**When Cells Fight Back: Acute Inflammation and Repair Mechanisms**
[Exploring the Cellular and Molecular Pathology of Human Diseases: A Case-Based Approach]

*Transcript updated on March 6, 2024*

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| **Slide 1** | *Title slide* |
| **Slide 2** | In this module, we will discuss two case studies to learn about ‘Acute Inflammation and Tissue Repair’. In ‘Acute Inflammation’, we will learn about ‘Vascular and Cellular Events’, ‘Inflammatory Cells’, ‘Chemical Mediators’, and ‘Outcomes of Acute Inflammation’. In the discussion on ‘Tissue Repair’, we will learn about ‘Regeneration’, the difference between ‘First and Second Intention Healing’, and the ‘Rate of Wound Healing’.  |
| **Slide 3** | You are a fourth-year kinesiology student eager to start a course to learn about athletic injuries. You will be supervised by Dr. Rodriguez, an experienced sports medicine physician, who will help walk you through cases of various patients visiting the clinic. |
| **Slide 4** | Your first patient is Emily, a 21-year-old college athlete. She comes to the clinic after sustaining a knee injury during a soccer match last night. |
| **Slide 5**  | Dr. Rodriguez examines Emily’s knee and observes signs of redness and swelling. She explains how these signs reflect the processes of vasodilation and increased vascular permeability, respectively. Vasodilation is the widening of blood vessels to increase blood flow. Vascular permeability means making blood vessels more porous to small molecules and whole cells.These vascular events are crucial for bringing immune cells and nutrients to the injured knee. She explains how inflammation is the body’s response to injury and proceeds the same way regardless of the source of injury. For example, inflammation will proceed the same way in response to infection, trauma, and metabolic injury. |
| **Slide 6** | You learn that an essential feature of inflammation is the accumulation of leukocytes at the site of injury. This process involves multiple cellular events.The first event is ‘Margination and Rolling’. Vascular permeability causes blood to become viscous, which pushes white blood cells (WBCs) to the periphery of the vasculature. WBCs roll and transiently stick to the endothelium via selectin molecules. |
| **Slide 7** | The next event is ‘Adhesion’. WBCs adhere firmly to the endothelium via integrins expressed on their cell surface.This is followed by ‘Transmigration’. WBCs squeeze between endothelial cells and pass through the basement membrane to enter tissue. |
| **Slide 8** | The fourth event is ‘Chemotaxis’. WBCs migrate towards the site of injury, attracted by a chemical gradient.The last event is ‘Activation and Phagocytosis’. Receptors on WBCs recognize offending agents. This induces intracellular signaling pathways leading to WBC activation and production of inflammatory mediators. WBCs then engulf and degrade offending agents. |
| **Slide 9** | *Knowledge check* |
| **Slide 10** | A blood test reveals elevated levels of inflammatory markers. Dr. Rodriguez discusses the role of chemical mediators, such as histamines and prostaglandins, in amplifying the inflammatory response. Histamines and prostaglandins are responsible for inducing hallmarks of inflammation, such as vasodilation, vascular permeability, fever, and pain. |
| **Slide 11**  | Dr. Rodriguez explains that there are three possible outcomes following acute inflammation: 1) complete resolution; 2) healing by connective tissue replacement; or 3) progression to chronic inflammation.Luckily for Emily, her knee is not severely injured and will likely undergo complete resolution. Dr. Rodriguez advises Emily to keep her knee on ice to bring down the swelling, rest well, and take ibuprofen if she experiences excessive pain. Ibuprofen is an anti-inflammatory drug, which blocks the production of prostaglandins.  |
| **Slide 12**  | *Knowledge check* |
| **Slide 13**  | *Check your understanding* |
| **Slide 14**  | Your second patient is Christopher, a 20-year-old hockey player, who sustained a painful scrape on his cheek during a recent game. Christopher is worried about how long the wound will take to heal because it is noticeable to others. He is also concerned about whether a large scar will remain. Dr. Rodriguez explains that several factors influence the rate of cutaneous wound healing and how tissue repair might occur. |
| **Slide 15**  | Dr. Rodriguez explains that tissue repair can occur by two types of reactions: ‘Regeneration’ or ‘Connective Tissue Deposition with Scar Formation’.  In ‘Regeneration’, the cells replacing the injured tissue are identical to those lost. Regeneration can occur in two ways: 1) the proliferation of remaining cells that are uninjured; or 2) the differentiation of tissue stem cells into an identical cell type.In ‘Connective Tissue Deposition with Scar Formation’, the cells replacing the injured tissue are different from those lost. This occurs by laying down connective tissue and results in scarring.Oftentimes, both regeneration and connective tissue deposition with scar formation work together to repair tissue. |
| **Slide 16** | Whether healing can occur by regeneration depends on two factors: The proliferative potential of thee injured cell type; and whether the extracellular matrix has been damaged. There are three types of proliferative potential: labile, stable, and permanent. Labile cells proliferate throughout life. Some examples of Labile cells are skin and blood cells. Stable cells have low levels of proliferation but can be stimulated to divide. This includes the epithelia of most parenchymal organs like the liver and kidney. Permanent cells cannot divide after birth. For instance, cardiac muscle cells cannot replicate. Thus, for permanent cells, regeneration is not possible, and healing must occur by scarring. Furthermore, if the extracellular matrix has been damaged, a new scaffold must be formed by scarring, regardless of the proliferative potential of the injured cell type. The newly formed extracellular matrix will never acquire 100% of its original strength. |
| **Slide 17**  | There are two types of healing: first intention and second intention. First intention healing occurs when the edges of a cutaneous wound are in close proximity, which minimizes the gap to be filled. Healing can then occur rapidly with minimal scarring. Second intention healing occurs in cutaneous wounds with significant tissue loss; thus, there is a large gap to fill. Granulation tissue will form at the site of injury 3-5 days post-injury. Granulation tissue is composed of capillaries, fibroblasts and inflammatory cells, and acts as a scaffold for further tissue repair. Second intention healing occurs slowly and will always cause scarring.  |
| **Slide 18** | Fortunately for Christopher, several factors apply to his case which increase the rate of cutaneous wound healing, including:* Wounds tend to heal faster in younger individuals.
* Our faces are well-vascularized. This means there is increased blood flow at Christopher’s site of injury to optimize healing.
* Skin epithelial cells are labile cells; and thus, proliferate throughout life.
* His wound has well-approximated edges, which enables rapid healing by 1st intention.

To promote healing further, Dr. Rodriguez advises Christopher to:* Irrigate and protect his wound from infection.
* Avoid tight dressings, which might reduce blood supply to the wound.
* Immobilize his site of injury, as much as possible.
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| **Slide 19** | *Knowledge check* |
| **Slide 20** | *Knowledge check* |