure 19.15

The flowchart depicts the short-term and long-term responses to decreased blood pressure and/or volume. In the short-term pathway, decreased blood pressure and volume trigger sympathetic activation, causing the adrenal glands to release epinephrine and norepinephrine, which increase cardiac output and peripheral vasoconstriction. These changes raise blood pressure, restoring homeostasis. In the long-term pathway, decreased blood pressure and volume cause the kidneys to produce renin and erythropoietin. Renin activates angiotensin II, leading to the release of antidiuretic hormone and secretion of aldosterone, as well as stimulation of thirst. These processes increase blood volume, while erythropoietin increases red blood cell formation, further increasing blood volume. The resulting rise in blood volume contributes to the restoration of homeostasis.

Figure 19.16

The flowchart depicts mechanisms that respond to decreased blood pressure and volume. The response divides into endocrine and neural mechanisms. The endocrine mechanism releases antidiuretic hormone (ADH), angiotensin II, aldosterone, and erythropoietin (EPO), which increase blood volume, leading to restoration of homeostasis. The neural mechanism stimulates baroreceptors and chemoreceptors, which activate cardiovascular centres and trigger general sympathetic activation, causing the release of norepinephrine and epinephrine. These actions increase cardiac output, cause peripheral vasoconstriction, raise blood pressure, and reduce venous reserve, ultimately restoring homeostasis.

Figure 19.17

The diagram shows the pulmonary circulation within the thoracic cavity, including the heart and lungs. The superior and inferior vena cavae carry deoxygenated blood into the right atrium of the heart, which then passes through the right ventricle and into the pulmonary trunk. The trunk branches into right and left pulmonary arteries that extend to the right and left lungs. Within each lung, the arteries branch into smaller vessels leading to the pulmonary capillaries, shown in a magnified inset where red and blue vessels intertwine. Oxygenated blood returns from the lungs through the right and left pulmonary veins to the left atrium of the heart. The ascending aorta and aortic arch emerge from the left ventricle and continue as the descending aorta.

Figure 19.18

The image shows an anterior view of a human body, highlighting the major systemic arteries in red, with labels identifying key vessels throughout the body. In the head and neck, the vertebral, right subclavian, right common carotid, left common carotid, and left subclavian arteries are labelled. The thoracic region includes the brachiocephalic trunk, aortic arch, ascending aorta, pulmonary trunk, axillary artery, and descending aorta. The abdominal region features the celiac trunk, diaphragm, renal arteries, superior mesenteric, gonadal, and inferior

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mesenteric arteries. The pelvis and lower limbs show the common iliac, internal iliac, and external iliac arteries branching into the femoral and deep femoral arteries. Farther down the leg, the descending genicular, popliteal, posterior tibial, anterior tibial, fibular, dorsalis pedis, and plantar arch arteries are identified. In the upper limbs, the brachial, radial, ulnar, and palmar arch arteries are labelled, showing the arterial network extending into the hands.

Figure 19.19

The image shows the major arteries branching from the aorta. The ascending aorta extends upward from the heart and gives rise to the right and left coronary arteries. The vessel curves into the aortic arch, from which the brachiocephalic artery, left common carotid artery, and left subclavian artery emerge. The brachiocephalic artery branches into the right subclavian and right common carotid arteries. Below the arch, the aorta continues as the descending aorta, which becomes the thoracic aorta and then the abdominal aorta.

Figure 19.20

The illustration shows arteries of the head and neck in a right lateral view, with vessels highlighted in red. The common carotid artery ascends along the neck and divides into the internal and external carotid arteries. The internal carotid extends upward toward the skull, while the external carotid branches into the occipital, lingual, facial, maxillary, and superficial temporal arteries. The carotid sinus is located at the base of the internal carotid. The vertebral artery runs upward through the cervical vertebrae, contributing to the blood supply of the brain.

Figure 19.21

The diagram shows the thoracic and abdominal aorta with major arterial branches. From the aortic arch, the thoracic aorta descends through the chest, giving rise to parietal branches, including the intercostal and superior phrenic arteries, and visceral branches, including the bronchial, esophageal, mediastinal, and pericardial arteries. The thoracic aorta passes through the diaphragm via the aortic hiatus to become the abdominal aorta. Below the diaphragm, branches include the inferior phrenic, adrenal, renal, gonadal, lumbar, and median sacral arteries. The celiac trunk divides into the left gastric, splenic, and common hepatic arteries, with the superior and inferior mesenteric arteries branching farther down. The abdominal aorta terminates by dividing into the common iliac arteries, which branch into internal and external iliac arteries.

Figure 19.22

The diagram lists unpaired and paired arterial branches of the thoracic and abdominal aorta along with their target structures. From the thoracic aorta, unpaired branches include the bronchial arteries supplying air passages and lung tissue, pericardial arteries supplying the pericardium, esophageal arteries supplying the esophagus, and mediastinal arteries supplying mediastinal structures. Paired thoracic branches include the intercostal arteries supplying vertebrae, spinal cord, back muscles, body wall, and skin, and the superior phrenic arteries supplying similar regions and the diaphragm. From the abdominal aorta, unpaired branches include the left gastric, splenic, and common hepatic arteries forming the celiac trunk, which supplies the stomach, spleen, pancreas, liver, gallbladder, duodenum, and part of the esophagus. The superior mesenteric artery supplies the pancreas, small intestine, appendix, and most of the large intestine, while the inferior mesenteric artery supplies the last third of the large intestine. Paired abdominal branches include the inferior phrenic arteries to the diaphragm and lower esophagus, adrenal arteries to the adrenal glands, renal arteries to the

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kidneys, gonadal arteries to the testes or ovaries, and lumbar arteries to the vertebrae, spinal cord, abdominal wall, and lumbar region. The diagram ends with the median sacral artery and the paired common iliac arteries branching from the lower abdominal aorta.

Figure 19.23

The diagram depicts arterial branches of the abdominal aorta, focusing on the iliac arteries and their major subdivisions. The abdominal aorta divides into the right and left common iliac arteries, with the left side following the same pattern as the right. The median sacral artery extends downward from the aortic bifurcation. The right common iliac supplies the pelvis and right lower limb and divides into the right external and right internal iliac arteries. The right external iliac continues to the right lower limb. The right internal iliac supplies pelvic muscles, skin, pelvic viscera, perineum, gluteal region, and medial thigh and branches into the superior gluteal, obturator, internal pudendal, and lateral sacral arteries. The superior gluteal supplies hip muscles and the hip joint; the obturator supplies the ilium, hip and thigh muscles, hip joint, and femoral head; the internal pudendal supplies the rectum, anus, perineal muscles, external genitalia, and lateral rotators of the hip; and the lateral sacral supplies the skin and muscles of the sacrum.

Figure 19.24

The image shows the arterial network of the right arm. The right subclavian artery continues into the axillary artery, which gives rise to the humeral circumflex and deep brachial arteries. The brachial artery extends along the upper arm, branching into the ulnar collateral artery near the elbow. In the forearm, the radial and ulnar arteries run parallel, joined by the anterior crural interosseous artery between them. Near the wrist, the radial and ulnar arteries contribute to the deep and superficial palmar arches, which give rise to the digital arteries that supply the fingers.

Figure 19.25

The diagram illustrates arterial branches from the aortic arch supplying the upper body and arms. The aortic arch arises from the left ventricle and gives rise to the brachiocephalic trunk, left common carotid, and left subclavian arteries. The brachiocephalic trunk divides into the right common carotid and right subclavian arteries. Each subclavian gives rise to the vertebral artery, thyrocervical trunk, and internal thoracic artery. The vertebral arteries ascend to supply the spinal cord and cervical vertebrae, joining within the cranium to form the basilar artery. The thyrocervical trunks supply the muscles, tissues, and skin of the neck and the thyroid gland, shoulders, and upper back. The internal thoracic arteries supply the skin and muscles of the chest and the abdomen, mammary glands, and pericardium. Each subclavian continues as the axillary artery, which supplies the pectoral and axilla muscles, then becomes the brachial artery, supplying the arm and elbow. The brachial artery divides into the radial and ulnar arteries, which run along the respective sides of the forearm and join in the hand to form the digital arteries.

Figure 19.26

The image shows anterior and posterior views of the arteries of the leg. In the anterior view, the common, external, and internal iliac arteries are visible at the upper pelvis, with branches including the lateral sacral, internal pudendal, and obturator arteries. The femoral artery extends down the thigh, giving rise to the deep femoral and lateral femoral circumflex arteries, then continues as the genicular and popliteal arteries near the knee. Below the knee, the

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anterior tibial, posterior tibial, and fibular arteries supply the lower leg, ending in the dorsalis pedis and dorsal arch at the foot. In the posterior view, the same major vessels are shown from behind, with the peroneal artery accompanying the tibial arteries down the leg and branching into the lateral and medial plantar arteries, which connect to the plantar arch in the foot.

Figure 19.27

The diagram outlines the arterial branches of the lower limb originating from the external iliac artery. The external iliac continues as the femoral artery, which supplies the thigh and gives rise to the descending genicular artery for the knee joint and leg skin. The deep femoral artery branches from the femoral and supplies the hip joint, femoral head, and deep thigh muscles. From the deep femoral artery, the median femoral circumflex artery supplies the adductor and obturator muscles and the hip joint, while the lateral femoral circumflex artery supplies the quadriceps muscles. The femoral artery continues as the popliteal artery, which supplies the leg and foot and divides into the anterior and posterior tibial arteries. The anterior tibial leads to the dorsalis pedis, dorsal arch, and plantar arch, which connect to the dorsal metatarsal and dorsal digital arteries supplying the distal foot and toes. The posterior tibial gives rise to the fibular and peroneal arteries, which also contribute to the lower leg and foot circulation.

Figure 19.28

The image shows an anterior view of the human body, highlighting the systemic veins in blue. In the head and neck, the external and internal jugular veins drain into the subclavian and brachiocephalic veins, which merge into the superior vena cava. The thoracic region includes the intercostal and hepatic veins connecting to the inferior vena cava. The upper limbs show the cephalic, basilic, brachial, axillary, and subclavian veins, with additional branches including the radial, ulnar, median antebrachial, and median cubital veins, as well as the palmar venous arches and digital veins in the hands. In the abdominal region, the renal, gonadal, and lumbar veins drain into the inferior vena cava. The pelvis and lower limbs feature the right and left common, external, and internal iliac veins, which connect to the femoral and deep femoral veins. The great saphenous, small saphenous, popliteal, fibular, anterior tibial, and posterior tibial veins continue down the legs, leading to the plantar and dorsal venous arches of the feet.

Figure 19.29

The image shows the major veins of the thoracic and abdominal regions in blue. The superior vena cava receives blood from the vertebral, internal jugular, external jugular, subclavian, brachiocephalic, axillary, and cephalic veins. Within the thorax, the mediastinal, esophageal, internal thoracic, intercostal, azygos, and hemiazygos veins drain into the superior vena cava. The inferior vena cava ascends through the abdomen, collecting blood from the hepatic, phrenic, adrenal, renal, gonadal, lumbar, and common iliac veins. The common iliac veins divide into internal and external iliac branches, which drain blood from the pelvis and lower limbs. The kidneys and adrenal glands are positioned on either side of the inferior vena cava, with their respective veins connecting directly to it.

Figure 19.30

The illustration shows the major veins of the head and neck in a right lateral view, highlighting venous sinuses and drainage pathways in blue. The superior and inferior sagittal sinuses, straight sinus, and occipital sinus converge posteriorly, connecting to the right transverse and sigmoid sinuses. The petrosal sinus links the cavernous sinus, located near the base of the skull,

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with the internal jugular vein. Additional labelled veins include the temporal, maxillary, facial, external jugular, and vertebral veins. The internal jugular vein descends alongside the neck to join the right subclavian vein, forming the superior vena cava via the brachiocephalic vein.

Figure 19.31

The image shows the superficial and deep veins of the right arm, indicated by different shades of blue. The superficial veins, shown in light blue, include the cephalic, basilic, median cubital, and median antebrachial veins, along with the palmar venous arches and digital veins in the hand. The deep veins, shown in dark blue, include the radial, ulnar, brachial, subscapular, axillary, and subclavian veins. The cephalic vein runs along the lateral side of the arm, while the basilic vein runs medially. The median cubital vein connects the cephalic and basilic veins near the elbow. Both superficial and deep veins drain blood from the hand and forearm into larger vessels that return to the subclavian vein near the shoulder.

Figure 19.32

The diagram illustrates major veins of the upper body and their drainage pathways leading to the superior vena cava. The right and left brachiocephalic veins converge into the superior vena cava, which empties into the right atrium. Each brachiocephalic vein receives blood from the vertebral, internal jugular, external jugular, subclavian, and internal thoracic veins. The vertebral veins collect blood from the cranium, spinal cord, and vertebrae, while the internal and external jugular veins drain the cranium, face, neck, scalp, and salivary glands. The subclavian veins collect blood from the upper limbs, with the left side detailed further: The axillary vein receives the cephalic and basilic veins, draining the lateral and medial surfaces of the arm, respectively, through the median cubital and median antebrachial veins. The internal thoracic veins collect blood from the anterior thoracic wall. Additional veins include the azygos and hemiazygos veins, which drain the intercostal and esophageal veins from the vertebrae, body wall, and esophagus, joining the superior vena cava through mediastinal connections.

Figure 19.33

The diagram shows the major veins draining into the inferior vena cava and their associated regions. The inferior vena cava carries blood to the right atrium and receives contributions from the hepatic veins draining the liver, the phrenic veins draining the diaphragm, the adrenal veins draining the adrenal glands, the renal veins draining the kidneys, the gonadal veins draining the testes or ovaries, and the lumbar veins draining the spinal cord and body wall. Below these, the right and left common iliac veins merge to form the inferior vena cava. Each common iliac divides into external and internal iliac veins. The external iliac veins drain the lower limbs, while the internal iliac veins drain pelvic muscles, skin, pelvic viscera, the perineum, and the gluteal region. The internal iliac veins give rise to the superior gluteal, internal pudendal, obturator, and lateral sacral veins, which return blood from their respective areas.

Figure 19.34

The image shows anterior and posterior views of the veins of the leg. In the anterior view, major veins include the common, external, and internal iliac veins, along with the gluteal, lateral sacral, internal pudendal, obturator, femoral, deep femoral, and femoral circumflex veins. The femoral vein continues downward to the popliteal vein behind the knee, which receives the great and small saphenous veins. Below the knee, the anterior tibial, posterior tibial, and fibular veins drain the lower leg. The foot contains the dorsal venous arch and digital veins. In the posterior view, the same veins are visible from behind, with the addition

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of the lateral and medial plantar veins and the plantar venous arch in the foot, which merge into the posterior tibial vein.

Figure 19.35

The diagram outlines the major veins of the lower limb and their connections. The external iliac vein continues as the femoral vein, which receives blood from the deep femoral vein draining the thigh and the great saphenous vein collecting blood from the superficial veins of the lower limb. The small saphenous vein joins the popliteal vein, which collects blood from the superficial veins of the leg and foot. The popliteal vein divides into the anterior tibial, posterior tibial, and fibular veins. These veins drain into the lateral and medial plantar veins as well as the dorsal and plantar arches of the foot. The metatarsal and digital veins collect blood from the distal foot and toes, feeding into these arches and then upward through the tibial and fibular veins.

Figure 19.36

The image shows the hepatic portal system and its associated veins draining the digestive organs. The hepatic portal vein, shown in black, receives blood from the superior mesenteric, splenic, and inferior mesenteric veins. The superior mesenteric vein, coloured green, drains the small intestine and portions of the large intestine through the intestinal, ileocolic, right colic, middle colic, pancreaticoduodenal, and gastro-omental veins. The splenic vein, shown in orange, collects blood from the spleen and receives the pancreatic and gastroepiploic veins. The inferior mesenteric vein, shown in purple, drains the distal portion of the large intestine through the superior rectal, sigmoid, and left colic veins. The hepatic portal vein also connects with the right gastric and cystic veins from the stomach and gallbladder. Blood from these vessels ultimately flows to the liver for processing before entering systemic circulation.

Figure 19.37

The image shows fetal circulation with labelled vessels and shunts. The umbilical vein carries oxygenated blood from the placenta to the fetus, where it passes through the ductus venosus into the inferior vena cava. Blood enters the right atrium and moves through the foramen ovale into the left atrium, then into the aorta for systemic circulation. Some blood flows from the pulmonary trunk through the ductus arteriosus into the aorta. Deoxygenated blood returns to the placenta through the paired umbilical arteries branching from the internal iliac arteries. The placenta, bladder, aorta, and major fetal vessels are shown in context.

Figure 20.1

The image shows the human lymphatic system with major organs, vessels, and structures highlighted. Green lymphatic vessels extend throughout the body, connecting lymph nodes, the spleen, thymus, and tonsils. The adenoid and tonsil are located in the head, the thymus in the upper chest, and the spleen in the upper left abdomen. The right lymphatic duct enters a large vein near the shoulder, returning lymph to circulation. The bone marrow in the leg is shown as a source of immune cells. Insets display the thymus as a lobed gland, a lymph node with labelled masses of lymphocytes and macrophages, and a close-up of tissue showing lymphatic capillaries, blood capillaries, interstitial fluid, and tissue cells.

Figure 20.2

The image shows lymph capillaries within tissue spaces and their relationship to surrounding structures. On the left, red arterioles, blue venules, and green lymphatic vessels are shown

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among tissue cells. Lymph capillaries collect tissue fluid that enters through overlapping endothelial flaps. The inset magnifies a section of lymphatic capillary, showing collagen fibres anchoring it to tissue, interstitial fluid between cells, lymph vessel endothelial cells forming one-way valves, and backflow prevention valves ensuring unidirectional lymph flow. Arrows indicate the movement of tissue fluid into the lymph capillary and through the lymphatic vessel.

Figure 20.3

The image shows the regions of the body drained by the right lymphatic duct and the thoracic duct. The right lymphatic duct, shown draining the upper right portion of the body shaded in purple, empties into the junction of the right subclavian and right internal jugular veins. The thoracic duct, shown in green, drains the remainder of the body and empties into the junction of the left subclavian and left internal jugular veins. The thoracic duct originates from the cisterna chyli, located near the lower abdomen. Insets show close-up views of each duct entering the subclavian veins on the right and left sides.

Figure 20.4

The diagram shows the development of blood cells from a multipotent hematopoietic stem cell, also called a hemocytoblast. After division, some cells remain stem cells, while others differentiate based on chemical signals into two main lineages: myeloid and lymphoid stem cells. The myeloid stem cell gives rise to megakaryoblasts, proerythroblasts, myeloblasts, and monoblasts. Megakaryoblasts form megakaryocytes, which produce platelets. Proerythroblasts become reticulocytes and then mature erythrocytes. Myeloblasts differentiate into basophils, neutrophils, and eosinophils, while monoblasts form monocytes that mature into macrophages. The lymphoid stem cell forms lymphoblasts, which give rise to natural killer cells and small lymphocytes. Small lymphocytes differentiate into T lymphocytes and B lymphocytes, with B lymphocytes further developing into plasma cells.

Figure 20.6

The image shows the lymphatic and immune structures of the upper body, along with thymus anatomy and microscopic details. The human figure depicts lymphatic vessels in green connecting the adenoids, tonsils, thymus, lymph nodes, spleen, and right lymphatic duct entering a large vein near the heart. The upper inset shows a histological section of the thymus with labelled cortex, medulla, trabeculae, and fibrous capsule. The lower inset illustrates thymic microanatomy, showing cortical epithelial cells, thymocytes, dendritic cells, macrophages, medullary epithelial cells, trabeculae, and blood vessels organized within the cortex and medulla beneath a fibrous capsule.

Figure 20.7

The image shows the structure of a lymph node through a histological section and a labelled diagram. The left side displays a microscope view with purple-stained tissue, identifying the connective tissue capsule, cortex, subcapsular sinus, and germinal centres. The accompanying diagram on the right depicts a cutaway view of a lymph node, showing afferent lymphatic vessels entering the node, the subcapsular sinus beneath the capsule, trabeculae extending inward, germinal centres within the cortex, and efferent lymphatic vessels exiting the node. The connective tissue capsule surrounds the entire node, maintaining its structure.

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Figure 20.8

The image shows the structure and histology of the spleen. In part A, a human figure indicates the spleen's location near the diaphragm, with a labelled cross-section showing the hilum, splenic artery, and splenic vein. A detailed view of splenic tissue illustrates red pulp, white pulp, trabeculae, arterioles, and venules. In part B, a magnified histological section shows the spleen's internal organization, including trabeculae, a marginal zone, central artery or arteriole, germinal centre, arterial capillaries, venous sinus, and surrounding red pulp.

Figure 20.9

The image shows the anatomy and histology of the tonsils. In part A, diagrams illustrate the locations of the pharyngeal, palatine, and lingual tonsils within the upper airway. The pharyngeal tonsil lies in the nasopharynx near the sphenoidal sinus and bone, while the palatine tonsil is located between the soft palate and tongue, and the lingual tonsil sits at the base of the tongue near the epiglottis. A photograph shows the palatine tonsils visible at the back of the throat, swollen due to infection. In part B, a histological section of the palatine tonsil shows crypts lined by stratified squamous epithelium and multiple germinal centres within lymphoid tissue.

Figure 20.11

The image illustrates innate and adaptive immunity. The upper section shows pathogens entering through the mouth and nose near the palatine tonsil. Arrows indicate the first line of innate defences, including surface barriers such as skin, hair, and mucus, and internal defences involving mast cells and basophils releasing histamine, natural killer cells, the complement system, and phagocytes such as monocytes, neutrophils, and macrophages. The lower section represents adaptive immunity in the germinal centre of a palatine tonsil, showing T lymphocytes, antigen-presenting cells, and B lymphocytes forming T effector cells, T memory cells, B effector cells, and B memory cells, with antibodies released into the surrounding area.

Figure 20.14

The image illustrates antigen processing and presentation by a dendritic cell. It begins with the dendritic cell engulfing a pathogen into a vesicle, where lysosomes release enzymes to digest it and extract antigens. These antigens bind to MHC class II proteins within the vesicle, and the MHC-antigen complexes are transported to the cell surface. The dendritic cell then displays the antigens on its membrane, allowing interaction with T cells whose receptors recognize and bind to the presented antigens, initiating an adaptive immune response.

Figure 20.15

The image illustrates the activation of cytotoxic T cells. A dendritic cell presents an antigen from a pathogen on its MHC class I protein to a naive cytotoxic T (TC) cell. The T cell receptor and CD8 molecule on the TC cell bind to the antigen-MHC complex, activating the TC cell. The activated TC cells then multiply, producing two groups: effector TC cells that destroy infected cells in the body and memory TC cells that remain to respond rapidly if the same antigen is encountered again.

Figure 20.17

The image compares the primary and secondary immune responses. On the left, the primary response begins when an antigen binds to a specific B cell receptor, activating the B cell and causing it to form clones. These clones differentiate into plasma cells, which secrete

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antibodies, and memory B cells, which remain in the body. On the right, the secondary response shows that when the same antigen is encountered again, memory B cells rapidly produce clones that generate plasma cells and antibodies in greater quantity and more quickly than in the primary response.

Figure 21.3

The image shows a sagittal section of the upper respiratory tract and surrounding structures. It labels key regions, including the nasal cavity (with nasal conchae, meatuses, and vestibule), paranasal sinuses (frontal and sphenoidal), and olfactory epithelium. The pharynx is divided into the nasopharynx, oropharynx, and laryngopharynx, with associated tonsils and the opening of the auditory tube. Lower structures include the larynx with the epiglottis, vocal and vestibular folds, thyroid and cricoid cartilages, and the hyoid bone.

Figure 21.5

The image shows the anatomy of the larynx in anterior and right lateral views. Major structures include the epiglottis, thyroid cartilage (with the laryngeal prominence), cricoid cartilage, and tracheal cartilages. Supporting membranes and ligaments include the thyrohyoid membrane, cricothyroid ligament, and cricotracheal ligament. The lateral view also shows the arytenoid, corniculate, and cuneiform cartilages as well as the vestibular and vocal folds, which are essential for voice production and airway protection.

Figure 21.15

The image illustrates lung volumes and capacities. Panel A shows a spirogram with labelled volumes: tidal volume, representing air exchanged during normal breathing; inspiratory reserve volume, the extra air that can be inhaled; expiratory reserve volume, the extra air that can be exhaled; and residual volume, the air remaining in the lungs after maximal exhalation. Panel B combines these volumes into capacities: inspiratory capacity, functional residual capacity, vital capacity, and total lung capacity, showing how different lung volumes sum together to form the total capacity of the lungs.

Figure 21.16

The image illustrates the neural control of breathing. It shows the brain stem regions involved, including the medulla and pons, with the medulla containing the ventral and dorsal respiratory groups (VRG and DRG) and the pons containing the pontine respiratory group (PRG), which includes the pneumotaxic and apneustic centres. Arrows indicate how these centres send stimulatory and inhibitory signals to regulate the diaphragm, external and internal intercostal muscles, and accessory respiratory muscles, coordinating inspiration and expiration.

Figure 21.17

The image illustrates Dalton's law of partial pressures. It shows three containers: one containing only oxygen molecules with a pressure of 159 millimetres of mercury, one containing only nitrogen molecules with a pressure of 597 millimetres of mercury, and one containing a mixture of oxygen and nitrogen molecules with a total pressure of 756 millimetres of mercury. The combined pressure in the mixed gas equals the sum of the partial pressures of oxygen and nitrogen, demonstrating that the total pressure of a gas mixture is the sum of the pressures each gas would exert independently.

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Figure 22.1

The diagram shows the human digestive system, labelling major organs and glands. Starting from the mouth, it includes the tongue, salivary glands (parotid, sublingual, and submandibular), pharynx, and esophagus, leading to the stomach. Connected organs include the liver, gallbladder, and pancreas. The intestines are divided into the small intestine (duodenum, jejunum, and ileum) and the large intestine (cecum, ascending, transverse, descending, and sigmoid colon), ending with the rectum, anal canal, and anus.

Figure 22.2

The diagram shows a cross-section of the gastrointestinal tract wall, highlighting its layers and structures. The innermost mucosa includes the epithelium, lamina propria, and muscularis mucosae surrounding the lumen, with glands and lymphatic tissue. The submucosa contains glands, the submucosal plexus (plexus of Meissner), and blood and lymphatic vessels. The muscularis layer has circular and longitudinal muscles with the myenteric plexus between them. The outermost serosa consists of areolar connective tissue and epithelium, with the mesentery containing arteries, veins, and nerves.

Figure 22.3

The diagram shows a cross-section of the abdominal cavity, identifying major organs and the peritoneal membranes. The spinal cord and vertebra are located posteriorly, with kidneys on either side, the liver and gallbladder on the left, and the spleen on the right. The pancreas lies behind the stomach, while the large and small intestines fill the central area. The visceral peritoneum covers organs, the parietal peritoneum lines the body wall, and the peritoneal cavity lies between them.

Figure 22.5

The diagram illustrates the digestive process from ingestion to defecation. Food enters through the mouth, passes the pharynx and esophagus to the stomach, and moves through the small and large intestines to the anus. Key functions are labelled: propulsion (swallowing and peristalsis), mechanical digestion (chewing, churning, and segmentation), chemical digestion (enzyme breakdown), and absorption (nutrients and water into blood and lymph vessels). The process ends with feces expelled during defecation.

Figure 22.6

The diagram shows an anterior view of the oral cavity with key structures labelled. It includes the superior and inferior lips connected by the labial frenula, gingivae (gums), and teeth (incisors, canines, premolars, and molars). The hard and soft palates form the roof, ending in the uvula. The palatoglossal and palatopharyngeal arches frame the fauces, with the palatine tonsil between them. The tongue is shown with its underside and lingual frenulum, along with the openings of the submandibular gland ducts.

Figure 22.14

The diagram shows the anatomy of the stomach, labelling its major regions and muscular layers. The stomach connects to the esophagus at the cardia and to the duodenum at the pyloric sphincter. The main sections include the fundus, body, pyloric antrum, and pyloric canal. The inner mucosa features folds called rugae, while the muscularis externa consists of three layers—longitudinal, circular, and oblique—that aid in churning and mixing food. The

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stomach's curvatures include the lesser curvature on the inner edge and the greater curvature on the outer edge.

Figure 22.15

The diagram shows the microscopic structure of the stomach wall, illustrating its four main layers: mucosa, submucosa, muscularis externa, and serosa. The mucosa contains surface epithelium, lamina propria, and muscularis mucosae, with gastric pits leading into gastric glands. These glands contain parietal cells that secrete hydrochloric acid, chief cells that produce pepsinogen, and enteroendocrine cells that release hormones. The muscularis externa includes oblique, circular, and longitudinal layers for churning and mixing, while the serosa forms the outer covering.

Figure 22.16

The diagram illustrates the three phases of gastric secretion regulation: cephalic, gastric, and intestinal. In the cephalic phase, the sight, thought, or smell of food activates the cerebral cortex and vagus nerve to stimulate gastric secretions, while loss of appetite or depression inhibits them. During the gastric phase, stomach distension and food chemicals trigger local and vagovagal reflexes and gastrin release, enhancing secretion, whereas excessive acidity or emotional stress inhibits it. In the intestinal phase, partially digested food in the duodenum briefly stimulates gastrin release, followed by inhibition through enterogastric reflexes and intestinal hormones such as secretin and cholecystokinin.

Figure 22.18

The image shows the structural organization of the small intestine, emphasizing its adaptations for nutrient absorption. Panel A illustrates the intestinal wall with circular folds, villi, and microvilli that increase surface area. Each villus contains blood vessels and a lacteal for nutrient and fat absorption, along with goblet cells for mucus secretion. The intestinal crypts and duodenal glands lie beneath the mucosal surface. Panels B and C show microscopic images of villi in tissue sections, while D displays the microvilli forming the brush border under high magnification.

Figure 22.20

The image shows the anatomy of the large intestine, labelling its major regions and structures. It begins where the ileum of the small intestine joins the cecum, which includes the vermiform appendix. From there, the ascending colon travels upward to the right colic (hepatic) flexure, across as the transverse colon, and down the descending colon to the sigmoid colon, rectum, and anal canal. The diagram highlights the large intestine's looping path around the abdominal cavity, connecting to the rectum at the lower end for waste elimination.

Figure 22.21

The image shows the structure of the large intestine. Panel A illustrates a section of the intestinal wall, showing deep intestinal glands (crypts) lined with absorptive cells that take in water and goblet cells that secrete mucus. The mucosa includes lymphatic nodules for immune defence, supported by smooth muscle fibres, the muscularis mucosae, and the submucosa. The inset diagrams highlight microvilli on absorptive cells and mucus-filled goblet cells. Panel B presents a microscopic view of the large intestine's lining, showing tightly packed tubular glands and numerous mucus-secreting goblet cells.

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Figure 22.23

The image shows the liver, gallbladder, pancreas, and associated ducts in relation to the digestive system. The liver is divided into four lobes—right, left, caudate, and quadrate. The right and left hepatic ducts merge to form the common hepatic duct, which joins the cystic duct from the gallbladder to create the common bile duct. This duct carries bile to the duodenum. The pancreas, located below and behind the stomach, connects via the pancreatic duct, which also empties into the duodenum. The spleen, shown to the left of the stomach, lies adjacent to the pancreas.

Figure 22.24

The image illustrates the microscopic structure of the liver, focusing on the hepatic lobules and blood flow. Each lobule is a hexagonal unit composed of plates of hepatocytes radiating from a central vein. Blood enters the lobule from branches of the portal vein and hepatic artery (portal venules and arterioles) located at the corners of the lobule. This blood flows through sinusoids—capillary-like channels—toward the central vein, where it eventually drains into the hepatic vein via the interlobular vein. Bile produced by hepatocytes flows in the opposite direction, from the centre toward bile ducts at the periphery. Connective tissue surrounds the lobules, and the overall organization allows efficient processing of blood and secretion of bile.

Figure 22.25

The image shows the structure and function of the pancreas, highlighting both its exocrine and endocrine components. The pancreas is divided into a head, body, and tail, with a central pancreatic duct that joins the common bile duct before emptying into the duodenum. The exocrine portion consists of lobules made up of acinar cells, which secrete digestive enzymes into the pancreatic ducts. These enzymes are essential for breaking down fats, proteins, and carbohydrates in the small intestine. The endocrine portion is represented by pancreatic islets, which contain hormone-secreting cells that release insulin, glucagon, and other hormones into the bloodstream to regulate blood glucose levels.

Figure 22.26

The image shows the gallbladder and its relationship with the liver and bile ducts. The gallbladder, located beneath the liver, is divided into three regions: the neck, body, and fundus. It stores and concentrates bile produced by the liver. Bile travels through the left and right hepatic ducts, which merge to form the common hepatic duct. The cystic duct connects the gallbladder to this duct, allowing bile to flow in and out of the gallbladder. When needed for digestion, especially after eating fatty foods, bile moves from the gallbladder through the cystic duct into the common bile duct, which delivers it to the small intestine for fat emulsification.

Figure 22.27

The illustration shows the human digestive tract and highlights the key digestive processes occurring at different stages. In the mouth, mechanical digestion involves chewing and swallowing, while chemical digestion begins with the breakdown of carbohydrates and fats. In the stomach, mechanical digestion continues through peristaltic mixing and propulsion, and chemical digestion targets proteins and fats; lipid-soluble substances like alcohol and aspirin are also absorbed here. The small intestine carries out mechanical digestion through segmentation; chemical digestion of carbohydrates, fats, polypeptides, and nucleic acids; and

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absorption of peptides, amino acids, glucose, fructose, fats, water, minerals, and vitamins. Finally, in the large intestine, mechanical digestion involves segmental mixing and propulsion, chemical digestion is limited to bacterial activity, and absorption focuses on ions, water, minerals, vitamins, and organic molecules.

Figure 22.28

The diagram illustrates the enzymatic breakdown of complex carbohydrates such as starch and glycogen into monosaccharides during digestion. Salivary amylase initiates this process by breaking starch and glycogen into short-branched polysaccharides (limit dextrins) and disaccharides like maltose, sucrose, and lactose. Limit dextrins are further digested by alpha-dextrinase into glucose. Maltose is split by maltase into two glucose molecules, sucrose is broken down by sucrase into one glucose and one fructose molecule, and lactose is digested by lactase into one glucose and one galactose molecule. The final products of carbohydrate digestion are monosaccharides—glucose, fructose, and galactose—that can be absorbed by the body.

Figure 22.29

A diagram illustrates the process of protein digestion and absorption in the human body. Protein digestion begins in the stomach, where hydrochloric acid and the enzyme pepsin break down proteins. Protein-digesting enzymes secreted from the pancreas enter the small intestine, which is the major site of protein digestion and where final digestion occurs. Additional protein-digesting enzymes are secreted from the brush border of the small intestine. Absorbed amino acids enter the bloodstream and travel to the liver, which regulates their distribution throughout the body. A small amount of dietary protein is lost in the feces. The diagram labels the liver, stomach, pancreas, and small intestine to indicate their roles in protein digestion and absorption.

Figure 22.30

This diagram illustrates water input, secretion, and reabsorption throughout the digestive system. It shows that about 2,000 milliliters of water enters the system through food and drink, while digestive secretions contribute additional fluids: 1,500 milliliters from saliva, 1,500 milliliters from gastric secretions, 1,000 milliliters of bile from the liver, 1,000 milliliters of pancreatic juice, 2,000 milliliters from intestinal secretions, and 200 milliliters from colonic mucus. Together, these total approximately 9,000 milliliters entering the small intestine. Of this, the small intestine reabsorbs about 7,800 milliliters, leaving around 1,200 milliliters to pass into the large intestine. The colon reabsorbs about 1,250 milliliters, with roughly 150 milliliters of water lost in the feces. The diagram emphasizes how most water is reclaimed during digestion, with minimal loss.

Figure 22.31

This diagram shows the absorption and transport of lipids in the small intestine. Fat digestion produces fatty acids and monoglycerides, which form micelles in the intestinal lumen. These micelles move into absorptive epithelial cells, where fatty acids and monoglycerides recombine to form triglycerides. Inside the Golgi apparatus, triglycerides combine with proteins to form chylomicrons. These chylomicrons are then released from the epithelial cells into lacteals, specialized lymphatic capillaries. Finally, lymph in the lacteals carries the chylomicrons away from the intestine, integrating them into the lymphatic and circulatory systems.

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Figure 23.1

The electron transport chain is shown across the inner mitochondrial membrane, with four protein complexes (I to IV) transferring electrons from NADH and FADH2 and pumping hydrogen ions (H plus) into the intermembrane space. Cytochrome c (Cyt c) carries electrons between complexes III and IV. The accumulated H plus ions flow back into the mitochondrial matrix through ATP synthase, a large enzyme, driving the conversion of ADP and phosphate into ATP. Oxygen serves as the final electron acceptor, combining with electrons and hydrogen ions to form water. The mitochondrial matrix is labelled below the membrane, and the intermembrane space is labelled above it.

Figure 23.2

A flowchart illustrates cellular respiration and ATP production from one glucose molecule through four main stages. In glycolysis, a six-carbon glucose splits into two three-carbon pyruvate molecules, producing 2 ATP (net) and 2 NADH, with 2 ATP used and 4 ATP generated. During pyruvate's transformation into acetyl CoA, each pyruvate releases CO2 and generates 1 NADH, for a total of 2 NADH. In the Krebs cycle, each acetyl CoA produces 1 ATP, 3 NADH, and 1 FADH2 per cycle, totalling 2 ATP, 6 NADH, and 2 FADH2 for both pyruvates. The electron transport chain uses these 10 NADH and 2 FADH2 to drive redox reactions, producing about 34 ATP through oxidative phosphorylation. Overall, cellular respiration yields about 36 ATP per glucose molecule after accounting for 2 ATP used to transport NADH into mitochondria.

Figure 23.3

A detailed diagram shows the structure of a lipoprotein particle, highlighting its main components. The outer shell is composed of a phospholipid monolayer represented by spherical molecules, which provides a hydrophilic surface that allows the particle to travel in blood. Embedded within this outer layer are apolipoproteins, shown as large blue structures, which serve roles in recognition and transport. Inside the particle, the hydrophobic core contains triglycerides illustrated as yellow branched structures, storing and transporting lipids through the circulatory system.

Figure 23.4

Diagram of the digestive system highlighting enzyme and hormone secretion sites. The esophagus leads to the stomach, where stomach cells secrete pepsin and hydrochloric acid (HCl) for protein digestion. The pancreas connects to the small intestine and releases trypsin, chymotrypsin, elastase, and sodium bicarbonate from its acinar cells to aid digestion and neutralize stomach acid. Intestinal cells secrete secretin and cholecystokinin (CCK), hormones that regulate pancreatic secretion and digestive activity. A magnified inset shows pancreatic ducts delivering enzymes into the small intestine, where most digestion occurs, and the pathway continuing to the large intestine for waste elimination.

Figure 23.5

Diagram illustrating nutrient absorption and insulin action during the absorptive state. Digested nutrients enter the bloodstream, raising blood glucose levels, which triggers insulin release from the pancreas. Insulin promotes glucose uptake by liver, muscle, and adipose cells. In the liver, glucose is converted to glycogen and amino acids are used for ketogenesis. Muscle cells store glucose as glycogen and use amino acids for actin and myosin synthesis. Adipose cells store excess lipids, increasing fat reserves. These processes lower blood glucose and restore homeostasis.

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Figure 23.6

This diagram illustrates the postabsorptive state, which occurs when no nutrients are entering the bloodstream from the digestive system. As blood glucose levels decline, the pancreas stops releasing insulin and begins secreting glucagon. Glucagon signals different tissues to mobilize stored energy: In liver cells, glycogen is broken down into glucose, and ketone oxidation helps generate ATP; in muscle cells, glycogen is broken down and proteins are catabolized into amino acids, which can contribute to glucose and ATP production; and in adipose tissue, stored lipids are released and used for glucose, ketone body, or ATP production. These processes collectively help restore and maintain blood glucose levels.

Figure 23.7

Diagram showing the feedback mechanisms of body temperature homeostasis. When body temperature drops below the normal range (36.5 to 37.5°C), temperature receptors in the hypothalamus activate heat-producing mechanisms: Superficial arteries constrict to reduce heat loss, blood flow to the digestive system decreases, shivering increases muscle respiration, and thyroid activity raises metabolic heat production, all of which increase body temperature back to normal. Conversely, when body temperature rises above the normal range, temperature receptors trigger heat-releasing mechanisms: Superficial arteries dilate to enhance heat loss, sweating begins, and thyroid activity decreases to reduce metabolic heat production, leading to a decrease in body temperature and restoration of homeostasis.

Figure 24.1

Illustration showing the anatomy of the urinary and reproductive systems in a sagittal section. Panel A depicts the female anatomy, including the uterus, urinary bladder, pubic bone, urethra, clitoris, labium minora, labium majora, ureter, cervix, rectum, vagina, and anus. Panel B shows the male anatomy, including the urinary bladder, pubic bone, ductus deferens, urethra, penis, epididymis, testis, ureter, seminal vesicle, prostate gland, rectum, and anus.

Figure 24.5

Frontal section of a kidney showing its internal anatomy and major structures. The outer cortex surrounds the inner medulla, which is organized into renal pyramids ending in papillae that project into minor calyces. These minor calyces merge into major calyces, which then drain into the renal pelvis, the funnel-shaped structure leading to the ureter. The renal column separates adjacent pyramids. The renal hilum is the entry and exit point for the renal artery, renal vein, and renal nerve. Blood supply is shown branching into interlobar, arcuate, and cortical blood vessels within the kidney. A small inset illustrates the kidneys' position in the body relative to the spine and adrenal glands.

Figure 24.6

Diagram showing the blood supply of the kidney and nephron. Blood enters through the renal artery, which branches into segmental, interlobar, arcuate, and cortical radiate arteries. The cortical radiate artery gives rise to afferent arterioles that supply the glomerulus, a capillary network where filtration occurs. Blood exits the glomerulus through efferent arterioles, which lead to the peritubular capillaries surrounding the nephron tubules. The blood then drains through cortical radiate, arcuate, and interlobar veins before exiting via the renal vein. The illustration highlights the close association between the nephron and its capillary network, essential for filtration, reabsorption, and secretion.

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Figure 24.7

Diagram of a nephron and associated blood vessels, showing the structure and flow of blood and filtrate during urine formation. Blood enters the glomerulus via the afferent arteriole and exits through the efferent arteriole. The glomerulus, enclosed by the glomerular capsule, filters blood into the proximal convoluted tubule. The filtrate then moves through the loop of the nephron, distal convoluted tubule, and collecting duct, where further processing occurs. The peritubular capillary network surrounds the tubules, facilitating reabsorption and secretion, and connects to the interlobular vein. Processed urine collects in the collecting duct and flows into the renal papilla for excretion.

Figure 24.10

Diagram of a renal corpuscle and its associated structures, showing the afferent arteriole bringing blood into the glomerulus and the efferent arteriole carrying blood away. The glomerulus is a network of capillaries surrounded by podocytes that form part of the filtration barrier. The proximal convoluted tubule extends from the renal corpuscle, beginning urine formation. The distal convoluted tubule (DCT) and macula densa are shown adjacent to the afferent arteriole, where specialized juxtaglomerular cells regulate blood pressure and filtration through renin secretion. The renal nerve is also shown influencing arteriole constriction.

Figure 24.11

Diagram of the renin-angiotensin-aldosterone system (RAAS), illustrating how low fluid flow or low sodium concentration sensed by the macula densa triggers juxtaglomerular cells in the kidney to secrete renin. Renin converts angiotensinogen, released by the liver, into angiotensin I, which is then converted to angiotensin II by angiotensin-converting enzyme (ACE) in the lungs. Angiotensin II causes widespread vasoconstriction and stimulates the adrenal cortex to release aldosterone. Aldosterone promotes sodium uptake in the distal convoluted tubule and collecting ducts, while antidiuretic hormone (ADH) increases water reabsorption by inserting aquaporins in the collecting duct, both of which help restore blood volume and pressure.

Figure 24.14

Diagram of solute and water movement along the nephron. Various substances, including glucose, amino acids, proteins, vitamins, ions (Na plus, K plus, Ca2 plus, Mg2 plus, Cl minus, HCO3 minus), water, urea, lactate, and uric acid, are reabsorbed from the filtrate back into the blood, mainly in the proximal convoluted tubule. Additional water and ions are reabsorbed in the loop of Henle and distal convoluted tubule. Substances like H plus, K plus, NH4 plus, urea, creatinine, and some drugs are secreted into the filtrate. Water and urea also move into the collecting duct, contributing to urine formation.

Figure 24.15

Diagram showing reabsorption and transport mechanisms in the proximal convoluted tubule. Sodium (Na plus) is actively transported out of the tubule cell into the interstitial space via the Na plus / K plus pump using ATP, creating a gradient that drives the cotransport of other substances. Chloride (Cl minus), calcium (Ca2 plus), phosphate (PO43 minus), amino acids, and glucose enter the tubule cell along with Na plus through cotransporters. Hydrogen ions (H plus) are exchanged for Na plus, contributing to acid-base balance. Water (H2O) and magnesium ions (Mg2 plus) follow passively by osmosis and diffusion. These substances then move into the bloodstream, aiding in the reabsorption of essential nutrients and ions.

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Figure 24.16

Diagram showing bicarbonate reabsorption and hydrogen ion secretion in the proximal convoluted tubule. Sodium (Na plus) is actively transported out of the tubule cell into the interstitial space using ATP, creating a gradient that drives Na plus reabsorption and H plus secretion. In the lumen, secreted H plus combines with bicarbonate (HCO3 minus) to form carbonic acid (H2CO3), which is quickly converted by carbonic anhydrase into water (H2O) and carbon dioxide (CO2). CO2 diffuses into the tubule cell, where it recombines with water to form H2CO3 again, which dissociates into H plus (recycled into the lumen) and HCO3 minus. The newly formed bicarbonate is transported into the bloodstream, helping regulate acid-base balance.

Figure 24.17

Diagram of the loop of Henle showing osmotic gradients and the movement of water, urea, and ions. The descending limb is permeable to water and urea, allowing them to move out into the increasingly concentrated interstitial fluid as osmolality rises from 300 to 1,200 milliosmoles per kilogram. The ascending limb is impermeable to water but actively transports sodium (Na plus) and chloride (Cl minus) ions out into the interstitium, lowering the filtrate's osmolality from 1,200 at the bottom of the loop to about 100 milliosmoles per kilogram at the top. This countercurrent mechanism helps establish the medullary osmotic gradient essential for urine concentration.

Figure 25.4

This diagram shows a sodium-potassium pump embedded in the cell membrane. In the first step, the pump is opened to the cytosol and closed to the extracellular fluid. First, three sodium ions move into the pump from the cytosol. An ATP molecule binds to the cytosol side of the pump, causing the pump to change shape and open to the extracellular fluid. The pump is now closed to the cytosol. The sodium ions are then released into the extracellular fluid, after which two potassium ions enter the pump. Also at this point, the used ADP detaches from the cytosol side of the pump, leaving a single phosphate attached. The pump then changes shape again so that it closes to the extracellular fluid and again opens to the cytosol. This releases the two potassium ions into the cytosol. The single phosphate also detaches from the pump at this point so that the cycle can start anew. Two bars along the right-hand side of the figure indicate that sodium normally diffuses into the cell down its concentration gradient, while potassium usually diffuses out of the cell down its concentration gradient. Therefore, the sodium-potassium pump is working against these natural concentration gradients.

Figure 25.5

Diagram illustrating fluid exchange across a capillary bed, showing filtration, no net movement, and reabsorption. At the arterial end, net filtration pressure is positive 10 millimetres of mercury, and fluid exits the capillary because capillary hydrostatic pressure (35 millimetres of mercury) exceeds blood colloidal osmotic pressure (25 millimetres of mercury). At the mid-capillary, net filtration pressure is 0 millimetres of mercury, and there is no net movement as pressures are balanced (25 millimetres of mercury each). At the venous end, net filtration pressure is negative 7 millimetres of mercury, and fluid reenters the capillary because capillary hydrostatic pressure (18 millimetres of mercury) is lower than blood colloidal osmotic pressure (25 millimetres of mercury).

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Figure 25.6

This diagram shows a carrier protein embedded in the plasma membrane between the cytoplasm and the extracellular fluid. There are several glucose molecules in the extracellular fluid. In the first step, the carrier protein is open to the extracellular fluid and closed to the cytosol. One of the glucose molecules travels from the extracellular fluid into the carrier protein. The protein then changes shape, closing at both ends. This pushes the glucose down into the carrier protein, closer to the cytosol end. The protein then opens on the cytosol side and closes on the extracellular fluid side, allowing the glucose to enter the cytosol.

Figure 25.7

This figure is a top-to-bottom flowchart describing the thirst response. The topmost box of the chart states that there is insufficient water in the body, which has two effects. The left branch of the chart leads to decreased blood volume, which leads to decreased blood pressure. This triggers an increase in angiotensin II. Angiotensin II stimulates the thirst centre in the hypothalamus. On the right branch, insufficient water in the body leads to increased blood osmolality, which causes dry mouth. Increased blood osmolality and dry mouth are sensed by osmoreceptors in the hypothalamus. This stimulates the thirst centre in the hypothalamus to increase thirst, giving a person the urge to drink. Drinking decreases blood osmolality back to homeostatic levels.

Figure 25.9

This diagram depicts a cross-section of the right wall of a kidney collecting tubule. The wall is composed of three block-shaped cells arranged vertically, one on top of the other. The lumen of the collecting tubule is to the left of the three cells. Yellow-coloured urine is flowing through the lumen. There is a small strip of blue interstitial fluid to the right of the three cells. To the right of the interstitial fluid is a cross-section of a blood vessel. Arrows show that water in the urine is entering the left side of the wall cells through aquaporins. The water travels through the cells and then leaves the kidney tubule through additional aquaporins in the right side of the wall cells. The water travels through the interstitial space and enters the blood in the blood vessel. The aquaporins in the wall cells are being released from aquaporin storage vesicles within their cytoplasm.

Figure 25.10

This flowchart shows how potassium and sodium ion concentrations in the blood are regulated by aldosterone. Rising K plus and falling Na plus levels in the blood trigger aldosterone release from the adrenal cortex. Aldosterone targets the kidneys, causing a decrease in K plus release from the kidneys, which reduces the amount of K plus in the blood back to homeostatic levels. Aldosterone also increases sodium reabsorption by the kidneys, which increases the amount of Na plus in the blood back to homeostatic levels.

Figure 25.11

This figure shows the hormone cascade that increases kidney reabsorption of Na plus and water. In the first step, the kidneys release renin into the bloodstream. The bloodstream is depicted with a red arrow pointing from left to right. At the same time, the liver releases angiotensinogen into the blood, which combines with the renin, yielding angiotensin I. The blood flow then leads to the lungs. Within the pulmonary blood, angiotensin-converting enzyme (ACE) converts angiotensin I to angiotensin II. The blood then flows to the adrenal cortex, where angiotensin II stimulates the adrenal cortex to secrete aldosterone.

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Aldosterone causes the kidney tubules to increase reabsorption of NA plus and water into the blood.

Figure 25.12

This top-to-bottom flowchart describes the regulation of pH in the blood. The left branch shows acidosis, which is when the pH of the blood drops. Acidosis stimulates brain and arterial receptors, triggering an increase in respiratory rate. This causes a drop in blood CO2 and H2CO3. A drop in these two acidic compounds causes the blood PH to rise back to homeostatic levels. The right branch shows alkalosis, which is when the PH of the blood rises. Alkalosis also stimulates brain and arterial receptors, but these now trigger a decrease in respiratory rate. This causes an increase in blood CO2 and H2CO3, which lowers the PH of the blood back to homeostatic levels.

Figure 25.13

This figure points out the symptoms of acidosis and alkalosis on a silhouette of a human torso. The effects of acidosis on the central nervous system include headache, sleepiness, confusion, loss of consciousness, and coma. The effects of acidosis are given on the left side of the diagram. The effects of acidosis on the respiratory system include shortness of breath and coughing. The effects of acidosis on the heart include arrhythmia and increased heart rate. The effects of acidosis on the muscular system include seizures and weakness. The effects of acidosis on the digestive system include nausea, vomiting, and diarrhea. The right side of the diagram describes the symptoms of alkalosis. The effects of alkalosis on the central nervous system include confusion, light-headedness, stupor, and coma. The effects of alkalosis on the peripheral nervous system include hand tremor and numbness or tingling in the face, hands, and feet. The effects of alkalosis on the muscular system include twitching and prolonged spasms. The effects of alkalosis on the digestive system include nausea and vomiting.

Figure 26.1

Illustration of the male reproductive system showing an uncircumcised penis with the prepuce (foreskin) and scrotum, a circumcised penis with the foreskin removed to expose the glans penis and corona, and a lateral view of the male reproductive system, including the prostate gland, urinary bladder, pubic symphysis, corpus cavernosum, corpus spongiosum, external urethral opening, ductus (vas) deferens, testis, epididymis, scrotum, spongy urethra, membranous urethra, muscles of the perineum, bulbourethral gland, ejaculatory duct, seminal vesicle, ampulla of the ductus deferens, and suspensory ligament of the penis.

Figure 26.4

Diagram illustrating spermatogenesis and a cross-section of a seminiferous tubule. On the left, the stages of spermatogenesis are shown: Spermatogonium (2n) undergoes mitosis to form primary spermatocytes (2n), which undergo meiosis I to form secondary spermatocytes (1n), then meiosis II to form spermatids (1n), which differentiate into mature spermatozoa. On the right, a histological cross-section of a seminiferous tubule shows labelled structures, including the lumen, spermatogonia, primary spermatocytes, early spermatids, Sertoli (sustentacular) cells, Leydig (interstitial) cells, peritubular capillary, interstitial tissue, lymphatic capillary, and arteriole.

Figure 26.6

Diagram comparing the penis in flaccid and erect states in both lateral and transverse views. In the flaccid state, the corpora cavernosa and corpus spongiosum are relaxed, cavernosal

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arteries are narrow, and penile venules and the deep dorsal vein remain uncompressed, allowing blood to exit freely. In the erect state, cavernosal arteries dilate, causing blood to engorge the corporal tissue, which swells and erects the penis. These swellings compress penile veins and venules, restricting blood outflow and maintaining an erection. Labels identify key structures such as the corpora cavernosa, corpus spongiosum, cavernosal arteries, spongy urethra, prepuce, and deep dorsal vein.

Figure 26.7

Diagram illustrating the hormonal regulation of the male reproductive system through the hypothalamic-pituitary-gonadal axis. The hypothalamus releases gonadotropin-releasing hormone (GnRH), which stimulates the anterior pituitary to release follicle-stimulating hormone (FSH) and luteinizing hormone (LH). LH stimulates Leydig (interstitial) cells in the testes to release testosterone, while FSH stimulates Sertoli cells to produce androgen-binding protein (ABP), which binds to testosterone to maintain high local concentrations. Sertoli cells also release inhibin, which negatively feeds back to the anterior pituitary to inhibit FSH release. Testosterone exerts negative feedback on both the hypothalamus and pituitary, reducing further release of GnRH, FSH, and LH. The seminiferous tubules and interstitial spaces are shown as sites of hormone action and sperm development.

Figure 26.8

Diagram of the female reproductive system showing two views. In the lateral view, the bladder, pubic symphysis, mons pubis, urethra, clitoris, labium minora, labium majora, uterus, ovary, fornix of uterus, cervix, rectum, vagina, and anus are labelled, illustrating the relationship of internal and external reproductive organs within the pelvic cavity. In the anterior view, the fimbriae, uterus, uterine tube (oviduct), cervix, vagina, ovary, ovarian ligament, broad ligament, labia minora, and labia majora are shown, highlighting the connections of the ovaries and fallopian tubes to the uterus and their supportive ligaments.

Figure 26.9

Diagram of the vulva showing external and internal structures. On the left, the external anterior view illustrates the prepuce, glans clitoris, labia minora, urethral opening, vaginal opening, labia majora, and anus. On the right, the internal anterolateral view reveals the corpus cavernosum, bulb of vestibule, urethral and vaginal openings, Bartholin's glands and their ducts, and deeper structures of the clitoris and labia, highlighting both superficial and internal components of the female external genitalia.

Figure 26.10

Diagram illustrating oogenesis, the development of the female gamete. It shows an oogonium (2n) undergoing mitosis to form a primary oocyte (2n), which begins meiosis I but arrests in prophase I before birth. After puberty, meiosis I resumes, producing a secondary oocyte (n) and the first polar body. The secondary oocyte arrests at metaphase II and will only complete meiosis II if penetrated by sperm, producing a mature ovum (n) and a second polar body. The process highlights key meiotic stages, timing before birth and after puberty, and the formation of polar bodies during oocyte development.

Figure 26.11

Diagram showing the stages of folliculogenesis and a detailed view of a secondary follicle. Part A illustrates the progression from a primordial follicle with an oocyte surrounded by

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cortex cells to a primary follicle with granulosa cells and a forming zona pellucida, then a secondary follicle with developing theca cells, followed by a tertiary follicle with an antrum. The mature follicle ovulates, releasing the oocyte, and the ruptured follicle transforms into the corpus luteum in the ovary. Part B shows a micrograph of a secondary follicle, labelling structures such as the oocyte, its nucleus and nucleolus, the corona radiata, zona pellucida, granulosa cells, developing antrum, theca cells, perifollicular capillaries, ovarian stroma, and cortex, illustrating the cellular organization supporting oocyte development.

Figure 26.12

Diagram illustrating the hormonal regulation of the ovarian cycle, divided into the follicular phase, ovulation, and luteal phase. In the follicular phase, the hypothalamus releases GnRH, stimulating the anterior pituitary to secrete LH and FSH, which promote follicle growth and estradiol production; estradiol causes endometrial thickening and provides negative feedback to inhibit GnRH, FSH, and LH. During ovulation, rising estradiol levels switch to positive feedback, enhancing GnRH, FSH, and LH secretion, with the LH surge triggering ovulation. In the luteal phase, LH stimulates the formation of the corpus luteum, which secretes progesterone to inhibit GnRH, FSH, and LH and maintain the endometrium; when the corpus luteum degenerates, progesterone levels fall, leading to the shedding of the stratum functionalis.

Figure 26.13

Diagram showing the female reproductive system and associated histology. The central illustration depicts the uterus, uterine tubes (oviducts), ovaries, and supporting ligaments. Labelled structures include the infundibulum, ampulla, isthmus, and fimbriae of the uterine tube, as well as the fundus, uterine isthmus, cervix, vagina, broad ligament, ovarian ligament, and suspensory ligament. Blood supply is shown via the ovarian, uterine, and vaginal arteries and veins. Insets provide histological views: on the left, the ovarian cortex with follicles beneath the tunica albuginea; on the right, a section of the uterine wall showing the endometrium, myometrium, and perimetrium layers.

Figure 26.14

Diagram showing the hormonal regulation and phases of the ovarian and uterine cycles during the menstrual cycle. The top panel illustrates follicular development: Primordial follicles mature into primary and secondary follicles, with most undergoing atresia, while one becomes the dominant tertiary follicle by days 1 to 7. The middle panels depict ovarian and uterine cycle phases across a 28-day cycle. The ovarian cycle includes the follicular phase (development of the tertiary follicle), ovulation around day 14, and the luteal phase (formation and regression of the corpus luteum). The uterine cycle shows menses, proliferative, and secretory phases, with the endometrium thickening after menstruation. The bottom panels present hormonal fluctuations: FSH and LH levels peak sharply around ovulation, while estrogen rises during the follicular phase and progesterone peaks in the luteal phase, coordinating follicle development and uterine preparation for possible implantation.

Figure 26.15

This image shows the anatomy and internal structure of the breast and mammary glands. The diagram illustrates the nipple and areola, which contain areolar glands, and highlights the branching lactiferous ducts that transport milk toward the nipple. These ducts expand into lactiferous sinuses, where milk is stored before release. The glandular tissue consists of

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lobules, which contain alveoli—the small sacs responsible for milk production. Surrounding the glandular tissue is fat tissue, which provides structure and protection, as well as suspensory ligaments that support the breast. The overall flow of milk is shown moving from the alveoli through the ducts and sinuses to exit at the nipple.

Figure 27.1

This image illustrates the process of fertilization, showing three main steps in which sperm interact with the oocyte. In step one, hundreds of sperm are attracted to the corona radiata, the outer layer of granulosa cells surrounding the oocyte, and begin breaking through this barrier as they approach the zona pellucida, a glycoprotein membrane around the egg. Step two shows that contact between sperm and the zona pellucida triggers the acrosome reaction, during which sperm release digestive enzymes that break down the zona's membrane to expose the oocyte's plasma membrane. In step three, a single sperm successfully burrows through the corona radiata and zona pellucida, then fuses its plasma membrane with that of the oocyte, releasing its nucleus into the cytoplasm of the oocyte, marking the completion of fertilization. The labelled structures include the acrosome, sperm nucleus, sperm receptors in the plasma membrane, the zona pellucida, the corona radiata, the oocyte cytoplasm, and the plasma membrane.

Figure 27.3

This image illustrates the stages of early human development from fertilization to implantation. It begins with an unfertilized oocyte, which becomes a fertilized oocyte after sperm penetration. The zygote undergoes cleavage, forming a two-cell stage, four-cell stage, and then an eight-cell stage and morula of 16 cells as it travels through the uterine tube. The morula develops into a blastocyst of 70 to 100 cells, consisting of a trophoblast, blastocoel, and inner cell mass. The blastocyst hatches by shedding the zona pellucida, rotates, and implants into the endometrium of the uterus, marking the beginning of pregnancy.

Figure 27.4

This diagram illustrates the stages of implantation in the uterus. In step one, the blastocyst begins implantation by digesting the uterine mucosa and embedding itself into the endometrium. In step two, the endometrium grows over and surrounds the embryo, securing it within the uterine lining. In step three, the implanted embryo continues to develop within the endometrium, shown here at seven to eight weeks after conception. The inset shows that implantation most commonly occurs on the posterior uterine wall, with both anterior and lateral views provided.

Figure 27.5

Diagram showing an implanted blastocyst in the endometrium, highlighting key structures of early development. The trophoblast consists of an outer syncytiotrophoblast layer and an inner cytotrophoblast layer, anchoring the embryo to the uterine lining. Inside, the embryonic disc is made up of the epiblast and hypoblast, with the amnion forming around the amniotic cavity above the epiblast. The blastocyst cavity, which will become the yolk sac, is shown adjacent to the hypoblast.

Figure 27.6

Two-panel diagram illustrating gastrulation. The top panel shows a blastocyst implanted in the endometrium with reestablished uterine mucosa, trophoblast, hypoblast, epiblast, and the amniotic cavity. The bottom panel shows the formation of three germ layers: ectoderm from the epiblast, mesoderm forming as cells migrate through the primitive streak, and endoderm

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as migrating cells displace most of the hypoblast. Insets highlight a cross-section at the primitive streak where these layers develop.

Figure 27.7

Diagram showing a cross-section of an early embryo implanted in the endometrium, surrounded by extraembryonic membranes. The amniotic cavity, filled with fluid, encloses the embryo, with the amnion and yolk sac lined with endoderm. The chorion, derived from the blastocyst membrane, connects to the maternal blood pool, and the allantois is visible near the base. Insets summarize the three germ layers and their derivatives: The endoderm forms the digestive system, liver, pancreas, and lung inner layers; the mesoderm forms the circulatory system, skeletal system, muscular system, and lung epithelial layers; and the ectoderm forms hair, nails, skin, and the nervous system.

Figure 27.8

Cross-section diagram of an implanted embryo in the uterus showing the developing placenta and associated structures. The image labels the yolk sac, amniotic fluid, amnion, chorion, and placenta, with the umbilical cord connecting the embryo to the placenta. A close-up of the placental interface shows chorionic villi extending into maternal blood in the intervillus space, with uterine arteries and veins supplying the area. The umbilical vein and arteries are labelled, illustrating nutrient and gas exchange between maternal and fetal blood.

Figure 27.9

Diagram showing fetal circulation, including the placenta, umbilical cord, and fetal heart. Oxygenated blood from the placenta enters the fetus through the umbilical vein and bypasses the liver via the ductus venosus to reach the inferior vena cava. Blood enters the right atrium, where the foramen ovale allows it to pass directly into the left atrium, bypassing the lungs. The ductus arteriosus connects the pulmonary artery to the aorta, diverting blood away from the lungs. Mixed blood circulates to the fetal body and returns to the placenta through the umbilical arteries.

Figure 27.12

Diagram showing the three stages of childbirth. Stage one is dilation, with the cervix expanding from closed to fully dilated at over 10 centimetres as the amniotic fluid surrounds the fetus. Stage two is birth, showing four steps—the head presenting through the birth canal, rotation and delivery of the anterior shoulder, delivery of the posterior shoulder, and delivery of the lower body and umbilical cord. Stage three is afterbirth, where the placenta detaches from the uterine wall and exits through the vagina, shown alongside a photo of a delivered placenta in a medical tray.

Figure 27.13

Diagram showing circulatory changes before and after birth. Before birth, the ductus arteriosus connects the pulmonary artery to the aorta, and the foramen ovale allows blood to flow between the atria. Immediately after birth, the ductus arteriosus constricts so blood from the right ventricle travels to the lungs, and the foramen ovale closes, forming the fossa ovalis and separating oxygenated and deoxygenated blood. Before birth, the ductus venosus shunts oxygenated blood from the umbilical vein toward the heart, bypassing the liver. After birth, the ductus venosus degenerates into the ligamentum venosum, the inferior vena cava carries only deoxygenated blood, and the umbilical vessels become ligaments.

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Figure 27.14

Diagram illustrating the milk ejection reflex during breastfeeding. Suckling by an infant triggers sensory nerve impulses in the areola, which travel to the hypothalamus and stimulate the posterior pituitary to release oxytocin. Oxytocin causes myoepithelial cells around mammary alveoli to contract, pushing milk into the lactiferous ducts. Milk pools in the lactiferous sinuses before being released through nipple pores. Increased milk production stimulates more suckling, forming a positive feedback loop.

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