Clinical Pharmacology and Prescribing Skills:

CLINICAL PHARMACOLOGY AND PRESCRIBING SKILLS:

Resources for Canadian Medical Trainees

DR ANNE HOLBROOK, MD, PHARMD, MSC, FRCPC

Pressbooks

Clinical Pharmacology and Prescribing Skills: Copyright © by Dr Anne

Holbrook, MD, Pharm D, MSc, FRCPC is licensed under a Ontario Commons License, except where otherwise noted.

CONTENTS

Introduction	1
Bibliography of CPT Important Terms, List of Common Abbreviations	2
Accessibility Statement	V
Main Body	
What is Clinical Pharmacology and Toxicology (CPT)?	7
What do we Mean by Prescribing Competence?	8
Why is CPT knowledge and Prescribing Competence critical to safe and effective medical practice?	9
Basic Pharmacology Principles for Prescribers	10
Toxicology	11
Drug Regulation and Formulary System in Canada	13
How to Avoid CPT and Prescribing Medicolegal Trouble	14
How to be an Effective Patient Advocate	15
Learning Objectives for CPT for Medical Students and Residents	16
Appropriateness of Prescribing Evaluation Tools	17
Essential Drugs List for Canadian Medical Students	18
Introduction to e-Prescribing Curriculum Resources	19
Introduction to Medication Safety	22
Approach to Antimicrobial Prescribing	23
Introduction to Drug Interactions and Adverse Drug Events	25
Recommended Clinical Pharmacology Case-Based Learning	26
Special Topics in CPT	33
Case-based CPT quizzes	34

Prescription Writing Practice and Feedback	35
Preparation for the Canadian Prescribing Safety Assessment	36
Medical Council of Canada Objectives on Prescribing Practices	39

This collection of resources, titled 'Clinical Pharmacology and Prescribing Skills: Resources for Canadian Medical Trainees', is intended to assist medical students and residents in understanding some key concepts in Clinical Pharmacology and Toxicology, find relevant and highly rated curricular resources, and understand the training and career opportunities in this new, smallest specialty of the Royal College of Physicians and Surgeons of Canada.

Funding statement

This project is made possible, in part, with funding by the Government of Ontario and through eCampus Ontario's support of the Virtual Learning Strategy. To learn more about the Virtual Learning Strategy visit: https://vls.ecampusontario.ca.

Licensing statement

This resource is licensed under an Ontario Commons License (Derivative Learning Object), except where otherwise noted.

Version 1.B. (Jan 2024)

BIBLIOGRAPHY OF CPT IMPORTANT TERMS, LIST OF COMMON ABBREVIATIONS

$\underline{A} | \underline{B} | \underline{C} | \underline{D} | \underline{E} | \underline{F} | \underline{G} | \underline{H} | \underline{I} | \underline{J} | \underline{K} | \underline{L} | \underline{M} | \underline{N} | \underline{O} | \underline{P} | \underline{Q} | \underline{R} | \underline{S} | \underline{T} | \underline{U} | \underline{V} | \underline{W} | \underline{X} | \underline{Y} | \underline{Z}$

top

Absorption Adherence Adverse drug event Adverse drug reaction **Affinity** Agonist Allele Allosteric modulator Antagonist Apparent volume of distribution (Vd) **AUC** top Bioavailability (F) Biological marker (biomarker) **Biotransformation** top Cheng-Prusoff equation Competitive antagonist Concentration-time curve top De-sensitization Dose-response relationships Drug concentration Drug transport top Efficacy Enteral drug administration Equilibrium dissociation constant (Kd)

First-pass effect	
Full agonist	
	<u>top</u>
Graded dose-response curve	
	<u>top</u>
Haplotype	
	<u>top</u>
IC50	
Informed consent document	
Inhibitory constant (Kj)	
Inverse agonist	
Irreversible antagonist	
	<u>top</u>
Metabolic drug tolerance	
Metabolism	
Metabolite	
Michaelis constant (Km)	
	<u>top</u>
Non-competitive antagonist	
1 0	
	<u>top</u>
Parent compound	<u>top</u>
- 0	<u>top</u>
Parent compound	<u>top</u>
Parent compound Parenteral drug administration	top
Parent compound Parenteral drug administration Partial agonist	<u>top</u>
Parent compound Parenteral drug administration Partial agonist Pharmacodynamics	top
Parent compound Parenteral drug administration Partial agonist Pharmacodynamics Pharmacogenetics	top
Parent compound Parenteral drug administration Partial agonist Pharmacodynamics Pharmacogenetics Pharmacogenomics	top
Parent compound Parenteral drug administration Partial agonist Pharmacodynamics Pharmacogenetics Pharmacogenomics Pharmacokinetics (PK)	top
Parent compound Parenteral drug administration Partial agonist Pharmacodynamics Pharmacogenetics Pharmacogenomics Pharmacokinetics (PK) Pharmacology	top
Parent compound Parenteral drug administration Partial agonist Pharmacodynamics Pharmacogenetics Pharmacogenomics Pharmacokinetics (PK) Pharmacology Potency	<u>top</u>
Parent compound Parenteral drug administration Partial agonist Pharmacodynamics Pharmacogenetics Pharmacogenomics Pharmacokinetics (PK) Pharmacology Potency	
Parent compound Parenteral drug administration Partial agonist Pharmacodynamics Pharmacogenetics Pharmacogenomics Pharmacokinetics (PK) Pharmacology Potency Prodrug	
Parent compound Parenteral drug administration Partial agonist Pharmacodynamics Pharmacogenetics Pharmacogenomics Pharmacokinetics (PK) Pharmacology Potency Prodrug	top
Parent compound Parenteral drug administration Partial agonist Pharmacodynamics Pharmacogenetics Pharmacogenomics Pharmacokinetics (PK) Pharmacology Potency Prodrug Quantal dose-responsive curve	top
Parent compound Parenteral drug administration Partial agonist Pharmacodynamics Pharmacogenetics Pharmacogenomics Pharmacokinetics (PK) Pharmacology Potency Prodrug Quantal dose-responsive curve Receptor pharmacology	top

4 | BIBLIOGRAPHY OF CPT IMPORTANT TERMS, LIST OF COMMON ABBREVIATIONS

Side effect	
Spare receptors	
	<u>top</u>
Tachyphylaxis	
Therapeutic index	
Therapeutics	
Tolerance	
	<u>top</u>
Wild type	

ACCESSIBILITY STATEMENT

The project team remains committed to creating an e-Book to meet requirements as set forth in the Accessibility for Ontarians with Disabilities Act (AODA) for publicly available online content. Pressbooks webbooks are designed to be accessible for users of all abilities and compatible with screen readers and other assistive technology (site maps, colour schemes, translations). As per Pressbooks accessibility recommendations, chapters, headings, and subheadings are used to organize content, described link text for links to web content are provided, and properly tagged table titles/captions and table headers/footers are available where appropriate. The webbook can be produced into two different types of PDF exports. 'PDF (for digital distribution)' exports use the <u>PDF/UA-1</u> profile, which means that these digital PDFs will be tagged for accessibility and are designed to be read on a screen with maximal accessibility.

Clinical pharmacology is a medical specialty concerned with the research, teaching and clinical application of what the human body does to drugs and what drugs do to humans. The knowledge and correct application of drug therapies is a core responsibility of every physician and crosses every disease and organ group. At a population level Canada, along with every other developed country, has noted that drugs form the fastest growing component of health care budgets. This means that there is tremendous pressure to ensure that medicines are provided in the most judicious (effective, safe and cost-effective) manner to optimize health. More recently, medication safety problems have been recognized as the most prominent single source of internal medicine patient adverse events and as a common source of disciplinary action against physicians. At an international, national and local level, it has been noted that trainees receive inadequate training in clinical pharmacology and therapeutics. In addition, overdose and drug use disorders are common and require toxicology knowledge and expertise.

Clinical pharmacologists with combined clinical expertise, critical appraisal abilities, knowledge of drug action and familiarity with regulatory and reimbursement policies influence healthcare at all levels (policy, provider and patient) and are in exceedingly short supply.

It is imperative that each practicing medicine specialist has a basic competence in safe prescribing and evidence-based therapeutics.

WHAT DO WE MEAN BY PRESCRIBING COMPETENCE?

Every physician, no matter what specialty, must learn to prescribe competently, which means choosing medications based on an accurate diagnosis, indication, prior therapies, applying high levels of evidence for effectiveness, safety and cost-effectiveness. In addition, prescribing competence requires ongoing monitoring for benefit and harm, expertise in patient communications, knowledge of the regulatory and formulary environment, and an ability to de-prescribe appropriately.

Institute for Safe Medical Practices

WHY IS CPT KNOWLEDGE AND PRESCRIBING COMPETENCE CRITICAL TO SAFE AND EFFECTIVE MEDICAL PRACTICE?

Clinical Pharmacology and Toxicology knowledge and Prescribing competence, especially in training and early years of practice, correlates with fewer medication errors, better licensing exam results, fewer professional disciplinary complaints, and improved sustainability of health care.

References:

- College of Physicians and Surgeons of Ontario. <u>PRESCRIBING DRUGS</u>. December 2019.
- World Health Organization. MEDICATION WITHOUT HARM. 2022.

BASIC PHARMACOLOGY PRINCIPLES FOR PRESCRIBERS

A few helpful pharmacology e-textbooks:

- Goodman & Gilman's: The Pharmacological Basis of Therapeutics, 14e | AccessMedicine | McGraw Hill Medical (mhmedical.com)
- Basic & Clinical Pharmacology, 15e | AccessMedicine | McGraw Hill Medical (mhmedical.com)
- The Washington Manual of Medical Therapeutics

Links to Dr. Mitch Levine's pharmacology talks:

*disclaimer: you need to have, and use, a Medportal login to access the links below

- Natural Health Products | Session · medportal
- Pharmacokinetics | Session · medportal
- Pharmacokinetics Part 2 | Session · medportal
- Clinical Pharmacology | Session · medportal

A Medical Toxicology curriculum for medical students has been suggested by a consensus group in the USA. See below for Prescribing Safety Assessment Domains:

Table 1: Prescribing Safety Assessment Question Domains

1. Review the exam format, time available, open book resources allowed. There are 8 domains tested in the PSA.

Prescription Writing	Writing a prescription requiring decisions regarding specific drug, dose, route and frequency based on clinical circumstances and supplementary information.
Prescription Review	Deciding which components of the current prescription list are inappropriate, unsafe, or ineffective based on clinical circumstances.
Planning Management	Deciding which combination of therapies would be the most appropriate to manage a particular clinical situation.
Providing Information	Deciding which are the important pieces of information that should be provided to patients to allow them to choose whether to take the medication, or to enhance its safety and effectiveness.
Calculation Skills	Making an accurate drug dosage calculation based on numerical information.
Adverse Drug Reactions	Identifying likely adverse reactions of specific drugs, drugs that are likely to be causing specific adverse drug reactions, potentially dangerous drug interactions and deciding on the best approach to managing a clinical presentation that results from the adverse effects of a drug.
Drug Monitoring	Deciding on how to monitor the beneficial and harmful effects of medicines.
Data Interpretation	Deciding on the meaning of the results of investigations as they relate to decisions about on-going drug therapy.

- 2. Since the Canadian PSA is open book, decide on resources that you want to use during the exam, for example, UptoDate, Lexicomp, RxTx, ODB formulary, etc.
- 3. Take time to do all of the practice exams allowed.

Holbrook A, Liu JT, Rieder M, Gibson M, Levine M, Foster G, et al. Prescribing competency assessment for Canadian medical students: a pilot evaluation. Canadian Medical Education Journal. 2019;10(1):e103-e110.

Liu J, Wong S, Foster G, Holbrook A. Prescribing Competency of Medical Students: National Survey of Medical Education Leaders. Journal of Population Therapeutics and Clinical Pharmacology January 2018; doi 10.22374/1710-6222.25.1.2

12 | TOXICOLOGY

Access the Canadian Antidote Guideline from the Quebec Poison Centre here (language can be switched to English if required) Antidote Guideline

The following poison control resources for health professionals can be found on the <u>Ontario Poison Centre</u> website:

Patient care resources – Resources

Priority – <u>Priority Queue</u>

Overdose management – Opioid Overdose Management

Antidotes – Antidotes

Personal health information – Privacy

<u>Toxicology Times Newsletter:</u>

- 1. Volume 1, Issue 1A Acetaminophen
- 2. Volume 1, Issue 1B <u>Acetaminophen</u>
- 3. Volume 1, Issue 2 <u>Mushrooms</u>

Below you will find the link to an informative talk on toxicology. *Disclaimer: you must have, and use, a medportal login to access this talk.

Toxicology | Session - Medportal

Toxicology Textbook: Students should review *Goldfrank's Toxicologic Emergencies (11th Edition)*. This text is available to purchase online, however students should be able to access this resource through their institutional library.

DRUG REGULATION AND FORMULARY SYSTEM IN CANADA

Canadians do not have universally funded Pharmacare. They do, however, in most provinces, have incomeadjusted access to a formulary of approximately 4000 medications. Health Canada's federal drug regulation system works similarly to the FDA in the USA and EMEA in Europe. Manufacturers bring drugs for approval based primarily on efficacy while demonstrating acceptable safety. Promising medications for serious conditions where there is a high need for better therapies are sometimes granted Notice of Compliance with Conditions (NoCC) where additional evidence must be gathered to confirm initial impressions of efficacy and safety. This is an important distinction from full Notice of Compliance (NoC) as NoCC medications frequently do not turn out to be safe and effective.

Once cleared by Health Canada with NoC, medications are usually submitted to the Common Drug Review at CADTH (Canadian Agency for Drugs and Technology in Health) for recommendations regarding funding through public formularies in the provinces and territories. This requires an additional and more rigorous standard of evidence based on societal value, systematic review of the evidence with economic analysis of cost-effectiveness, and burden of illness.

The recommendations from the expert advisory committees based on the above review, are then considered by the individual provinces/territories and a formulary designation made. In Ontario, this is managed by the Ontario Public Drug Benefit Program. This program covers, seniors 65 years and older, children and youth 25 years and younger, those on disability or social assistance, and those with extreme drug expenditures relative to household income.

Drug Product Database online query (canada.ca) Formulary Search (gov.on.ca) The Drug Review and Approval Process in Canada

CADTH. Reimbursement Reviews. 2020.

CMPA. Medication Safety. 2021.

HOW TO AVOID CPT AND PRESCRIBING MEDICOLEGAL TROUBLE

It has been shown that poor training in medical school and poor communication skills with patients, predict medicolegal trouble in practice. Trainees are referred to earlier chapters on Advice on Prescribing from the CPSO. Careful review of advice from the Canadian Medical Protective Association (CMPA), is also crucial to safe and successful practice.

HOW TO BE AN EFFECTIVE PATIENT **ADVOCATE**

Health Advocacy is a key role and competency for physicians in Canada, so much so that it is one of the main CanMEDS competencies.

In our discipline, typical patient advocacy roles include:

- a) completing forms regarding restricted access to expensive non-formulary medications for patients meeting criteria or where there is no other option
- b) continually working with patients to reduce and discontinue their exposure to harmful medications including alcohol, tobacco, cocaine and similar stimulants, high dose opioids, etc.
- c) recognizing and remediating vulnerable situations where patients are at risk of lethal overdoses or poisonings.
- d) participating in high quality research with patients that will address important medication-related questions.
- e) discouraging use of expensive, supplements and natural health products which lack adequate evidence of effectiveness and safety, and are not regulated in terms of contamination.

CMPA. Participating in Health Advocacy.

LEARNING OBJECTIVES FOR CPT FOR MEDICAL STUDENTS AND RESIDENTS

One or more interactive elements has been excluded from this version of the text. You can view them online here: https://ecampusontario.pressbooks.pub/

clinicalpharmacologyandprescribingskillsformedicine/?p=34

APPROPRIATENESS OF PRESCRIBING **EVALUATION TOOLS**

APPROPRIATENESS OF PRESCRIBING QUESTIONNAIRE (APEQ) DOMAINS Holbrook, AM et al.

(More specific criteria are developed for each drug/drug family)

- 1. Indication appropriate diagnosis?
- 2. Indication appropriate prior therapy?
- 3. Benefit/Harm optimal Drug Choice based on RCT Evidence?
- 4. Dosage correct?
- 5. Directions correct (where relevant)?
- 6. Clinically important drug-drug interactions?
- 7. Clinically important drug-disease interactions (contraindications)?
- 8. Unnecessary therapeutic duplication?
- 9. Duration acceptable duration to next physician assessment?
- 10. Cost-effectiveness relative to other drugs or treatments in the same therapeutic class?

Reference:

 A comprehensive appropriateness of prescribing questionnaire was validated by nominal consensus group

ESSENTIAL DRUGS LIST FOR CANADIAN MEDICAL STUDENTS

List curated by CPT specialists, internal medicine and pediatric specialists, regularly updated. This is modelled after the long-standing World Health Organization concept of an essential drugs list for poor countries, however our list has been modified to be relevant for Canadian practice. Most physicians will prescribe most frequently a core list of approximately 50-80 medications throughout their career. Our Essential Drugs List deliberately attempts to influence what that list should include.

Holbrook A. McMaster Essential/Core Drugs List for Medical Students. MacSphere, McMaster University: Medicine Publications collection; Hamilton ON, 2022. http://hdl.handle.net/11375/27291



An interactive H5P element has been excluded from this version of the text. You can view it online here:

https://ecampusontario.pressbooks.pub/ clinicalpharmacologyandprescribingskillsformedicine/?p=38#h5p-2

INTRODUCTION TO E-PRESCRIBING **CURRICULUM RESOURCES**

This product of a previous eCampusOntario grant provides a curated list of key e-curriculum resources that have been evaluated by clinical, research, usability and e-learning experts. Most resources are international (for example, the Australian National Prescribing Curriculum (NPC) is excellent), therefore Canadian preambles are provided for areas of translation.

General Preamble

Our own work with Canadian medical students shows that many lack basic clinical pharmacology and therapeutics knowledge, and prescribing skills as schools struggle to meet all of their required curricula objectives. 1, 2 Expertise in this broad-based specialty is scarce, and most medical schools no longer have dedicated clinical pharmacology courses. However, for the first time, the Medical Council of Canada has recently launched specific Prescribing Practices objectives that schools must cover.³

Safe prescribing is a complex activity requiring detailed knowledge of dozens of drug families, accurate patient diagnosis and individual risk assessment, excellent communication and interprofessional collaboration skills, and professionalism. More than 700 million prescriptions are written annually in Canada for drugs from approximately 1100 therapeutic groups. 4 Medication errors are common, usually go unrecognized and can pose a serious patient safety hazard.^{2, 5-8} Medical students and residents are especially vulnerable, with prescribing errors on 7-10% of their prescriptions.⁵

Competent prescribing and medication management is even more essential as years go on, given the dozens of new medications introduced each year, primarily high-risk medications and very expensive medications, increasing numbers of patients with extreme polypharmacy, lethal problems with drug overdose and poisoning, and poor adherence with effective medications.

- a. Royal College of Physicians and Surgeons of Canada: The Prescribing Safely Canada Physician Prescribing Competencies – Executive Summary
- b. The Prescribing Safely Canada Physician Prescribing Competencies- https://oracle.royalcollege.ca/ mssites/prescribingsafely/EN/PSCCOMP2018.pdf
- c. College of Physicians and Surgeons of Ontario's Advice to the Profession on Prescribing Drugs CPSO Prescribing Drugs CPSO - Advice to the Profession: Prescribing Drugs Additional, valuable documents for learners on the prescribing competence topic include:

- d. The World Health Organization's Guide to Good Prescribing: A Practical Manual useful not specifically for the patient examples or specific drug examples, but for the recommended process of prescribing.
- e. The Essential Drugs List for McMaster Medical Students: http://hdl.handle.net/11375/27291 useful for specific drug and drug family examples that should become familiar to every medical trainee
- f. The Institute for Safe Medication Practices Canada (ISMP Canada)'s resources including i) DO NOT USE List of Dangerous Abbreviations Symbols and Dose Designations abbreviations, symbols, and dose designations reported as being frequently misinterpreted and contributing to harmful medication errors, and ii) List of High-Alert Drugs medications with an increased risk of causing significant patient harm when they are used inappropriately, including lack of indication, wrong dose, contraindications, etc. ^{2, 10}
- g. Health Canada's Drug Product Database provides access to the full product monographs from all manufacturers of medications approved for use in Canada. Product monographs are the 'bottom line' on your medico-legal responsibilities. In other words, if a medication does not have an official indication for the disease or condition that you are treating or does not have clear, supportive randomized trial evidence, and you cannot justify that you have tried all other reasonable avenues and the patient was aware of and agreed with your rationale to prescribe the drug, then if a major adverse event related to the drug occurs, you will be at risk of successful legal and disciplinary challenge.
- h. Drug formulary and coverage is an essential consideration when prescribing any medication. Formularies in Canada are based on the highest quality cost-effectiveness information and evaluation. Each province and territory has their own that can be accessed individually. For Ontario, this can be accessed via: https://www.formulary.health.gov.on.ca/formulary/.
- i. Conflicts of Interest Physicians must avoid conflicts of interest to ensure that their professional
 priorities remain patients and advancing healthcare, particularly when dealing with the pharmaceutical
 and device industry.¹²

References:

- 1. Holbrook A, Liu JT, Rieder M, Gibson M, Levine M, Foster G, et al. Prescribing competency assessment for Canadian medical students: a pilot evaluation. Can Med Educ J. 2019;10(1):e103-e10. ↑
- 2. Liu J, Wong S, Foster G, Holbrook A. Prescribing Competency of Medical Students: National Survey of Medical Education Leaders. J Popul Ther Clin Pharmacol. 2018;25(1):e18-e24. ↑
- 3. MCC. Prescribing Practices Ottawa, Canada: MCC; 2022 [Available from: https://mcc.ca/objectives/expert/key/125/]. \(\dagger
- 4. Canada Health Infoway. Current prescribing and dispensing landscape in Canada: CHI; 2017

[Available from: https://infocentral.infoway-inforoute.ca/en/resources/docs/medmgmt/ 1778-report-2017-current-prescribing-and-dispensing-landscape-in-canada. Accessed on 23 Apr 2019].

- 5. Dornan T, Ashcroft D, Heathfield H, Lewis P, Miles J, Taylor D, et al. An in-depth investigation into causes of prescribing errors by foundation trainees in relation to their medical education: EQUIP study. London: General Medical Council. 2009:1-215. \(\dagger
- 6. Lazarou J, Pomeranz BH, Corey PN. Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. JAMA. 1998;279(15):1200-5. 1
- 7. Ryan C DP, Francis J, Johnston M, Ker J, Lee AJ, et al. The Prevalence of Prescribing Errors amongst Junior Doctors in Scotland. Basic and Clinical Pharmacology and Toxicology. Basic and Clinical Pharmacology and Toxicology. 2011;109(35). 1
- 8. Young H. Lack of pharmacological training causes overuse and misuse of drugs. CMAJ. 2008;178(3):276.
- 9. ISMP. Do Not Use: Dangerous Abbreviations, Symbols and Dose Designations. Toronto, ON: ISMP 2018 [Available from: https://www.ismp-canada.org/download/ $\underline{ISMPCanadaListOfDangerousAbbreviations.pdf}]. \uparrow$
- 10. ISMP. ISMP List of High-Alert Medications in Acute Care Settings. Toronto, ON: ISMP; 2018 [Available from: https://www.ismp.org/sites/default/files/attachments/2018-08/highAlert2018-Acute-Final.pdf]. \(\daggerap
- 11. CADTH. Guidelines for the Economic Evaluation of Health Technologies: Canada. Ottawa, ON: CADTH; 2017. 1
- 12. CPSO. Physicians' Relationships with Industry: Practice, Education and Research. Toronto, ON: CPSO; 2014 [Available from: https://www.cpso.on.ca/Physicians/Policies-Guidance/Policies/ Physicians-Relationships-with-Industry-Practice]. \(\Delta\)

Holbrook A, Patel D, Yoo L. Introductory Preambles to Clinical Pharmacology and Toxicology eCurriculum Resources for Canadian Medical Students [MacSphere]. McMaster University, Department of Medicine: Hamilton, Ontario; 2022. Available from http://hdl.handle.net/11375/27381

INTRODUCTION TO MEDICATION SAFETY

Links to Australian National Prescribing Curriculum course with Canadian adaptation (eg, <u>Choosing Wisely Canada</u>), and Vanessa's Law reporting obligations, with interpretation preambles for medical students.

Understanding Medication Safety

Preamble:

Differences in terms used:

- a. Registrar vs Resident (Canada)
- b. Specialised vs Specialized
- c. Concept of Open Disclosure Open discussion with patients and/or family members

Therapeutics:

- a. Scenario 1: Methotrexate Overdose real example from a teaching hospital in Australia. Emphasize not using 'ad' in Australia which is 'od' in Canada. The drug is prescribed weekly.
- b. Scenario 2: Inadvertent Rx for Fentanyl in an incorrect patient's chart

Resources:

- a. The statistics used for medication errors are Australia based
 - i. E.g. % of prescribing error, % of reported errors, % of administration errors etc.
- b. Understanding and Reporting medication errors
 - i. CMIRPS
 - Canadian Medication Incident Reporting and Prevention System Program | ISMP Canada
 - ii. NCC MERP Index for Categorizing Medication Errors
 Types of Medication Errors | NCC MERP

APPROACH TO ANTIMICROBIAL **PRESCRIBING**

PHAC Antibiogram for Ontario



An interactive H5P element has been excluded from this version of the text. You can view it online here:

https://ecampusontario.pressbooks.pub/ clinicalpharmacologyandprescribingskillsformedicine/?p=44#h5p-12

Dr. Spellberg's video recording for grand rounds:

Short Course Antibiotic Therapy. Youtube [internet]. Los Angeles County, University of Southern California; October 13 2022 [cited October 20 2022]. Available from Short Course Antibiotic Therapy – YouTube.



One or more interactive elements has been excluded from this version of the text. You can view them online here: https://ecampusontario.pressbooks.pub/

clinicalpharmacologyandprescribingskillsformedicine/?p=44#oembed-1

Link to Dr. Spellberg's antibiotics website: Shorter Is Better | mysite (bradspellberg.com) Access the National Prescribing Curriculum (NPC) here https://learn.prescribing.edu.au/ NPC course: https://learn.nps.org.au/

Preamble:

Differences in terms used:

- a. Optimising vs Optimizing
- b. Multi-resistant gram-negative (MRGN) organisms vs. ??? Multi-drug resistant organisms
- c. Australian suburban hospital → Canadian suburban hospital
- d. Emergency Senior Registrar → Senior Resident
- e. General practitioner → Family doctor

24 | APPROACH TO ANTIMICROBIAL PRESCRIBING

- $f. Loin \rightarrow Flank$
- g. EMMS / NIMC vs EMR / patient chart

Therapeutics:

a. 7-10 days therapy is usually sufficient for targeted therapy. No need for 14 days

Resources:

- a. IDSA guidelines
- b. Antimicrobial Stewardship resource
- c. C. diff risk with broad spectrum use

INTRODUCTION TO DRUG INTERACTIONS AND ADVERSE DRUG EVENTS

Link to useful introduction on the importance of Drug Interactions to Adverse Drug Events:

• Preventable Adverse Drug Reactions

*disclaimer: you must have, and use, a Medportal login to access the link below

- Adverse Drug Reactions | Session · medportal
- Drug Interactions | Session · medportal
- Drug Metabolism | Session · medportal

RECOMMENDED CLINICAL PHARMACOLOGY CASE-BASED LEARNING

Mandatory National Prescribing Curriculum modules for Transitions to Clerkship

To access the Australian National Prescribing Curriculum modules, you must first create a *free* account <u>here</u> (only limited modules will allow guest access).

Our team has rated the quality and relevance of the Australian National Prescribing e-curriculum the highest and created Canadian 'translation' preambles for key modules, which can be accessed <u>here.</u>

Type 2 Diabetes: Initiating Treatment

Preamble: The case description and details about symptoms, vitals, history etc. are reasonable and should be understood by the Canadian learners.

Differences in terms used:

- a. Haemoglobin vs hemoglobin
- b. Capillary Blood Glucose Level (BGL) vs Blood Glucose (BG) (*they also use mmol/L as the unit of measurement)
- c. Anaemia vs anemia
- d. TDS vs TID

Laboratory Values:

Parameter	Module	2018 Diabetes Canada Clinical Practice Guidelines	Hamilton Regional Laboratory	
Triglycerides (TG)	< 2 mmol/L	<1.5 mmol/L		
Albumin to Creatinine Ratio (ACR)	> 2.5 mg/mmol in men and > 3.5 mg/mmol in women is indicative of microalbuminuria	2 – 20 mg/mmol is the range considered for microalbuminuria. uACR>20 mg/mmol is considered overt nephropathy		
Potassium	3.2 – 4.3	N/A	3.5 – 5.2 mmol/L	
Serum Creatinine	60 – 120	N/A	60 – 110 umol/L	
ALT		N/A		
AST		N/A		
ALP		N/A		
GGT		N/A		
Albumin	$34-48\mathrm{g/L}$	N/A	42 – 50 g/L	
Target Blood Glucose Ranges	"Generally, the HbA1c target for most people with type 2 diabetes is ≤ 53 mmol/mol (7%) and the fasting blood glucose level is between 6 and 8 mmol/L."	FBG: 4 – 7 mmol/L (or 4 – 5.5 mmol/L if diabetes is not well controlled)	N/A	
		2-hour post-prandial: 5 – 10 mmol/L (or 5 – 8 if diabetes is not well-controlled)	IN/A	

Therapeutics:

- a. Metformin: Module states, "Metformin is available in a fixed dose combination with glibenclamide. Due to risk of hypoglycaemia with glibenclamide, blood glucose levels should be monitored when switching a patient to the fixed dose combination." Glibenclamide is known as glyburide in Canada.
- b. Long term safety and outcome data DPP-4 inhibitors have on diabetes related complications are lacking - not necessarily true; we have CV outcome data from SAVOR-TIMI, CARMELINA, etc.
- c. Metformin: Dose: 500 mg once daily PO increasing to maximum 1 g tds PO ◊ ["TDS" = "TID"]; According to the 2018 Diabetes Canada guidelines, the maximum dose of metformin is 2.55 grams per day (i.e. 1000 mg QAM + 500 mg at lunch + 1000 mg QPM)
- d. Vildagliptin: Vildagliptin is not available in Canada
- e. Semaglutide is missing from the list of GLP1-RA drugs (the list only includes exenatide, liraglutide, and dulaglutide)
- f. Acarbose: Module states that the maximum dose is "maximum 600 mg daily". The maximum dose is

- 100 mg TID, i.e. 300 mg daily (total)
- g. Glipizide is not available in Canada
- h. Canagliflozin is missing from the list of SGLT2 inhibitor drugs (the list only includes dapagliflozin, empagliflozin, and ertugliflozin)
- i. Dapagliflozin also comes in 5 mg tablets (not just 10 mg tablets) in Canada
- j. Fiasp (faster insulin aspart) is missing from the list of ultra-short acting insulins
- k. For the insulins, there should be a table that outlines the onset, peak, and duration of action for each group/type of insulin
- 1. There should be a note that ultra-short acting insulins (i.e. rapid-acting insulins) can also be used in CSII (insulin pump) regimens
- m. Short-acting insulin is also referred to as "Insulin Regular" in Canada (not "Insulin Neutral" as in the module). Canadian Brand Names for short-acting insulin/insulin regular include: "Humulin R", "Novolin GE Toronto", "Novolin R", "Entuzity"
- n. Insulin degludec (Tresiba) is not missing from the list of long-acting insulins
- o. In Section "15. More prescription feedback", there are a number of statements pertaining to the preference for Sulfonylureas as add-on therapy after metformin:
 - i. In Sub-Section 1, it says: "If metformin cannot be tolerated or is contraindicated, a sulfonylurea would be an alternative first-line medication. Sulfonylureas are associated with weight gain and hypoglycaemia, which is why metformin is the preferred first-line treatment wherever possible. As Richard has no previous intolerance to metformin and no contraindications, metformin is the best choice for initial treatment." → Sulfonylureas have fallen out of favour and are no longer the preferred alternative to metformin for second-line therapy. Either an agent with proven CV benefit (if the patient has CV risk factors or has CVD) is preferred and if not, then another class of antihyperglycemics like SGLT2 inhibitors, DPP4 inhibitors are preferred.
 - ii. In Sub-Section 3, it says, "Sulfonylureas are considered add-on therapy to metformin when glycaemic targets are not met on monotherapy. Before intensifying treatment by adding a sulfonylurea, make an assessment of compliance to the metformin dosing regimen, and specifically ask about the presence of troubling gastrointestinal adverse effects. Sulfonylureas are considered a reasonable alternative for first-line treatment if there are contraindications to using metformin."
 - iii. In subsection 4, it says, "It would be unusual to initiate treatment of type 2 diabetes with a DPP-4 inhibitor. Sulfonylureas are the usual initial add-on medicine if monotherapy with metformin is not effective at achieving blood glucose targets. DPP-4 inhibitors (or SGLT2 inhibitors) are an alternative to sulfonylureas as add-on therapy, after considering patient preference, the presence of problematic hypoglycaemia, weight gain or other adverse effects."
- p. Sulfonylureas are considered a reasonable alternative for first-line treatment if there are contraindications to using metformin.

Resources:

- a. Diabetes Canada 2018 Clinical Practice Guidelines
- b. FIT (Forum for Injection Technique) Guidelines

Other Problems:

"Glycated haemoglobin (HbA1C) is reimbursable through Medicare for the diagnosis of type 2 diabetes in asymptomatic patients determined to be at high risk (e.g. ethnic background, score of 12 or greater using the Australian type 2 diabetes risk assessment tool [AUSDRISK]).

<u>Urinary Tract Infection</u>

Preamble:

Differences in terms used:

- a. Loin pain vs flank pain
- b. Bacteraemia vs Bacteremia
- c. Amenorrhea vs Amenorrhea
- d. Systemic Inflammatory Response Syndrome (SIRS) ?? Canadian equivalent
- e. Leucocytes vs Leukocytes
- f. Consumer Medicine Information (CMI) vs. Patient Information Leaflet

Therapeutics:

a. For uncomplicated UTI – we usually recommend Nitrofurantoin 100mg po bid x 5 days **OR** SMX/ TMP DS 1-tab po bid x 3 days (Note that the NPS module recommended Trimethoprim 300mg po daily x 3 days)

Resources:

- a. Module has a resource for asking your patients about sexual history in a sensitive way need to identify something Canadian (Sexually Transmitted Diseases)
- b. IDSA instead of Australasian Society of Infectious Diseases
- c. Urinary Tract Infections IDSA guidelines

Postoperative Pain and Vomiting Analgesia for Low Back Pain **Polypharmacy**

Chronic obstructive pulmonary disease (COPD) exacerbation

Preamble: Important clarifications for Canadian medical students:

Differences in medical terms used, for example:

- a. **o**edema vs. **e**dema
- b. **registrar** vs. senior resident ("You make a diagnosis of acute exacerbation of COPD. You discuss this with your registrar, who agrees and states that Mary should receive bronchodilators..."). The term "Registrar", in Canada, would be equivalent to a senior resident.

Potential differences in normal reference ranges for certain laboratory values:

a. Note there may be slight differences in the normal ranges of certain laboratory parameters contained within this module and the standard reference values used in Canada. Reference lab values are often institution- or site-specific; for example, the Hamilton Health Sciences and St. Joseph's Healthcare Hamilton follow the references ranges set by the Hamilton Regional Laboratory Medicine Program (HRLMP), which is one of the largest integrated laboratory service programs in Canada. Please see:

<u>Laboratory Test Information Guide</u> and <u>Hamilton Regional Laboratory Medicine Program</u> for more information.

Potential differences in therapeutics:

- a. Choice of Antibiotic for acute COPD exacerbation: The Australian module recommends Amoxicillin or Doxycycline. Canadian recommendations vary depending on risk for Pseudomonas infection, inpatient vs outpatient setting, etc. Outpatient setting and low risk for Pseudomonas antibiotic choices are typically amoxycillin-clavulanate or a respiratory quinolone. Patients with multiple (more than 2) exacerbations per year are occasionally treated with azithromycin.
- b. The module talks about recommending COPD patients for influenza and pneumococcal vaccine and then provides a link to The Australian Immunisation Handbook. Canadian physicians would follow NACI guidance: Immunization of persons with chronic diseases: Canadian Immunization Guide Canada.ca
- c. There is a link to Australian VTE prophylaxis resource (in the scenario that patient will have limited mobility and admitted) we refer to Thrombosis Canada: thrombo-prophylaxis in the hospitalized medical patient
- d. The GOLD (Global Initiative for Chronic Obstructive Lung Disease) Guidelines have published a <u>Pocket Guide to COPD Diagnosis, Management, and Prevention for Healthcare Professionals</u> (updated as of 2020).

Canadian-Specific Resources:

- a. Two Canadian organizations for respiratory health that provide exceptional resources are outlined below, along with specific and relevant resources from each:
 - i. The Ontario Lung Association (also known as "The Lung Health Foundation")
 - 1. Clinical Tools
 - 2. <u>E-Modules</u>
 - ii. The Canadian Lung Association (also known as "Breathe: The Lung Association")
 - 1. How to use your inhaler
- b. Some of the newer inhalation devices may be prone to errors in usage and technique, which may pose potential efficacy and safety risks. The Institute for Safe Medication Practices Canada (ISMP Canada) produced a 1-page document outlining pertinent counselling points when training and educating patients about the appropriate use of these devices: <u>InhalationDevices-ReferencePoster (ismp-</u> canada.org)
- c. The Canadian Thoracic Society (CTS) has a <u>library of guidelines</u>, <u>updates/notices</u>, <u>and position</u> statements pertaining not just to asthma and COPD but other relevant topics such as COVID-19, spirometry, home mechanical ventilation, pulmonary vascular disease, sleep disorders, etc.

<u>Hypertension</u>

Prevention of Venous Thromboembolism Child with Acute Otitis Media

Strongly suggested but not mandatory NPC Modules

- Antimicrobials: bacteremia (online course)
- Antimicrobials: surgical prophylaxis (online course)
- Antimicrobials: catheter-associated urinary tract infections (online course)
- Antimicrobials: community-acquired pneumonia (online course)
- Acute pulmonary edema (NPC module)
- Chronic heart failure (NPC module)Alcohol withdrawal delirium (NPC module)
- Lipid and CVD risk management (NPC)
- Delirium in an older person (NPC)
- Insomnia (NPC)
- H. pylori infection (NPC)
- Iron deficiency (NPC)
- Anticoagulation in atrial fibrillation (NPC)
- Management of acute coronary syndrome (NPC)

32 | RECOMMENDED CLINICAL PHARMACOLOGY CASE-BASED LEARNING

- Depression in adolescents (NPC)
- Acute mania in bipolar disorder (NPC)
- Preventing fractures: where to start with osteoporosis (NPC)

It is important to read **Katzung's Basic & Clinical Pharmacology, 16th Edition.** Student should be able to access this resource through their institutional library, and/or online here.

SPECIAL TOPICS IN CPT

Interests and Conflicting Interests



An interactive H5P element has been excluded from this version of the text. You can view it online here:

https://ecampusontario.pressbooks.pub/clinicalpharmacologyandprescribingskillsformedicine/?p=48#h5p-7

Goldfine C, Lung D, Beauchamp G, O'Connor A, Stolbach A, Kao L, Judge B, Wax P, Patwari R, Kazzi Z. Consensus Development of a Core Content for a Standardized Medical Toxicology Curriculum for Medical Students. J Med Toxicol. 2022 Apr;18(2):139-144. doi: 10.1007/s13181-021-00874-z. Epub 2022 Jan 28. PMID: 35089533; PMCID: PMC8796743.

A review of CPT 'Pearls of the Week' introduced by the University of Calgary is encouraged and can be accessed here <u>UCalgary CPT Pearl of the Week</u>

 st disclaimer: you will need to have, and use, a Medportal login to access the links below

- Maternal Fetal Pharmacology | Session · medportal
- Drug Use in Renal Dysfunction | Session · medportal

Please review the special presentation on opioid use below:



An interactive H5P element has been excluded from this version of the text. You can view it online here:

https://ecampusontario.pressbooks.pub/clinicalpharmacologyandprescribingskillsformedicine/?p=48#h5p-6

CASE-BASED CPT QUIZZES

Opioids and Non-opioids in the Management of Pain: Time for Change



An interactive H5P element has been excluded from this version of the text. You can view it online here:

https://ecampusontario.pressbooks.pub/clinicalpharmacologyandprescribingskillsformedicine/?p=50#h5p-6

Just say KNOW to drugs



An interactive H5P element has been excluded from this version of the text. You can view it online here:

https://ecampusontario.pressbooks.pub/clinicalpharmacologyandprescribingskillsformedicine/?p=50#h5p-8

PRESCRIPTION WRITING PRACTICE AND **FEEDBACK**

Please visit the College of Physicians and Surgeons of Ontario (CPSO) for an introduction of have to correctly write prescriptions here.

We are developing a computerized prescription writing assessment tool that will allow much broader formative practice, assessment and feedback for medical students and residents to practice their therapeutics and prescribing skills in a safe environment. This will be a form of ClinPharmTox simulation.

In the meantime, try this Prescription Writing simulation:



An interactive H5P element has been excluded from this version of the text. You can view it online here:

https://ecampusontario.pressbooks.pub/ clinicalpharmacologyandprescribingskillsformedicine/?p=52#h5p-10

Click here to Download this exercise.

Reference:

• Khatami A, Holbrook A, Levinson AJ, Keshavjee K. Software Architecture for Automated Assessment of Prescription Writing [MacSphere]. McMaster University, Department of Medicine: Hamilton, Ontario; 2022. Available from http://hdl.handle.net/11375/27383

PREPARATION FOR THE CANADIAN PRESCRIBING SAFETY ASSESSMENT

Concerns about prescribing competence are not isolated to North American medical graduates. The EQUIP study in England reviewed 124,260 medication orders finding an error rate as high as 10.3% amongst junior housestaff. In response to this study and a series of serious medication safety incidents, education leaders in clinical pharmacology and the British Pharmacological Society instituted the Prescribing Safety Assessment (PSA), an online exam that final year medical students must pass prior to their licensing exams. The full PSA consists of 60 questions and lasts for two hours, drawing on a large database of validated questions. Students participate in the PSA at the end of medical school a few months before their medical licensure examinations, and are encouraged to prepare using practice resources.(14) Approximately 53,000 students have completed the exam in the last five years, with very positive feedback on fairness and the helpfulness of the exam to their competence to practice. These students expressed appreciation for the initiative taken to address the prescription competency concerns, for increased their confidence when prescribing as a first year resident, and for making them aware of key prescribing resources such as formularies.

The Canadian PSA is a 30-question, 1 hour exam modified by Dr Holbrook from the British PSA. It has been tried consistently at McMaster University and sporadically at other Ontario medical schools over a 7-year period, with very good face validity. The exam is meant to be a formative assessment near the end of medical school as a measure of readiness for residency. Practice exams are made available for the Transitions to Clerkship period.

Recommendations to prepare for the PSA exam include:

1. Review the exam format, time available, open book resources allowed. There are 8 domains tested in the PSA.

Table 1: Prescribing Safety Assessment Question Domains

Prescription Writing	Writing a prescription requiring decisions regarding specific drug, dose, route and frequency based on clinical circumstances and supplementary information.
Prescription Review	Deciding which components of the current prescription list are inappropriate, unsafe, or ineffective based on clinical circumstances.
Planning Management	Deciding which combination of therapies would be the most appropriate to manage a particular clinical situation.
Providing Information	Deciding which are the important pieces of information that should be provided to patients to allow them to choose whether to take the medication, or to enhance its safety and effectiveness.
Calculation Skills	Making an accurate drug dosage calculation based on numerical information.
Adverse Drug Reactions	Identifying likely adverse reactions of specific drugs, drugs that are likely to be causing specific adverse drug reactions, potentially dangerous drug interactions and deciding on the best approach to managing a clinical presentation that results from the adverse effects of a drug.
Drug Monitoring	Deciding on how to monitor the beneficial and harmful effects of medicines.
Data Interpretation	Deciding on the meaning of the results of investigations as they relate to decisions about on-going drug therapy.

- 2. Since the Canadian PSA is open book, decide on resources that you want to use during the exam, for example, UptoDate, Lexicomp, RxTx, ODB formulary, etc.
- 3. Take time to do all of the practice exams allowed.

References:

- Holbrook A, Liu JT, Rieder M, Gibson M, Levine M, Foster G, et al. Prescribing competency assessment for Canadian medical students: a pilot evaluation. Canadian Medical Education Journal. 2019;10(1):e103-e110.
- Liu J, Wong S, Foster G, Holbrook A. Prescribing Competency of Medical Students: National Survey of Medical Education Leaders. Journal of Population Therapeutics and Clinical Pharmacology January 2018; doi 10.22374/1710-6222.25.1.2.

MEDICAL COUNCIL OF CANADA **OBJECTIVES ON PRESCRIBING PRACTICES**

Available at: https://www.mcc.ca/objectives/expert/key/125/. Accessed June 14, 2021

PRESCRIBING PRACTICES — 125

Rationale:

Prescribing medications safely is a central component of most physicians' activities and requires appropriate medical knowledge, skill, professional judgment, and an understanding of the applicable legislation related to prescribing.

Key Objectives:

To safely and effectively manage a patient presenting with a condition that requires prescription medication, the candidate will first undertake a thorough clinical assessment and then apply principles of evidence-based medicine and cost effectiveness in prescribing.

Enabling Objectives:

Given a patient that requires a medication to be prescribed safely and effectively, the candidate will

- 1. Undertake a thorough clinical assessment, including:
 - a. complete medication history, including allergies and intolerances;
 - b. a review for adherence and effectiveness of the patient's current medications;
 - c. address polypharmacy and the options for deprescribing; and
- 2. Apply principles of clinical pharmacology in prescribing medication to:
 - a. address the effect of comorbidities, current medications, liver and renal function, genetics, age, and pregnancy on the risks and benefits of prescribing the medication;
 - b. apply an evidence-based approach to clinical and cost effectiveness, including prescribing generic medications when appropriate;
 - c. anticipate the potential for adverse effects and take steps to mitigate them (e.g., prescribing appropriate routes, strengths, and quantities of medication);
 - d. recognize potential medical interactions when prescribing new medications;
 - e. recognize barriers to patients access to the medication (e.g., affordability, accessibility, supply) and advocate to resolve these where possible; and
- 3. Document the prescription appropriately, including:
 - a. generating a clear and legible prescription that meets legal requirements;
 - b. recognizing common cases of medication errors and how they can be prevented;
 - c. creating contemporaneous clinical notes of prescribing decisions;

40 | MEDICAL COUNCIL OF CANADA OBJECTIVES ON PRESCRIBING PRACTICES

- d. documenting appropriate follow-up plans for review of the effectiveness of the prescribed medication and any adverse effects encountered; and
- 4. Communicate with the patient or, if appropriate, their family or caregivers to:
 - a. build a therapeutic relationship that encourages adherence but respects the patient's
 - b. values, beliefs, and expectations about medications and their right to refuse treatment;
 - c. ensure they understand the rationale for the prescription;
 - d. provide them with information about any adverse effects, how to report them, and what they should do if adverse effects occur;
 - e. ensure that those involved in sharing care or transfer of prescribing responsibilities are adequately informed about the prescription.