Pharmacology Learning Objectives

2026 Edition

September 2026

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PREFACE TO THE 2026 EDITION

The 2026 *Pharmacology Learning Objectives (PLOs)* provide a contemporary guide for teaching and learning pharmacology across health professions programs. Formerly titled the *Pharmacology Knowledge Objectives*, the change in title reflects an expanded emphasis on learning outcomes that extend beyond knowledge acquisition to the application and integration of pharmacological concepts. The PLOs are intended to support faculty in developing, delivering, and assessing pharmacology content while allowing flexibility to adapt their use to the goals, structure, and instructional time of individual curricula.

This revised edition is the result of a collaborative effort by the AMSPC and ASPET's Division for Pharmacology Education, involving pharmacology educators and subject-matter experts from diverse health professions programs. We gratefully acknowledge the Section Teams and the many faculty and subject-matter experts who contributed their time, expertise, and thoughtful feedback throughout the revision process. Their collective efforts have helped shape a contemporary and adaptable resource for pharmacology education across the health professions.

The 2026 edition represents a substantive revision guided by several principles that inform both the development and use of this document:

1. **Learning outcomes and higher-order thinking**: The learning objectives have been revised using Bloom's Taxonomy, with greater emphasis on higher-order cognitive skills such as application, analysis, comparison, prediction, justification, and evaluation. This approach supports active learning, clinical reasoning, and pharmacotherapeutic decision-making, while moving beyond factual recall alone.

2. **Integration and clinical application:** The PLOs have been reorganized around the mechanism of action and effects, pharmacokinetics, pharmacogenomics (where applicable), therapeutic uses, adverse effects, drug monitoring, contraindications, and drug interactions. The mechanism of action and therapeutic use objectives incorporate pathophysiology and other foundational sciences, reflecting the integrated nature of pharmacology.

3. **Drug selection and representation:** Drug tables have been streamlined and reorganized by major drug classes and relevant subclasses, emphasizing clinically relevant and prototypical agents rather than exhaustive drug lists. All drugs are presented using their generic (nonproprietary) names. Drugs in ALL CAPITAL LETTERS represent major or prototypical drugs considered essential for student learning, whereas other relevant drugs are presented in lowercase.

4. **Curricular flexibility and adaptability:** The PLOs are not intended to serve as a comprehensive syllabus or student study guide. Rather, they provide flexible guidance that faculty can adapt to their programs and use to design instruction, active-learning activities, clinical cases, and assessments. Intentional overlap

among topics is retained when individual drugs or drug classes are relevant across multiple clinical contexts.

5. **Suggested time allocation:** Approximate teaching time is included for each topic to assist with curriculum planning. These estimates are intended as general guidance and may be adjusted based on the structure and emphasis of each academic program, including integrated curricula in which pharmacology contact hours are limited.

The PLOs are intended to serve as a dynamic resource that evolves with advances in pharmacology, therapeutics, and health professions education. Educators and other users are encouraged to provide feedback to support continued refinement and ensure that future editions remain accurate, relevant, and useful across diverse health professions programs.

For additional background on the history of the Association of Medical School Pharmacology Chairs (AMSPC) and the origins of the Pharmacology Knowledge Objectives, see ***The Pharmacologist***.

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PREFACE TO THE 2022 EDITION

The Preface to the First Edition is provided below this current preface. It is included to provide some historical perspective on the development and purpose of the Knowledge Objectives. The last iteration of the Knowledge Objectives occurred in 2012. A few sections were updated around 2017, but a full update did not occur. This iteration is the result of an agreement with Association of Medical School Pharmacology Chairs (AMSPC) and ASPET's Division for Pharmacology Education (DPE). Both groups realize the value of such a document to provide consistency to the pharmacology education of our future healthcare providers. Members of both organizations have worked together to update this document and make it available to all who need the guidance it contains. The Editors thank the Section Chairs and the members of each Committee for their hard work and dedication to creating this update.

Several important points need to be made to help facilitate the purpose of this document.

1. This document is intentioned to be used by faculty as a guide, or recommendation, for faculty to use to develop content for presentations, lectures, self-study modules, small-group activities, etc., for students.
2. It is not a compendium of information, but rather suggestions of the content to be presented, suggestions from pharmacologists who have expertise and experience in each field or section.
3. There will be some redundancy of content in various topics. Each faculty member should decide for themselves what to use, and how to use the information suggested for each topic to best suit the goals of their curriculum.
4. The drugs noted in the document show major, prototypical drugs in CAPS. Other drugs that may be important in an area, but are not major and/or prototypical, are in lowercase. The drug lists are NOT all inclusive, nor should they be. There may be an appendix developed with a more comprehensive list of drugs in each topic section. However, the Knowledge Objectives should be succinct and confine drugs listed to only the minimum drugs that are exemplary for a topic being addressed.
5. There is a suggested curricular time for each topic area. This is to provide some guidance as to the importance of each topic. However, with the wide variability of curricula today, these may be hard to align with any given academic program. Yet, this information is the best estimate from the body of experts who have updated the Knowledge Objectives.

In summary, this document is intended for use by experienced faculty, junior faculty, or new faculty, and faculty who may be charged with presentations in areas of pharmacology they have not presented before. It is NOT intended as a study guide for students, or as a comprehensive compendium of information students should have to move into their clinical training. Faculty may share this information with students if they so choose, but hopefully with the above caveat. If anyone notes a discrepancy or error in this document, the editors would appreciate being notified of such an instance. As with all knowledge,

this should be considered a ‘work in progress’ that needs updating periodically, especially considering the dynamic nature of the discipline of pharmacology.

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Information for the 2024 Update
This update, completed June, 2024, includes reviews and updates of all sections except Basic Principles, Autacoids/Nonsteroidal Anti-inflammatory/Asthmatic Drugs, and Toxicology.

PREFACE TO THE FIRST EDITION

It is the purpose of this document to identify the minimum essential knowledge in pharmacology which every medical student trained as an undifferentiated physician must have at the time of graduation from medical school. These knowledge objectives were developed by a committee of the Association of Medical School Pharmacology Chairs (AMSP) charged with developing an essential knowledge base in pharmacology for medical students. This document is intended to assist faculty members in medical schools in the United States in organizing their pharmacology curricula. Each topic was generated by a special subcommittee of the Association of Medical School Pharmacology chairmen with expertise in a particular area of pharmacology. The objectives were not designed for any particular medical pharmacology course, but instead are meant to serve as guidelines for the minimum knowledge of pharmacology that medical students should possess when they graduate from medical school.

Even though the essential knowledge objectives included in this document have been oriented toward the second-year medical pharmacology course, curricula may differ in some schools where these principles and objectives are covered in other years of the medical school curriculum.

An attempt has been made to define the essential learning or knowledge objectives and the minimum number of drugs which should be taught. Whenever possible prototypical or model drugs are included with major emphasis on teaching the principles of pharmacology. Drugs in current use will usually be used in each organizing element. However, in certain instances drugs which are not currently used in therapeutics or drugs which may be used as pharmacological tools may be included if they better demonstrate a principle or special pharmacologic mechanism. Thus, the reasons for including a drug are: 1) extent of therapeutic use by being listed in the 200 most commonly prescribed drugs in the United States (e.g., *National Prescription Audit); or 2) its recommendation by one of the expert committees listed at the beginning of each section based on its demonstrating a principle of drug action or being of historical interest. The drugs listed as PRIMARY drugs (ALL CAPITALS) in the index are considered by the above criteria to be the most important drugs and are strongly recommended to be taught in every medical pharmacology course. Some selected SECONDARY drugs (small letters) are also included in the index which are considered less important but should be taught if time permits.

The principles and knowledge objectives included in this document will usually center around mechanisms of action, actions on organ systems, pharmacokinetics, therapeutic indications including some disease entities, adverse effects, contraindications and drug interactions. Every effort has been made to reduce the number of drugs being taught in medical schools today and focus on the essence of pharmacology emphasizing principles and knowledge objectives. Some areas of pharmacology and some drug classes such as diagnostic agents, special nutritional materials and some agents with a limited specific use are not covered in this document. These materials are best learned at the time of exposure to a particular clinical specialty.

The results of surveys of medical school pharmacology departments carried out in 1983 by P.N. Bogner and M.D. Alschuler at the University of Illinois; for the Association of Medical School Pharmacology (AMSP) carried out by Ted Brody at Michigan State University (1984-85); and by a questionnaire under the combined auspices of the ASPET Educational Affairs subcommittee on medical education and AMSP were used as guides in determining the total number of contact hours for a medical pharmacology course and the number of hours devoted to each topic area. We hope this document will provide guidance for medical school pharmacology departments as well as clinical departments in pharmacology and will better prepare physicians in pharmacology, therapeutics and toxicology for the practice of medicine on a scientific basis.

*conducted by IMS America, Ltd., Ambler, Pa.

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SECTION 1

GENERAL PRINCIPLES OF PHARMACOLOGY & THERAPEUTICS

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1.1 General Principles of Pharmacology & Therapeutics	
Recommended Curriculum Equivalent: 7.0 hr	
Terminology	
Definitions & Terminology	**Drug Development**
pharmacology drugs receptors targets	generic drugs biologics biosimilars
Pharmacokinetics	**Pharmacodynamics**
routes of administration drug absorption bioavailability drug distribution drug metabolism elimination excretion clearance area under the curve (auc) drug half-life first and zero order kinetics steady-state concentration loading dose maintenance dose	mechanisms of drug action structure-activity relationships (SAR) quantal and gradient concentration/dose-effect relationships types of agonists and antagonists mechanisms of adverse effects mechanisms of drug interactions therapeutic index
Learning Objectives	
1.1.1 Definitions and Terminology 1. Evaluate the role of pharmacology in therapeutic decision-making to justify strategies that ensure safe patient care and minimize medication errors. 2. Explain how pharmacology integrates with other biomedical sciences (e.g., physiology, biochemistry, microbiology, anatomy) to guide clinical reasoning and patient care. 3. Differentiate between receptor-mediated and non-receptor-mediated drug actions (e.g., osmotic, chemical, and physical) to predict unique pharmacokinetic and pharmacodynamic outcomes.	
1.1.2 Pharmacokinetics 1. Evaluate how key principles of pharmacokinetics guide safe and effective drug therapy. 2. Predict how route of administration and processes that govern Absorption, Distribution, Metabolism, and Excretion affect time-course of drug concentration at its target site and in the body. 3. Apply knowledge of drug half-life and clearance in evidence-based dosing regimens. 4. Evaluate how drug chemical structure and its physicochemical properties (e.g., pKa, polarity, solubility, partition coefficient) influence pharmacokinetics of small molecule drugs, and differentiate these principles from those governing biologics 5. Predict how drug movement across membranes, including the action of drug transporters, affects bioavailability and clearance.	

6. Analyze how body compartments and physiological barriers (e.g., blood-brain barrier, Placenta) influence the apparent volume of distribution and drug disposition within the target tissues.
7. Predict how physicochemical properties (lipid solubility, pH) and other variables (perfusion, route of administration) affect drug bioavailability.
8. Apply core pharmacokinetic concepts (e.g., half-life, apparent volume of distribution, area under the curve, bioavailability, first-pass metabolism, and clearance) to predict time to steady-state in clinical scenarios., and to formulate, adjust and justify individualized dosing regimens, including loading doses and maintenance doses.
9. Compare first-order, mixed-order, and zero-order kinetics to analyze their influence on drug clearance, half-life, dosing and other clinically relevant concepts.
10. Interpret concentration-time curves and data following intravenous administration, and estimate core parameters (clearance, elimination half-life, and volume of distribution).
11. Differentiate renal and non-renal contributions to Clearance to guide dose adjustments for patients with renal or hepatic impairment.
12. Predict how drug-protein binding and tissue sequestration alter the free (active) drug fraction and evaluate their impact on pharmacological effects, drug distribution, and dosing requirements.
13. Apply knowledge of Phase I and Phase II metabolism (including CYP450 enzymes) to predict the effects of enzyme induction or inhibition on drug disposition and therapeutic response
14. Assess how patient-specific factors (e.g., age, sex, genetics, disease states) influence key pharmacokinetic parameters to inform individualized drug dosing and therapeutic decision-making.
15. Differentiate drug elimination from drug excretion and evaluate how each process influences dosing and clinical outcomes.
16. Identify and analyze major and specialized routes of Drug Excretion to predict drug behavior in specific clinical contexts (e.g., biliary excretion, lactation).

1.1.3 Pharmacodynamics

1. Evaluate how principles of pharmacodynamics inform therapeutic decision-making.
2. Classify major drug targets and molecular interactions and predict target-mediated, including effects at the subcellular level.
3. Relate a drug's mechanism of action and drug–receptor interaction to its clinical use, adverse effects, and drug interactions.
4. Distinguish ligand selectivity from specificity.
5. Explain the concept of spare receptors and determine their functional significance for drug action and signal transduction pathways.
6. Contrast drug potency and drug efficacy and appraise their relevance to drug selection and dosing.
7. Interpret graded and quantal dose/concentration-response relationships, to calculate potency, efficacy, and therapeutic index for safe patient care.
8. Explain the concepts of agonists (full, partial, inverse) and antagonists (competitive, non-competitive, irreversible) and predict how their distinct molecular interactions alter the dose/concentration-response relationship.
9. Apply quantal dose-response curves to determine therapeutic index.

10. Compare and contrast therapeutic index to therapeutic window and propose how they inform clinical decisions.
11. Explain the core concept of the drug molecule and structure-activity relationships (SAR) to infer how molecular modifications influence receptor binding, activation, and drug development strategies for small molecule drugs.
12. Evaluate mechanism governing receptor regulation (such as desensitization, down-regulation, super-sensitivity, and up-regulation) to predict how these adaptive responses alter drug response over time (such as tolerance and rebound effects).

1.1.4 Pharmacogenetics/Pharmacogenomics

1. Apply the key principles of Pharmacogenetics and Pharmacogenomics to justify the use of precision medicine in optimizing therapeutic efficacy and minimizing adverse effects.
2. Explain how genetic polymorphisms (e.g., single nucleotide polymorphisms, deletions, amplifications) alter protein structure or expression and predict their impact on drug response, toxicity, and clinical outcomes.
3. Identify the major clinically relevant polymorphic genes affecting drug metabolism and disposition, toxicity and therapeutic response, including genes coding for Phase I enzymes (such as CYP2D6, CYP2C9, CYP2C19; pseudocholinesterase), Phase II enzymes (such as, NAT2, TPMT), drug transporters, receptors, and effector systems, and evaluate their implications for individual variations in drug response, including risk of adverse effects and therapeutic efficacy.
4. Evaluate monogenic pharmacogenetic traits to predict drug response, toxicity risks, and medication-specific considerations in clinical scenarios.

1.1.5 Drug Interactions

1. Explain mechanisms (both pharmacokinetic and pharmacodynamic) underlying drug interactions with other drugs, nutrients, herbal products, supplements, recreational drugs, and other substances and evaluate their clinical significance for therapeutic decision-making and patient safety.
2. Analyze drug interactions (additivity, synergy, potentiation, antagonism) to predict clinical outcomes and justify therapeutic decisions, including when interactions may be therapeutically beneficial.
3. Interpret a comprehensive patient medication, supplement, and substance-use history to predict and prevent clinically significant drug interactions and ensure patient safety.

1.1.6 Drug Development, Evaluation, and Regulation

1. Explain drug development process from preclinical through clinical stages.
2. Analyze key principles for regulatory approval of new drugs, including generics, biologics, and biosimilars, to ensure safety, efficacy and therapeutic equivalence.
3. Compare and contrast how each phase of clinical trials (I-IV) contributes to evaluating drug efficacy and safety, including identification of rare adverse drug reactions.
4. Explain the rationale for post-marketing surveillance (Phase IV) and analyze how ongoing safety and effectiveness data are collected and evaluated to identify rare adverse drug reactions, long-term outcomes, and real-world drug use patterns across diverse patient populations.

5. Evaluate drug information sources (e.g., pharmacopoeias, clinical databases, and peer-reviewed literature) to interpret evidence quality and justify safe, evidence-based prescribing decisions.
6. Apply critical appraisal to ensure safe and evidence-informed therapeutic decision-making when using generative artificial intelligence.

SECTION 2

AUTONOMIC PHARMACOLOGY

Khalil Eldeeb (section chair), Mark Hernandez, Scott Ochs,
Ken Dretchen, Teresa Wilborn

2.1 Neuronal Drugs

Recommended Curriculum Equivalent: 1.0 hr

Drug Classes and Drugs

AMPHETAMINE
BOTULINUM TOXIN
CARBIDOPA
TETRABENAZINE
cocaine
entacapone
physostigmine

Learning Objectives

2.1.1 Mechanism of Action and Effects

1. Differentiate the anatomical organization and neurotransmitter profiles of the sympathetic and parasympathetic divisions of the autonomic nervous system, including their craniosacral and thoracolumbar projections.
2. Analyze the synthesis, storage, release, and termination of autonomic neurotransmitters, including acetylcholine and catecholamines.
3. Predict physiological responses of end organs based on activation or inhibition of specific adrenergic and cholinergic receptor subtypes.
4. Relate the concept of dominant autonomic tone to baseline regulation of organ systems and responses to pharmacologic modulation.
5. Differentiate the functional roles of muscarinic and nicotinic receptors at autonomic ganglia and effector organs.
6. Evaluate mechanisms by which neuronal drugs alter autonomic neurotransmission through effects on neurotransmitter synthesis, storage, release, reuptake, or metabolism.
7. Analyze regulatory mechanisms that modulate autonomic neurotransmission, including presynaptic autoreceptors and cotransmitters.

2.1.2 Pharmacokinetics

1. Compare the mechanisms that terminate autonomic neurotransmitter signaling, including enzymatic degradation of acetylcholine and reuptake of norepinephrine via neuronal transporters.
2. Analyze how inhibition of catecholamine metabolism by monoamine oxidase (MAO) or catechol-O-methyltransferase (COMT) alters adrenergic neurotransmitter availability and signaling.
3. Predict how drugs that alter neurotransmitter synthesis, transport, metabolism, or reuptake influence synaptic neurotransmitter concentrations and duration of signaling.
4. Evaluate the pharmacokinetic effects of peripheral COMT inhibition and dopa-decarboxylase inhibition on catecholamine and levodopa metabolism.

2.1.3 Therapeutic Uses

1. Apply principles of autonomic pharmacology to explain therapeutic uses of neuronal drugs that act on autonomic receptors, enzymes that affect neuronal activity, or alter neurotransmitter release.

2.1.4 Adverse Effects, Contraindications, and Drug Interactions

1. Predict adverse effects and/or clinical outcomes resulting from excessive or deficient cholinergic or adrenergic neurotransmission based on underlying receptor-mediated mechanisms or neurotransmitter related mechanism.
2. Evaluate clinically significant pharmacodynamic interactions between drugs that affect catecholamine metabolism, reuptake, or release.

2.2 Cholinergic and Nicotinic Agonists			
Recommended Curriculum Equivalent: 3.0 hr			
Drug Classes and Drugs			
Direct Acting Cholinergic Agonists		**Indirect Acting Cholinergic Agonists**	
Muscarinic	**Nicotinic**	**Cholinesterase Inhibitors**	**Related Drugs**
BETHANECHOL PILOCARPINE	NICOTINE varenicline	**Reversible** NEOSTIGMINE PYRIDOSTIGMINE physostigmine **Irreversible** parathion (pesticide) sarin (nerve agent)	PRALIDOXIME

Learning Objectives

2.2.1 Mechanism of Action and Effects

1. Identify pharmacologic targets that modify the processes of synthesis, vesicular storage, calcium-dependent release, and enzymatic inactivation of acetylcholine at cholinergic synapses
2. Analyze how the structural features of the acetylcholinesterase active site determine interactions with substrates and inhibitors.
3. Contrast the mechanisms of reversible and irreversible acetylcholinesterase inhibition (e.g., including the functional consequences of carbamylation, phosphorylation, and aging) and identify the mechanism of antidote.
4. Predict the organ-system effects of broad muscarinic and nicotinic stimulation based on receptor subtype activation.

2.2.2 Pharmacokinetics

1. Differentiate pharmacokinetic properties of direct-acting and indirect-acting to both cholinergic agonists (tertiary or quaternary).
2. Relate the duration of acetylcholinesterase inhibition to the type and stability of enzyme binding, including reversible carbamylation and irreversible phosphorylation.
3. Analyze how structural features of cholinesterase inhibitors (including irreversible “aging”) influence pharmacokinetics, central nervous system penetration, and therapeutic use.

2.2.3 Therapeutic Uses

1. Justify the therapeutic uses of cholinergic agonists in various clinical conditions.
2. Explain why nicotine itself has limited therapeutic applications beyond smoking cessation due to its pharmacologic and adverse-effect profile.

2.2.4 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions

1. Predict adverse effects and clinical manifestations of cholinergic agonists (direct and indirect) based on excessive muscarinic or nicotinic receptor activation or in combination with other therapeutics and justify the therapeutic management
2. Predict contraindications to cholinergic agonists.

2.2.5 Notes

Cross-References

- Use of acetylcholinesterase inhibitors in neuromuscular disorders such as myasthenia gravis is cross-referenced with neuromuscular pharmacology sections.
- Acetylcholinesterase inhibitors used in Alzheimer disease are addressed in CNS pharmacology section (Drugs for the Treatment of Alzheimer Disease).

Clinical Guidelines

- Refer to American Academy of Ophthalmology (AAO) guidelines for the role of pilocarpine in acute angle-closure glaucoma.
- Refer to Myasthenia Gravis Foundation of America (MGFA) for treatment standards involving pyridostigmine and other therapies for myasthenia gravis.
- Smoking cessation recommendations involving nicotine replacement therapy and partial nicotinic agonists are provided by major public health organizations such as the American Thoracic Society. (https://www.cdc.gov/tobacco/php/tobacco-control-programs/cessation-materials.html)

Historical

- Acetylcholine is included for physiological context as the endogenous neurotransmitter but is not used therapeutically due to its rapid degradation.
- Organophosphate agents such as sarin and parathion are included to illustrate mechanisms of irreversible acetylcholinesterase inhibition and cholinergic toxicity rather than therapeutic use.

2.3 Cholinergic Antagonists		
Recommended Curriculum Equivalent: 2.0 hr		
Drug Classes and Drugs		
Muscarinic Receptor Antagonists		
General Muscarinic Antagonists	**Respiratory Muscarinic Antagonists**	**Genitourinary Muscarinic Antagonists**
ATROPINE SCOPOLAMINE glycopyrrolate	IPRATROPIUM TIOTROPIUM	OXYBUTYNIN TOLTERODINE darifenacin solifenacin

Gastrointestinal	Ophthalmic Agents
dicyclomine	tropicamide

Nicotinic Receptor Antagonists	
Neuromuscular Junction Blockers	
Nondepolarizing (Competitive)	**Depolarizing**
CISATRACURIUM ROCURONIUM VECURONIUM	SUCCINYLCHOLINE
Other Nicotinic Receptor Antagonist and Related Agents	
Neuromuscular Junction Reversal	**Ganglionic Blockers**
SUGAMMADEX	mecamylamine

Learning Objectives

2.3.1 Mechanism of Action and Effects

1. Differentiate muscarinic (M1–M3) and nicotinic (Nm, Nn) receptor subtypes based on molecular coupling, subunit composition, anatomic distribution, and physiological roles.
   Predict the organ-system effects of muscarinic receptor antagonism by applying receptor distribution
2. Contrast the mechanisms of competitive (nondepolarizing) and depolarizing neuromuscular blockers with respect to receptor interaction, end-plate potential changes, and stages of neuromuscular blockade.
3. Analyze the biphasic pharmacologic actions of succinylcholine (initial depolarization followed by desensitization) and their implications for skeletal muscle paralysis.
4. Predict the physiological consequences of autonomic ganglionic blockade based on the dominant baseline sympathetic or parasympathetic tone of individual organs.
5. Explain the mechanism by which selective relaxant binding agents (e.g., sugammadex) reverse steroidal neuromuscular blockade.

2.3.2 Pharmacokinetics

1. Differentiate tertiary amine and quaternary ammonium cholinergic antagonists based on physicochemical properties, blood–brain barrier penetration, and resultant central nervous system effects.

2. Predict how route of administration (e.g., inhaled, topical ophthalmic, parenteral) alters drug distribution, systemic exposure, and clinical selectivity of muscarinic antagonists.
3. Compare onset, duration, and recovery characteristics of depolarizing and nondepolarizing neuromuscular blocking agents
4. Analyze metabolism and elimination pathways of neuromuscular blockers.
5. Justify drug and dose selection in patients with hepatic or renal impairment based on clearance mechanisms and risk of prolonged neuromuscular blockade.
6. Predict the pharmacokinetic and clinical consequences of impaired or inhibited plasma cholinesterase activity on succinylcholine duration of action.

2.3.3 Pharmacogenomics

1. Analyze the effect of butyrylcholinesterase (pseudocholinesterase) genetic variants on succinylcholine metabolism, duration of neuromuscular blockade, and risk of prolonged postoperative apnea.
2. Recommend alternative neuromuscular blocking or reversal strategies for patients with known or suspected cholinesterase deficiency.
3. Evaluate how cytochrome P450 polymorphisms (e.g., CYP2D6) alter metabolism, efficacy, and adverse-effect risk of selected muscarinic antagonists (e.g., tolterodine).
4. Justify adjustments or selection of alternative agents in patients identified as poor or ultra-rapid metabolizers of relevant CYP enzymes.

2.3.4 Therapeutic Uses

1. Apply principles of autonomic physiology and pathophysiology to select appropriate muscarinic antagonists for related systems indications.
2. Justify the selection of specific antimuscarinic agents and routes of administration based on receptor selectivity, pharmacokinetics, adverse-effect profiles, and patient-specific factors
3. Design perioperative neuromuscular blockade strategies that incorporate appropriate agent selection and reversal approaches.
4. Evaluate the role of atropine in emergency and toxicologic settings, including symptomatic bradycardia and organophosphate poisoning.

2.3.5 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions

1. Predict the adverse effects of muscarinic antagonists from receptor distribution and loss of parasympathetic tone
2. Differentiate peripheral from central anticholinergic toxicity and propose appropriate risk-mitigation or management strategies, e.g in older adults.
3. Analyze the adverse effects of depolarizing and nondepolarizing neuromuscular blocking agents, e.g., malignant hyperthermia susceptibility
4. Predict physiologic consequences of autonomic ganglionic blockade based on disruption of dominant sympathetic or parasympathetic tone.
5. Interpret neuromuscular monitoring data (e.g., train-of-four) to assess depth of blockade and adequacy of recovery in perioperative settings.
6. Evaluate patient-specific contraindications to muscarinic antagonists
7. Analyze pharmacodynamic interactions that increase cumulative anticholinergic burden during polypharmacy (e.g., antihistamines, TCAs, antipsychotics) and predict associated toxicity.

2.3.6 Notes

Cross-References

- Neuromuscular blocking agents are also discussed within CNS Pharmacology section (under anesthesia drugs) due to their perioperative use.
- Respiratory muscarinic antagonists (short- and long-acting inhaled agents) are detailed further in the Pulmonary Pharmacology section.
- The anticholinergic toxidrome and its management are cross-referenced with toxicology content under Toxicology and Treatment of Intoxication section.

Clinical Guidelines

- Refer to Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines for standardized use of inhaled muscarinic antagonists in COPD. (refer to the Pulmonary Pharmacology section)
  Refer to American Heart Association (AHA) Advanced Cardiac Life Support (ACLS) guidelines for emergency use of atropine in symptomatic bradycardia. (refer to CVS section)

Historical

- Tubocurarine is retained for instructional purposes but is no longer used clinically.

2.4 Adrenergic Agonists		
Recommended Curriculum Equivalent: 3.5 hr		
Drug Classes and Drugs		
Endogenous Catecholamines	**Selective Alpha-Adrenergic Agonists**	
EPINEPHRINE (alpha 1, 2, beta 1, 2, 3) NOREPINEPHRINE (alpha 1, 2, beta 1 >> beta 2) dopamine (D1, B1, Alpha1, NE release)	brimonidine (alpha 2) clonidine (alpha 2) methyldopa (alpha 2) phenylephrine (alpha 1)	
Nonselective Alpha-Adrenergic Agonists	**Nonselective Beta-Adrenergic Agonists**	**Selective Beta-Adrenergic Agonists**
OXYMETAZOLINE	isoproterenol (beta 1, 2)	ALBUTEROL (beta 2) MIRABEGRON (beta 3) dobutamine (beta 1)
Indirect Acting Agents	**Mixed Acting Agents**	
amphetamine cocaine tyramine (dietary component)	DOPAMINE (alpha 1, 2, beta 1, DA 1, release NE) ephedrine (alpha 1, 2, beta 1, 2, release NE) pseudoephedrine (alpha 1, 2, beta 1, 2, release NE)	
Learning Objectives		
2.4.3 Mechanism of Action and Effects 1. Contrast the pharmacologic mechanisms of direct-acting, indirect-acting, and mixed-acting adrenergic agonists based on receptor selectivity in enhancing sympathetic neurotransmission. 2. Explain how activation of central α2-adrenergic receptors reduces sympathetic outflow and contributes to the pharmacologic effects of drugs such as clonidine and methyldopa.		
2.4.4 Pharmacokinetics 1. Differentiate pharmacokinetic properties of adrenergic agonist drugs and how those influence their clinical uses and justify their selection for therapeutic administration.		
2.4.5 Therapeutic Uses 1. Differentiate the role of indirect and direct acting (selective versus nonselective adrenergic agonists) based on receptor selectivity and justify their therapeutic uses. 2. Evaluate the therapeutic role of central α2-adrenergic agonists and similar drugs		
2.4.6 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions 1. Predict adverse effects, contraindications, and clinically significant interactions of adrenergic agonists based on the receptor selectivity and the mechanisms underlying their toxicity. 2. Interpret the clinical rationale for laboratory monitoring such as a Coombs test during methyldopa therapy.		

2.4.7 Notes

Cross-References

- Cardiovascular uses of catecholaminergic agonists are discussed further in Cardiovascular System Pharmacology.
- Inhaled β_2-adrenergic agonists used as bronchodilators are discussed in Pulmonary Pharmacology section.
- The clinical uses of adrenergic agonists and psychostimulants are discussed in Central Nervous System Pharmacology sections

Clinical Guidelines

- Refer to Global Initiative for Asthma (GINA) and Global Initiative for Chronic Obstructive Lung Disease (GOLD) for recommendations regarding the use of β_2-agonists in asthma and COPD management. https://pmc.ncbi.nlm.nih.gov/articles/PMC10111975/
- Refer to American Heart Association / ACC guidelines for the use of vasopressors and adrenergic agonists in ACLS and shock management

2.5 Adrenergic Antagonists		
Recommended Curriculum Equivalent: 1.5 hr		
Drug Classes and Drugs		
Nonselective Beta-Adrenergic Antagonists (beta 1, beta 2)	**Selective Beta 1-Adrenergic Antagonists**	
PROPRANOLOL timolol	ATENOLOL METOPROLOL esmolol nebivolol	
Nonselective Alpha-Antagonists (alpha 1, alpha 2)	**Selective Alpha 1-Adrenergic Antagonists**	**Mixed Alpha- and Beta-Adrenergic Antagonists**
phenoxybenzamine (irreversible) phentolamine (reversible)	PRAZOSIN tamsulosin terazosin	CARVEDILOL (alpha 1, beta 1, 2) LABETALOL (alpha 1, beta 1, 2)

Learning Objectives

2.5.1 Mechanism of Action and Effects

1. Predict the pharmacological consequences of reversible or irreversible adrenergic and/or mixed α/β-adrenergic receptor blockade.
2. Compare the pharmacologic effects of selective and nonselective adrenergic antagonists and relate receptor selectivity to therapeutic actions.

2.5.2 Pharmacokinetics

1. Differentiate pharmacokinetic properties of adrenergic antagonists and justify their therapeutic uses.

2.5.3 Therapeutic Uses

1. Differentiate the therapeutic roles of adrenergic antagonists based on receptor selectivity and patient-specific factors and justify their therapeutic uses.
2. Justify the sequence of α-adrenergic blockade before β-blockade in the management of excessive adrenergic stimulation (e.g., pheochromocytoma).

2.5.4 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions

1. Predict adverse effects, contraindications, and clinically significant drug interactions of adrenergic antagonists.

2.5.5 Notes

Cross-References

- Therapeutic uses of adrenergic antagonists is discussed in Cardiovascular Pharmacology section.
- Use of alpha-1 adrenergic antagonists is discussed in Endocrine Pharmacology section.

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Clinical Guidelines

- Refer to American Heart Association / ACC guidelines for evidence-based use of β-blockers and α-blockers in cardiovascular disease.
- Refer to American Urological Association (AUA) guidelines for the use of α-blockers in benign prostatic hyperplasia.

SECTION 3

CENTRAL NERVOUS SYSTEM PHARMACOLOGY

Scott Ochs (section chair), Diptiman Boss, Carl Faingold, James O'Donnell, Jennelle Durnett Richardson, Monzurul Roni

3.1 Drugs for the Treatment of Parkinson Disease			
Recommended Curriculum Equivalent: 1.0 hr			
Drugs Classes and Drugs			
Dopamine Precursor	**AADC Inhibitor**	**Dopamine Agonist**	
LEVODOPA	CARBIDOPA	PRAMIPEXOLE apomorphine ropinirole	
MAO-B Inhibitors	**COMT Inhibitors**	**Anticholinergic Agents**	**Other**
SAFINAMIDE SELEGILINE rasagiline	ENTACAPONE	BENZTROPINE trihexyphenidyl	AMANTADINE ISTRADEFYLLINE

Learning Objectives

3.1.1 Mechanism of Action and Effect

1. Analyze the opposing roles of dopamine and acetylcholine in regulating movement, and justify why both dopaminergic and anticholinergic agents are therapeutically rational strategies for managing Parkinson disease.
2. Differentiate the mechanisms of action of dopaminergic Parkinson disease drug classes including the dopamine precursor levodopa, dopamine receptor agonists, and inhibitors of enzymes that metabolize dopamine or levodopa.

3.1.2 Pharmacokinetics

1. Evaluate how monoamine oxidase-B (MAO-B) inhibitors and catechol-O-methyltransferase (COMT) inhibitors elevate brain dopamine levels and attenuate dopamine fluctuations, and hypothesize the clinical significance of their action.
2. Analyze the pharmacokinetic properties of Parkinson disease drugs and justify the clinical rationale for selecting delayed-release or extended-release formulations over immediate-release alternatives.

3.1.3 Therapeutic Uses

1. Justify the selection of specific Parkinson disease drugs as monotherapy versus adjuncts, and defend the use of particular agents for defined clinical scenarios such as off-periods.
2. Justify why certain Parkinson disease drugs are more appropriate for treatment of the early stage of the disease compared to the middle- or late- disease stages.
3. Evaluate the relative efficacy of Parkinson disease drug classes and hypothesize the clinical consequences of levodopa's diminishing effectiveness with long-term use, including the therapeutic implications for disease management.

3.1.4 Adverse Effects, Contraindications, and Drug Interactions

1. Compare and contrast the central nervous system (CNS) adverse effect profiles of levodopa and dopamine receptor agonists, and evaluate the clinical relevance of these differences when

individualizing therapy.

2. Evaluate the gastrointestinal and cardiovascular adverse effects of Parkinson disease drugs and propose evidence-based strategies to minimize their impact on patient care.
3. Analyze the mechanism underlying the levodopa–protein interaction and design a patient counseling approach that optimizes meal timing to ensure adequate CNS drug delivery.

3.2 Drugs for the Treatment of Alzheimer Disease		
Recommended Curriculum Equivalent: 0.7 hr		
Drugs Classes and Drugs		
Cholinesterase Inhibitors	**NMDA Receptor Antagonist**	**Anti-amyloid Monoclonal Antibodies**
DONEPEZIL galantamine rivastigmine	MEMANTINE	donanemab lecanemab
Learning Objectives		
3.2.1 Mechanism of Action and Effects 1. Rationalize why acetylcholinesterase inhibitors, NMDA receptor antagonists, and anti-amyloid-β-immunotherapy are indicated for Alzheimer disease based on their mechanism of action.		
3.2.2 Pharmacokinetics 1. Apply knowledge of the specific pharmacokinetic properties of the drugs used for the management of Alzheimer disease as it relates to their administration and therapeutic use.		
3.2.3 Therapeutic Uses 1. Evaluate the efficacy and limitations of each Alzheimer disease drug, differentiating which disease stages they target and assessing the degree and clinical meaningfulness of the cognitive improvement they provide.		
3.2.4 Adverse Effects, Contraindications, and Drug Interactions 1. Compare and contrast the significant adverse effects of cholinesterase inhibitors versus NMDA receptor antagonists for Alzheimer disease.		

3.3 Drugs for the Treatment of Huntington Disease and Amyotrophic Lateral Sclerosis		
Recommended Curriculum Equivalent: 0.3 hr		
Drugs Classes and Drugs		
Dopamine-depleting Agents	**Antipsychotics**	**Disease-modifying Agents (ALS)**
TETRABENAZINE deutetrabenazine	HALOPERIDOL aripiprazole olanzapine quetiapine risperidone	EDARAVONE RILUZOLE

Learning Objectives

3.3.1 Mechanism of Action and Effects

1. Rationalize why reducing dopaminergic activity helps to treat Huntington disease, and describe mechanistically how this is achieved by either blocking dopamine receptors or depleting dopamine.
2. Rationalize why each disease-modifying drug class for amyotrophic lateral sclerosis (ALS) slows the progression of the disease.

3.3.2 Pharmacokinetics

1. Apply knowledge of the specific pharmacokinetic properties of the drugs used for the management of Huntington disease and ALS as it relates to their administration and therapeutic use.

3.3.3 Therapeutic Uses

1. Differentiate disease-modifying ALS drugs from symptom-managing agents, and justify this distinction based on a critical analysis of their mechanisms of action.
2. Evaluate the limitations of pharmacological treatments for Huntington disease and ALS, and assess how these limitations shape realistic therapeutic goals for patients.

3.3.4 Adverse Effects, Contraindications, and Drug Interactions

1. Analyze the major adverse effects of drugs used for Huntington disease and ALS, and assess how these risks influence prescribing decisions and patient monitoring strategies.
2. Compare and contrast the significant adverse effects of antidopaminergic agents versus the use of atypical antipsychotics for Huntington’s disease.

3.4 Drugs for the Treatment of Mental Health Diseases and Psychoses		
Recommended Curriculum Equivalent: 1.5 hr		
Drug Classes and Drugs		
First-generation (typical) Antipsychotics (D_2 receptor antagonist)		
Phenothiazines	**Butyrophenone**	
CHLORPROMAZINE fluphenazine perphenazine	HALOPERIDOL	
Second-generation (atypical) Antipsychotics (D_2 and 5-HT_{2A} receptor antagonist, 5-HT_{1A} receptor partial agonist)		
D_2>5-HT_{2A}	**5-HT_{2A}>D_2**	**D_2:5-HT_{2A}:5-HT_7**
quetiapine	CLOZAPINE OLANZAPINE RISPERIDONE paliperidone ziprasidone	ASENAPINE LURASIDONE
Third-generation Antipsychotics (D_2 receptor partial agonist and 5-HT_{2A} receptor antagonist)		
5-HT_{2A}> D_2 (D_2 partial agonist/antagonist)	**D_2> 5-HT_{2A} and 5-HT_{1A} partial agonist**	
LUMATEPERONE	ARIPIPRAZOLE BREXPIPRAZOLE CARIPRAZINE	
Dopamine Depleting Agent		
Vesicular Monoamine Transporter 2 (VMAT2) Inhibitor		
Valbenazine		
Learning Objectives		
3.4.1 Mechanism of Action and Effects 1. Compare and contrast the actions of phenothiazines and haloperidol with those of second- and third-generation antipsychotics, and relate these differences to theories of antipsychotic mechanisms. 2. Analyze and evaluate prevailing theories of the therapeutic actions of antipsychotic medications, focusing on their immediate and long-term effects on dopaminergic and serotonergic pathways in the CNS.		
3.4.2 Therapeutic Uses 1. Compare and contrast the effectiveness of classical and atypical antipsychotics in the treatment of both positive and negative symptoms of schizophrenia. 2. Evaluate the current evidence regarding pharmacological management of cognitive impairments associated with schizophrenia. 3. Justify the use of specific antipsychotic agents for indications beyond schizophrenia, including bipolar disorder, agitation, and Tourette syndrome. 4. Evaluate the role of dopamine depleting agents in the management of Tourette syndrome.		

3.4.3 Adverse effects, Contraindications, and Drug Interactions

1. Differentiate the side effect profiles of low-potency versus high-potency first-generation antipsychotics based on their receptor binding characteristics, and provide a mechanistic explanation for these differences.
2. Predict the adverse effects of antipsychotic drugs based on their interactions with dopaminergic, serotonergic, muscarinic, histaminergic, and adrenergic receptor systems.
3. Compare the adverse effect profiles of first-generation and second-/third-generation antipsychotics and justify agent selection in patients with comorbid diseases.
4. Differentiate the time course, clinical presentation, and management of antipsychotic drug-induced movement disorders, including acute dystonia, akathisia, drug-induced Parkinsonism, and tardive dyskinesia.
5. Analyze the clinical features, pathophysiology, and management of neuroleptic malignant syndrome.

3.5 Drugs for the Treatment of Depression, Bipolar Disorder, and Anxiety		
Recommended Curriculum Equivalent: 2.5 hr		
Drug Classes and Drugs		
Drugs for Depression		
Monoamine Uptake Inhibitors		
Selective Serotonin (SSRI)	**Serotonin and NE (SNRI)**	**Norepinephrine and Dopamine**
FLUOXETINE escitalopram paroxetine sertraline vilazodone	duloxetine venlafaxine	bupropion
Tricyclic Antidepressants (TCAs)	**Monoamine Oxidase Inhibitors (MAOIs)**	**Extrasynaptic $GABA_A$ Receptor Positive Allosteric Modulator**
amitriptyline desipramine imipramine nortriptyline protriptyline	phenelzine tranylcypromine	zuranolone
NMDA Receptor Antagonist	**Serotonin Modulator**	
esketamine	trazodone	
Drugs for Bipolar Disorders		
Lithium	**Antiepileptics**	**Antipsychotics**
lithium carbonate lithium citrate	carbamazepine lamotrigine valproic acid	aripiprazole olanzapine quetiapine risperidone
Drugs for Anxiety Disorders		
SSRI	**Benzodiazepines**	**5-HT_{1A} Receptor Agonist**
FLUOXETINE sertraline	alprazolam diazepam lorazepam	buspirone
Antihistamines	**Gabapentinoids**	
doxepin hydroxyzine	gabapentin pregabalin	
Learning Objectives		
3.5.1 Mechanism of Action and Effects 1. Compare the primary cellular targets of the major antidepressant drug classes including TCAs, SSRIs, SNRIs, atypical antidepressants, serotonin modulators, and MAO inhibitors. 2. Predict how these mechanisms contribute to therapeutic effects in depressive disorders and relate to the current neurochemical and neurotrophic theories of depression.		

3. Analyze the mechanisms proposed to account for the delayed onset of therapeutic action of antidepressants.
4. Compare the mechanisms of action of drugs used to treat bipolar disorder including lithium, anticonvulsants, and antipsychotics; and where mechanisms are established, predict the pharmacological consequences of each.
5. Differentiate the mechanisms of action among the major drug classes used to treat anxiety disorders including SSRIs, benzodiazepines, buspirone, gabapentinoids, and antihistamines; and relate these mechanisms to their clinical use.

3.5.2 Pharmacokinetics

1. Contrast the pharmacokinetic profiles of the different classes of antidepressant drugs.
2. Justify switching protocols between antidepressant medications based on pharmacokinetic properties including the clinical significance of active metabolite formation.
3. Justify the necessity of regular plasma lithium level monitoring given its narrow therapeutic index, and predict the clinical consequences of subtherapeutic and supratherapeutic concentrations.

3.5.3 Therapeutic Uses

1. Justify the selection of specific antidepressant drug classes for indications beyond unipolar depression, including obsessive-compulsive disorder, panic disorder, PTSD, neuropathic pain, smoking cessation, enuresis, and generalized anxiety disorder.
2. Evaluate the relative roles of anticonvulsants, lithium, and antipsychotics in the pharmacological management of bipolar disorder.
3. Justify the use of benzodiazepines and antipsychotics in the management of anxiety disorders including an analysis of the benefits and limitations of each.
4. Evaluate the evidence for herbal antidepressants, including St. John's wort, and compare their pharmacological profile and limitations with those of conventional pharmacotherapy.
5. Apply knowledge of patient-specific factors such as comorbidities, adverse effect profiles, pharmacokinetic considerations, and prior treatment response to propose appropriate pharmacotherapy for a patient presenting with a mood or anxiety disorder.
6. Apply knowledge of the pharmacokinetics of SSRIs as it relates to the initiation and the discontinuation of therapy

3.5.4 Adverse Effects, Contraindications, and Drug Interactions

1. Compare the adverse effect profiles of the major antidepressant classes including TCAs, SSRIs, SNRIs, MAOIs, and atypical agents; and explain the receptor-based mechanisms underlying these effects.
2. Predict clinically significant drug and dietary interactions with antidepressants, with particular emphasis on MAOI interactions.
3. Justify regular plasma lithium level monitoring in the clinical management of bipolar disorder, and recognize the signs and symptoms of lithium toxicity along with its appropriate management.
4. Differentiate the clinical presentations of tricyclic antidepressant toxicity and serotonin syndrome, and propose evidence-based treatment strategies for each condition.
5. Predict the pharmacokinetic and pharmacodynamic drug interactions of St. John's wort.

6. Predict the significance of concomitant use of ethanol and drugs used to treat depression.

3.6 Drugs for the Treatment of Sleep Disorders		
Recommended Curriculum Equivalent: 1.5 hr		
Drug Classes and Drugs		
Drugs for Insomnia		
$GABA_A$ Receptor Positive Allosteric Modulators	**Melatonin Receptor Agonist**	**Orexin Receptor Antagonist**
ESZOPICLONE ZALEPLON ZOLPIDEM estazolam flurazepam quazepam temazepam triazolam	RAMELTEON tasimelteon	SUVOREXANT lemborexant
Serotonin Modulator	**Antihistamine**	
trazodone	doxepin	
Drugs for Excessive Daytime Sleepiness		
Stimulants	**H_3 Receptor Inverse Agonist**	
MODAFINIL solriamfetol	pitolisant	
Learning Objectives		
3.6.1 Mechanism of Action and Effects 1. Compare the mechanisms of action of selective versus nonselective GABA-enhancing agents, melatonin receptor agonists, and orexin receptor antagonists in the treatment of insomnia. 2. Differentiate the pharmacological mechanisms underlying treatments for narcolepsy and excessive daytime sleepiness, including CNS stimulants and H3 receptor inverse agonist.		
3.6.2 Pharmacokinetics 1. Differentiate the pharmacokinetic profiles of benzodiazepine and how these differences influence appropriate clinical selection for insomnia.		
3.6.3 Therapeutic Uses 1. Justify the selection of specific pharmacological agents for insomnia and hypersomnia based on the pathophysiology of these disorders.		
3.6.4 Adverse Effects, Contraindications, and Drug Interactions 1. Compare the adverse effect profiles of benzodiazepine and non-benzodiazepine sedative-hypnotics, including REM sleep suppression, daytime hangover, anterograde amnesia, and risk of dependence. 2. Predict the drug interactions associated with sedative-hypnotic agents that arise from CYP3A4-mediated metabolism.		

3.7 Drugs for the Treatment of ADHD	
Recommended Curriculum Equivalent: 1.0 hr	
Drug Classes and Drugs	
Stimulants	
Amphetamines	**Methylphenidate Derivatives**
AMPHETAMINE DEXTROAMPHETAMINE LISDEXAMFETAMINE	METHYLPHENIDATE
Non-stimulants	
NE Reuptake Inhibitors	**Alpha$_2$-adrenergic Agonists**
atomoxetine viloxazine	clonidine guanfacine
Learning Objectives	
3.7.1 Mechanism of Action and Effects 1. Elucidate the molecular mechanisms by which stimulants increase dopaminergic and noradrenergic neurotransmission in the prefrontal cortex and striatum. 2. Differentiate the mechanism of action of stimulant versus nonstimulant medications in managing ADHD symptoms. 3. Relate the dysregulation of dopamine and norepinephrine signaling to the rationale for using stimulant and nonstimulant therapies in ADHD.	
3.7.2 Pharmacokinetics 1. Apply the concept of prodrug design to justify the pharmacokinetic advantages of lisdexamfetamine over d-amphetamine. 2. Analyze how differences in formulation of methylphenidate affect dosing schedules and clinical outcomes.	
3.7.3 Therapeutic Uses 1. Integrate the pathophysiology of ADHD when selecting appropriate pharmacotherapy, considering patient age, comorbidities, and evidence-based guidelines. 2. Justify the selection of a stimulant versus a nonstimulant agent based on patient-specific factors such as history of substance use disorder, cardiovascular risk, or comorbid anxiety. 3. Evaluate the evidence base for the use of α2-adrenoceptor agonists as adjuncts or alternatives in ADHD management.	
3.7.4 Adverse Effects, Contraindications, and Drug Interactions 1. Predict the cardiovascular adverse effects of stimulants, including increased heart rate, increased blood pressure, and risk of arrhythmia, that warrant caution in patients with pre-existing cardiac conditions. 2. Differentiate the adverse effect profiles of stimulant versus nonstimulant agents, including the risk of dependence, abuse, somnolence, and suicidality. 3. Evaluate the contraindications to stimulant use, including concurrent MAOI therapy, uncontrolled hypertension, and structural cardiac abnormalities. 4. Analyze clinically significant drug interactions of stimulants, including interactions with MAOIs,	

antihypertensives, and serotonergic agents.

3.8 Drugs Used for Seizures		
Recommended Curriculum Equivalent: 1.5 hr		
Drug Classes and Drugs		
$GABA_A$ Receptor Positive Allosteric Modulators	**GABAergic Agents**	**Na^+ Channel Blockers**
LORAZEPAM PHENOBARBITAL clonazepam diazepam	VALPROIC ACID cenobamate tiagabine topiramate vigabatrin	CARBAMAZEPINE LAMOTRIGINE PHENYTOIN lacosamide
Ca^{2+} Channel Blockers		**SV2A Inhibitor**
N-type	**T-type**	LEVETIRACETAM
gabapentin pregabalin	ETHOSUXIMIDE	

Carbonic Anhydrase Inhibitor	AMPA Receptor Antagonist	Serotonergic Agent	Other
acetazolamide	perampanel	fenfluramine	cannabidiol

Learning Objectives

3.8.1 Mechanism of Action and Effects

1. Compare the cellular mechanisms of action of the major antiseizure drug classes including $GABA_A$ positive allosteric modulators, GABAergic agents, Na^+ channel blockers, Ca^{2+} channel blockers, SV2A inhibitors, carbonic anhydrase inhibitors, AMPA receptor antagonists, and serotonergic agents.
2. Examine the differential effect of antiseizure medications on the various Na^+ channel states.
3. Predict how these mechanisms confer antiseizure efficacy in treating the most common types of seizure forms including generalized tonic-clonic, absence, focal (partial) onset, and status epilepticus.
4. Differentiate anticonvulsant from antiepileptic drug actions with respect to acute seizure termination versus prophylactic suppression of seizures, and distinguish between seizures and epilepsy as distinct clinical entities.
5. Evaluate the principles of antiepileptic therapy including monotherapy versus polypharmacy, strategies for drug withdrawal, and the factors that contribute to treatment failure.

3.8.2 Pharmacokinetics

1. Explain the nonlinear pharmacokinetics of phenytoin and predict the clinical consequences of dose escalation on drug clearance and plasma concentrations.
2. Justify the clinical practice of therapeutic drug monitoring for antiepileptic drugs based on pharmacokinetic variability and narrow therapeutic indices.

3.8.3 Therapeutic Uses

1. Recommend antiseizure medications for the appropriate seizure type including generalized tonic-clonic, absence, focal (partial) onset, and status epilepticus based on mechanism of action and clinical evidence.

2. Propose a stepwise pharmacological management plan for status epilepticus, justifying the rationale for agent selection at each stage of treatment. 3. Justify the use of antiseizure drugs for conditions other than epilepsy including neuropathic pain, migraine prophylaxis, and mood stabilization. 4. Evaluate the limitations of epilepsy management with antiseizure medications and relate this to future drug development.
3.8.4 Adverse Effects, Contraindications, and Drug Interactions 1. Compare the adverse and teratogenic effect profiles of major antiseizure drugs with a particular emphasis on valproic acid 2. Attribute the effects of long-term treatment and significant adverse effects on patient adherence. 3. Predict the consequences of hepatic enzyme induction by antiseizure medications on epilepsy management and on drug interactions with agents used for comorbid conditions. 4. Examine the various antiseizure medications and their risk for sudden unexpected death in epilepsy (SUDEP).

3.9 Drugs for the Treatment of Spasticity Disorders	
Recommended Curriculum Equivalent: 1.0 hr	
Drug Classes and Drugs	
Centrally Acting	
GABAergic Agents	**Alpha$_2$-adrenergic Agonists**
BACLOFEN DIAZEPAM clonazepam	TIZANIDINE clonidine
Anticholinergic Antispasmodic	**Other Antispasmodics**
CYCLOBENZAPRINE	METHOCARBAMOL metaxalone
Peripherally Acting	
Ryanodine Receptor Antagonist	**Acetylcholine Release Inhibitor**
DANTROLENE	onabotulinumtoxinA
Learning Objectives	

3.9.1 Mechanism of Action and Effects

1. Differentiate the mechanisms of action of centrally acting versus peripherally acting agents for spasticity and muscle spasm.
2. Elucidate the role of spinal $GABA_B$ receptors in mediating the antispasticity effects of baclofen and relate this to its therapeutic and adverse effect profile.
3. Relate the role of α_2-adrenergic agonists on spinal interneurons to its mechanism of action.
4. Explain the mechanism by which dantrolene inhibits skeletal muscle contraction by blocking ryanodine receptor-mediated calcium release.
5. Distinguish between spasticity caused by upper motor neuron disorders and muscle spasms, and relate these distinctions to therapeutic drug selection.

3.9.2 Pharmacokinetics

1. Justify the clinical rationale for intrathecal versus oral administration of baclofen in patients with severe spasticity, based on pharmacokinetic principles and CNS penetration.
2. Apply knowledge of botulinum toxin mechanism of action to its administration and therapeutic use in spastic disorders.

3.9.3 Therapeutic Uses

1. Integrate the pathophysiology of upper motor neuron disorders such as multiple sclerosis, spinal cord injury, and cerebral palsy when selecting appropriate antispasticity pharmacotherapy.
2. Differentiate the clinical indications for centrally acting agents versus peripherally acting agents in the management of spasticity versus malignant hyperthermia.
3. Justify the use of botulinum toxin for focal spasticity and predict the expected duration of effect based on its mechanism of action.

3.9.4 Adverse Effects, Contraindications, and Drug Interactions

1. Predict the CNS adverse effects of baclofen, diazepam, and tizanidine and justify the need for gradual dose tapering.

2. Compare the adverse effect profiles of centrally acting muscle relaxants versus dantrolene, particularly regarding sedation and hepatotoxicity.
3. Evaluate the contraindications and precautions for using oral agents for spasticity including liver and renal disease.
4. Analyze drug interactions between CNS muscle relaxants and other CNS depressants and propose patient counseling strategies.

3.10 Drugs Used for Pain Management and General Anesthetics			
Recommended Curriculum Equivalent: 1.5 hr			
Drug Classes and Drugs			
Inhaled Anesthetics			
Volatile Halogenated Agents		**Inorganic Gases**	
SEVOFLURANE desflurane halothane (historic)*		NITROUS OXIDE (N_2O)	
Intravenous Agents	**Adjuncts**		
ETOMIDATE KETAMINE PROPOFOL dexmedetomidine thiopental (historic)	**Opioids**	**Benzodiazepines**	
	REMIFENTANIL fentanyl meperidine morphine sufentanil	midazolam	

Learning Objectives

3.10.1 Mechanism of Action and Effects

1. Identify the primary receptor targets of inhaled and intravenous anesthetics and relate these to their pharmacological effects.
2. Apply the Meyer-Overton rule to predict the relative potencies of inhaled anesthetics based on lipid solubility and explain its limitations.
3. Define minimum alveolar concentration (MAC) and apply it to compare the potencies of inhaled anesthetics and predict drug interactions.
4. Differentiate the mechanisms of action of the intravenous anesthetics and predict their respective effects on cardiovascular, respiratory, and central nervous systems.

3.10.2 Pharmacokinetics

1. Apply Fick's law of diffusion to explain the role of alveolar pressure and ventilation in determining the rate of onset of inhaled anesthetics.
2. Differentiate between the blood/gas partition coefficient and the oil/gas partition coefficient and apply these concepts to predict onset of action and recovery time for specific inhaled agents.
3. Define alveolar fractional concentration (FA/FI ratio) and relate changes in this ratio to the clinical induction and emergence phases of inhaled anesthetics.
4. Define context-sensitive half-time and apply it to the pharmacokinetic properties of intravenous anesthetics
5. Analyze the roles of redistribution and hepatic metabolism in determining the duration of action of intravenous anesthetics.

3.10.3 Therapeutic Uses

1. Define balanced anesthesia and justify the rationale for combining multiple drug classes such as inhaled anesthetics, IV induction agents, opioids, benzodiazepines, and neuromuscular blockers to achieve its goals.
2. Relate the unique pharmacological profile of the various inhaled and intravenous anesthetics to their clinical application.

3. Evaluate the relative advantages and limitations of intravenous versus inhaled anesthetics in specific clinical scenarios.
4. Apply knowledge of adjunct agents to their roles in general anesthesia.

3.10.4 Adverse Effects, Contraindications, and Drug Interactions

1. Predict the cardiovascular and respiratory effects of inhaled anesthetics and relate these to monitoring priorities.
2. Evaluate the risk of malignant hyperthermia associated with volatile anesthetics and succinylcholine, and justify dantrolene as the treatment of choice.
3. Compare the adverse effect profiles of propofol, etomidate, and ketamine and justify agent selection in patients.
4. Predict how the concomitant use of adjunct agents reduces MAC and analyze its clinical implications for titrating inhaled anesthetic concentrations.
5. Differentiate the adverse effects of common adjunct anesthetics.

3.10.5 Notes

Historical/Toxicology Context

- *Halothane is still widely used in the developing world. It is a core medicine in the World Health Organization's "Essential Drugs List." It's not a first-line agent in high-income settings.

3.11 Local Anesthetics		
Recommended Curriculum Equivalent: 1.0 hr		
Drug Classes and Drugs		
Amide-type Agents	**Ester-type Agents**	**Adjuncts**
BUPIVACAINE LIDOCAINE ROPIVACAINE	BENZOCAINE chloroprocaine cocaine tetracaine	EPINEPHRINE sodium bicarbonate

Learning Objectives

3.11.1 Mechanism of Action and Effects

1. Elucidate the molecular mechanism by which local anesthetics block voltage-gated sodium channels, differentiating tonic from use-dependent, frequency-dependent, block.
2. Differentiate how benzocaine, a neutral ester at physiological pH, exerts its blocking effect from that of ionizable amide and ester agents, and predict the clinical implications of this difference.
3. Relate the resting, threshold, and refractory states of Na^+ channels to the mechanism and selectivity of local anesthetic blockade.
4. Apply the Henderson-Hasselbalch equation to predict the ionization state of a local anesthetic in normal tissue versus tissue in a patient with inflammation, acidosis, or infection and relate this to the achieving adequate anesthesia in the affected tissue.

3.11.2 Pharmacokinetics

1. Apply principles of drug ionization and lipid solubility to predict differences in onset, potency, and duration of action among local anesthetic agents.
2. Justify how the frequency of nerve impulse transmission, fiber size, and tissue vascularity influence the clinical efficacy of local anesthetics.
3. Differentiate the metabolic pathways of amide local anesthetics, which is primarily hepatic CYP450, versus ester local anesthetics, which is metabolized by plasma pseudocholinesterase, and relate these differences to drug interactions, systemic toxicity risk, and contraindications.

3.11.3 Therapeutic Uses

1. Integrate the pathophysiology of pain conduction and sensory nerve fiber subtypes when selecting appropriate local anesthetic agents and administration routes for specific clinical scenarios.
2. Justify the selection of specific local anesthetic agents and routes of administration such as topical, infiltration, nerve block, epidural, and intrathecal for different clinical applications, including which agents cannot be used topically or by infiltration and why.
3. Evaluate the clinical rationale for adding epinephrine or sodium bicarbonate to local anesthetic solutions and predict the effect on onset, duration, and systemic absorption.
4. Justify the requirement for preservative-free formulations when administering local anesthetics intrathecally or epidurally, and predict the consequences of using preserved formulations in this context.
5. Compare and contrast the benefits and risks of epidural versus spinal administration of local anesthetics and apply this to clinical use.

3.11.4 Adverse Effects, Contraindications, and Drug Interactions

1. Predict the central nervous system and cardiovascular adverse effects of local anesthetic based on the specific agent and how it was used.
2. Differentiate the allergic potential of ester-type local anesthetics which have a para-aminobenzoic acid metabolite versus amide-type local anesthetics and evaluate implications for patient selection in cases of reported allergy.

3.12 Opioid Analgesics		
Recommended Curriculum Equivalent: 2.5 hr		
Drug Classes and Drugs		
Agonists	**Partial Agonist**	**Antagonists**
CODEINE FENTANYL HEROIN HYDROCODONE HYDROMORPHONE METHADONE MORPHINE OXYCODONE REMIFENTANIL TRAMADOL	BUPRENORPHINE	NALOXONE NALTREXONE

Learning Objectives

3.12.1 Mechanisms of Action and Effects

1. Apply knowledge of opioid receptor G protein signaling to explain how opioids modulate nociceptive transmission at peripheral, spinal, and supraspinal sites, including activation of descending analgesic pathways.
2. Differentiate how activation of mu, delta, and kappa opioid receptors contribute to distinct therapeutic and adverse effects.
3. Explain the mechanisms underlying opioid tolerance and physical dependence and distinguish these from addiction.

3.12.2 Pharmacokinetics

1. Predict how renal impairment alters the accumulation and clinical effects of morphine metabolites.
2. Evaluate pharmacokinetic differences between codeine and heroin in terms of onset of action, CNS morphine exposure, and variability in opioid effects.
3. Explain how extensive tissue binding of methadone influences euphoria and withdrawal.
4. Predict how the co-formulation of naloxone with buprenorphine influences the effects of sublingual versus intravenous administration.

3.12.3 Pharmacogenomics

1. Analyze how CYP2D6 genetic polymorphisms influence the analgesic and adverse effects of codeine.

3.12.4 Therapeutic Uses

1. Evaluate opioid selection for pain management based on pain severity (mild, moderate, or severe) and pain type (acute, chronic, cancer, or neuropathic).
2. Differentiate morphine, fentanyl, and remifentanil for intraoperative use in terms of onset, duration, accumulation, and hemodynamic stability.
3. Predict the effects of combining opioids with other CNS depressants.
4. Differentiate the therapeutic roles of naloxone, naltrexone, methadone, and buprenorphine in opioid overdose and opioid use disorder based on their opioid receptor pharmacology.

5. Compare methadone and buprenorphine for treatment of opioid use disorder in terms of mechanism of action, adverse effects, overdose risk and reversibility with opioid receptor antagonists, consequences of concurrent opioid or sedative use, and severity of withdrawal symptoms.
6. Explain prescription opioid misuse and diversion and identify strategies to minimize these occurrences.
7. Predict additional health risks associated with illicit opioids compared to prescription opioids.

3.12.5 Adverse Effects, Contraindications, and Drug Interactions

1. Relate the anatomical location of opioid receptors to the physiological mechanisms underlying the opioid toxidrome and other adverse effects.
2. Illustrate how opioid receptor activation in the mesolimbic reward pathway contributes to the development of opioid use disorder.
3. Explain how lipophilicity influences the addictive potential of opioids.
4. Predict opioid withdrawal symptoms and evaluate how opioid half-life influences the severity and duration of withdrawal.
5. Compare the toxicity and withdrawal syndromes associated with opioids versus other CNS depressants.
6. Predict how inclusion of acetaminophen in hydrocodone and oxycodone combination products alters the adverse effect profile.
7. Explain how the mechanism of tramadol accounts for an adverse effect profile that differs from morphine.
8. Explain how oral administration of morphine can alter the absorption of other oral drugs.

3.13 Drugs for the Treatment of Neuropathic Pain		
Recommended Curriculum Equivalent: 0.5 hr		
Drug Classes and Drugs		
TCA	**SNRI**	**Gabapentinoids**
NORTRIPTYLINE amitriptyline	DULOXETINE venlafaxine	GABAPENTIN PREGABALIN
Learning Objectives		
3.13.1 Mechanisms of Action and Effects 1. Compare the mechanisms by which tricyclic antidepressants (TCAs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and gabapentinoids modulate neuropathic pain transmission.		
3.13.2 Therapeutic Uses 1. Differentiate patient comorbidities that favor or warrant avoidance of TCAs, SNRIs, and gabapentinoids in the treatment of neuropathic pain. 2. Explain the risks associated with abrupt discontinuation of TCAs and SNRIs and propose strategies to mitigate these risks.		
3.13.3 Adverse Effects, Contraindications, and Drug Interactions 1. Explain how pharmacologic targets of TCAs, SNRIs, and gabapentinoids lead to differences in their adverse effect profiles. 2. Evaluate the misuse and overdose risks associated with gabapentinoids, particularly when combined with opioids.		

3.14 Drugs for the Treatment of Primary Headache Disorders			
Recommended Curriculum Equivalent: 2.0 hr			
Drug Classes and Drugs			
Drugs for Migraine Headache			
NSAIDS	**Acetaminophen**	**Triptan**	**CGRP Antagonist**
ASPIRIN CELECOXIB IBUPROFEN KETOROLAC NAPROXEN	ACETAMINOPHEN	SUMATRIPTAN dihydroergotamine	ERENUMAB RIMEGEPANT

Beta-adrenergic Antagonist	Antidepressants	Antiepileptic
PROPRANOLOL	AMITRIPTYLINE VENLAFAXINE	TOPIRAMATE

Drugs for Tension Headache		
NSAIDS	**Acetaminophen**	**TCA**
ASPIRIN IBUPROFEN KETOROLAC NAPROXEN	ACETAMINOPHEN	AMITRIPTYLINE

Drugs for Cluster Headache		
Triptan	**Calcium Channel Blocker**	**Other**
SUMATRIPTAN	VERAPAMIL	OXYGEN

Drugs for Trigeminal Neuralgia
Antiepileptic
CARBAMAZEPINE

Learning Objectives

3.14.1 Mechanisms of Action and Effects

1. Explain how the mechanisms of action of medications used to treat migraine, cluster headache, tension headache, and trigeminal neuralgia modulate the underlying neurovascular and nociceptive pathways.

3.14.2 Pharmacokinetics

1. Compare the routes and dosing frequencies of CGRP antagonists used for migraine prevention and explain how these differences influence treatment selection.
2. Explain the different routes of administration of triptans and the impact on onset of action.

3.14.3 Therapeutic uses

1. Differentiate pharmacologic treatments of migraine, cluster headache, tension headache, and trigeminal neuralgia based on their clinical roles in acute symptom relief versus preventive therapy.
2. Differentiate patient comorbidities that favor or warrant avoidance of specific classes of

medications used for migraine prevention. 3. Evaluate the role of caffeine as an adjuvant to NSAIDs and acetaminophen in the treatment of migraine and tension headaches. 4. Develop a treatment plan for migraines accompanied by significant nausea or vomiting that addresses barriers to effective oral therapy. 5. Identify appropriate treatment for acute migraines during pregnancy and explain safety concerns of other treatments
3.14.4 Adverse Effects, Contraindications, and Drug Interactions 1. Compare adverse effects of pharmacologic treatments for migraine, cluster headache, tension headache, and trigeminal neuralgia and relate these effects to the drugs' mechanisms of action. 2. Compare medication classes associated with medication overuse headaches and identify strategies to prevent its development.

3.15 Drugs for the Treatment of Alcohol Use Disorder		
Recommended Curriculum Equivalent: 0.3 hr		
Drug Classes and Drugs		
Drugs for Alcohol Use Disorder		
Aldehyde Dehydrogenase Inhibitor	**μ-opioid Antagonist**	
DISULFIRAM	NALTREXONE (oral)	
Glutamate Modulator	**Antiepileptics**	
acamprosate	gabapentin topiramate	
Drugs for the Management of Withdrawal		
Benzodiazepines		
CHLORDIAZEPOXIDE lorazepam		
Alcohol Toxicity		
Toxins		
METHANOL ethylene glycol		
Drugs for Toxic Alcohol Ingestion		
Alcohol Dehydrogenase Inhibitor	**Competitive Substrate**	**Other**
FOMEPIZOLE	ETHANOL (second line; see Notes)*	thiamine
Learning Objectives		
3.15.1 Mechanism of Action and Effects 1. Analyze the mechanisms by which ethanol modulates $GABA_A$ and NMDA receptor activity in the CNS, and relate these interactions to its acute behavioral and physiological effects. 2. Contrast the mechanisms of action of disulfiram, naltrexone, and acamprosate in the long-term management of alcohol use disorder. 3. Evaluate the mechanistic rationale for fomepizole as an antidote in the management of methanol and ethylene glycol toxicity.		
3.15.2 Pharmacokinetics 1. Apply knowledge of ethanol's absorption, distribution, zero-order metabolism, and excretion to predict clinical outcome. 2. Predict the effects of chronic moderate or heavy alcohol use on ethanol metabolism and organ function.		
3.15.3 Therapeutic Uses 1. Evaluate the therapeutic rationale and clinical evidence for disulfiram, naltrexone, and acamprosate in the long-term management of alcohol use disorder. 2. Justify the use of benzodiazepines in the management of the ethanol abstinence syndrome.		

3. Apply clinical evidence to justify fomepizole as the treatment of choice for methanol or ethylene glycol toxicity, and evaluate the role of ethanol as an alternative agent when fomepizole is unavailable.
4. Summarize the limited accepted therapeutic applications of ethanol.
5. Critique the ethical and practical limitations of using disulfiram for ethanol use disorder based on its mechanism of action and adverse effects.

3.15.4 Adverse effects, Contraindications, and Drug Interactions

1. Differentiate the acute and chronic organ toxicities of ethanol, methanol, and ethylene glycol.
2. Compare and contrast the signs and symptoms of the ethanol abstinence syndrome with those following chronic use of barbiturates, benzodiazepines, or opioids, including differences in morbidity and mortality.
3. Predict drug-drug and drug-food interactions involving ethanol, including cross-tolerance and cross-dependence with other CNS depressants.
4. Identify prescription and over-the-counter drugs that require avoidance of alcohol due to clinically significant interaction risks.
5. Compare and contrast the morbidity and mortality associated with chronic alcohol use disorder with that of other substances of abuse.

3.15.5 Notes

Historical/Toxicology Context

- *The accepted therapeutic uses of ethanol are very limited. It was historically used to stimulate gastric acid production and remains a second-line option for trigeminal neuralgia (by injection). It serves as an alternative antidote for methanol or ethylene glycol overdose when fomepizole is unavailable; however, achieving and maintaining a therapeutic blood ethanol concentration after ingestion is problematic, and exacerbation of CNS depression is a significant concern.

3.16 Substance Use Disorders: General Principles	
Recommended Curriculum Equivalent: 0.2 hr	
Definitions	
Definitions Related to Substance Use Disorders	**Definitions Related to Drug Classes**
Dependence Addiction Tolerance Withdrawal syndrome	Psychostimulant Hallucinogen Psychedelic Dissociative drug Sedative-hypnotic
Learning Objectives	
3.16.1 Definitions and Terminology 1. Define the terms related to substance use disorders: dependence, addiction, tolerance, and withdrawal syndrome. 2. Differentiate between the following drug classes: psychostimulant, hallucinogen, psychedelic, dissociative drug, and sedative-hypnotic.	

3.17 Substance Use Disorders: Psychostimulants		
Recommended Curriculum Equivalent: 0.5 hr		
Drug Classes and Drugs		
Dopaminergic and Noradrenergic	**Nicotinic Agonist**	**Other**
AMPHETAMINES COCAINE METHAMPHETAMINE METHYLPHENIDATE	NICOTINE VARENICLINE	BUPROPION CAFFEINE ephedrine phentermine
Learning Objectives		
3.17.1 Mechanism of Action and Effects 1. Predict the effects of methamphetamine, cocaine, and nicotine on various organ systems based on their molecular mechanism of action. 2. Compare and contrast the mechanism of action of cocaine and amphetamine.		
3.17.2 Therapeutic Uses 1. Propose appropriate smoking cessation therapy based on patient specific factors such as age, comorbidities, and use of concomitant drugs.		
3.17.3 Adverse Effects, Contraindications, and Drug Interactions 1. Compare abuse liability among the psychostimulants including amphetamine, methamphetamine, cocaine, methylphenidate, and nicotine. 2. Predict the adverse effects of stimulants that target cholinergic, dopaminergic and noradrenergic receptors. 3. Compare and contrast patterns of tolerance and the withdrawal syndromes for different psychostimulants. 4. Discuss the contraindications of bupropion. 5. Describe the adverse effects of nicotine and other constituents of tobacco products. 6. Compare and contrast morbidity and mortality of misuse of stimulants with other drugs of abuse. 7. Identify the treatment for acute overdose on psychostimulant drugs such as amphetamine or cocaine. 8. Predict the implications of drug interactions of MAO inhibitors on the effects of psychostimulants.		

3.18 Substance Use Disorders: Hallucinogens and Psychedelics		
Recommended Curriculum Equivalent: 0.3 hr		
Drug Classes and Drugs		
Psychedelics	**Dissociative Drugs**	**Other**
LYSERGIC ACID DIETHYLAMIDE (LSD) MESCALINE PSILOCYBIN	KETAMINE (Special K) PHENCYCLIDINE (PCP)	METHYLENEDIOXYMETHAMPHETAMINE (MDMA, Ecstasy)
Learning Objectives		
3.18.1 Mechanism of Action and Effects 1. Predict the effects of hallucinogens on central nervous system based on their molecular mechanism of action on serotonin and NMDA receptors. 2. Compare and contrast the mechanism of action of psychedelics and dissociative drugs.		
3.18.2 Adverse Effects, Contraindications, and Drug Interactions 1. Discuss tolerance and cross-tolerance among the various hallucinogens. 2. Differentiate hallucinogens from other drugs of abuse in terms of dependence, addiction, tolerance, and withdrawal. 3. Compare the toxidromes expected for LSD, MDMA, and PCP. 4. Evaluate the consequences relating to acute ingestion of these drugs and relate this to appropriate patient management.		

3.19 Substance Use Disorders: Sedatives and Hypnotics		
Recommended Curriculum Equivalent: 0.5 hr		
Drug Classes and Drugs		
Benzodiazepines	**Barbiturates**	**GABA Analog**
ALPRAZOLAM CHLORDIAZEPOXIDE DIAZEPAM FLUNITRAZEPAM clonazepam	BUTALBITAL† PENTOBARBITAL amobarbital secobarbital	GAMMA HYDROXYBUTYRATE (GHB)*
Alpha$_2$-adrenergic Agonist	**Meprobamates**	**Benzodiazepine Antagonist**
XYLAZINE	MEPROBAMATE carisoprodol	FLUMAZENIL

Learning Objectives

3.19.1 Mechanism of Action and Effects

1. Predict the sedative effects of benzodiazepines, barbiturates, meprobamate derivatives, GHB, and xylazine based on their receptor binding and activity in the central nervous system.
2. Differentiate the mechanism of action of benzodiazepines and barbiturates and predict their effects in various organ systems.

3.19.2 Pharmacokinetics

1. Predict the abuse potential of benzodiazepines and barbiturates based on their onset of action, half-life, and route of administration.
2. Compare and contrast the route of administration of sedatives and hypnotics to other drugs of abuse.

3.19.3 Therapeutic Uses

1. Propose an appropriate therapy for the management of an acute overdose with a sedative or hypnotic agent.
2. Devise an appropriate strategy for managing acute and chronic withdrawal symptoms in patients with sedative, hypnotic, or anxiolytic use disorder.
3. Assess the clinical use of flumazenil and its limited application in the treatment of benzodiazepine overdose.

3.19.4 Adverse effects, Contraindications and Drug Interactions

1. Differentiate the mechanism of action of benzodiazepines and barbiturates and relate this to their differences in toxicity.
2. Compare and contrast the acute toxicity profile of sedatives and hypnotics with other drugs of abuse.
3. Compare and contrast the relative abuse potential of the various sedatives and hypnotics based on tolerance, dependence, and withdrawal symptoms and relate this to the other drugs of abuse.

3.19.5 Notes

Clinical Guidelines

- *FDA approved as sodium oxybate for the management of cataplexy or excessive daytime sleepiness associated with narcolepsy.

Historical/Toxicology Context

- †Commonly abused barbiturate that is available in combination products with aspirin and acetaminophen prescribed for headaches.

3.20 Substance Use Disorders: Inhalants		
Recommended Curriculum Equivalent: 0.2 hr		
Drug Classes and Drugs		
Aromatic Hydrocarbons	**Aliphatic Hydrocarbons**	**Halogenated Hydrocarbons**
TOLUENE benzene xylene	BUTANE gasoline*	bromochlorodifluoromethane
Ketones	**Nitrites**	**Anesthetics**
ACETONE METHYL ETHYL KETONE	amyl nitrite	NITROUS OXIDE

Learning Objectives

3.20.1 Mechanisms of Action and Effects

1. Predict the neurological effects of commonly abused inhalants based on proposed neurobiological targets and activities.
2. Organize abused inhalants based on the commercial product in which they are found.
3. Compare and contrast the epidemiology of inhalant use to other drugs of abuse.

3.20.2 Adverse effects, Contraindications, and Drug Interactions

1. Examine the acute and long-term adverse effects of inhalant use in the central nervous system and other organs and their psychosocial effects.
2. Propose an appropriate therapy for the management of acute inhalant intoxication.

3.20.3 Notes

Historical/Toxicology Context

- *Gasoline is a complex mixer of hydrocarbons. Most of the hydrocarbons in gasoline are aliphatic, however aromatic hydrocarbons such as benzene, toluene, and xylene are used as additives.

3.21 Cannabinoids and Cannabis Use Disorder	
Recommended Curriculum Equivalent: 0.5 hr	
Drug Classes and Drugs	
Phytocannabinoids	
CANNABIDIOL (CBD) DELTA-9-TETRAHYDROCANNABINOL (THC) MARIJUANA	
Synthetic Cannabinoids	**Butyrophenone Antiemetic**
delta-8-THC delta-10-THC DRONABINOL (Δ^9-THC) K2 Spice THC-O	DROPERIDOL
Learning Objectives	
3.21.1 Mechanism of Action and Effects 1. Differentiate the receptor binding and activities of THC with cannabidiol. 2. Compare and contrast the potency, psychological effects, physiological effects, and route of administration of THC, marijuana, and synthetic cannabinoids.	
3.21.2 Pharmacokinetics 1. Compare and contrast the potency, absorption, and the onset and duration of action of inhaled cannabinoids with those of ingested cannabinoids. 2. Compare and contrast the routes of administration and preparations of cannabinoids to other drugs of abuse and relate this to the increased risk of accidental ingestion, particularly by children.	
3.21.3 Therapeutic Uses 1. Differentiate between the various cannabinoids and their approved clinical uses including Lennox-Gastaut syndrome, Dravet syndrome, tuberous sclerosis complex, chemotherapy induced nausea and vomiting, and cachexia in patients with AIDS. 2. Propose additional therapeutic uses of THC, marijuana, and cannabidiol beyond current FDA approved indications based on recent evidence-based studies. 3. Propose an appropriate therapy for the management of cannabinoid hyperemesis syndrome and justify the use of butyrophenone antiemetics over other antiemetic agents.	
3.21.4 Adverse Effects, Contraindications, and Drug Interactions 1. Compare and contrast the relative abuse potential of the various cannabinoids based on tolerance, dependence, and withdrawal symptoms and relate this to the other drugs of abuse. 2. Differentiate the clinical manifestations of acute cannabis intoxication in children and adults. 3. Compare and contrast the adverse effects and toxicity of THC, marijuana, and synthetic cannabinoids and relate this to other drugs of abuse. 4. Evaluate a patient for the signs, symptoms, and functional impairment meeting the criteria for diagnosing cannabis use disorder and predict the persistent symptoms of chronic cannabinoid	

use.

5. Examine the legal implications of using cannabinoids clinically and recreationally with respect to federal and state laws*.

3.21.5 Notes

Clinical Guidelines

- McDonagh MS, Morasco BJ, Wagner J, Ahmed AY, Fu R, Kansagara D, Chou R. Cannabis-Based Products for Chronic Pain: A Systematic Review. Ann Intern Med. 2022 Aug;175(8):1143-1153. doi: 10.7326/M21-4520. Epub 2022 Jun 7. PMID: 35667066.
- Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for Medical Use: A Systematic Review and Meta-analysis. JAMA. 2015;313(24):2456–2473. doi:10.1001/jama.2015.6358

Historical/Toxicology Context

- *Currently the ambiguous federal status and regulation of cannabinoids compared to state laws has created barriers to the clinical research and use of cannabinoids for medicinal purposes. Current deregulation of cannabinoids to schedule C-III has increased their potential use in research though comprehensive clinical application remains equivocal.

SECTION 4

CARDIOVASCULAR PHARMACOLOGY

Mark Hernandez (section chair), Andy Chen, Youssef Soliman,
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4.1 Drugs Used for the Management of Arrhythmia		
Recommended Curriculum Equivalent: 3.0 hr		
Drug Classes and Drugs		
CLASS I (Voltage-gated Na^+ channel blockers)		
Class IA	**Class IB**	**Class IC**
PROCAINAMIDE disopyramide quinidine	LIDOCAINE mexiletine	FLECAINIDE propafenone
CLASS II (Beta antagonists)	**CLASS III (Voltage dependent K^+ channel blockers, membrane-stabilizing drugs)**	**CLASS IV (Calcium channel blockers)**
PROPRANOLOL esmolol	AMIODARONE ibutilide sotalol	DILTIAZEM verapamil
For the Management of Tachyarrhythmias		
Other Specific	**Autonomic Activator**	**Adenosine A1 Receptor Activator**
MAGNESIUM	DIGOXIN	ADENOSINE
For the Management of Bradyarrhythmias		
Beta-adrenergic Receptor Agonist	**M2 Receptor Antagonist**	
ISOPROTERENOL	ATROPINE	

Learning Objectives

4.1.1 Mechanism of Action and Effects

1. Explain the molecular mechanism of action of each antiarrhythmic drug in each drug class and organize those according to the modernized classification inspired by the Vaughan-Williams framework, recognizing the limitations of this classification system.
2. Justify drug selection based on their phase-specific effects on cardiac action potentials in normal and diseased myocardial and conduction tissue.
3. Analyze how antiarrhythmic drugs differentially modify fast (sodium-dependent) and slow (calcium-dependent) cardiac action potentials and use these mechanisms to justify the selection of specific agents for ventricular versus supraventricular arrhythmias
4. Apply knowledge of extracardiac pharmacologic actions to predict adverse effects and monitoring needs associated with other antiarrhythmic drugs.
5. Analyze major indirect autonomic actions of these drugs to predict the hemodynamic consequences.

4.1.2 Pharmacokinetics

1. Explain how pharmacokinetic differences among antiarrhythmic drugs account for variability in onset, duration of action, and toxicity.
2. Distinguish the onset and duration of action of drugs used in the management of arrhythmias.
3. Predict the impact of reduced cardiac output (e.g., in MI or cardiomyopathy) on

pharmacokinetics (e.g., half-life) and justify dosage adjustments and prevent toxicity.
4. Predict how aging and multi-organ dysfunction (renal/hepatic) can affect the pharmacokinetics of drugs used to manage arrhythmias.
5. Analyze the significance of electrolyte and acid-base imbalance on arrhythmia generation and their influence on antiarrhythmic drug action.
6. Explain how pharmacokinetic differences among antiarrhythmic drugs account for variability in onset, duration of action, and toxicity.
7. Distinguish the onset and duration of action of drugs used in the management of arrhythmias.
8. Predict the impact of reduced cardiac output (e.g., in MI or cardiomyopathy) on pharmacokinetics (e.g., half-life) and justify dosage adjustments and prevent toxicity.
9. Predict how aging and multi-organ dysfunction (renal/hepatic) can affect the pharmacokinetics of drugs used to manage arrhythmias.
10. Analyze the significance of electrolyte and acid-base imbalance on arrhythmia generation and their influence on antiarrhythmic drug action.

4.1.3 Pharmacogenomics

1. Differentiate the molecular basis of congenital versus drug-induced Long QT Syndrome (LQTS) and identify the specific ion channels involved as drug targets.
2. Analyze the impact of inherited cardiac channelopathies on patient responsiveness to antiarrhythmic therapy.
3. Evaluate the clinical role of quinidine in the management of short-QT syndrome.
4. Justify individualized antiarrhythmic therapy based on a patient's genetic susceptibility to proarrhythmia and sudden cardiac death.

4.1.4 Therapeutic uses

1. Evaluate the appropriateness of pharmacologic strategies for management of arrhythmia based on current clinical guidelines for safe and effective care.
2. Analyze the evidence for rate control versus rhythm control in atrial fibrillation to justify patient-specific pharmacotherapeutic decisions.

4.1.5 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions

1. Analyze the mechanisms of antiarrhythmic and non-antiarrhythmic drugs to predict cardiac and extracardiac toxicities, clinically significant drug interactions, and contraindications in patients with conduction abnormalities, heart failure, or risk for acquired long QT syndrome.
2. Apply principles of pharmacodynamics and pharmacokinetics to predict clinically important drug–drug interactions and arrhythmia risk associated with combination therapy.

4.2 Drugs Used for the Management of Acute and Chronic Heart Failure			
Recommended Curriculum Equivalent: 2.0 hr			
Drug Classes and Drugs			
Drugs Affecting the Renin-angiotensin Aldosterone System			
ACE Inhibitors	**Angiotensin Receptor Blockers**	**Aldosterone Antagonists**	**Angiotensin Receptor-Neprilysin Inhibitor (ARNI)**
CAPTOPRIL ENALAPRIL lisinopril	LOSARTAN VALSARTAN candesartan	SPIRONOLACTONE eplerenone finerenone	SACUBITRIL-VALSARTAN
Sympathetic Agents			
Beta Blockers		**Beta Agonists**	
CARVEDILOL METOPROLOL bisoprolol		DOBUTAMINE dopamine	
Inotropes/Others			
Cardiac Glycosides	**Diuretics**	**SGLT2 Inhibitors**	
DIGOXIN	FUROSEMIDE HYDROCHLOROTHIAZIDE amiloride	DAPAGLIFLOZIN empagliflozin	
PDE3 Inhibitors	**Vasodilators**	**Other agents**	
MILRINONE	HYDRALAZINE/ISOSORBIDE DINITRATE NITROGLYCERIN	ivabradine mavacamten vericiguat	

Learning Objectives

4.2.1 Mechanism of Action and Effects

1. Analyze how the different heart failure drug classes modify cardiac function and hemodynamics (heart rate, contractility, preload, afterload, coronary perfusion, and cardiac remodeling) based on their mechanisms of action.
2. Evaluate the extracardiac effects of heart failure therapies, including their impact on renal perfusion and systemic vascular physiology, and relate these effects to therapeutic benefit and adverse outcomes.

4.2.2 Pharmacokinetics

1. Analyze the pharmacokinetic parameters that determine digoxin loading and maintenance dosing, including volume of distribution, renal clearance, bioavailability, and patient-specific factors.
2. Explain how drug-specific differences in absorption, metabolism, and excretion and patient-specific factors such as aging—interact to influence onset of action, duration, therapeutic outcomes, and risk of toxicity in the pharmacologic management of heart failure.

4.2.3 Pharmacogenetics

1. Evaluate genetic polymorphisms in cardiovascular signaling pathways with pharmacogenomic evidence to justify individualized selection of heart failure therapies and predict variability in efficacy and toxicity across patient populations.

4.2.4 Therapeutic uses

1. Evaluate the appropriateness of pharmacologic strategies for management of acute and chronic heart failure based on current clinical guidelines for safe and effective care.

4.2.5 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions

1. Analyze how cardiac and extracardiac side effects, drug-drug interactions, and comorbid disease states (e.g., hypothyroidism) intersect to mitigate risks and optimize pharmacologic management in heart failure patients.
2. Evaluate the clinical impact of drug-induced electrolyte shifts (K+, Na+, Ca2+, Mg2+) and formulate monitoring strategies to prevent life-threatening complications such as digoxin toxicity or arrhythmias.
3. Apply principles of pharmacology and physiology to predict how drug–drug and drug–disease interactions alter the safety, efficacy, and dosing of heart failure therapies, including but not limited to potassium-sparing medications, thyroid disease, and NSAID use.

4.2.6 Notes

Cross-References

- Objectives for RAAS agents are covered under Vasoactive Peptides.
- Sympathetic drug objectives are also covered under the Autonomic Nervous System.

Clinical Guidelines

- Drug update: Mavacamten is a first-in-class drug approved for the treatment of obstructive hypertrophic cardiomyopathy. It is used for the treatment of adult patients with symptomatic New York Heart Association (NYHA) class II-III obstructive hypertrophic cardiomyopathy (oHCM). https://www.acc.org/latest-in-cardiology/articles/2022/05/02/12/27/fda-update-mavacamten-approved-for-obstructive-hcm
- The VICTOR (**Vericiguat** in Patients With Chronic Heart Failure and Reduced Ejection Fraction) study results showed minimal hospitalization reduction but signaled mortality benefit.https://www.acc.org/Latest-in-Cardiology/Articles/2026/01/05/17/47/Vericiguat-in-Heart-Failure
- For clinical guideline updates on heart failure refer to 2024 ACC Expert Consensus Decision Pathway for Treatment of Heart Failure With Reduced Ejection Fraction: A Report of the American College of Cardiology Solution Set Oversight Committee | JACC

4.3 Drugs Used for the Management of Hypertension				
Recommended Curriculum Equivalent: 4.0 hr				
Drug Classes and Drugs				
Drugs Inhibiting the Renin-angiotensin Aldosterone System				
ACE Inhibitors		**Angiotensin Receptor Blockers**		**Renin Inhibitor**
ENALAPRIL CAPTOPRIL LISINOPRIL		LOSARTAN VALSARTAN candesartan Olmesartan		aliskiren
Adrenergic Receptor Antagonists				
Alpha		**Beta**		**Mixed α and β**
Nonselective	**α_1 Selective**	**Nonselective**	**β_1 Selective**	
phenoxybenzamine phentolamine	PRAZOSIN doxazosin	PROPRANOLOL pindolol	METOPROLOL atenolol nebivolol	CARVEDILOL LABETALOL
Other Agents				
Centrally Acting Agents	**Vasodilators**			
	Venous	**Arterial**	**Both**	
CLONIDINE guanfacine methyldopa	ISOSORBIDE DINITRATE nitroglycerin	AMLODIPINE HYDRALAZINE diltiazem minoxidil nicardipine verapamil	NITROPRUSSIDE	
Diuretics		**Dual Endothelin Receptor Antagonist**		**Hypertensive Emergency and Urgency**
HYDROCHLOROTHIAZIDE amiloride chlorthalidone eplerenone furosemide spironolactone		aprocitentan		LABETALOL NITROPRUSSIDE esmolol clevidipine fenoldopam nicardipine nitroglycerin
Learning Objectives				
4.3.1 Mechanism of Action and Effects 1. Analyze how antihypertensive drug classes act on organ systems involved in blood pressure regulation to achieve therapeutic effects. 2. Evaluate the link between hypertension-induced organ damage and the protective mechanisms of blood pressure treatments.				

4.3.2 Pharmacokinetics

1. Predict the onset and duration of action of commonly prescribed antihypertensive drugs based on their pharmacokinetic properties.
2. Analyze how differences in absorption, metabolism, and excretion among antihypertensive drugs contribute to variability in efficacy, duration of action, and toxicity.

4.3.3 Pharmacogenomics

1. Analyze how genetic and epigenetic variation in the renin–angiotensin–aldosterone system (RAAS) influences individual responsiveness to antihypertensive drug classes.
2. Evaluate the potential and limitations of genetic biomarkers and polygenic risk scores in guiding selection of antihypertensive therapies.
3. Justify individualized antihypertensive pharmacotherapy based on genetic predispositions to adverse drug reactions (e.g., ACE inhibitor–associated angioedema or statin-associated myopathy).

4.3.4 Therapeutic uses

1. Evaluate the appropriateness of pharmacologic strategies for management of hypertension including special populations (e.g., pregnancy, hypertensive emergencies, resistant hypertension, diabetes, renal failure, and isolated systolic hypertension and/or other secondary causes), based on current clinical guidelines for safe and effective care.

4.3.5 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions

1. Analyze the cardiac and extracardiac adverse effects of antihypertensive drugs, including physiologic reflex responses.
2. Evaluate the benefits and risks of combination antihypertensive therapy.
3. Predict clinically significant drug interactions between antihypertensive agents and medications that alter blood pressure regulation, including non-prescription drugs (e.g., pseudoephedrine, NSAIDs, and herbal stimulants).
4. Analyze clinically significant pharmacokinetic interactions involving antihypertensive drugs, including CYP-mediated metabolism and transporter effects, and their impact on drug exposure and toxicity.

4.3.6 Notes

Cross-References

- Objectives for RAAS agents are covered under Vasoactive Peptides.
- Sympathetic drug objectives are also covered under the Autonomic Nervous System.

Clinical Guidelines

- For clinical guideline updates on Prevention, Detection, Evaluation and Management of High Blood Pressure in Adults refer to 2025 AHA/ACC/AANP/AAPA/ABC/ACCP/ACPM/AGS/AMA/ASPC/NMA/PCNA/SGIM
- The 2025 American Heart Association/American College of Cardiology guideline now recommends the PREVENT (Predicting Risk of Cardiovascular Disease Events) equations to provide more precise, representative risk estimates for cardiovascular disease, including heart failure. It calculates 10-year cardiovascular risk, lowering the threshold for initiating medication

in Stage 1 Hypertension (130-139/80-89 mmHg) to ≥7.5%. For low-risk patients (< 7.5%), medication is now recommended if BP remains ≥ 130/80 mmHg after 3-6 months of lifestyle changes.

- New BP guidelines focus on addressing social determinants like structural, economic, and environmental factors to reduce cardiovascular disease (CVD) disparities.
- The 2025 American Heart Association/American College of Cardiology guideline update emphasizes an **individualized, race-agnostic approach**. While it still acknowledges that certain medications (Thiazides, CCBs) are highly effective in Black adults, the focus has shifted toward using **single-pill combinations** (two medications in one pill) as first-line therapy for most patients to improve adherence.
- New classes of hypoglycemic agents, sodium-glucose cotransporter inhibitors (SGLT2i) and GLP-1 receptor agonists have been demonstrated to slow decline in kidney function whether or not diabetes is present and may have some beneficial effects on BP.

4.4 Drugs Used for the Management of Angina and Coronary Artery Disease		
Recommended Curriculum Equivalent: 1.0 hr		
Drug Classes and Drugs		
Beta Blockers	**Calcium Channel Blockers**	**Organic Nitrates**
ATENOLOL METOPROLOL PROPRANOLOL	DILTIAZEM VERAPAMIL amlodipine nifedipine (extended- release)	NITROGLYCERIN ISOSORBIDE MONONITRATE isosorbide dinitrate
Metabolic Modulators	**Cardiac Rate Control**	
ranolazine	ivabradine	

Learning Objectives

4.4.1 Mechanism of Action and Effects

1. Contrast the therapeutic objectives for chronic ischemic states and acute coronary events, formulating plans that prioritize symptom control and mortality reduction in stable coronary artery disease versus immediate myocardial salvage in acute coronary syndrome.
2. Analyze the mechanisms of anti-anginal pharmacotherapy to evaluate how shifts in heart rate, contractility, preload, and afterload optimize the myocardial oxygen supply-demand balance in patients with stable coronary artery disease.

4.4.2 Pharmacokinetics

1. Analyze how differences in absorption, first-pass metabolism, and excretion among antianginal drugs contribute to variability in bioavailability, onset, duration of action, efficacy, and toxicity.
2. Evaluate the mechanisms underlying nitrate tolerance and dosing strategies that minimize its development.

4.4.3 Pharmacogenomics

1. Justify individualized antianginal pharmacotherapy based on genetic predispositions to adverse drug reactions and altered drug metabolism.
2. Analyze how genetic variation in drug-metabolizing enzymes (e.g., CYP450), drug transporters, and intracellular signaling pathways (including β-adrenergic receptor signaling) influence responsiveness to antianginal therapy in ischemic heart disease.

4.4.4 Therapeutic Uses

1. Evaluate the appropriateness of pharmacologic strategies for management of classic and/or vasospastic angina based on current clinical guidelines for safe and effective care.
2. Analyze the role of antianginal drugs in myocardial preservation during acute myocardial infarction, with emphasis on adrenergic receptor antagonists.

4.4.5 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions

1. Analyze the physiologic consequences and clinically significant adverse effects of drugs used in the management of angina and coronary artery disease.
2. Evaluate contraindications to antianginal and anti–coronary artery disease therapies, including interactions with PDE5 inhibitors and agents with negative chronotropic, inotropic, or dromotropic effects.

3. Analyze clinically significant pharmacokinetic interactions affecting antianginal drugs, including cytochrome P450–mediated effects involving beta-blockers, calcium channel blockers, and ranolazine.
4. Predict pharmacodynamic interactions between antianginal agents and commonly co-prescribed medications that increase the risk of hypotension, bradycardia, or atrioventricular block.

4.4.6 Notes

Cross-References

- Disease-Modifying Therapy: Antiplatelet agents (e.g., aspirin, clopidogrel), lipid-lowering therapies (e.g., statins), and renin–angiotensin system modulators (ACE inhibitors and ARBs) that reduce cardiovascular morbidity and mortality in patients with coronary artery disease are addressed in hemostasis and blood-forming organs Section.
- Genetic determinants of antiplatelet and lipid-lowering therapy are addressed in hemostasis and blood-forming organs Section. (STEMI/ACS). (Dyslipidemia/Chronic Cardiovascular Disease) and should be integrated with antianginal pharmacotherapy in patients with stable coronary artery disease.
- Objectives for sympathetic nervous system drugs are covered under the Autonomic Nervous System.

Clinical Guidelines

- Management strategies for stable ischemic heart disease and secondary prevention should be interpreted in the context of current AHA/ACC clinical practice guidelines.
- For clinical guideline updates refer to 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA Guideline for the Management of Patients with Chronic Coronary Disease: A Report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines.
- Colchicine, a widely available gout medication, has received FDA approval to be used in low dose to prevent cardiovascular events in patients with proven coronary disease.https://www.jacc.org/doi/10.1016/j.jacc.2023.05.055?_ga=2.232404063.1737016906.1712245024-844464207.1695759712 (see section on gout/rheumatology).

4.5 Drugs Used for the Management of Dyslipidemias		
Recommended Curriculum Equivalent: 1.0 hr		
Drug Classes and Drugs		
Bile Acid sequestrants	**Fibric Acid Derivatives**	**HMG CoA Reductase Inhibitors**
CHOLESTYRAMINE colesevelam colestipol	GEMFIBROZIL fenofibrate	ATORVASTATIN ROSUVASTATIN pravastatin simvastatin

Other Agents	PCSK9-inhibitors
bempedoic acid ezetimibe icosapent ethyl lomitapide niacin	evolocumab inclisiran

Learning Objectives

4.5.1 Mechanism of Action and Effects

1. Analyze how the mechanisms of action of lipid-lowering drugs determine their effects on lipoprotein profiles.
2. Evaluate the therapeutic advantages of combination pharmacotherapy in the management of high-risk patients with refractory dyslipidemia.
3. Analyze the non–lipid-lowering (pleiotropic) effects of drugs to justify their use in acute coronary syndromes regardless of baseline LDL levels.
4. Discuss drug-induced alterations in plasma lipids (e.g., protease inhibitor-induced hyperlipidemia; estrogen-induced hypolipidemia).
5. Review the role of thyroid hormone in affecting serum lipids and the findings in hyper- and hypothyroidism.

4.5.2 Pharmacokinetics

1. Analyze how differences in statin metabolism and duration of action influence clinical management and therapeutic efficacy.

4.5.3 Pharmacogenetics

1. Justify the selection of lipid-lowering therapies (e.g., PCSK9 inhibitors) for patients with familial hypercholesterolemia and high risk for recurrent coronary events based on genetic risk profiles.
2. Predict statin-associated muscle symptoms using genetic variation in drug transporters (e.g., SLCO1B1) to guide an individualized statin selection and dosing regimen.

4.5.4 Therapeutic uses

1. Evaluate the appropriateness of pharmacologic strategies for management of dyslipidemias based on current clinical guidelines for safe and effective care.

4.5.5 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions

1. Predict clinically significant adverse effects of drugs used in the management of dyslipidemias

and coronary artery disease, with emphasis on muscle and hepatic toxicity.

2. Predict clinically relevant drug–drug interactions that alter digoxin or warfarin absorption, increase myopathy risk, or interfere with drug metabolism.
3. Analyze clinically significant pharmacokinetic interactions affecting statins and other lipid-lowering agents, including CYP3A4- and transporter-mediated effects.
4. Predict pharmacodynamic interactions that increase the risk of myopathy and hepatotoxicity during combination lipid-lowering therapy.

4.5.6 Notes

Cross-References

- Objectives for nicotinic acid (niacin) are also found under Vitamins section.

Clinical Guidelines

- For clinical guideline updates on management of adults with dyslipidemia refer to: https://www.ahajournals.org/doi/10.1161/CIR.0000000000001423 .

SECTION 5

RENAL PHARMACOLOGY

Andy Chen (section chair), Joe Blumer, Helmut Gottlieb, Gerald Call

5.1 Diuretics			
Recommended Curriculum Equivalent: 2.0 hr			
Drug Classes and Drugs			
Carbonic Anhydrase Inhibitor	**Osmotic Diuretic**	**SGLT2 Inhibitors**	**Loop Diuretics**
ACETAZOLAMIDE brinzolamide	mannitol	CANAGLIFLOZIN dapagliflozin empagliflozin	FUROSEMIDE ethacrynic acid torsemide

Thiazide Diuretics	**K-sparing Diuretics**	
	Aldosterone Antagonist	**Na^+ Channel Blocker**
HYDROCHLOROTHIAZIDE chlorthalidone metolazone	SPIRONOLACTONE eplerenone	AMILORIDE

Learning Objectives

5.1.1 Mechanism of Action and Effects

1. Analyze the mechanisms of action of major diuretic classes by examining their targeted nephron transport processes and the pharmacologic basis for SGLT2 inhibitor-induced osmotic diuresis.
2. Evaluate the systemic physiological consequences of diuretic therapy by predicting changes in electrolyte and water excretion, hemodynamics, and extra-renal effects.

5.1.2 Pharmacokinetics

1. Analyze how organic anion/cation transporters and protein binding influence the renal delivery and action of diuretics.
2. Compare the pharmacokinetic profiles of aldosterone antagonists with other diuretic classes to determine implications for clinical use.
3. Evaluate the impact of organ dysfunctions (e.g., renal or hepatic impairment) on diuretic pharmacokinetics and therapeutic effectiveness.

5.1.3 Therapeutic Uses

1. Evaluate how renal and extra-renal mechanisms of diuretics, including their effects on ion transporters and channels, contribute to the treatment of hypertension and edema in heart, liver, or kidney failure.
2. Analyze the role of sodium transport in modulating reabsorption of other ions and water, and how these principles explain the therapeutic use of diuretics in conditions such as nephrogenic diabetes insipidus, primary aldosteronism, and glaucoma.
3. Assess how alterations in renal or systemic pathophysiology (e.g., intrinsic renal disease, hormonal changes) influence diuretic effectiveness and safety in conditions such as toxic nephropathy and organ dysfunction.

4. Evaluate the physiological basis for the use of diuretics indicated for specialized applications such as seizure management, cystic fibrosis, and diagnostic testing for bronchial hyperreactivity.
5. Evaluate how manipulation of tubular fluid pH can enhance renal excretion of certain drugs, including alkalinization for salicylate toxicity.
6. Analyze how thiazide-induced reduction in urinary calcium excretion contributes to the prevention of calcium-containing kidney stones and may benefit patients with osteopenia who require thiazide therapy.

5.1.4 Adverse effects, Drug Monitoring, Contraindications, and Drug Interactions

1. Analyze the mechanisms by which thiazide and loop diuretics induce metabolic alkalosis.
2. Evaluate the risk factors and pathophysiology of hyponatremia and potassium imbalances during diuretic therapy.
3. Assess the clinical significance of metabolic changes in glucose, urate, lipids, calcium, and magnesium caused by diuretic therapy.
4. Appraise the impact of reduced renal perfusion on the efficacy and safety of thiazide diuretics.
5. Contrast the unique adverse effect profiles of specific diuretics to optimize drug selection in diverse clinical scenarios.
6. Evaluate the clinical consequences of interactions between diuretics and drugs such as lithium, cardiac glycosides, oral hypoglycemic agents, uricosurics, nephrotoxic antibiotics, NSAIDs, and renin-angiotensin system inhibitors.
7. Evaluate the clinical significance of sulfonamide structures among thiazide and loop diuretics, including the potential for cross-reactivity in patients with sulfonamide allergies.

5.1.5 Notes

Cross-References

- Objectives for diuretic use in cardiovascular diseases are covered under the Cardiovascular Section.
- Objectives for renin-angiotensin-system modulating drugs are covered under the Cardiovascular Section and Bioactive Peptides in the Autacoid Section.
- Objectives for SGLT2 Inhibitors are covered under the Endocrine Section.
- Objectives for drugs influencing plasma Ca^{2+} and PO_4^{3-} levels are covered under the Endocrine Section.
- Objectives for drugs used in renal transplantation are covered under the Immunopharmacology Section.

5.2 Agents Affecting the Renal Conservation of Water	
Recommended Curriculum Equivalent: 1.0 hr	
Drug Classes and Drugs	
Vasopressin Agonists	**Vasopressin Antagonists**
DESMOPRESSIN (V_2R) vasopressin ($V_1R > V_2R$)	conivaptan ($V_{1a}R$, V_2R) tolvaptan (V_2R)
Learning Objectives	
5.2.1 Mechanisms of Action and Effects 1. Analyze the physiological and pathophysiological mechanisms regulating urine concentration and dilution, the renal and extra-renal effects of vasopressin and desmopressin, and how drugs mimic or interfere with these processes.	
5.2.2 Pharmacokinetics 1. Explain how altering the structure of vasopressin affects its pharmacokinetic and pharmacodynamic properties.	
5.2.3 Therapeutic uses 1. Evaluate therapeutic strategies for disorders of water balance—central and nephrogenic diabetes insipidus, syndrome of inappropriate ADH secretion, and hypervolemic hyponatremia in heart failure—based on underlying physiology and pathophysiology. 2. Appraise the clinical use of vasopressin receptor antagonists (e.g., tolvaptan) in polycystic kidney disease, considering mechanism and therapeutic impact. 3. Assess the role of desmopressin in managing von Willebrand disease and enuresis, focusing on mechanism and clinical outcomes.	
5.2.4 Adverse Effects, Drug Monitoring, Contraindications, Drug Interactions 1. Analyze the renal mechanisms by which NSAIDs and lithium modify vasopressin-mediated water reabsorption. 2. Discuss contraindications with use of V2 receptor antagonists and clinical limitations of tolvaptan therapy based on its organ safety profile. 3. Evaluate the need for hospital initiation or re-initiation of vasopressin antagonists to monitor the rate of hyponatremia correction and minimize the risk of adverse effects such as osmotic demyelination syndrome.	
5.2.5 Notes **Cross-References** • Objectives for desmopressin-enhanced clotting factor release are covered under the Hemostasis and Blood-Forming Organs section.	

- Similar objectives for vasopressin agonist and antagonists are covered under the Endocrine Section.

SECTION 6

HEMOSTASIS AND BLOOD-FORMING ORGANS

Peter Oldenburg (section chair), David McMillan, Sarah Lerchenfeldt

6.1 Pharmacology of Blood-Forming Organs	
Recommended Curriculum Equivalent: 1.5 hr	
Drug Classes and Drugs	
Drugs for Treating Anemia	
Minerals	**Vitamins**
DEFEROXAMINE FERROUS SULFATE ferrous gluconate iron dextran	CYANOCOBALAMIN FOLIC ACID VITAMIN B12
Hematopoietic Growth Factors	
ERYTHROPOIETINS EPOETIN ALFA FILGRASTIM Darbepoetin alfa myeloid growth factors pegfilgrastim sargramostim thrombopoietic growth factors interleukin-11 thrombopoietin	
Learning Objectives	
6.1.1 Mechanism of Action and Effects 1. Diagram the normal physiological control of hematopoietic growth factors and the effect of kidney failure on erythropoiesis. 2. Relate factors that can lead to abnormal iron balance including genetic hemochromatosis to the iron absorption and transport pathways. 3. Compare and contrast the biochemical systems, which are impaired in B12 and folic acid deficiency, and the role of cyanocobalamin and folic acid in correcting the metabolic defect in DNA thymine and methionine synthesis. 4. Elucidate the molecular mechanism of action of each drug in each drug class. 5. Describe the pharmacological effects of each class of drugs on the hematopoietic system.	
6.1.2 Pharmacokinetics 1. Elucidate the possible etiologies which should be considered if a delayed or diminished response to doses of recombinant erythropoietin within the recommended dose range occurs. 2. Analyze how the pharmacokinetics and therapeutic effects of epoetin alfa and darbepoetin alfa differ between normal and anemic dialysis patients. 3. Illustrate the sources, transport, metabolism, storage, and excretion of vitamin B12 and folic acid. 4. Elucidate the factors, which influence the bioavailability of vitamin B12 and folic acid.	
6.1.3 Therapeutic Uses 1. Apply the criteria for oral therapy versus parenteral iron therapy to a patient with iron deficiency anemia.	

2. Compare and contrast the predicted rates of response of oral versus parenteral iron therapy in patients with iron deficiency anemia.
3. Justify the use of parenteral iron therapy for rapid repletion in patients with severe iron deficiency anemia, iron malabsorption, or oral iron intolerance.
4. Evaluate the risks of acute iron poisoning in children and describe its treatment.
5. Evaluate the pharmacologic management of chronic iron overload disease (e.g., secondary to chronic blood transfusion, iron absorption disturbances, etc.).
6. Justify the appropriate management of the patient with a megaloblastic anemia.
7. Compare and contrast acute and chronic management of megaloblastic anemia. Propose the vitamin dosage and describe the expected response.
8. Explain why folic acid supplementation improves erythropoiesis but allows neurological damage to progress in patients with pernicious anemia.
9. Justify the use of folic acid in patients with elevated serum levels of homocysteine or spina bifida?
10. Illustrate the therapeutic applications for myeloid growth factors with those for thrombopoietic growth factors.
11. Differentiate approaches to treatment of folate-dependent vs B12-dependent megaloblastic anemia; describe how laboratory tests guide choice of treatment.
12. Differentiate cancer vs non-cancer indications for myeloid growth factors.
13. Delineate specific types of cancer where these growth factors are contradicted.

6.1.4 Adverse effects, Contraindications, and Drug Interactions

1. Predict the principal adverse effects and describe the contraindications of the drugs in each class.
2. Compare and contrast the associated side effects of oral versus parenteral iron therapy.
3. Describe the adverse events associated with erythropoietin use in cancer patients, and explain black box warning on erythropoietin preparations.
4. Predict the implications of drugs that decrease iron absorption (e.g., antacids, calcium, tetracyclines, fluoroquinolones, levothyroxine).
5. Explain chelation interactions between iron and certain antibiotics or thyroid medications
6. Illustrate interactions that increase the risk of aluminum toxicity (deferoxamine + aluminum-containing products).
7. Predict the implications of drugs that reduce vitamin B12 absorption (e.g., metformin, PPIs, H2 blockers).
8. Evaluate the interaction between folic acid and methotrexate (i.e., reduced toxicity vs reduced efficacy).
9. Illustrate the risk of increased thrombosis when hematopoietic growth factors are combined with other pro-thrombotic agents.

6.2 Anticoagulant Drugs			
Recommended Curriculum Equivalent: 1.0 hr			
Drug Classes and Drugs			
Indirect Thrombin Inhibitors	**Direct Thrombin Inhibitors**	**Factor Xa Inhibitors**	**Inhibitors of Clotting Factor Synthesis**
HEPARIN LOW MOLECULAR WEIGHT HEPARINS (LMWH) PROTAMINE SULFATE (antidote)	DABIGATRAN bivalirudin argatroban Idarucizumab (antidote)	ENOXAPARIN RIVAROXABAN fondaparinux andexanet-alfa (antidote)	WARFARIN VITAMIN K (antidote)

Learning Objectives

6.2.1 Mechanism of Action and Effects

1. Explain the role of the coagulation cascade in the regulation of hemostasis.
2. Illustrate the synthesis of the vitamin K-dependent clotting factors, and explain the role of antithrombin in the regulation of hemostasis.
3. Examine the pathogenesis of venous thrombosis.
4. Differentiate the molecular mechanism of action of the drugs in each drug class.
5. Compare and contrast the structural features of unfractionated heparin, low molecular weight heparins, direct thrombin inhibitors and factor Xa inhibitors that determine their target specificity.
6. Compare and contrast the effect of direct versus indirect thrombin and factor Xa inhibitors on their free and clot-bound targets.
7. Evaluate the structural similarity of warfarin to vitamin K to explain the mechanism of action of inhibitors of clotting factor synthesis.
8. Elucidate the effect of warfarin on anticoagulant factors protein S and protein C.
9. Analyze the effect of heparin on platelet aggregation and plasma lipids.

6.2.2 Pharmacokinetics

1. Differentiate the oral versus parenteral anticoagulants.
2. Compare the rates of onset of action of heparin, LMWH, Direct thrombin inhibitors, Factor Xa inhibitors, and warfarin in regard to their routes of administration and mechanisms of action.
3. Explain how warfarin inhibits vitamin K-dependent clotting factor synthesis (II, VII, IX, X), leading to gradual depletion of active factors based on their half-lives and resulting in delayed anticoagulant activity.

6.2.3 Pharmacogenomics

1. Explain how genetic polymorphisms in CYP2C9 and VKORC1 can affect the patient response to warfarin.

6.2.4 Therapeutic Uses

1. Evaluate parenteral and oral anticoagulant therapy for initial and long-term management of patients with venous thrombosis and pulmonary embolism.
2. Propose an appropriate treatment plan for a patient requiring the transition from heparin to outpatient anticoagulant therapy.

3. Propose an appropriate treatment plan for a patient requiring the pharmacological management of thromboembolic complications from heparin-induced thrombocytopenia.
4. Elucidate the goals of anticoagulant therapy to its use in patients with atrial fibrillation, prosthetic heart valves, myocardial infarction, and stroke.
5. Illustrate the advantages and disadvantages of treatment with dabigatran or rivaroxaban, instead of warfarin for oral anticoagulant therapy.

6.2.5 Adverse Effects, Drug monitoring, Contraindications, and Drug Interactions

1. Predict bleeding risk across anticoagulants (heparin, DOACs, warfarin), including factors that increase risk (e.g., concomitant antiplatelets/NSAIDs, renal impairment, high INR).
2. Describe the incidence and typical onset of heparin-induced thrombocytopenia (HIT), and recognize its paradoxical thrombotic risk.
3. Explain the use of reversal agents (e.g., protamine for heparin and vitamin K for warfarin) and apply them to manage anticoagulant-associated bleeding.
4. Explain the teratogenic effects of warfarin (e.g., fetal bone and CNS abnormalities) and identify safer alternatives (e.g., heparin) during pregnancy.
5. Differentiate monitoring strategies for anticoagulants by interpreting aPTT (heparin) and INR (warfarin) to assess therapeutic effect and bleeding risk.
6. Evaluate the implications of drugs that increase bleeding risk when combined with anticoagulants (e.g., antiplatelets, NSAIDs, thrombolytics).
7. Evaluate the impact of food, drink, and herbal products on warfarin therapy, including vitamin K-rich foods (↓ INR), alcohol use (acute ↑ INR, chronic ↓ INR), and supplements (e.g., cranberry, grapefruit, St. John's wort, ginseng) that alter anticoagulant effect and bleeding risk.
8. Predict the implications of drug interactions of CYP inhibitors on the effects of warfarin.

6.3 Antiplatelet Drugs				
Recommended Curriculum Equivalent: 0.75 hr				
Drug Classes and Drugs				
Cyclooxygenase Inhibitors	**ADP $P2Y_{12}$ Inhibitors**	**Phospho-diesterase Inhibitors**	**GPIIb/IIIa inhibitors**	**Inhibitors of PAR-1**
ASPIRIN (acetylsalicylic acid) Ibuprofen	CLOPIDOGREL prasugrel ticagrelor	dipyridamole	TIROFIBAN eptifibatide	VORAPAXAR

Learning Objectives

6.3.1 Mechanism of Action and Effects

1. Explain the role of platelet aggregation in the regulation of hemostasis.
2. Describe the pathogenesis of thrombosis with respect to the platelet activation.
3. Explain the molecular mechanism of action of each drug in each drug class, and illustrate the site of action of each drug in the platelet aggregation process.
4. Describe how inhibition of prostaglandin synthesis affects platelet aggregation, specifically differentiating the role of COX-1 and COX-2.
5. Compare and contrast the mechanism of action for antiplatelet drugs (e.g., aspirin, dipyridamole, clopidogrel, tirofiban, vorapaxar).

6.3.2 Pharmacokinetics

1. Contrast the effects and time course of aspirin with nonsteroidal anti-inflammatory agents (NSAIDs) and cyclooxygenase 2 (COX2) inhibitors on platelet function.
2. Demonstrate how manipulation of the dosing regimen for aspirin can reduce adverse effects, particularly on the GI tract.
3. Evaluate the difference in routes of administration for different classes of antiplatelet drugs.

6.3.3 Pharmacogenomics

1. Explain how genetic polymorphisms in *CYP2C19* can affect the patient response to clopidogrel.
2. Justify alternative antiplatelet therapy in patients with *CYP2C19* poor metabolizing status receiving clopidogrel.

6.3.4 Therapeutic Uses

1. Discuss the approach to the management of the patient on short term and long-term antiplatelet therapy.
2. Explain the role of the platelet glycoprotein IIb/IIIa inhibitors in the diagnosis and management of coronary artery disease.
3. Elucidate appropriate clinical indications for antiplatelet agents and propose an appropriate treatment plan for a patient requiring antiplatelet therapy.

6.3.5 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions

1. Describe the principal adverse effects and contraindications of the drugs in each class.
2. Compare and contrast the effects of aspirin, dipyridamole, clopidogrel, and propranolol for primary post MI prophylaxis.

3. Illustrate how concomitant use of NSAIDs, e.g., ibuprofen, can interfere with the antiplatelet actions of aspirin.
4. Contrast the effects of reversible with irreversible inhibitors on duration of action.
5. Predict the implications of drugs that have an additive bleeding risk when combined with anticoagulants or other antiplatelets.
6. Illustrate how ibuprofen competitively and reversibly occupies the COX-1 binding site on platelets, preventing aspirin's irreversible acetylation and thereby reducing aspirin's antiplatelet effect when taken concurrently or prior to aspirin.
7. Explain the role of CYP2C19 inhibition in reducing clopidogrel activation (e.g., omeprazole).

6.3.6 Notes

Cross-References

- The anti-inflammatory, analgesic, and antipyretic effects of aspirin and NSAIDs, including COX-2 inhibitors, are discussed further in the Analgesics Learning Objectives.

6.4 Thrombolytic Drugs	
Recommended Curriculum Equivalent: 0.25 hr	
Drug Classes and Drugs	
Plasminogen Activators	**Inhibitors of Fibrinolysis**
t-PA ALTEPLASE reteplase tenecteplase	aminocaproic acid
Learning Objectives	
6.4.1 Mechanism of Action and Effects 1. Illustrate the role of plasminogen in thrombolysis. 2. Describe the role of thrombolysis in the physiology of hemostasis. 3. Compare and contrast the molecular mechanism and site of action of alteplase with aminocaproic acid. 4. Illustrate the pharmacologic effects of alteplase on thrombi.	
6.4.2 Pharmacokinetics 1. Differentiate between the pharmacokinetic properties of t-PA, alteplase and tenectaplase.	
6.4.3 Therapeutic Uses 1. Justify the use of thrombolytic drug therapy and propose a treatment plan for patients with treatment of myocardial infarction, ischemic stroke, deep venous thrombosis, or pulmonary embolism. 2. Describe the use of aminocaproic acid (EACA) to prevent clot breakdown and reduce bleeding, particularly in patients with hemophilia or von Willebrand disease during dental procedures or bleeding episodes.	
6.4.4 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions 1. Identify and differentiate major adverse effects of fibrinolytics and aminocaproic acid, including severe bleeding (e.g., intracranial, GI) versus thrombotic complications. 2. Assess patient-specific risk factors that increase complications (e.g., recent surgery, hypertension, concurrent anticoagulants for bleeding; prothrombotic states for aminocaproic acid). 3. Develop a monitoring plan for patients to identify clinical signs of complications, including bleeding, reperfusion arrhythmias, hypotension, and muscle toxicity. 4. Predict the implications of the increased bleeding risk that occurs when fibrinolytics are combined with anticoagulants or antiplatelet drugs. 5. Illustrate the direct antagonism between fibrinolytics and aminocaproic acid.	

SECTION 7

PULMONARY PHARMACOLOGY

Sandeep Bansal (section chair), Helmut Gottlieb, Kent Vrana

7.1 Drugs for the Management of Pulmonary Disorders		
Recommended Curriculum Equivalent: 1.0 hr		
Drug Classes and Drugs		
Anti-inflammatory Drugs		
Glucocorticoids	**Leukotriene Receptor Antagonists**	**5-LO Inhibitor**
Inhaled agents: BUDESONIDE BECLOMETHASONE FLUTICASONE MOMETASONE **Systemic agents:** DEXAMETHASONE PREDNISONE	MONTELUKAST	ZILEUTON
Immunomodulators		
IL Antagonists	**Anti-IgE**	
DUPILUMAB RESLIZUMAB	OMALIZUMAB	
Bronchodilators		
β_2 Agonists		**Phosphodiesterase 4 Inhibitors**
Short-Acting beta 2 agonists (SABA)	**Long-Acting beta 2 agonists (LABA)**	
ALBUTEROL	FORMOTEROL SALMETEROL	Roflumilast
Muscarinic Receptor Antagonists		
Short-acting antimuscarinic agents (SAMA)	**Long-acting antimuscarinic agents (LAMA)**	
IPRATROPIUM	TIOTROPIUM	
Learning Objectives		
7.1.1 Mechanisms of Action and Effects 1. Analyze the molecular mechanism of action of each of the above-listed drug classes within the framework of the pathogenesis of asthma and chronic obstructive pulmonary disease (COPD). 2. Based on molecular mechanism of action, distinguish between agents that modify the disease process versus those that relieve symptoms of asthma and COPD. 3. Distinguish the effects of the above listed agents on bronchial smooth muscle tone and inflammatory processes.		

7.1.2 Pharmacokinetics

1. Apply the pharmacokinetics in determining the relative merits of inhaled versus systemic (oral or intravenous) administration of drugs in the management of asthma (episodic and chronic) and COPD.
2. Compare the onset and duration of action of inhaled beta 2 agonists and antimuscarinic agents.

7.1.3 Therapeutic Uses

1. Integrate the pathophysiology of asthma and COPD in selecting appropriate treatments for the disorders.
2. Compare and contrast the role of beta 2 agonists, antimuscarinic agents, systemic and inhaled glucocorticoids, leukotriene inhibitors, and emerging therapies in the management of acute and chronic asthma, as per the latest guidelines.
3. Apply the pathophysiology of asthma in recommending pharmacotherapy for the management of asthma in special patient populations (e.g., pediatric and pregnant and/or lactating females).
4. Design an evidence-based treatment plan for a patient with exercise-induced asthma, integrating preventive and therapeutic strategies.
5. Evaluate the role of emerging therapies in the management of asthma and chronic obstructive pulmonary disease.

7.1.4 Adverse Effects, Contraindications, and Drug Interactions

1. Differentiate the adverse effects and potential contraindications for each class of agents.
2. Evaluate the risk factors and underlying molecular mechanisms that contribute to aspirin-induced bronchoconstriction in asthma and justify clinical management strategies.

7.1.5 Notes

Cross-References

- Information on many of the drugs in this section may also be found in the Autonomics Section.
- Information on asthma and COPD is also found in the Autacoid Section.
- Note also that in addition to asthma and COPD, other diseases affecting respiration may employ these agents (e.g., see relevant sections on antimicrobials and/or neoplasias).

Clinical Guidelines

- It is noteworthy that the clinical guidelines for the treatment of asthma and COPD continuously evolve and are updated yearly. To that end, instructors are urged to consult online sources such as:
- Global Initiative for Asthma. www.ginasthma.org (look for the current treatment report)
- National Asthma Education and Prevention Program. 2020. https://www.nhlbi.nih.gov/health-topics/asthma-management-guidelines-2020-updates

Historical/Toxicology Context

- Theophylline (a methylxanthine) and cromolyn (a mast cell stabilizer) are mentioned here because of their historical perspective, and frequent appearance on board exams. Both drugs are no longer included on the WHO List of Essential Medications and are considered as last line drugs for the treatment of asthma. According to the GINA (Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2021; available from: www.ginasthma.org),

theophylline is not recommended because of low efficacy, high risk of severe side effects and possible drug-drug interactions. Cromolyn is not even mentioned on the GINA guidelines.

SECTION 8

AUTACOIDS, BIOACTIVE PEPTIDES, AND GOUT

Teresa Wilborn (section chair), Pius Fasinu

8.1 Histamine Antagonists	
Recommended Curriculum Equivalent: 1.5 hr.	
Drug Classes and Drugs	
H2 Receptor Antagonists	**Histamine Release Modifiers**
CIMETIDINE famotidine	CROMOLYN OMALIZUMAB
H1 Receptor Antagonists	
First Generation	**Second Generation**
DIPHENHYDRAMINE chlorpheniramine hydroxyzine	FEXOFENADINE LORATADINE cetirizine

Learning Objectives

8.1.1 Mechanism of Action and Effects

1. Differentiate the effects of H1 and H2 histamine receptor antagonists including their molecular mechanisms and sites of therapeutic action.
2. Compare and contrast the mechanisms by which cromolyn and omalizumab decrease histamine activity, and their effects on cytokines and leukotrienes.
3. Compare the cells targeted by cromolyn and omalizumab.

8.1.2 Pharmacokinetics

1. Compare and contrast first-generation and second-generation antihistamine CNS penetration, receptor selectivity, and metabolic elimination.

8.1.3 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions

1. Differentiate the adverse effect profile of first and second-generation H1 antihistamines, and comorbidities that could be exacerbated by their use.
2. Describe the adverse effects of cimetidine that are related to its endocrine effects in comparison to other H2 antihistamines.
3. Summarize recommendations for anaphylaxis and serum sickness-like reaction monitoring when initiating therapy with omalizumab.
4. 4) Explain omalizumab indications which require determination of IgE baseline levels prior to initiating therapy.
5. Predict the risks associated with combining H1 first generation antihistamines with drugs that have muscarinic receptor antagonist or CNS suppressing effects.
6. Describe the effects of cimetidine on CYP enzymes and drug transporters and the associated risk for drug interactions.

8.1.4 Notes

Cross-References

- Additional objectives for H1-receptor antagonists are covered in the Gastrointestinal Section.
- Additional objectives for H2-receptor antagonists are covered in the Gastrointestinal Section.

8.2 5-Hydroxytryptamine (5-HT, Serotonin): Agonists & Antagonists	
Recommended Curriculum Equivalent: 1.0 hr	
Drug Classes and Drugs	
5HT 1B/1D Agonists (Triptans)	**5HT3 Antagonists**
DIHYDROERGOTAMINE SUMATRIPTAN eletriptan	ONDANSETRON palonosetron

Learning Objectives

8.2.1 Mechanism of Action and Effects

1. Compare and contrast the action of 5HT1B/1D and 5HT1F receptor agonists in the trigemino-vascular system including their target cells (nerve vs vascular) and effects on proinflammatory peptides and vascular tone.
2. Describe the mechanism by which 5HT3 receptor antagonists decrease input into the vomiting center.

8.2.2 Pharmacokinetics

1. Distinguish triptan route of administration to onset of action and relative effects.

8.2.3 Therapeutic Uses

1. Describe the use of the triptans and dihydroergotamine as abortive therapy for migraine and cluster headaches.
2. Explain the use of the 5HT3 antagonists in the treatment of chemotherapy induced nausea and vomiting (CINV), radiation therapy induced nausea and vomiting (RINV), postoperative nausea and vomiting (PONV), carcinoid syndrome associated diarrhea and acute, severe nausea and vomiting.

8.2.4 Adverse Effects, Drug Interactions, and Contraindications

1. Describe adverse effects of the 5HT1B/1D receptor agonists and 5HT3 receptor antagonists including the cardiovascular adverse effects of the triptans and contraindications associated with these effects.
2. Compare the risk of serotonin syndrome with the triptans and 5HT3 antagonists.
3. Explain the effects of ondansetron on the cardiac QTc and the potential consequences of this effect.
4. Distinguish additional activities of dihydroergotamine at alpha adrenergic receptors and adverse effects associated with these activities.

8.2.5 Notes

Cross-References

- Serotonergic drugs used for psychiatric disorders are covered in the CNS Pharmacology Section.
- Additional objectives for 5HT3 antagonists are covered in the Gastrointestinal Pharmacology Section.
- Additional objectives for 5HT1B/1D agonists are covered in the CNS Pharmacology Section.

Clinical Guidelines

- Ergotamine preparations such as dihydroergotamine are 5HT1B/1D agonists that have been used in the treatment of acute migraine in combination with antiemetics, however for migraine specific medications, guidelines from the American College of Physicians (2025) recommend triptans as front line therapy. https://www.acpjournals.org/doi/10.7326/ANNALS-24-03095.

Historical/Toxicology Context

- Lasmiditan, a 5HT1F agonist is being discontinued in the USA by the manufacturer (2026).

8.3 Nitric Oxide (NO) and Nitric Oxide-cGMP Signaling Drugs		
Recommended Curriculum Equivalent: 0.5 hr		
Drug Classes and Drugs		
Agonist	**PDE-5 Inhibitors**	**NO Donors**
NITRIC OXIDE/NO (gas)	SILDENAFIL tadalafil	NITROGLYCERIN SODIUM NITROPRUSSIDE isosorbide mononitrate

Learning Objectives

8.3.1 Mechanism of Action and Effects

1. Explain the action of NO and phosphodiesterase V inhibitors on vascular smooth muscle and prostatic smooth muscle.
2. Contrast the mechanisms by which the organic nitrates and sodium nitroprusside liberate nitric oxide.

8.3.2 Pharmacokinetics

1. Discuss the onset and duration of action of sodium nitroprusside, its metabolism to nitric oxide and cyanide, and the major pathway involved in cyanide detoxification.
2. Distinguish the bioactivation of nitroglycerin and isosorbide mononitrate.
3. Contrast the onset and relative duration of action of sublingual, topical and transdermal nitroglycerin, and the occurrence of tolerance with chronic exposure.

8.3.3 Therapeutic Uses

1. Differentiate the use of NO donors in cardiac disorders including angina, hypertensive emergency, and acute decompensated heart failure.
2. Distinguish the use of nitric oxide and PDE-5 inhibitors in the treatment of pulmonary hypertension.
3. Differentiate the use of PDE-5 inhibitors in erectile dysfunction and benign prostatic hyperplasia.

8.3.4 Adverse Effects, Drug Interactions, and Contraindications

1. Describe the principal adverse effects and contraindications of the drugs in each class.
2. Explain the risk of methemoglobinemia with the organic nitrates and sodium nitroprusside.
3. Discuss clinically important drug interactions of the drugs in each class, including the interaction of the nitric oxide donors and phosphodiesterase V inhibitors.

8.3.5 Notes

Cross-References

- Additional objectives for nitric oxide donors are included in the Cardiac pharmacology section.
- Additional objectives for PDE V inhibitors are included in the Endocrine pharmacology section.

Clinical Guidelines

- Guidelines for the treatment of erectile dysfunction are available from multiple organizations including the American Urological Association which are found at https://www.auanet.org/guidelines-and-quality/guidelines/erectile-dysfunction-(ed)-guideline

- Guidelines for the treatment of benign prostatic hyperplasia are available from multiple organizations including the American Urological Association which are found at https://www.auanet.org/guidelines-and-quality/guidelines/benign-prostatic-hyperplasia-(bph)-guideline

8.4 Eicosanoids: Agonists & Antagonists		
Recommended Curriculum Equivalent: 1.0 hr		
Drug Classes and Drugs		
Prostanoids		
Prostacyclin Analogs	**Prostaglandin Analogs and Prostanoids**	
	Ocular Formulations	**Systemic, Topical and Local Formulations**
EPOPROSTENOL treprostinil	LATANOPROST bimatoprost	ALPROSTADIL MISOPROSTOL dinoprostone

*Cyclooxygenase (COX) Inhibitors	**Leukotriene Modifiers
ACETAMINOPHEN ASPIRIN (ACETYLSALICYLIC ACID) CELECOXIB DICLOFENAC IBUPROFEN KETOROLAC MELOXICAM NAPROXEN Indomethacin	MONTELUKAST zafirlukast zileuton

Learning Objectives

8.4.1 Mechanism of Action and Effects

1. Summarize the molecular mechanism by which prostanoids reduce intraocular pressure, relax pulmonary artery vascular tone, and decrease gastric acid secretion.
2. Elucidate the effects by which local/topical prostanoids produce cervical softening and dilation, increase uterine contractions, and dilate cavernosal arteries in male erectile tissue.

8.4.2 Pharmacokinetics

1. Compare and contrast the pharmacokinetics of inhaled, oral, and parenteral formulations of the prostacyclin analogs.
2. Summarize the pharmacokinetic differences of the IV, SC, oral, and inhaled formulations of the prostacyclin analogs.

8.4.3 Therapeutic Uses

1. Describe the use of prostanoid analogs in the treatment of glaucoma, ocular hypertension, pulmonary artery hypertension, NSAID-induced GI toxicity, cervical ripening, labor induction, medication abortion, and erectile dysfunction.

8.4.4 Adverse Effects, Drug Interactions, and Contraindications

1. Define the major adverse effects, contraindications, and clinically important drug interactions of the prostanoid analogs.
2. Explain the rationale for using misoprostol with NSAIDs.

8.4.5 Notes

Cross-References

- *COX Inhibitors are covered in the CNS Pharmacology section, Immunopharmacology section, and hemostasis and blood-forming organs Section.
- **Leukotriene Modifiers are covered in the Pulmonary Pharmacology and the Immuno-pharmacology section.

8.5 Bioactive Peptides		
Recommended Curriculum Equivalent: 0.5 hr		
Drug Classes and Drugs		
Neuropeptide Antagonists		
Substance P (Neurokinin I)	**Calcitonin Gene-Related Peptide (CGRP)**	**Orexin**
APREPITANT netupitant	ERENUMAB UBROGEPANT rimegepant	SUVOREXANT
Bradykinin Antagonists		
ICATIBANT		
Learning Objectives		

8.5.1 Mechanism of Action and Effects

1. Appraise the rationale for using NK1 receptor antagonists in the treatment of emesis.
2. Summarize the action of CGRP in trigeminovascular pain transmission and neurogenic inflammation in migraine and the role of CGRP antagonists used in its prevention or treatment.
3. Describe the action of orexin at the OX1R and OX2R receptors in the CNS and the consequences of dual orexin receptor antagonist (DORA) therapy.
4. Summarize the symptoms of angioedema associated with C1 esterase deficiency and bradykinin and infer the mechanism by which a bradykinin B2 receptor antagonist is effective in its treatment.

8.5.2 Pharmacokinetics

1. Describe the routes of administration and pharmacokinetics of the drugs in each class.

8.5.3 Therapeutic Uses

1. Summarize the use of NK1 antagonists in the treatment of nausea and vomiting, and the rationale for combining them with glucocorticoids and 5HT3 antagonists in chemotherapy induced nausea and vomiting.
2. Differentiate the use of oral or parenteral CGRP antagonists in the prevention and/or treatment of migraine.
3. Relate the use of orexin antagonist therapy for sleep disorders and compare/contrast with benzodiazepines and Z-compounds.
4. Describe the use of icatibant in the treatment of an acute attack of hereditary angioedema.

8.5.4 Adverse Effects, Drug Interactions, and Contraindications

1. Describe the principal adverse effects and contraindications of the drugs in each class.
2. Compare the risk of NK1, CGRP and orexin antagonist interactions associated with drugs that affect cytochrome P450 (CYP450) and/or drug transporter activities.

8.5.5 Notes

Cross-References

- Additional objectives for NK1 antagonists are in the CNS Pharmacology

- Additional objectives for the CGRP antagonists are in the CNS Pharmacology
- Additional objectives for the orexin antagonists are in the CNS Pharmacology

Clinical Guidelines

- Guidelines for the acute treatment of migraine are available from multiple organizations including the American College of Physicians https://www-acpjournals-org.uab.idm.oclc.org/doi/10.7326/ANNALS-24-03095
- Guidelines for the prevention of migraine are available from multiple organization including the American College of Physicians https://www-acpjournals-org.uab.idm.oclc.org/doi/10.7326/ANNALS-24-03095

8.6 Gout			
Recommended Curriculum Equivalent: 1.0 hr			
Drug Classes and Drugs			
Acute Gout Attack	**Xanthine Oxidase Inhibitors**	**Uricosurics**	**Uricase**
Colchicine *NSAIDs *glucocorticoids	ALLOPURINOL febuxostat	PROBENECID	PEGLOTICASE RASBURICASE

Learning Objectives

8.6.1 Mechanisms of Action and Effects

1. Summarize the role of urate in the pathophysiology of gout and how inhibition of xanthine oxidase is an effective drug mechanism.
2. Describe the consequence of human lack of urate oxidase/uricase and the role recombinant uricase in gout therapy.
3. Identify the role of the renal transporter involved in urate renal secretion and the drug class for which it is the target.
4. Elucidate the role of neutrophils in the inflammatory response to urate crystals in synovial fluid and tissues and how neutrophil chemotaxis to these sites is prevented by colchicine.

8.6.2 Pharmacokinetics

1. Summarize the clinically relevant PK parameters of each drug class.
2. Describe the role of CYP3A4 and P-glycoprotein in the disposition of colchicine.
3. Associate the influence of oxypurinol on allopurinol's duration of action.

8.6.3 Pharmacogenetics

1. Summarize the risk of severe cutaneous adverse reactions (SCAR) associated with allopurinol therapy in persons with an HLA-B*5801 polymorphism and populations most likely to be at risk.
2. Explain the contraindication of uricase therapy in persons with G6PD deficiency.

8.6.4 Therapeutic Uses

1. Summarize the use of xanthine oxidase inhibitors and recombinant uricase therapy for the prevention and treatment of gout and tumor lysis syndrome.
2. Distinguish the drugs used in the treatment of acute gout attacks from prophylactic therapies.
3. Compare and contrast urate lowering therapies in people that overproduce uric acid with those that underexcrete uric acid.
4. Rationalize the use of probenecid to enhance beta-lactam serum levels in the treatment of syphilis.
5. Explain the use of allopurinol to prevent recurrent calcium nephrolithiasis associated with hyperuricemia.
6. Describe the use of colchicine in the treatment of Familial Mediterranean fever.

8.6.5 Adverse Effects, Drug Interactions, and Contraindications

1. Discuss the principal adverse effects and contraindications of the drugs of each class.
2. Review clinically important drug interactions of the drugs of each class including the contraindication of xanthine oxidase inhibitors with thiopurines.

3. Summarize drugs that interact with urate lowering therapies based on their interference with the renal excretion of uric acid
4. Describe the mechanism of gouty flare-up associated with initiation of treatment of chronic tophaceous gout.

8.6.6 Notes

Cross-References

- *NSAIDs are covered in several sections including CNS and Immunopharmacology
- *Glucocorticoids are covered in several sections including Endocrine and Immunopharmacology

Clinical Guidelines

- Guidelines for the treatment of gout can be found at multiple sites including those from the American College of Rheumatology https://assets.contentstack.io/v3/assets/bltee37abb6b278ab2c/blt04d52e3b6ff5112f/632cab5b258fb55f6b2186af/gout-guideline-2020.pdf

SECTION 9

GASTROINTESTINAL PHARMACOLOGY

Sean Thatcher (section chair), Laurel Gorman, Matthew Henry, Carol Beck

9.1 Acid Reducers: Antihistamines, Protein Pump Inhibitors, & Potassium Competitive Acid Blockers	
Recommended Curriculum Equivalent: 0.75 hr	
Drug Classes and Drugs	
Protein Pump Inhibitors (PPI)	**Potassium-Competitive Acid Blockers (PCAB)**
ESOMEPRAZOLE OMEPRAZOLE dexlansoprazole lansoprazole pantoprazole rabeprazole	VONOPRAZAN
H_2 Receptor Antagonists	
First Generation	**Second Generation**
CIMETIDINE	FAMOTIDINE NIZATIDINE
Learning Objectives	
9.1.1 Mechanism of Action and Effects 1. Describe the molecular mechanism of action of the major categories of drugs described. 2. Distinguish between agents that are competitive and non-competitive, irreversible inhibitors.	
9.1.2 Pharmacokinetics 1. Describe the pharmacokinetics of major and prototypical drugs identified.	
9.1.3 Pharmacogenomics 1. Identify patient populations most likely to have reduced PPI metabolism. 2. List the hepatic CYPs responsible for PPI metabolism.	
9.1.4 Therapeutic Uses 1. List the therapeutic uses for the acid reducing agents. 2. Select the antibiotic agents used in combination with vonoprazan for the treatment of *H. pylori*. 3. Select antibiotic agents and acid reducers used in combination with proton pump inhibitors used for the treatment of *H. pylori*.	
9.1.5 Adverse effects, Contraindications, and Drug Interactions 1. Describe the principal adverse effects of H2 receptor antagonists, PPIs, and PCABs. 2. Describe the clinically important principal contraindications. 3. Compare and contrast the adverse effects, and contraindications between first and second generation H2-receptor antagonists. 4. Identify the H2-receptor antagonist with the greatest likelihood of drug-drug interactions.	

9.2 Acid Reducers: Acid Neutralizers	
Recommended Curriculum Equivalent: 0.25 hr	
Drug Classes and Drugs	
Selected Antacids	
Single Agent	**Mixed Preparations**
ALUMINUM HYDROXIDE CALCIUM CARBONATE MAGNESIUM HYDROXIDE sodium bicarbonate sodium citrate	MAGNESIUM HYDROXIDE/ ALUMINUM HYDROXIDE bismuth subsalicylate calcium carbonate/magnesium hydroxide magnesium carbonate/aluminum hydroxide
Learning Objectives	
9.2.1 Mechanism of action and effects 1. Describe the mechanism of action of antacid medications.	
9.2.2 Pharmacokinetics 1. Describe the absorption of antacid preparations. 2. Compare and contrast the differences in onset and duration of action of each antacid preparation. 3. Identify agents that can impact systemic electrolyte balance.	
9.2.3 Therapeutic Uses 1. List the therapeutic uses for the antacids. 2. Select antibiotic and acid reducing agents used in combination with bismuth subsalicylate for treatment of *H. pylori*. 3. Compare the efficacy of antacids to other agents used to treat acid-peptic disease.	
9.2.4 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions 1. Describe the principal adverse effects of each antacid preparation. 2. Identify the principal precautions and contraindications in the use of antacids. 3. Predict the impact of antacids on the absorption of drugs that are weak acids and weak bases. 4. Describe clinically important drug interactions with antacids.	

9.3 Other Drugs Used for the Treatment of Peptic Ulcer Disease		
Recommended Curriculum Equivalent: 0.25 hr		
Drugs Classes and Drugs		
Cytoprotectant and Antimicrobial Agents		
Endogenous Ligand Analog	**Surface Protectant**	**Misc. Antimicrobial Effects Mixed Properties**
MISOPROSTOL	SUCRALFATE	BISMUTH SUBSALICYLATE

Learning Objectives

9.3.1 Mechanism of Action and Effects

1. Describe the mechanism of action of each drug with cytoprotective benefits.

9.3.2 Pharmacokinetics

1. Describe the absorption, distribution metabolism and excretion of each drug.

9.3.3 Therapeutic Uses

1. Describe the primary indications for use of each drug.

9.3.4 Adverse Effects, Contraindications, and Drug Interactions

1. Describe the principal adverse effects of each drug.
2. Describe clinically important drug interactions of the drugs in each class.
3. Identify the principal contraindications of each agent and the black box warnings concerning the use of misoprostol.

9.3.5 Notes

Cross-References

- Antimicrobial agents against *H. pylori* are also covered in the Antimicrobial Section.

9.4 Prokinetic Drugs and Laxatives		
Recommended Curriculum Equivalent: 1.0 hr		
Drug Classes and Drugs		
Drugs Used to Treat Upper GI Motility Disorders		
Dopamine Antagonists	**Motilin Agonists**	**Serotonin Agonists (5HT-4)**
METOCLOPRAMIDE domperidone	ERYTHROMYCIN azithromycin	PRUCALOPRIDE
Drugs Used to Treat Lower GI Motility Disorders (Constipation)		
Prokinetic Categories & Drugs (Receptor Mediated)		
Chloride Channel-2 Agonists/ Prostaglandin Analogs	**Cholinomimetics**	**Guanylate Cyclase-C Agonists**
LUBIPROSTONE	bethanechol neostigmine	LINACLOTIDE plecanatide
Mu-opioid Antagonists	**Serotonin Agonists (5HT-4)**	**Sodium/Hydrogen Exchange-3 Transporter Inhibitor**
METHYLNALTREXONE NALOXEGOL alvimopan naldemedine	tegaserod	tenapanor
Laxatives (Mechanical/Chemical)		
Bulk-forming (Fiber-related)	**Lubricants**	**Osmotic/ Hyperosmotic**
METHYLCELLULOSE PSYLLIUM	mineral oil	MAGNESIUM HYDROXIDE POLYETHYLENE GLYCOL SODIUM PHOSPHATE lactulose
Stimulant	**Surfactant**	
BISACODYL cascara sagrada castor oil senna	DOCUSATE	
Learning Objectives		
9.4.1 Mechanism of Action and Effects 1. Describe the molecular mechanism of action of each drug. 2. Discuss how drugs can be used to compensate for changes in neural and hormonal control of gastrointestinal motility. 3. Describe why some drugs are selective for upper GI motility disorders and why others are selective for lower GI motility disorders.		
9.4.2 Pharmacokinetics 1. Describe the relevant pharmacokinetic features of each drug.		

9.4.3 Therapeutic uses

1. List the main therapeutic uses of the drugs of each class of prokinetics and laxatives.
2. Distinguish between the clinical uses of drugs used in the treatment of upper and lower GI disorders.

9.4.4 Adverse Effects, Drug Interactions, and Contraindications

1. Describe the principal adverse effects of the drugs of each class.
2. Predict neurological adverse effects for drugs antagonizing dopamine D2 receptors.
3. Describe clinically significant drug-drug interactions with each drug class.
4. Describe the principal contraindications for use of laxatives.

9.4.5 Notes

Cross Reference

- Antacids, proton pump inhibitors (PPIs), H2-receptor blockers are discussed in other sections

9.5 Anti-diarrheal Drugs		
Recommended Curriculum Equivalent: 0.5 hr		
Drug Classes and Drugs		
Opioid agonists	**Alpha$_2$ Adrenergic Agonists**	**Somatostatin Analog**
LOPERAMIDE diphenoxylate	clonidine (*refer to autonomics*) lofexidine	octreotide
Muscarinic Antagonists		**Misc. Antidiarrheal**
ATROPINE DICYCLOMINE hyoscyamine scopolamine		BISMUTH SUBSALICYLATE bismuth citrate
Learning Objectives		
9.5.1 Mechanisms of action and effects 1. Differentiate the molecular mechanism of action of each drug in each drug class.		
9.5.2 Pharmacokinetics 1. Describe the absorption distribution metabolism and secretion of each drug.		
9.5.3 Therapeutic Uses 1. List the specific therapeutic applications of each class of drug. 2. Describe management of opioid withdrawal diarrhea. 3. Differentiate between use of agents in infectious diarrhea versus chronic diarrhea caused by irritable bowel syndrome, inflammatory bowel disorders, and medication-induced diarrhea.		
9.5.4 Adverse Effects, Drug Interactions and Contraindications 1. Describe the principal adverse effects of the drugs of each class. 2. Identify which opioid agonist can be given with atropine sulfate. 3. Describe the clinically important drug interactions of the drugs of each class. 4. Describe the principal contraindications of the drugs of each class.		

9.6 Drugs for the Treatment of Inflammatory Bowel Disease (IBD) & Irritable Bowel Syndrome (IBS)		
Recommended Curriculum Equivalent: 0.5 hr		
Drug Classes and Drugs		
IBD Treatments		
Salicylates	**Corticosteroids**	
5-AMINO SALICYLIC ACID SULFASALAZINE	BUDESONIDE PREDNISONE	
Antimetabolite Immunosuppressants*	**JAK Inhibitors**	
METHOTREXATE azathioprine 6-mercaptopurine	upadacitinib	
Monoclonal Antibodies		
Anti-TNF-alpha	**Anti-Integrin**	**IL-12/23 Inhibitors**
ADALIMUMAB INFLIXIMAB	vedolizumab	RISANKIZUMAB USTEKINUMAB guselkumab
IBS Treatments		
Laxatives & Antidiarrheals	**Intestinal fluid regulators**	
	Secretagogues	**Retainagogues**
IBS-C: Many laxatives **IBS-D:** LOPERAMIDE	LINACLOTIDE LUBIPROSTONE plecanatide	TENAPANOR
Neuromodulators		
Serotonergic	**Mixed opioid**	**Tricyclic Antidepressant**
alosetron	ELUXADOLINE	AMITRIPTYLINE
Antibiotics	**Bile Acid Sequestrants**	
RIFAXIMIN	CHOLESTYRAMINE	
Learning Objectives		
9.6.1 Mechanism of Action and Effects 1. Describe the mechanism of action of each IBD drug class and how this reduces inflammation. 2. Differentiate between the treatment goals and desired actions of the drugs used to treat IBD versus IBS. 3. Distinguish between the mechanisms of drugs used to treat IBS based on predominant symptoms. 4. Describe the underlying processes mediating the effects of neuromodulator agents on the gut.		

9.6.2 Pharmacokinetics

1. Predict how the routes of routes of administration of drugs impact their selection and onset of effects.
2. Elaborate on the role of onset of effects in drug selection.
3. Compare and contrast the duration of action for different agents.
4. Describe the metabolism, bioactivation, distribution, and elimination of drugs used to treat IBD or IBS.

9.6.3 Therapeutic Uses

1. List the therapeutic use of each class of drug for the treatment of acute and chronic symptoms.
2. Compare and contrast drugs utilized in the treatment of acute versus chronic IBD.
3. Develop a treatment plan using pharmacologic and dietary therapy for long-term management of IBD or IBS based on patient history, comorbidities, and presenting concerns.

9.6.4 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions

1. List the major acute and chronic toxicities associated with each agent/class
2. Weigh the benefits and risk of different treatment options in a patient with presenting comorbidities.
3. Elaborate on processes to reduce infection risk and monitor for reactivation of latent infections while utilizing agents that promote immunosuppression.
4. Describe the clinically important drug interactions of the drugs of each class.
5. Identify agents contraindicated in pregnancy or in patients with other significant comorbidities.

9.6.5 Notes

Cross-References

- Immunomodulatory antibodies are covered in the Immunopharmacology section, Antihistamines are in the Autocoids and anti-inflammatory section.

Clinical Guidelines

- Many IBS drugs are commonly used off label as they were approved for a different purpose.

Historical/Toxicology Context

- *Used off label for Crohn Disease

9.7 EMETIC AND ANTI-EMETIC DRUGS			
Recommended Curriculum Equivalent: 1.0 hr			
Drug Classes and Drugs			
Emetic Drugs			
Dopamine Receptor Agonist		**Nonselective Emetics**	
apomorphine		SYRUP OF IPECAC	
Anti-emetic Drugs			
Dopamine D2 Receptor Antagonists	**5-HT$_3$ Receptor Antagonists**	**Cannabinoid Receptor Agonists**	**Histamine Receptor Antagonists**
METOCLOPRAMIDE PROCHLORPERAZINE haloperidol	GRANISETRON ONDANSETRON PALONOSETRON	DRONABINOL nabilone marinol	DIMENHYDRINATE DIPHENHYDRAMINE cyclizine hydroxyzine meclizine promethazine
Neurokinin Receptor Antagonists	**Corticosteroids**	**Herbal or Natural Agents**	**Muscarinic Receptor Antagonists**
APREPITANT	METHYL-PREDNISOLONE PREDNISONE dexamethasone	VITAMIN B6 (pyridoxine) peppermint ginger	SCOPOLAMINE

Learning Objectives

9.7.1 Mechanisms of Action and Effects

1. Describe the mechanism of action of anti-emetic and emetic drugs.
2. Compare and contrast central and peripheral mechanisms and organ effects of different classes of antiemetic drugs.
3. Predict how medications impacting the vestibular system produce anti-emetic actions based upon the underlying physiological regulation of balance and motion sickness.
4. Elaborate on how some medications used for other purposes can reduce nausea and vomiting as an additional benefit.

9.7.2 Pharmacokinetics

1. Characterize benefits of using different routes of administration of different agents relative to the patient's presenting condition(s).
2. Elaborate on how the absorption, distribution, metabolism and excretion of different drugs impacts their selection for different patients.
3. Describe how pharmacokinetic parameters can alter the onset and efficacy of anti-emetics.

9.7.3 Therapeutic Uses

1. Distinguish between agents used to treat nausea and vomiting acutely with those used for longer term management of a disease or chemotherapy-induced nausea and vomiting.
2. Justify the use of anti-emetics with different underlying mechanisms in multi-drug nausea and vomiting protocols based on patient comorbidities

3. Discuss the roles of anti-emetic drugs and natural products in reducing nausea and vomiting in pregnancy.
4. Develop a treatment plan for use of appropriate emetics in reducing overdose related toxicity.

9.7.4 Adverse Effects, Drug monitoring, Contraindications, and Drug Interactions

1. Differentiate between adverse effects of acute and long-term use of various classes of antiemetic drugs.
2. Describe the clinically important drug interactions of the antiemetic drugs and natural products.
3. Predict monitoring processes necessary when specific antiemetics are used in multitherapeutic processes like chemotherapy or post-operative recovery.
4. Discuss relative and absolute contraindication for antiemetics and emetics.
5. Predict the adverse effects of using emetics in patients with differing comorbidities.
6. Identify contraindications for use of emetics.

9.7.5 Notes

Cross-References

- Several drug classes are also covered in the CNS Section which includes dopamine receptor antagonists and cannabinoids.
- Muscarinic antagonists are covered in the Autonomic Section, corticosteroids are covered in the Endocrine Section, and antihistamines are covered in the Pulmonary Pharmacology section.

9.8 Other Gastrointestinal Drugs		
Recommended Curriculum Equivalent: 0.25 hr		
Drug Classes and Drugs		
Anti-flatulent	**Pancreatic Enzyme Replacement**	**Gallstones Dissolution Agents, Cholesterol Absorption Inhibitor or Binder**
SIMETHICONE activated charcoal	PANCRELIPASE	ezetimibe (*refer to antihyperlipidemics*) cholestyramine (*refer to antihyperlipidemics*) obeticholic acid ursodiol
Probiotics	**Chloride Channel Activators**	**Herbs and Natural Products**
Lactobacillus Bifidobacterium	LUBIPROSTONE	aloe vera
Learning Objectives		
9.8.1 Mechanisms of Action and Effects 1. Describe the mechanism of action of each of the major classes of drugs.		
9.8.2 Pharmacokinetics 1. Describe the route of administration, absorption, distribution, and elimination for drugs in each class. 2. Discuss how route of administration impacts drug selection based on presenting concerns and patient comorbidities.		
9.8.3 Therapeutic Uses 1. List the therapeutic uses for agents in each drug category. 2. Describe when activated charcoal should be utilized in the treatment of an oral drug overdose.		
9.8.4 Adverse Effects, Contraindications, and Drug Interactions 1. Describe the principal adverse effects of the drugs of each class. 2. Identify the principal contraindications of the drugs of each class.		

SECTION 10

ENDOCRINE PHARMACOLOGY

Laurel Gorman (section chair), Sandeep Bansal, Rheaclare Fraser-Spears, Gerald Sterling

10.1 Hypothalamus and Anterior Pituitary Pharmacology		
Recommended Curriculum Equivalent: 2.0 hr		
Drug Classes and Drugs		
Growth Hormone (GH)-related Therapy		
Agonist		
Recombinant GH	**Recombinant IGF-1**	**GH Releasing Hormone (GHRH)**
SOMATROPIN lonapegsomatropin	MECASERMIN	SERMORELIN
Inhibitors of GH		
Somatostatin Agonists [inhibits GH release]	**GH Receptor Antagonist**	
LANREOTIDE OCTREOTIDE	PEGVISOMANT	
Prolactin Inhibitors		
Dopamine agonists		
BROMOCRIPTINE CABERGOLINE		
Gonadotropins		
FSH Agonists	**LH Agonists**	**FSH + LH**
follitropin alfa urofollitropin	CHORIONIC GONADOTROPIN (hCG)	menotropins (hMG)
GnRH Agonist	**GnRH Antagonist**	
GOSERELIN LEUPROLIDE buserelin histrelin nafarelin triptorelin	DEGARELIX cetrorelix ganirelix	
ACTH	**TSH**	
Agonist	**Agonist**	
COSYNTROPIN	THYROTROPIN ALFA	
Learning Objectives		

10.1.1 Mechanism of Action and Effects

1. Describe the mechanisms of hormone action for all endocrine therapy regulated by the hypothalamic-pituitary-adrenal axis, including receptors and signal transduction pathways (receptor location, molecular events activated by hormones at cell membrane or intracellular receptors, and second messenger systems).
2. Describe the regulatory mechanisms of the hypothalamic-anterior pituitary axis, including releasing hormones (GHRH, GnRH), release-inhibiting hormones (somatostatin, dopamine), and trophic hormones (GH, prolactin, ACTH, TSH, LH and FSH), and their actions on target

tissues.

3. Explain the physiological actions of growth hormone, including its effects on insulin sensitivity, glucose metabolism, and the stimulation of peripheral insulin-like growth factor 1 (IGF-1) production.
4. Predict the consequences of deficiency or excess of GH, GnRH, and anterior pituitary trophic hormones on feedback regulation within the hypothalamic-anterior pituitary-target organ axis.
5. Analyze how drugs acting as agonists or antagonists of the hypothalamic-anterior pituitary axis impact hormone secretion, growth, metabolism processes, lactation, and gonadal hormone production.
6. Compare and contrast the use of direct antagonists vs agonist to trigger negative feedback in the treatment of hormone-sensitive neoplasia.

10.1.2 Pharmacokinetics

1. Describe the routes of administration and pharmacokinetic properties (absorption, distribution, metabolism and excretion) of drugs within each class.
2. Identify drug-, or formulation-related factors that alter the pharmacokinetic properties of these drugs.
3. Predict the impact of underlying patient conditions on pharmacokinetic parameters.

10.1.3 Therapeutic Uses

1. Discuss the rationale for use therapeutic use of hormones and hormone analogs as agonists/antagonists.
2. Describe the therapeutic roles of drugs that modulate the growth hormone axis by stimulating GH secretion, inhibiting GH release, or blocking GH receptors.
3. Extrapolate how using drugs altering prolactin secretion impacts reproduction and lactation.
4. Differentiate the therapeutic uses of agonists and antagonists of gonadotropin-releasing hormone and FSH and LH analogs on gonadal hormone regulation.
5. Compare the therapeutic consequences of intermittent (infertility) versus continuous administration (endometriosis, uterine fibroids, prostate cancer) of GnRH analogs.
6. Explain how cosyntropin and thyrotropin alfa are used in diagnosing pituitary-adrenal disorders.

10.1.4 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions

1. Describe the adverse effects, contraindications, clinically significant drug interactions associated with GH therapy in children and adults, including glucose regulation, fluid retention, and malignancy risk.
2. Compare and contrast the adverse effects, contraindications, and drug interactions associated with drugs that alter prolactin secretion and dopaminergic signaling.
3. Analyze the adverse effects, and clinically significant drug interactions of GnRH agonists and antagonists as they relate to n bone loss, vasomotor symptoms, and reproductive function.
4. Predict the monitoring requirements of therapeutics based on risks of adverse effects on different organ systems.

10.2 Hypothalamus and Posterior Pituitary Pharmacology	
Recommended Curriculum Equivalent: 1.0 hr	
Drug Classes and Drugs	
Vasopressin	
ADH Agonists	**ADH Antagonists**
DESMOPRESSIN VASOPRESSIN (ADH) terlipressin	CONIVAPTAN TOLVAPTAN
Oxytocin	
OXYTOCIN	
Learning Objectives	
10.2.1 Mechanism of Action and Effects 1. Identify posterior pituitary hormones and their effects on primary target organs. 2. Distinguish between the mechanisms of action and effects of vasopressin agonists (vasopressin, desmopressin) versus antagonists (conivaptan, tolvaptan) on renal water reabsorption. 3. Describe the mechanism of action and vascular effects of the vasopressin analogs on vascular smooth muscle to cause vasoconstriction. 4. Explain the mechanism of action and physiological effect of oxytocin on uterine smooth muscle contraction and milk ejection.	
10.2.2 Pharmacokinetics 1. Describe the routes of administration and key PK properties (absorption, distribution, metabolism, elimination) of posterior pituitary drugs and relate these to onset, peak effect, and duration at their target tissues (kidney, vasculature, uterus, breast). 2. Identify drug-, or formulation-related factors that can alter the pharmacokinetic properties of these drugs (e.g., pregnancy physiology, hepatic/renal impairment, CYP3A interactions, intranasal variability, controlled-release formulations). 3. Predict how pregnancy physiology alters pharmacokinetic variables	
10.2.3 Therapeutic Uses 1. Differentiate drugs used in the management of neurogenic (central) and nephrogenic diabetes insipidus and the syndrome of inappropriate secretion of antidiuretic hormone (SIADH). 2. Explain the rationale for the use of vasopressin agonists and antagonists in disorders of water balance, including diabetes insipidus and SIADH. 3. Compare and contrast the uses of oxytocin use in labor induction, labor augmentation, and postpartum hemorrhage.	
10.2.4 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions 1. Describe the common and serious adverse effects associated with vasopressin, desmopressin, and vasopressin antagonists (vaptans). 2. Describe the adverse effects and major contraindications associated with oxytocin and tocolytic agents, including cardiovascular and uterine risks.	

3. Explain key drug interactions affecting vasopressin agonists, vasopressin antagonists, oxytocin, and tocolytics that alter pharmacokinetics or enhance adverse effects.
4. Create a drug monitoring plan (e.g., serum sodium, fluid status, blood pressure, heart rate, uterine activity) used to optimize safety and therapeutic effectiveness of these agents.
5. Predict how altered pharmacokinetic properties or patient-specific factors may influence clinical response and adverse risk, including hyponatremia, hypotension or ischemia, tachycardia, and uterine hyperstimulation.

10.2.5 Notes

Cross-References

- Tocolytics are covered in the female reproductive section

10.3 Drugs Affecting the Adrenal Cortex and Endocrine Pharmacology		
Recommended Curriculum Equivalent: 1.5 hr		
Drug Classes and Drugs		
Glucocorticoid Receptor Agonists	**Mineralocorticoid Agonists**	**Mineralocorticoid Antagonists**
BETAMETHASONE BUDESONIDE DEXAMETHASONE FLUTICASONE HYDROCORTISONE METHYL PREDNISOLONE PREDNISONE TRIAMCINOLONE beclomethasone mometasone	FLUDROCORTISONE	SPIRONOLACTONE eplerenone

Glucocorticoid Receptor Antagonists	Adrenal Synthesis Inhibitors
MIFEPRISTONE	KETOCONAZOLE METYRAPONE OSILODROSTAT etomidate mitotane spironolactone

Learning Objectives

10.3.1 Mechanism of Action and Effects

1. Describe the hormones and regulatory steps of the hypothalamic, pituitary, adrenal (HPA) axis and the roles of ACTH and the renin–angiotensin system in adrenal steroid synthesis.
2. Explain the molecular mechanisms and physiologic effects of glucocorticoid and mineralocorticoid receptor agonists and antagonists.
3. Characterize how the mechanism of glucocorticoid and mineralocorticoid agonists impact onset of effects.
4. Differentiate between inhibitors of different steroidogenic enzymes (e.g., 11β-hydroxylase) in terms of impact on cortisol synthesis precursors, and downstream adrenal steroid hormone levels.

10.3.2 Pharmacokinetics

1. Describe the routes of administration and core pharmacokinetic properties of corticosteroid drugs, including absorption, distribution, metabolism, and elimination.
2. Explain how corticosteroid disposition (protein binding, biotransformation, and enzyme induction or inhibition) can necessitate adjustments in dosing regimens.
3. Evaluate patient-, drug-, and formulation-related factors that modify corticosteroid pharmacokinetics, including the effects of prolonged exposure and HPA axis suppression.

10.3.3 Therapeutic Uses

1. Justify corticosteroid use for hormone replacement, anti-inflammatory and immunosuppressive

treatment, and diagnostic evaluation of HPA-axis disorders, including Addison disease (replacement therapy) and Cushing syndrome (suppression and stimulation testing).

2. Differentiate therapeutic indications for glucocorticoids versus mineralocorticoids and apply the role of fludrocortisone in mineralocorticoid replacement for states of aldosterone deficiency.
3. Explain the use of mineralocorticoid receptor antagonists and steroid synthesis inhibitors in conditions of adrenal steroid excess, including primary hyperaldosteronism and Cushing syndrome.
4. Identify rare, specialty, or diagnostic uses for betamethasone, triamcinolone, mifepristone, and metyrapone.
5. Integrate the use of steroid hormone modulators in disorders of gonadal steroid imbalance, including treatment strategies for hyperandrogenism and endocrine-mediated hypogonadism.

10.3.4 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions

1. Identify major adverse effects and contraindications associated with glucocorticoid and mineralocorticoid therapy, including effects of excessive mineralocorticoid activity.
2. Compare the selectivity and anti-androgen effects of the mineralocorticoid receptor antagonists.
3. Explain alternate-day glucocorticoid therapy and the need for gradual dose tapering following chronic corticosteroid use to prevent adrenal insufficiency.
4. Analyze clinically significant drug interactions involving corticosteroids and steroid synthesis inhibitors that require monitoring or dose adjustment (e.g. cytochrome P450 enzymes and P-glycoprotein).
5. Predict how organ dysfunction and metabolic activation influence corticosteroid safety and efficacy.
6. Create a monitoring plan to assess for metabolic, catabolic, immune, electrolyte disturbances associated with adrenal steroid agonist therapy.

10.4 Drugs Affecting Thyroid Hormone Functions and Endocrine Pharmacology		
Recommended Curriculum Equivalent: 1.0 hr		
Drug Classes and Drugs		
Thyroid Hormone Preparations		
LEVOTHYROXINE (T4) LIOTHYRONINE (triiodothyronine, T3)		
Antithyroid Agents		
Thioamides	**Radioactive Iodine**	**Beta Blockers***
METHIMAZOLE (MMI) PROPYLTHIOURACIL (PTU)	RADIOIODINE 131 (^{131}I)	PROPRANOLOL nadolol
Iodides	**Biologic agent**	
POTASSIUM IODIDE	teprotumumab	
Learning Objectives		
10.4.1 Mechanism of Action and Effects 1. Delineate the mechanisms of action of thyroid hormone preparations at nuclear thyroid hormone receptors and relate these actions to systemic metabolic effects. 2. Compare the molecular mechanisms by which thioamides, radioiodine and iodide inhibit thyroid hormone synthesis and release. 3. Analyze how β-adrenoceptor antagonists mitigate the peripheral manifestations of thyrotoxicosis. 4. Explain the mechanism by which teprotumumab modulates insulin-like growth factor-1 receptor (IGF-1R) signaling in thyroid eye disease.		
10.4.2 Pharmacokinetics 1. Differentiate levothyroxine and liothyronine with respect to absorption, half-life, protein binding, potency, and clinical utility. 2. Justify the preferential use of levothyroxine for chronic thyroid hormone replacement therapy based on its pharmacokinetics. 3. Apply pharmacokinetic principles to select appropriate antithyroid therapy in non-pregnant patients, during pregnancy, and thyroid storm.		
10.4.3 Therapeutic Uses 1. Integrate thyroid pathophysiology to select appropriate pharmacologic therapy for hypothyroidism and hyperthyroidism, including special populations such as elderly patients, pregnant patients, and those with coronary artery disease. 2. Propose rational drug combinations for the management of thyroid storm based on mechanism of action. 3. Evaluate the therapeutic role of radioiodine, antithyroid drugs, and surgery in the management of Graves' disease and toxic nodular goiter. 4. Justify the use of teprotumumab in patients with moderate to severe thyroid eye disease.		
10.4.4 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions 1. Evaluate the adverse effects of thioamides, including agranulocytosis and hepatotoxicity, in		

treating a patient with hyperthyroidism.
2. Differentiate the teratogenic risks of methimazole and propylthiouracil and justify trimester-specific drug selection in pregnancy.
3. Identify cardiovascular risks associated with excessive thyroid hormone replacement.
4. Analyze clinically significant drug–disease and drug–drug interactions involving thyroid hormones and antithyroid agents.
5. Identify laboratory parameters used to monitor the adequacy of thyroid hormone replacement and antithyroid therapy.

10.4.*5* Notes

Cross-References

- *Objectives related to β-adrenoceptor antagonists are covered in greater detail in the Autonomic Nervous System section.

Clinical Guidelines

- American Thyroid Association. https://www.thyroid.org/professionals/ata-professional-guidelines/practice-guidelines-pocketcards/
- American Association of Clinical Endocrinology. https://pro.aace.com/clinical-guidance/thyroid
- Society for Endocrinology. https://www.endocrinology.org/endocrinologist/144-summer-22/features/the-latest-guidance-in-managing-thyroid-disease/

10.5 Parathyroid/Calcium and Phosphate Homeostasis			
Recommended Curriculum Equivalent: 0.5 hr			
Drug Classes and Drugs			
Bisphosphonates	**Vitamin D**	**Calcimimetics**	**Phosphate Binder**
ALENDRONATE IBANDRONATE RISEDRONATE PAMODRONATE ZOLEDRONATE	CALCIFEDIOL CALCITRIOL CHOLECALCIFEROL ERGOCALCIFEROL PARICALCITOL	CINACALCET	SEVELAMER
RANK Ligand Inhibitor	**Sclerostin Antibody**	**Hormones**	**Diuretics**
DENOSUMAB	ROMOSOZUMAB	TERIPARATIDE calcitonin selective estrogen receptors modulators (SERMs)	FUROSEMIDE
Glucocorticoids		**Minerals**	
DEXAMETHASONE HYDROCORTISONE PREDNISOLONE		CALCIUM PHOSPHATE STRONTIUM	

Learning Objectives

10.5.1 Mechanism of Action and Effects

1. Analyze how bisphosphonates, denosumab, and calcitonin suppress osteoclast-mediated bone resorption by targeting distinct molecular pathways involved in osteoclast function and survival.
2. Differentiate the mechanism of action of calcimimetics and phosphate binders in the management of secondary hyperparathyroidism.
3. Predict the effects of targeting sclerostin versus parathyroid hormone receptors on bone remodeling dynamics in osteoporosis.
4. Relate the mechanism of actions of vitamin D analogs to intestinal calcium absorption and bone mineralization.
5. Compare and contrast the mechanism of action of bisphosphonates, RANK-ligand inhibitors, calcitonin, loop diuretics, and glucocorticoids in the management of hypercalcemia of malignancy.

10.5.2 Therapeutic Uses

1. Compare pharmacologic strategies for the management of hypoparathyroidism and hyperparathyroidism.
2. Integrate calcium–phosphate physiology to guide drug selection in chronic kidney disease–related mineral and bone disorders.
3. Justify the use of bisphosphonates, RANK-ligand inhibitors, calcitonin, and loop diuretics, glucocorticoids in the management of hypercalcemia of malignancy.
4. Evaluate the role of pharmacotherapy in the prevention and treatment of rickets, osteomalacia, and osteoporosis.
5. Justify the role of bisphosphonates and calcitonin in the management of Paget disease of bone.

6. Describe the role of cholecalciferol and calcium supplements in the prevention and management of rickets/osteomalacia, and vitamin D deficiency.
10.5.3 Adverse Effects, Contraindications, and Drug Interactions 1. Predict adverse effects of bisphosphonates, RANK-ligand inhibitors, PTH analogs, calcimimetics, phosphate binders, loop diuretics, and glucocorticoids used in the management of disorders affecting the bone-mineral homeostasis. 2. Identify risks associated with excessive calcium and vitamin D supplementation, including hypercalcemia and nephrolithiasis. 3. Analyze contraindications and clinically significant drug interactions associated with bisphosphonates, calcimimetics, and parathyroid hormone analogs.

10.6 Endocrine Pancreas Pharmacology		
Recommended Curriculum Equivalent: 1.5 hr		
Drug Classes and Drugs		
Drug Categories and Classes for the Treatment of Diabetes Mellitus		
Insulins	**Insulin Sensitizer Agents**	
ASPART DEGLUDEC GLARGINE LISPRO NPH INSULIN REGULAR glulisine	**Biguanides**	**Thiazolidinediones**
	METFORMIN	PIOGLITAZONE rosiglitazone
Insulin Secretagogue Agents		
Sulfonylureas	**Meglitinides**	
GLIPIZIDE	nateglinide repaglinide	
Incretin Agents		
GLP1 Agonists	**GLP1/GIP Agonist**	**DDP-4 Inhibitors**
EXENATIDE LIRAGLUTIDE SEMAGLUTIDE	TIRZEPATIDE	SITAGLIPTIN linagliptin
Glucosuric Agents		
SGLT2 Inhibitors	**SGLT1/SGLT2 Dual inhibitor**	
CANAGLIFLOZIN DAPAGLIFLOZIN EMPAGLIFLOZIN bexagliflozin	SOTAGLIFLOZIN	
Misc. Agents		
Alpha Glucosidase Inhibitor	**Amylin Analog**	
ACARBOSE	pramlintide	
Treatment of Medication-induced Hypoglycemia		
GLUCAGON		
Drug Table abbreviations: GLP1 = Glucagon-like peptide 1; GIP = Glucose-dependent insulinotropic polypeptide; DDP-4= Dipeptidyl peptidase; SGLT=Sodium-glucose co-transporter		
Learning Objectives		
10.6.1 Mechanism of Action and Effects 1. Explain the molecular mechanisms of action of insulin in glucose uptake, metabolism, and anabolic processes. 2. Compare the physiologic effects of endogenous incretins with the mechanism of exogenously		

administered incretin analogues or GLP-1 or GLP-1/GIP agonists.
3. Compare and contrast the mechanisms of different subclasses of insulin secretagogues versus different subclasses of insulin sensitizers.
4. Explain the mechanisms of SGLT2 inhibitors, alpha-glucosidase inhibitors, and amylin in treating type 2 diabetes.
5. Differentiate between the mechanism of diabetes medications causing weight gain versus the mechanism of diabetes medications promoting weight loss.
6. Evaluate the effects of different diabetes therapeutics on pathophysiological and physiological processes relevant to comorbidities like heart and kidney function.
7. Explain the mechanism of glucagon in reversing medication-induced hypoglycemia.

10.6.2 Pharmacokinetics

1. Compare the pharmacokinetic parameters of insulins with emphasis on onset and duration of action.
2. Justify rationale for the use of insulin preparations based on pharmacokinetic parameters.
3. Describe the absorption, distribution, metabolisms, and elimination of all classes of type 2 diabetes medication.
4. Justify the use of differing subclasses of type 2 medications based on route of administration and patient characteristics.

10.6.3 Therapeutic Uses

1. Discuss therapeutic indications for drugs used in treating type I, type 2, or gestational diabetes.
2. Compare efficacy and benefits of the different classes of type 2 medications in patients with different underlying comorbidities and characteristics
3. Evaluate choice of insulin based on onset and duration relative to type 1 or type 2 or gestational diabetes patient needs for bolus, basal, and/or postprandial insulin coverage.
4. Differentiate between insulin therapy using an insulin pump versus bolus and basal coverage using injections.
5. Weigh pros and cons of utilizing “tight” glycemic control in differing populations.
6. Analyze patient A1c levels to inform monotherapy vs polytherapy and/or insulin therapy to maintain ideal glycemic control.
7. Create a treatment plan for acute management of ketoacidosis or hyperglycemic hyperosmolar syndrome
8. Describe treatment of medication-induced hypoglycemia.
9. Identify drug-drug interactions that can impact medication efficacy and glycemic control for patients with diabetes
10. Create a treatment plan that coordinates pharmacologic therapy with diet and exercise to improve patient prognosis.

10.6.4 Adverse Effects, Drug Interactions, and Contraindications

1. Describe the adverse effects of all diabetes medications within therapeutic and the clinical manifestations of overdose.
2. Differentiate between medications with high risks of hypoglycemia versus options with low risk.
3. Evaluate medication choices based on propensity to cause weight gain in patients with type 2 diabetes and comorbid obesity.
4. Identify major drug-drug interactions that can impact medication efficacy, glycemic control, and

hypoglycemia risk in patients with diabetes.

5. Compare and contrast diabetes medication choices based on adverse effect risks and underlying patient comorbidities.
6. Create a plan to monitor efficacy and adverse effects in the long-term management of diabetes.

10.6.5 Notes

Cross-References

- There is overlap in learning objectives between diabetes medications and some of the anti-obesity medications.

Clinical Guidelines

- American Association of Clinical Endocrinology (AACE). Clinical guidelines on treatment of diabetes: https://pro.aace.com/clinical-guidance/diabetes
- American Diabetes Association (ADA) Clinical Updates 2025 Diabetes Medications: https://diabetesjournals.org/books/book/57/2025-26-Guide-to-Medications-for-the-Treatment-of

10.7 Female Reproductive Hormone Pharmacology		
Recommended Curriculum Equivalent: 1.5 hr		
Drug Classes and Drugs		
Estrogen-related Therapy		
Estrogen Full Agonists	**Selective Estrogen Receptor Modulators (SERMS)**	**Selective Estrogen Receptor Down-regulators (SERD)**
CONJUGATED ESTROGENS ETHINYL ESTRADIOL estradiol 17ß estrone mestranol phytoestrogens	CLOMIPHENE RALOXIFENE TAMOXIFEN bazedoxifene toremifene	FULVESTRANT
Progestin- and Progesterone-related Therapy		
Progestin and Progesterone Agonist	**Progesterone Antagonist**	
DROSPIRENONE ETONOGESTREL LEVONORGESTREL MEDROXYPROGESTERONE NORETHINDRONE PROGESTERONE desogestrel norgestimate norgestrel ulipristal	MIFEPRISTONE	
Androgen-related Therapy		
Partial Agonist	**Agonist**	**Androgen Antagonist**
danazol	testosterone	DROSPIRENONE SPIRONOLACTONE
Aromatase Inhibitors (Ais)	**Gonadotropin-Releasing Hormone Analogues**	
ANASTROZOLE EXEMESTANE LETROZOLE	LEUPROLIDE	
Drugs for Vasomotor Symptoms of Menopause		
Neurokinin-3 Receptor Antagonists	**Antidepressants**	
FEZOLINETANT	VENLAFAXINE ESCITALOPRAM	
Learning Objectives		
10.7.1 Mechanism of Action and Effects 1. Explain the molecular mechanism of action of therapeutically administered female reproductive hormones as well as phytoestrogens.		

2. Compare and contrasts the effects of estrogen and progesterone-based therapeutic with those of endogenous female reproductive hormones.
3. Characterize how estrogen and progesterone therapies can be used to trigger negative feedback processes to inhibit ovulation, regulate endogenous hormone levels, and provide contraception.
4. Differentiate between androgenic and progestogenic properties of therapeutic progestins.
5. Elaborate on hormonal replacement therapy (HRT) mechanisms in resolving or reducing pathophysiological events triggered by hypoestrogenic and/or hypo-androgenic states In menopause or other conditions.
6. Explain the therapeutic benefits of using a progestin or progesterone with estrogen in patients with a uterus based on the pharmacodynamic properties of these agents.
7. Differentiate between the mechanisms of selective estrogen receptor modulators (SERMs), estrogen receptor antagonists, aromatase inhibitors., and progesterone antagonists.
8. Predict the physiological effects of estrogen, progesterone, androgen agonist and/or antagonists in cis and transgender patients.
9. Differentiate between the properties and effects of acute vs chronic continuous administration of gonadotropin releasing hormone analogues.
10. Describe the mechanism of non-hormonal medications treating estrogen-deficiency vasomotor symptoms.

10.7.2 Pharmacokinetics

1. Compare the routes of administration, absorption, distribution, metabolism, elimination and relative duration of synthetic and natural estrogens, including phytoestrogens.
2. Compare the routes of administration, absorption, distribution, metabolism, elimination and relative duration of action of synthetic progestins, progesterone agonists and antagonists, and androgen agonist and antagonists,
3. Compare the routes of administration, absorption and relative duration of SERMs, SERDs, and aromatase inhibitors.
4. Describe relevant pharmacokinetics of Neurokinin-3 Receptor antagonists and antidepressants used to treat menopausal vasomotor symptoms.

10.7.3 Therapeutic Uses

1. Describe the use of drugs such as clomiphene and gonadotropic drugs for the treatment of infertility.
2. Identify commonly used estrogen-progestin or progestin-only hormonal contraceptive agents.
3. Compare and contrast the therapeutic benefits and concerns based on androgenicity of various progestins used in contraception.
4. Distinguish between the benefits and concerns associated with various dosage schedules (e.g., biphasics, triphasics) and routes of administration (oral, transdermal patch, topical, vaginal ring, etc) for contraception using combination (estrogen-progestin) therapy.
5. Identify agents and doses used for postcoital contraception.
6. Elaborate on gynecologic uses of estrogens, progestin, and androgen therapeutics beyond contraception and hormone replacement therapy.
7. Justify use of progestin-only or long-acting progestin contraception based on patient characteristics.

8. Describe the rationale and appropriate indications for estrogens and estrogen/progestin hormonal replacement therapy (HRT) in postmenopausal women as well as hormonal supplementation for hypogonadism or gender affirming care.
9. Describe the use of SERMs, estrogen receptor antagonists, and aromatase inhibitors in treatment of breast cancer.
10. Characterize the use of SERMs in post-menopausal osteoporosis.
11. Explain appropriate uses of progesterone antagonists as abortifacients.
12. Compare and contrast the benefits and risks of using HRT versus neurokinin 3 receptor antagonists or antidepressants to reduce menopausal vasomotor symptoms.

10.7.4 Adverse Effects, Drug Interactions, and Contraindications

1. Explain major adverse effects and major contraindications for estrogens and progestins alone and in combination
2. Differentiate between the adverse effects of progestins based on relative potency to stimulate androgenic receptors.
3. Evaluate the risk of blood clots for estrogen formulations administered by oral vs non-oral routes.
4. Compare and contrast the adverse effects of SERMs, SERDs, and aromatase inhibitors.
5. Predict the adverse effects of androgen agonists and antagonists.
6. Describe the adverse effects of progesterone antagonists.
7. Describe the most common drug interactions with estrogen, progesterone/progestin, and androgen-based therapeutics.
8. Select hormonal contraception in clinical scenarios based on comorbidities and known contraindications.
9. Create a treatment plan for ER+/PR+ breast cancer using a SERM, SERD, or aromatase inhibitors based on patient characteristics and comorbidities.

10.7.5 Notes

Clinical Guidelines

- Association of Clinical Obstetricians and Gynecologists (ACOG) Treatment Guidelines: https://www.acog.org/clinical/search?t=#f:@selectedcontenttype=[Clinical%20Practice%20Guideline]
- Menopause Society (NAMS) Professional guidelines and resources: https://menopause.org/professional-resources/practice-pearls-nm https://menopause.org/professional-resources/menopause-practice-textbook
- JNCCN Breast Cancer treatment guidelines: https://jnccn.org/view/journals/jnccn/22/5/article-p331.xml?content=pdf-7340&print

10.8 Female Reproductive Labor and Delivery Pharmacology			
Recommended Curriculum Equivalent: 1.0 hr			
Drug Classes and Drugs			
Uterine Stimulants			
Oxytocin Analogue	**Prostaglandin Analogues**	**Antiprogesterone Abortifacient**	
OXYTOCIN	CARBOPROST ERGONOVINE MISOPROSTOL TROMETHAMINE dinoprostone	MIFEPRISTONE	
Tocolytics*			
NSAID	**Anticonvulsant/ Tocolytic**	**Calcium Channel Blocker**	**Selective Beta 1-adrenergic agonist**
INDOMETHACIN	MAGNESIUM SULFATE	NIFEDIPINE	terbutaline
Other Preterm Labor Agents			
Corticosteroids			
BETAMETHASONE DEXAMETHASONE			
Learning Objectives			
10.8.1 Mechanism of Action and Effects 1. Describe how uterine stimulants and tocolytics impact uterine myometrial contractions. 2. Compare and contrast the effects of endogenous versus exogenous oxytocin on labor and delivery. 3. Explain how the progression of gestation alters the responsiveness of uterine myometrial tissue to oxytocin and tocolytics. 4. Discuss how prostaglandin analogues impact uterine and cervical contraction. 5. Predict the effects of mifepristone in early and late gestation stages. 6. Predict the physiological effects of administering tocolytic agents systemically on the blood sugar, cardiovascular function, and smooth muscle relation. 7. Differentiate between the mechanisms and effects of calcium channel blockers and magnesium sulfate in preeclampsia patients. 8. Explain the mechanistic benefits of administering corticosteroids during preterm labor.			
10.8.2 Pharmacokinetics 1. Discuss the usual route(s) of administration, onset and duration of action of the various oxytocic and tocolytic agents. 2. Compare and contrast the benefits of the route(s) and duration of action of various prostaglandin analogues. 3. Identify the benefits of using long-duration corticosteroids in preterm labor.			
10.8.3 Therapeutic Uses 1. Describe the appropriate and inappropriate clinical use of oxytocin.			

2. Justify the rationale for administering long-acting corticosteroids in mothers at risk of preterm birth.
3. Discuss the utilization of mifepristone versus prostaglandins in therapeutic abortion.
4. Debate the potential benefits and risks of administering tocolytic agents to the mother and baby.
5. Differentiate between the use of different labor and delivery medications in patients experiencing preeclampsia.
6. Predict the benefits and concerns of using prostaglandins and oxytocin to control enhance post-delivery uterine tonicity and reduce post-partum hemorrhage.
7. Identify the benefits of using long-duration corticosteroids in preterm labor.
8. Compare the efficacy and appropriate use of different abortifacients in varying gestational phases.

10.8.4 Adverse Effects, Drug Interactions, and Contraindications

1. Describe the potential adverse effects of the oxytocic agents in the mother (uterine, extrauterine) and in the neonate.
2. Explain the adverse effects of tocolytic agents on the mother and baby.
3. Identify major contraindications to using oxytocic, prostaglandins, and tocolytic agents.
4. Compare the adverse effects and contraindications of abortifacient agents.
5. Create a maternal and fetal adverse effects monitoring plan during use of oxytocin, uterine stimulants, and tocolytics (if preterm labor).

10.8.5 Notes

Cross-References

- Some learning objectives overlap with the pituitary hormone section

Clinical Guidelines

- Association of Clinical Obstetricians and Gynecologists (ACOG) labor and delivery medications guidelines: https://www.acog.org/clinical

Historical/Toxicology Context

- *No tocolytics are FDA approved but they are used off label clinically.

10.9 Male Reproductive Gonadal Hormone Pharmacology		
Recommended Curriculum Equivalent: 0.5 hr		
Drug Classes and Drugs		
Androgenic Agents		
Androgenic Agonists	**Agonists & Anabolic Steroid**	
DIHYDROTESTOSTERONE TESTOSTERONE androstenedione dehydroepiandrosterone methyltestosterone	OXANDROLONE fluoxymesterone nandrolone	
Antiandrogenic Agents		
5alpha-reductase Inhibitors	**Androgen Antagonists**	**Other Androgen Synthesis Inhibitors**
FINASTERIDE dutasteride	FLUTAMIDE bicalutamide	SPIRONOLACTONE abiraterone ketoconazole
Gonadotropin-related Drugs Used for Male Reproductive Disorders		
DEGARELIX** LEUPROLIDE**		
Learning Objectives		
10.9.1 Mechanism of Action and Effects 1. Describe the molecular mechanism of action of androgenic agonists 2. Characterize the roles of androgen therapy in sexual differentiation, puberty, and sexual maturation when used 3. Discuss mechanisms for how androgen antagonists and androgen synthesis inhibitors reduce androgen levels in precocious puberty, and androgen hormone-responsive neoplasms. 4. Delineate the importance of reducing metabolism of testosterone to dihydrotestosterone on pathophysiological processes mediating prostate hyperplasia 5. Compare the mechanisms and effects of different classes of medications reducing androgen hormone level or function. 6. Predict the physiological effects (therapeutic and adverse) of antagonizing androgen receptors and/or depleting androgens in males. 7. Compare the anabolic actions vs androgenic effects of androgens. 8. Predict the mechanistic benefit of initially adding flutamide to leuprolide therapy in treating prostate concern		
10.9.2 Pharmacokinetics 1. Compare the routes of administration, pharmacokinetic characteristics and relative duration of action of androgenic agonists and antagonists		
10.9.3 Therapeutic Uses 1. Describe the use of testosterone replacement therapy in men with hypogonadism, youth with delayed puberty, gender-affirming care, and chronic catabolic conditions.		

2. Weigh the pros and cons of using androgen antagonists, androgen synthesis inhibitors, and other types of hormonal therapy in the treatment of either benign prostate hyperplasia or prostate cancer.
3. Create a plan to monitor the efficacy of androgen antagonist in treating prostate hyperplasia or prostate cancer.

10.9.4 Adverse Effects, Drug Interactions, and Contraindications

1. Predict the adverse effects of androgenic agonists and anabolic steroids and overdosage
2. Compare the adverse effects of androgen antagonists and androgen synthesis inhibitors used to treat prostate cancer.
3. List the most common drug-drug interactions with gonadotropin therapeutics.
4. Create a plan to monitor the adverse effects of long-term androgen depletion therapy in prostate cancer.

10.9.5 Notes

Cross-References

- **These drugs are also covered in the Hypothalamus and Anterior Pituitary Pharmacology Objectives, and Female Reproductive Hormone Pharmacology.

10.10 Male Urogenital Pharmacology		
Recommended Curriculum Equivalent: 0.5 hr		
Drug Classes and Drugs		
Alpha 1-adrenergic Antagonists	**5-Alpha Reductase Inhibitors***	**PDE Inhibitors**
TAMSULOSIN alfuzosin doxazosin silodosin terazosin	FINASTERIDE dutasteride	SILDENAFIL TADALAFIL avanafil vardenafil
Prostaglandins	**Anticholinergics**	**Beta 3-adrenoceptor Agonists**
alprostadil (Prostaglandin E1)	DARIFENACIN OXYBUTYNIN SOLIFENACIN tolterodine	MIRABEGRON vibegron

Learning Objectives

10.10.1 Mechanism of Action and Effect

1. Explain the mechanism of action of drugs used to treat prostate hyperplasia, erectile dysfunction, and overactive bladder.
2. Identify drugs used for other purposes that may contribute to or cause erectile dysfunction.
3. Predict the effects of prostate hyperplasia medications on smooth muscle contraction and relaxation to allow urination.
4. Compare the effects of alpha1 antagonist, PDE inhibitors, 5-alpha reductase inhibitors on physiological processes, including pathophysiological processes in prostate hyperplasia.

10.10.2 Pharmacokinetics

1. Describe the route of administration, absorption, distribution, and elimination for drugs in each class.
2. Identify drugs where the route of administration may limit use.

10.10.3 Therapeutic Uses

1. Compare the benefits of different drugs used in the treatment of benign prostatic hyperplasia.
2. Describe drugs used to treat erectile dysfunction (ED) and identify appropriate uses in patients with different underlying comorbidities.
3. Compare the benefits and adverse effects of different drugs used to treat overactive bladder.

10.10.4 Adverse Effects, Drug Interactions, and Contraindications

1. List the major or most common adverse effects of drugs from each class.
2. Explain major contraindications of drugs from each class.
3. Describe drug interactions, especially those with significant risk of morbidity and mortality in patients treated vasodilators for hypertension or cardiac disease.
4. Analyze the clinically significant interaction between PDE inhibitors and vasodilators such as nitroglycerin and the potential for severe hypotension.

10.10.5 Notes

Cross-References

- *Covered in male reproductive section.
- Androgen antagonists used to treat prostate cancer are listed in the gonadal hormone section.

10.11 Anorexiant and Anti-Obesity Agents		
Recommended Curriculum Equivalent: 1.0 hr		
Drug Classes and Drugs		
Stimulant	**Stimulant/Antiepileptic Combination**	**GLP1 Agonists**
PHENTERMINE	PHENTERMINE/ TOPIRAMATE	LIRAGLUTIDE ORFORGLIPRON SEMAGLUTIDE

Mixed GLP1/GIP Agonist	**Atypical Antidepressant**
TIRZEPATIDE	BUPROPION
Antidepressant /Opioid Antagonist Combination	**Lipase Inhibitors**
BUPROPION/ NALTREXONE	ORLISTAT

Learning Objectives

10.11.1 Mechanism of Action and Effects

1. Identify drugs promoting anorexia and weight loss.
2. Describe molecular mechanism of action for individual agents and the synergistic effects of approved combination therapies.
3. Elaborate on efficacy relative to underlying central and/or peripheral mechanisms of action.

10.11.2 Pharmacokinetics

1. Describe the absorption, distribution, metabolism, and elimination of commonly used selected agents
2. Justify the use of agents based on oral or parenteral routes of administration
3. Elaborate on patient variables that may alter pharmacokinetic and dosing parameters.

10.11.3 Therapeutic Uses

1. Predict drug efficacy based on specified patient characteristics
2. Explain how medications are used in combination with lifestyle and behavioral modification in short-term and long-term treatment of obesity.
3. Justify the use of agents based on patient comorbidities independent of obesity.
4. Identify non-pharmacologic obesity management strategies and elaborate on how pharmacological agents are used in combination with surgery, counseling, and/or lifestyle modifications.

10.11.4 Adverse Effects, Drug Interactions Contraindications, and Drug Monitoring

1. Compare and contrast the adverse effects of different classes of agents.
2. Predict which agents are contraindicated based on adverse effect profile and inherent risks associated with patient comorbidities.
3. Differentiate between use of agents based on drug interactions, disease-drug interactions, and the drug-related needs for monitoring and follow-up
4. Create a treatment monitoring plan to assess the efficacy of a selected agent in reducing

weight, A1C levels, or other relevant obesity-related disorders.

10.11.5 Notes

Cross-References

- Some medications overlap with diabetes pharmacology.

Clinical Guidelines

- National Institute Health: Approved obesity medications: https://pmc.ncbi.nlm.nih.gov/articles/PMC10327684/
- AACE 2025 Guidelines for Anti-obesity Therapeutics: https://www.endocrinepractice.org/article/S1530-891X(25)00977-2/fulltext

SECTION 11

CANCER PHARMACOLOGY

Rachel Linger (section chair), Kelly Quesnelle, Kent Vrana

11.1 Classical Cytotoxic Antineoplastic Agents		
Recommended Curriculum Equivalent: 2.0 hr		
Drugs Classes and Drugs		
Adducting Agents	**Antimetabolites**	**Mitotic Spindle Poisons**
CARBOPLATIN CISPLATIN CYCLOPHOSPHAMIDE carmustine ifosfamide lomustine melphalan oxaliplatin procarbazine temozolomide	5-FLUOROURACIL CAPECITABINE CYTARABINE GEMCITABINE METHOTREXATE 6-mercaptopurine 6-thioguanine azacitidine fludarabine hydroxyurea pemetrexed pralatrexate	PACLITAXEL VINCRISTINE docetaxel vinblastine vinorelbine

Antitumor Antibiotics	Topoisomerase Inhibitors
BLEOMYCIN DAUNORUBICIN DOXORUBICIN dactinomycin epirubicin idarubicin	ETOPOSIDE IRINOTECAN topotecan

Learning Objectives

11.1.1 Mechanism of Action and Effects

1. Integrate the biochemical pathways of purine and pyrimidine biosynthesis with the specific inhibitory targets of antimetabolites (e.g., DHFR, Thymidylate Synthase).
2. Differentiate between cell-cycle specific (CCS) and cell-cycle non-specific (CCNS) agents based on their interference with DNA replication, repair pathways, and topoisomerase activity.
3. Analyze the molecular dynamics of mitotic spindle inhibitors (vinca alkaloids vs taxanes) and their impact on chromosomal regulation.
4. Explain the biochemical rationale for leucovorin as both a “rescue” agent (methotrexate) and a “potentiator” (5-fluorouracil).

11.1.2 Pharmacokinetics

1. Compare the intracellular bioactivation requirements of prodrugs such as cyclophosphamide (hepatic) and capecitabine (enzymatic triple-step).
2. Predict the risk of severe toxicity in patients with genetic deficiencies in drug-metabolizing enzymes (e.g., DPD deficiency with fluoropyrimidines or TPMT polymorphism with thiopurines).
3. Evaluate the role of metabolic byproducts, specifically identifying acrolein’s role in urotoxicity and the necessity of mesna for neutralization.
4. Discuss the role of dexrazoxane in treating anthracycline extravasation and preventing doxorubicin-mediated cardiomyopathies.

11.1.3 Therapeutic Uses

1. Justify the use of combination chemotherapy protocols to overcome drug resistance and achieve synergistic cell kill.
2. Analyze the roles of induction, maintenance, adjuvant, and neoadjuvant chemotherapy in the treatment of cancer.
3. Apply the knowledge of cell cycle, doubling time, and growth fraction to explain the rationale for repetitive intermittent treatment of cancer.
4. Analyze the role of anticancer pharmacotherapy as an adjunct to surgery and radiation therapy in the treatment of relevant cancers.
5. Analyze factors that may limit the effectiveness of anticancer drug treatment, including tumor burden, tumor genotype, patient comorbidities, and drug access and cost.

11.1.4 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions

1. Distinguish between general cytotoxic effects (myelosuppression, mucositis, alopecia) and drug-specific "signature" toxicities (e.g., cisplatin ototoxicity, bleomycin pulmonary fibrosis).
2. Describe adverse effects of anticancer drugs and approaches to minimizing adverse effects.
3. Critique the dose-limiting cumulative cardiotoxicity of anthracyclines and the mechanistically driven use of dexrazoxane as a cardioprotectant.
4. Anticipate the clinical presentation of tumor lysis syndrome (TLS) in high-bulk malignancies and formulate a prevention strategy using allopurinol or rasburicase.
5. Formulate a monitoring plan for patients on drugs with narrow therapeutic indices, focusing on renal clearance (methotrexate/cisplatin) and hepatic function.
6. Analyze potential drug-drug interactions, such as the inhibition of xanthine oxidase by allopurinol and its effect on 6-mercaptopurine metabolism.
7. Assess patient comorbidities (e.g., pre-existing heart failure or renal impairment) to determine absolute and relative contraindications for specific cytotoxic agents.

11.2 Pathway-Targeted Antineoplastic Agents		
Recommended Curriculum Equivalent: 1.0 hr		
Drug Classes and Drugs		
Kinase Inhibitors	**Monoclonal Antibodies & Fusion Proteins**	**Miscellaneous Agents**
ERLOTINIB IMATINIB LAPATINIB PALBOCICLIB abemaciclib afatinib crizotinib dasatinib gefitinib sorafenib sunitinib vemurafenib	CETUXIMAB NIVOLUMAB PEMBROLIZUMAB RITUXIMAB TRASTUZUMAB atezolizumab bevacizumab ipilimumab panitumumab pertuzumab	BORTEZOMIB EVEROLIMUS carfilzomib temsirolimus vorinostat

Cellular & Gene Therapies	Antibody-Drug Conjugates
TISAGENLECLEUCEL axicabtagene ciloleucel brexucabtagene autoleucel sipuleucel-T	ADO-TRASTUZUMAB EMTANSINE FAM-TRASTUZUMAB DERUXTECAN brentuximab vedotin

Learning Objectives

11.2.1 Mechanism of Action and Effects

1. Integrate the molecular biology of oncogenic “driver” mutations (e.g., *BCR-ABL*, *BRAF*, *V600E*, and *HER/neu*) with the specific inhibitory mechanisms of small molecule inhibitors and monoclonal antibodies.
2. Analyze the immune checkpoint signaling pathways (PD-1/PD-L1 and CTLA-4) and predict how their inhibition restores T-cell-mediated anti-tumor surveillance.
3. Compare and contrast pharmacologic strategies of competitive kinase inhibition (e.g., imatinib) versus extracellular ligand-binding blockade (e.g., cetuximab).
4. Differentiate the mechanisms of action for advanced delivery systems, including fusion proteins and antibody-drug conjugates (ADCs), focusing on intracellular toxin release.

11.2.2 Pharmacokinetics

1. Compare the absorption, distribution, and elimination half-lives of small molecule "nib" drugs (oral, intracellular targets) versus monoclonal "mab" therapies (parenteral, extracellular targets).
2. Evaluate the pharmacokinetic hurdles of cell-based therapies (e.g., CAR-T), specifically regarding "expansion" and persistence within the host.

11.2.3 Pharmacogenomics

1. Correlate specific molecular biomarkers (e.g., *KRAS* mutation status, *HER2* amplification) with the predicted efficacy or primary resistance to targeted therapies.

2. Appraise the necessity of companion diagnostics (genotyping/IHC) in selecting regimens to satisfy the requirements of "personalized" oncology.
11.2.4 Therapeutic Uses 1. Justify the rationale for combination "vertical" or "horizontal" pathway inhibition to bypass metabolic bypass loops and prevent acquired drug resistance. 2. Select the appropriate targeted agent based on a clinical vignette providing tumor histology and cytogenetic data. 3. Compare and contrast the strategies and outcomes from standard cytotoxic chemotherapy and targeted therapies.
11.2.5 Adverse Effects, Contraindications, and Drug Interactions 1. Distinguish "off-target" toxicities from "on-target, off-tumor" toxicities (e.g., premature release of ADC payload into the bloodstream vs EGFR inhibitors causing acneiform rash or trastuzumab-induced cardiotoxicity). 2. Analyze the unique profile of Immune-Related Adverse Events (irAEs) associated with checkpoint inhibitors, contrasting them with the myelosuppression of classical cytotoxics. 3. Identify rare but life-threatening syndromes, such as Cytokine Release Syndrome (CRS) in CAR-T therapy or infusion-related anaphylaxis with chimeric antibodies. 4. Predict potential drug-drug interactions involving the CYP34A system, which frequently metabolizes oral tyrosine kinase inhibitors (TKIs). 5. Assess contraindications for immunotherapy in the context of pre-existing autoimmune pathology.

11.3 Drugs for Hormone Sensitive Cancers		
Recommended Curriculum Equivalent: 1.0 hr		
Drugs and Drug Classes		
Glucocorticoids	**GnRH Agonists**	**Antiandrogens**
PREDNISONE dexamethasone methylprednisolone prednisolone	LEUPROLIDE goserelin	ABIRATERONE ACETATE BICALUTAMIDE apalutamide enzalutamide darolutamide

GnRH Antagonists	Aromatase Inhibitors
degarelix relugolix	ANASTROZOLE EXEMESTANE letrozole
Selective Estrogen Receptor Modulators (SERMs)	**Selective Estrogen Receptor Downregulators (SERDs)**
TAMOXIFEN raloxifene	FULVESTRANT elacestrant

Learning Objectives

11.3.1 Mechanism of Action and Effects

1. Explain the role of hormone signaling in cancer cell growth.
2. Differentiate estrogen- and androgen-dependent signaling pathways in breast and prostate cancer.
3. Describe the mechanisms of action of the glucocorticoids in immune suppression and anticancer activities.
4. Compare how GnRH agonists and GnRH antagonists suppress androgenic signaling.
5. Diagram how an aromatase inhibitor decreases estrogen signaling.
6. Compare and contrast the mechanisms of SERMs, injectable SERDs, and oral SERDs.

11.3.2 Pharmacokinetics

1. Explain the two phases of GnRH agonist therapies for prostate cancer.
2. Explain why SERM pharmacokinetics is impacted in hepatically impaired patients, but not renally impaired patients.

11.3.3 Pharmacogenomics

1. Describe the clinical biomarkers that determine treatment approaches to hormone sensitive breast cancer.

11.3.4Therapeutic Uses

1. Detail how the pathologic work-up of breast cancer determines the recommended course of treatment.
2. Describe how the consequences of prostate cancer therapy may present a barrier to patient compliance.

11.3.5 Adverse Effects and Drug Interactions

1. Describe dose-limiting toxicities of long-term corticosteroid use.
2. Explain how the use of anti-estrogens and aromatase inhibitors represent a double-edged sword in terms of benefits versus costs.

11.4 Appendix of Additional Anticancer Drugs that are Less Important During Health Professions Education		
Drug Classes and Drugs		
Adducting Agents	**Antimetabolites**	**Antibiotics**
bendamustine busulfan chlorambucil dacarbazine lurbinectedin mechlorethamine trabectedin	cladribine TAS-102 (trifluridine and tipiracil)	mitoxantrone valrubicin
Cellular & Gene Therapies	**Antibody-Drug Conjugates**	**Miscellaneous Agents**
idecabtagene vicleucel lisocabtagene maraleucel	enfortumab vedotin gemtuzumab ozogamicin inotuzumab ozogamicin polatuzumab vedotin	betamethasone ixazomib olaparib tretinoin venetoclax
Antiestrogens	**GnRH Agonists**	**Antiandrogens**
megestrol acetate	buserelin triptorelin	flutamide nilutamide

Kinase Inhibitors	Monoclonal Antibodies & Fusion Proteins
alectinib axitinib bosutinib cabozantinib ceritinib cobimetinib dabrafenib ibrutinib idelalisib lenvatinib midostaurin neratinib nilotinib osimertinib pazopanib ponatinib regorafenib ribociclib ruxolitinib trametinib tucatinib vandetanib	alemtuzumab avelumab blinatumomab daratumumab dinutuximab durvalumab elotuzumab necitumumab obinutuzumab ramucirumab ziv-aflibercept

SECTION 12

ANTIMICROBIAL PHARMACOLOGY

Katharina Brandl (section chair), Gagani Athauda, Willmann Liang, Shantanu Rao

12.1 Cell Wall Synthesis Inhibitors and Cell Membrane Active Agents			
Recommended Curriculum Equivalent: 2.0 hr			
Drug Classes and Drugs			
Cell Wall Synthesis Inhibitors			
Beta-lactams			
Penicillins	**Cephalosporins**	**Carbapenems**	**Monobactams**
AMOXICILLIN +/- CLAVULANATE AMPICILLIN +/- SULBACTAM OXACILLIN PENICILLIN G PIPERACILLIN + TAZOBACTAM dicloxacillin nafcillin penicillin V pivmecillinam	CEFEPIME CEFTAROLINE CEFTRIAXONE CEFUROXIME CEPHALEXIN Cefazolin Cefiderocol Cefotaxime Cefotetan Cefoxitin Ceftazidime Ceftobiprole	IMIPENEM + CILASTATIN MEROPENEM doripenem sulopenem	AZTREONAM
Others			
VANCOMYCIN bacitracin dalbavancin* fosfomycin teicoplanin telavancin*			
Cell Membrane Active Agents			
COLISTIN DAPTOMYCIN polymyxin B (drugs marked with * from sections above may also have cell membrane activity)			
Learning Objectives			
12.1.1 Mechanism of Action and Effects 1. Differentiate the mechanism of action of β-lactam antibiotics. 2. Explain the principle of combination of inhibitors of β-lactamase with penicillins (List such combinations). 3. Illustrate the pharmacological basis for combining imipenem with cilastatin. 4. Describe the mechanism of action of non-beta-lactam cell wall synthesis inhibitors and cell membrane active agents.			

5. Explain why certain cell wall inhibitors are effective in the treatment of methicillin-resistant staphylococcal infections and others are not.

12.1.2 Pharmacokinetics

1. Evaluate the effect of probenecid on penicillin and vancomycin elimination.
2. Describe the role of repository penicillins.
3. Justify the use of imipenem with cilastatin.
4. Justify the use of intravenous versus oral vancomycin in the treatment of systemic infections.

12.1.3 Therapeutic Uses

1. Compare the anti-bacterial spectrum and uses of different beta-lactams.
2. Differentiate the five generations of cephalosporins with specific examples. Compare and contrast the differences in their antimicrobial spectrum.
3. Discuss the uses of vancomycin in anthrax, clostridial, corynebacterial, enterococcal, pneumococcal, staphylococcal, and streptococcal infections.
4. Discuss the uses of different cephalosporins in either gram-positive or gram-negative infections.
5. Describe the use of topical bacitracin in gram-positive infections.
6. Describe the uses of fosfomycin, pivmecillinam and sulopenem in urinary tract infections.
7. Explain the role of the carbapenem class of antibacterial agents (imipenem, meropenem) in serious systemic bacterial infections.

12.1.4 Adverse Effects and Contraindications

1. Identify common and life-threatening adverse effects of the drugs listed above.
2. Examine the terms superinfection and cross-hypersensitivity.

12.2 Protein Synthesis Inhibitors		
Recommended Curriculum Equivalent: 1.5 hr		
Drug Classes and Drugs		
Aminoglycosides	**Macrolides**	**Streptogramins**
GENTAMICIN amikacin neomycin streptomycin tobramycin	AZITHROMYCIN CLARITHROMYCIN ERYTHROMYCIN	QUINUPRISTIN / DALFOPRISTIN
Lincosamides	**Oxazolidinones**	**Tetracyclines**
CLINDAMYCIN	LINEZOLID tedizolid	DOXYCYCLINE TIGECYCLINE minocycline tetracycline
Others		
MUPIROCIN chloramphenicol		
Learning Objectives		
12.2.1 Mechanism of Action and Effects 1. Illustrate the mechanism of action of each class of protein synthesis inhibitors. 2. Evaluate the mechanism of acquired drug resistance to aminoglycosides, tetracyclines, and macrolides. 3. Justify the rational basis for combination therapy with an aminoglycoside and a penicillin, cephalosporin, or vancomycin.		
12.2.2 Pharmacokinetics 1. Outline the pharmacokinetic properties of each class of protein synthesis inhibitors, including their routes of administration. 2. Illustrate the importance of peak and trough levels of aminoglycosides. 3. Inspect the need of and examine the method of dose adjustment for aminoglycosides in patients with compromised renal function.		
12.2.3 Therapeutic Uses 1. Compare and contrast the antibacterial spectrum and uses of different protein synthesis inhibitors. 2. Discuss the therapeutic options for treating skin and soft tissue infections, and systemic infections due to methicillin-resistant or vancomycin-resistant bacteria. 3. Evaluate the uses of tetracyclines in the treatment of Rickettsial infections and Lyme disease. 4. Justify the uses of macrolides and tetracyclines in the treatment of *Chlamydia* infections. 5. Analyze the topical uses of mupirocin.		

12.2.4 Adverse Effects and Drug Interactions

1. Identify common and serious adverse effects of the drugs listed above, e.g. aminoglycoside-associated ototoxicity and nephrotoxicity, tetracycline-associated phototoxicity and effects on calcified tissues, and chloramphenicol-associated gray baby syndrome and aplastic anemia.
2. Analyze the major drug interactions of macrolides due to inhibition of cytochrome P450 enzymes.
3. Assess the MAO inhibitory activity of linezolid.

12.3 Inhibitors of Nucleic Acid Synthesis	
Recommended Curriculum Equivalent: 1.0 hr	
Drug Classes and Drugs	
Fluoroquinolones	**RNA Polymerase Inhibitors**
CIPROFLOXACIN LEVOFLOXACIN gemifloxacin moxifloxacin	FIDAXOMICIN RIFAMPIN rifaximin
Nitroimidazole	**Folate Synthesis Inhibitors**
METRONIDAZOLE	COTRIMOXAZOLE (Trimethoprim-Sulfamethoxazole) [TMP-SMX]
Others	
NITROFURANTOIN gepotidacin zoliflodacin	
Learning Objectives	
12.3.1 Mechanism of Action and Effects 1. Illustrate the mechanism of action of each class of antibiotics. 2. Evaluate the synergistic inhibition due to sequential blockade with cotrimoxazole.	
12.3.2 Pharmacokinetics 1. Evaluate the pharmacokinetics properties of each class of antibiotics. 2. Analyze the drug interactions of fluoroquinolones, including the effect of ingested cations on drug absorption.	
12.3.3 Therapeutic Uses 1. Compare and contrast the advantages of more recently developed fluoroquinolones over ciprofloxacin. 2. Illustrate the major therapeutic indications of cotrimoxazole. 3. Analyze the emergence of microbial resistance to cotrimoxazole and fluoroquinolone drugs, and its implications for the treatment of urinary tract infections. 4. Compare the role of fidaxomicin (preferred first-line), vancomycin (alternative), and metronidazole (no longer first-line) in the treatment of *Clostridioides difficile* infections.	
12.3.4 Adverse Effects and Drug Interactions 1. Identify common and serious adverse effects of the antimicrobial agents listed above, e.g. cotrimoxazole-associated Stevens-Johnson syndrome, fluoroquinolone-associated tendon rupture, QT prolongation, CNS effects. 2. Analyze the strong enzyme induction effects of rifampin (CYP3A4), including reduced efficacy of oral contraceptives, antiretrovirals, and immunosuppressive drugs.	

12.4 Antimycobacterial Drugs
Recommended Curriculum Equivalent: 1.0 hr
Drugs
DAPSONE ETHAMBUTOL ISONIAZID PYRAZINAMIDE RIFABUTIN RIFAMPIN RIFAPENTINE amikacin azithromycin clarithromycin clofazimine cycloserine levofloxacin moxifloxacin streptomycin thalidomide
Learning Objectives
12.4.3 Mechanism of Action and Effects 1. Outline first-line antitubercular agents (RIPE therapy: isoniazid, rifampin, pyrazinamide, ethambutol) and summarize their mechanisms of action, spectrum of activity, and major adverse effects. 2. Outline the plan of tuberculosis treatment, including the intensive phase (four-drug therapy) and continuation phase (two-drug therapy), and assess the rationale for combination therapy to prevent resistance and improve efficacy. 3. Inspect the relationship between bacterial metabolic states (actively replicating vs dormant organisms) and the activity of specific antitubercular drugs.
12.4.4 Pharmacokinetics 1. Outline the pharmacokinetic profile of isoniazid and rifampin. 2. Analyze the impact of *N*-Acetyl Transferase in terms of therapeutic efficacy and occurrence of adverse effects of isoniazid.
12.4.5 Therapeutic Uses 1. Categorize treatment regimens for latent and active tuberculosis, including duration and drug selection. 2. Investigate the pharmacologic approach to drug-resistant tuberculosis, including use of second line and newer agents (e.g., bedaquiline, linezolid). 3. Explain mechanisms of resistance in *Mycobacterium tuberculosis* and their clinical implications. 4. Describe the role of directly observed therapy (DOT) in improving treatment adherence and outcomes of non-tuberculous mycobacterial infections (e.g., *Mycobacterium avium* complex).

5. Summarize the drugs used in the treatment of leprosy and their mechanism of action.
6. Categorize the drugs used for reversing the lepra reactions and the erythema nodosum leprosum reaction.
7. Explain the WHO regimen for treatment of leprosy.

12.4.6 Adverse Effects and Drug Interactions

1. Assess the adverse effects of isoniazid, rifampin, ethambutol and pyrazinamide.
2. Outline the drug interactions of rifampin with anticoagulants and other drugs, such as oral contraceptives. Inspect the hematologic adverse effects of dapsone.
3. Examine the teratogenic effects of thalidomide.
4. Examine key pharmacokinetic and clinical considerations in tuberculosis therapy, including tissue penetration (e.g., CNS penetration), drug–drug interactions, and monitoring of treatment response.
5. Investigate variability in isoniazid metabolism (fast vs slow acetylators) and its clinical implications.

12.4.6 Notes

Clinical Guidelines

- https://www.cdc.gov/tb/treatment/index.html

12.5 Antiparasitic Drugs
Recommended Curriculum Equivalent: 1.0 hr
Drugs
ALBENDAZOLE IVERMECTIN METRONIDAZOLE PRAZIQUANTEL atovaquone iodoquinol mebendazole nitazoxanide paromomycin pyrantel pamoate tinidazole
Learning Objectives
12.5.1 Mechanism of Action and Effects 1. Differentiate the mechanisms of action of the different antiparasitic drugs.
12.5.2 Therapeutic Uses 1. Assess the preferred therapeutic agents for helminth infections. 2. Examine the broad-spectrum anthelmintic drugs. 3. Outline the opportunistic parasitic infections commonly known to occur in HIV/AIDS patients and summarize the drugs used for their treatment. 4. Categorize the drugs used to treat amebiasis (differentiate between the treatment regimen for asymptomatic versus intestinal/extraintestinal disease), giardiasis, trypanosomiasis, and leishmaniasis.

12.6 Antimalarial drugs
Recommended Curriculum Equivalent: 1.0 hr
Drugs
ATOVAQUONE/PROGUANIL ARTESUNATE ARTEMETHER/LUMEFANTRINE CHLOROQUINE DOXYCYCLINE MEFLOQUINE PRIMAQUINE QUININE
Learning Objectives
12.6.1 Mechanism of Action and Effects 1. Examine the targets of the antimalarial drugs in the life cycle of malarial parasites. 2. Differentiate the mechanisms of action of the various antimalarial drugs. 3. Analyze the genetic and biochemical bases for chloroquine resistance in malaria parasites.
12.6.2 Pharmacokinetics 1. Examine the pharmacokinetic properties of chloroquine and relate it to the selection of malarial treatment regimens. 2. Apply the pharmacokinetic properties and metabolism of artesunate and artemether in making therapeutic decisions.
12.6.3 Therapeutic Uses 1. Propose the treatment of choice for uncomplicated illness and severe illness due to *P. vivax, P. ovale, P. malariae* and *P. falciparum*. 2. Compare and contrast the prophylaxis and treatment of *P. vivax, P. ovale, P. malariae,* and *P. falciparum*. 3. Outline the therapeutic indications for artemisinin derivatives.
12.6.4 Adverse Effects and Drug Interactions 1. Explain the mechanism of hemolytic anemia induced by primaquine in G6PD deficient patients. 2. Describe cinchonism and the drugs that cause it. 3. Summarize the toxic effects of chloroquine and other antimalarial agents. 4. Analyze the implications of drug interactions in patients with malaria and concurrent HIV infection due to polypharmacy and effects especially on CYP3A4 activity.

12.7 Antifungal Drugs
Recommended Curriculum Equivalent: 1.0 hr
Drugs
AMPHOTERICIN B CASPOFUNGIN FLUCONAZOLE ITRACONAZOLE VORICONAZOLE flucytosine ketoconazole micafungin nystatin posaconazole terbinafine sulfamethoxazole-trimethoprim (cotrimoxazole)
Learning Objectives
12.7.1 Mechanism of Action and Effects 1. Compare and contrast the mechanism of action of each class of antifungal drugs.
12.7.2 Pharmacokinetics 1. Outline the pharmacokinetic properties of the various antifungal drugs.
12.7.3 Therapeutic Uses 1. Assess the major therapeutic indications of the antifungal drugs, including current recommendations for treating aspergillosis, blastomycosis, superficial and systemic candidiasis, coccidioidomycosis, cryptococcosis, histoplasmosis and mucormycosis. 2. Justify the use of trimethoprim-sulfamethoxazole in the treatment of *Pneumocystis jirovecii* infections. 3. Evaluate optimal treatment durations for fungal infections and assess the role of surgical debridement in the management of subcutaneous mycoses. 4. Examine the host factors that predispose patients to fungal infections. 5. Differentiate the azole antifungal drugs according to the route of administration. 6. Discuss the advantages of liposomal preparations of amphotericin B in the treatment of fungal infections.
12.7.4 Adverse Effects and Drug Interactions 1. Examine and outline the important adverse effects of the various antifungal drugs. 2. Analyze the implications of interactions of antifungal agents with CYP450.

12.8 Antiviral Drugs
Recommended Curriculum Equivalent: 1.0 hr
Drugs
ACYCLOVIR ENTECAVIR FOSCARNET GANCICLOVIR NIRMATRELVIR-RITONAVIR OSELTAMIVIR PEGYLATED INTERFERON ALFA REMDESIVIR RIBAVIRIN TENOFOVIR amantadine cidofovir famciclovir glecaprevir ledipasvir pibrentasvir sofosbuvir valacyclovir valganciclovir velpatasvir zanamivir
Learning Objectives
12.8.1 Mechanism of Action and Effects 1. Arrange antiviral drugs based on their site of action in the viral replication cycle. 2. Compare and contrast the mechanisms of action of major antiviral drug classes, including nucleoside analogs, neuraminidase inhibitors, protease inhibitors, and polymerase inhibitors, and relate these mechanisms to viral targets and selectivity. 3. Infer how viral enzyme specificity (e.g., viral thymidine kinase) contributes to selective toxicity of antiviral drugs.
12.8.2 Pharmacokinetics 1. Assess how pharmacokinetic properties (e.g., bioavailability, renal elimination, tissue penetration) of acyclovir, valacyclovir, ganciclovir, and valganciclovir. 2. Apply the knowledge of pharmacokinetics of these agents in selecting route of administration and drug selection in antiviral therapy.
12.8.3 Therapeutic Uses 1. Describe major therapeutic indications for antiviral drugs based on viral pathogen (e.g., HSV, CMV, influenza, hepatitis viruses, SARS-CoV-2).

2. Compare antiviral regimens used for treatment and prevention of common viral infections (e.g., HSV, CMV, influenza). 3. Assess the role of combination antiviral therapy in chronic viral infections (e.g., hepatitis B, hepatitis C). 4. Illustrate the mechanism of antiviral resistance and their clinical implications. 5. Outline the clinical use of nirmatrelvir-ritonavir (oral, early outpatient treatment) and remdesivir (IV, hospitalized or high-risk patients).
12.8.4 Adverse Effects 1. List the adverse effects and therapeutic complications of antiviral drugs. 2. Relate major toxicities to drug mechanisms and organ-specific accumulation (e.g., nephrotoxicity with renally cleared agents, bone marrow suppression with nucleoside analogs). 3. Inspect potential drug interactions for antiviral drugs. 4. Explain how major drug interaction related to antiviral agents (especially CYP3A4 inhibition by ritonavir) influence the selection of antiviral agents for combination therapy.

12.9 Anti-HIV Drugs	
Recommended Curriculum Equivalent: 1.0 hr	
Drugs Classes and Drugs	
Nucleoside Reverse Transcriptase Inhibitors (NRTI)	**Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)**
ABACAVIR (ABC) LAMIVUDINE (3-TC) TENOFOVIR DISOPROXIL (TDF) ZIDOVUDINE (AZT) EMTRICITABINE (FTC) didanosine stavudine	EFAVIRENZ (EFV) NEVIRAPINE (NVP)
HIV-1 Protease Inhibitors	**Fusion Inhibitors**
ATAZANAVIR (ATV) RITONAVIR (RTV) darunavir indinavir lopinavir nelfinavir saquinavir	ENFUVIRTIDE MARAVIROC
Integrase Strand Transfer Inhibitors (INSTIs)	
DOLUTEGRAVIR bictegravir raltegravir	
Learning Objectives	
12.9.1 Mechanism of Action and Effects 1. Classify anti-HIV drugs based on their site of inhibition in the HIV replication cycle (entry, reverse transcription, integration, and maturation). 2. Explain the mechanisms of action of major antiretroviral drug classes (NRTIs, NNRTIs, INSTIs, protease inhibitors, and entry inhibitors) and relate each class to its viral target. 3. Compare and contrast the mechanisms of action of NRTIs and NNRTIs. 4. Compare and contrast the mechanism of action of NRTIs and NNRTIs. 5. Explain the importance of performing a tropism assay before use of maraviroc-containing regimen.	
12.9.2 Pharmacokinetics 1. Explain how pharmacokinetic boosting (e.g., ritonavir, cobicistat) increases drug levels and contributes to significant drug–drug interactions.	

12.9.3 Pharmacogenomics

1. Analyze the clinical implications of HLA-B*5701 testing before use of abacavir-containing regimen.

12.9.4 Adverse effects and Drug Interactions

1. Categorize major class-specific adverse effects of antiretroviral drugs (e.g., mitochondrial toxicity with NRTIs, CNS effects with NNRTIs, metabolic effects with protease inhibitors).
2. Assess the major drug interactions of anti-HIV drugs, with emphasis on interactions involving inhibition or induction of cytochrome P450 enzymes.

12.9.5 Therapeutic Uses

1. Categorize currently preferred HIV regimens, including integrase inhibitor-based combinations (e.g., bictegravir- or dolutegravir-based regimens), and the use of two-drug regimens and long-acting injectable therapies.
2. Explain the rationale for combination antiretroviral therapy, including prevention of resistance and targeting multiple stages of the HIV lifecycle.
3. Assess the rationale and components of once-a-day formulations for treating HIV infections.
4. Examine the use of drugs for pre-exposure prophylaxis (PrEP) and post-exposure prophylaxis (PEP)

12.9.6 Notes

Clinical Guidelines

- CDC guidelines on the management of HIV infection: https://www.cdc.gov/hivnexus/hcp/guidelines/index.html
- American Academy of HIV Medicine: https://aahivm.org/hiv-treatment-guidelines/

SECTION 13

IMMUNOPHARMACOLOGY

Carolina Restini (section chair), Pamela E. Potter, Israel Castillo Gonzalez, Patrick Murphy

13.1 Anti-inflammatory Agents (Excluding Corticosteroids)	
Recommended Curriculum Equivalent: 2.0 hr	
Drug Classes and Drugs	
Salicylates	**COX 1 And 2 Inhibitors**
ACETYLSALICYLIC ACID MESALAMINE SULFASALAZINE	DICLOFENAC IBUPROFEN KETOROLAC MELOXICAM NAPROXEN indomethacin
COX 2 Inhibitor	**Leukotriene Modifiers**
CELECOXIB	MONTELUKAST ZAFIRLUKAST ZILEUTON
Learning Objectives	
13.1.1 Mechanism of Action and Effects 1. Analyze the role of eicosanoid pathways (prostaglandins, thromboxane, leukotrienes) in mediating inflammation, pain, fever, platelet aggregation, and bronchoconstriction to correlate with the targets for the drugs. 2. Differentiate the molecular targets of salicylates, nonselective COX inhibitors, COX-2 selective inhibitors, and leukotriene modifiers. 3. Predict downstream physiological and clinical consequences resulting from selective versus nonselective COX inhibition. 4. Explain how eicosanoid physiology and pathway disruption alter inflammatory responses across organ systems (e.g., gastrointestinal tract, kidney, lung, cardiovascular system) to predict how drugs affect those systems. 5. Delineate the pharmacologic interventions in eicosanoid pathways in the management of pain, inflammation, cardiovascular/pulmonary disorders, and reproduction.	
13.1.2 Pharmacokinetics 1. Specify key pharmacokinetic parameters of agents within a drug class, including the routes of administration, in relation to differential treatment paradigms. 2. Apply pharmacokinetic principles (absorption, distribution, metabolism, elimination, route of administration) to select appropriate anti-inflammatory agents for specific clinical contexts. 3. Analyze how dosing, duration of therapy, and formulation influence therapeutic outcomes and toxicity risk.	
13.1.3 Therapeutic Uses 1. Identify the use of a particular anti-inflammatory class/agent in the treatment of organ-specific inflammatory disorders. 2. Justify the selection of specific anti-inflammatory drug classes or agents for the management of organ-specific inflammatory conditions (e.g., arthritis, inflammatory bowel disease, asthma). 3. Integrate mechanistic, pharmacokinetic, and safety considerations to optimize anti-inflammatory therapy in clinical decision-making.	

13.1.4 Adverse Effects, Contraindications, and Drug Interactions

1. List the major acute and chronic toxicities associated with each agent and/or class.
2. Analyze patient-specific risk factors that predispose to NSAID-associated toxicities (e.g., gastrointestinal bleeding, renal dysfunction, cardiovascular risk).
3. Identify patient populations in which these agents should not be used.
4. Identify organ-specific toxicities (e.g., GI ulceration) elicited by these agents.
5. Compare and contrast therapeutic and adverse effects of anti-inflammatory agents on gastrointestinal, renal, cardiovascular, pulmonary, and reproductive systems.
6. Evaluate how COX selectivity influences efficacy and toxicity in organ-specific inflammatory disorders.

13.2 Corticosteroids		
Recommended Curriculum Equivalent: 1.0 hr		
Drug Classes and Drugs		
Glucocorticoids	**Corticosteroid Synthesis Inhibitors**	**Corticosteroid Receptor Antagonists**
BECLOMETHASONE CORTISONE AND DEXAMETHASONE HYDROCORTISONE METHYLPREDNISOLONE PREDNISONE TRIAMCINOLONE	KETOCONAZOLE	MIFEPRISTONE SPIRONOLACTONE eplerenone finerenone

Learning Objectives

13.2.1 Mechanism of Action and Effects

1. Recognize the glucocorticoid biosynthetic pathway as a target for corticosteroid synthesis inhibitors.
2. Describe the regulation of corticosteroid synthesis by ACTH and feedback inhibition.
3. Explain the molecular mechanism of action of agonists and antagonists in each drug class.
4. Recognize receptor-independent effects via 11-beta-steroid hydroxylase on corticosteroid specificity.
5. Differentiate genomic and non-genomic mechanisms of action of corticosteroid agonists and antagonists.
6. Analyze how receptor specificity and enzyme modulation (e.g., 11β-hydroxysteroid dehydrogenase) influence corticosteroid activity and tissue selectivity.
7. Compare the cellular/molecular mechanisms of action of endogenous corticosteroids vs synthetic corticosteroids and describe their effect on intermediary metabolism, growth, electrolyte homeostasis, immune and inflammatory responses, and stress responses.
8. Discuss endogenous versus synthetic glucocorticoids with respect to potency, duration of action, and route-dependent effects
9. Discuss the importance of synthetic glucocorticoids, especially those modifications that enhance pharmacodynamic activity and/or determine activity based on route of administration.

13.2.2 Pharmacokinetics

1. Describe the significance of corticosteroid disposition (protein binding, biotransformation, enzyme induction) that may necessitate changes in dosage regimens and routes of administration.
2. Apply principles of protein binding, hepatic biotransformation, enzyme induction/inhibition, and route of administration to adjust corticosteroid dosing regimens.
3. Predict how altered hepatic function or drug interactions modify corticosteroid exposure and clinical response.
4. Discuss PK of prednisone activation to identify populations at risk for reduced efficacy (e.g., severe liver disease). e.g., prednisone is a prodrug and may be poorly activated in patients with severe liver disease

13.2.3 Therapeutic Uses

1. Analyze the physiological basis for gradual tapering following chronic glucocorticoid therapy.
2. Explain the rationale for corticosteroid use in replacement therapy, as anti-inflammatory and immunosuppressive agents, and as diagnostic agents in hypothalamic-pituitary adrenocortical disease/dysfunction.
3. Explain the rationale for slow withdrawal following chronic therapy with glucocorticoids.
4. Apply mechanistic reasoning for clinical indications to select the different drugs in each class (example: a) rationale for spironolactone in treating primary hyperaldosteronism; b) roles of mifepristone in managing the symptoms associated with Cushing syndrome).

13.2.4 Adverse Effects, Drug Interactions, and Contraindications

1. List the adverse effects/contraindications related to corticosteroid use.
2. Differentiate adverse effects associated with short-term versus chronic corticosteroid therapy.
3. Evaluate patient-specific contraindications and risk-mitigation strategies when prescribing corticosteroids.
4. Analyze ketoconazole-mediated CYP3A4 and P-glycoprotein inhibition to anticipate clinically significant drug interactions. Apply the example of Ketoconazole, as a potent inhibitor of both CYP3A4 and P-glycoprotein, to discuss safety and monitoring patients receiving other drug therapies that are modulated by this transporter (P-gp) and drug metabolizing enzyme (3A4).

13.3 Cytotoxic Agents		
Recommended Curriculum Equivalent: 0.5 hr		
Drug Classes and Drugs		
Antimetabolites	**Inhibitors of Purine Synthesis**	**Alkylating Nitrogen Mustards**
AZATHIOPRINE METHOTREXATE	MYCOPHENOLATE MOFETIL	CYCLOPHOSPHAMIDE

Learning Objectives

13.3.1 Mechanism of Action and Effects

1. Analyze the role of inappropriate immune cell function and dysregulation of the immune system leading to chronic inflammation, organ transplant rejection, and organ-specific diseases such as IBD, psoriasis, and rheumatic diseases.
2. Distinguish the mechanism of action of each drug class and the differential target of each agent in mediating immunosuppression and inhibiting lymphocyte proliferation and function.
3. Compare and contrast the actions(s) of each drug class on specific aspects of immune cell function leading to immunosuppression.

13.3.2 Pharmacokinetics

1. Specify key pharmacokinetic parameters of each of these agents, including the route of administration, in relation to differential treatment paradigms.
2. Explain metabolic steps leading to drug activation, if applicable.
3. Identify pathways for metabolism and elimination that may result in toxicity in liver or kidney disease.

13.3.3 Therapeutic Uses

1. Identify the most appropriate pharmacotherapeutic agent for treatment of organ-specific inflammatory disorders
2. Explain the use of appropriate pharmacotherapeutic agents for prevention of organ transplant rejection.
3. Identify which agents can be used for rescue organ transplants.

13.3.4 Adverse Effects, Drug Interactions, and Contraindications

1. List the major acute and chronic toxicities associated with each agent/class.
2. Explain patient-specific contraindications to use of each drug class or specific agent.
3. Identify specific organ toxicities for each of the drugs.
4. Discuss the concern of increased risk of infection.
5. Identify agents considered teratogenic that are contraindicated in pregnancy.

13.4 Cytokine Modulators And Inhibitors		
Recommended Curriculum Equivalent: 2 hrs.		
Drug Classes and Drugs		
Cytokine Modulators	**Interleukin Inhibitors**	
INTERFERON α, β, γ	BASILIXIMAB BENRALIZUMAB TOCILIZUMAB anakinra ustekinumab	
Janus Kinase Inhibitors	**MTOR Inhibitors**	**TNF-alpha Inhibitors**
TOFACITINIB	SIROLIMUS everolimus	ADALIMUMAB ETANERCEPT INFLIXIMAB certolizumab golimumab thalidomide
Learning Objectives		
13.4.1 Mechanism of Action and Effects 1. Analyze the role of cytokines in stimulating or suppressing the immune response and dysregulation of cytokine secretion and immune cell function in the setting of viral infection, specific autoimmune disorders, and organ transplant rejection. 2. Distinguish the effect of specific agents on their specific physiological targets. 3. Explain how these interactions attenuate an exaggerated organ-specific inflammatory response, regulate T-cell activation and phagocyte activation, and induce downregulation of viral/bacterial protein synthesis. 4. Compare and contrast the actions(s) of each drug class/agent in modulating the immune system resulting in either activation of immune cell function (interferons) or immunosuppression. 5. Identify drugs acting to suppress activation of T-cells versus those suppressing other activators of immune function or inflammation.		
13.4.2 Pharmacokinetics 1. Specify key pharmacokinetic parameters of agents within a drug class, including the route of administration and duration of action. 2. Identify factors affecting absorption and metabolism of drugs with narrow therapeutic ranges, and possible routes for drug interactions arising from pharmacokinetics.		
13.4.3 Therapeutic Uses 1. Apply knowledge of the mechanism of each agent in predicting its use in the treatment of immune disorders. 2. Identify drugs used for prevention of organ transplant rejection. 3. Detail the use of TNFα inhibitors and JAK inhibitors in treating musculoskeletal rheumatic diseases and inflammatory bowel disease. 4. Discuss the use of interleukin inhibitors in musculoskeletal dermatologic and rheumatic diseases		

and arteritis. 5. Identify clinical uses of each type of interferon.
13.4.4 Adverse Effects, Drug Interactions, and Contraindications 1. List the major acute and chronic toxicities associated with each class/agent, and the contraindications associated with each drug class or specific agent. 2. Identify agents contraindicated in pregnancy 3. Identify underlying disease states which would necessitate alternative therapy 4. Analyze the risk-benefit ratios for drugs with the potential to develop/reactivate neoplasm or infectious diseases in patients treated with these agents. 5. Identify organ-specific toxicities elicited by these agents. 6. Formulate a plan for management of potential severe reactions resulting from treatment with these agents.

13.5 Drugs Inhibiting T-Cells		
Recommended Curriculum Equivalent: 0.5 hr		
Drug Classes and Drugs		
Calcineurin Inhibitors	**Co-stimulation Inhibitors**	**Immunoglobulins**
CYCLOSPORINE TACROLIMUS	BELATACEPT ALEMTUZUMAB	antithymocyte globulin (ATG)

Learning Objectives

13.5.1 Mechanism of Action and Effects

1. Describe the physiology of T-cell activation, including the role of calcineurin and co-stimulation receptors.
2. Elaborate on the result of selective blockade of T-cell activation by inhibiting calcineurin.
3. Explain how the co-stimulation receptors can be used to deplete T-cells.
4. Describe the mechanism of action of the drugs on activation, proliferation, or depletion of T-cells.
5. Analyze the effects of each drug on various types of blood cells, joints, CNS, and heart.

13.5.2 Pharmacokinetics

1. Identify factors that can affect metabolism and elimination, in particular the metabolic pathway for calcineurin inhibitors with a very narrow therapeutic range.
2. Discuss the requirement for individualized dosing of these drugs to the trough level.
3. Describe how the presence of absence of food can affect the level of calcineurin inhibitors.

13.5.3 Therapeutic Uses

1. Describe the therapeutic applications for drugs which deplete of T-cells.
2. Identify which drugs are used for preventing or rescuing organ transplant or for stem cell transplant.
3. Explain why belatacept is only used in patients who are Epstein-Barr positive.

13.5.4 Adverse Effects, Drug Interaction, and Contraindications

1. Elucidate the risk of serious infections in patients receiving these drugs and consider the need for prophylaxis against common opportunistic infections such as cytomegalovirus, herpes, and *P. jirovecii*.
2. Describe the risk of inducing leukopenia, lymphopenia or other malignancies with use of these drugs.
3. Recognize the risk of infusion reactions and serious hypersensitivity reactions with ATG and alemtuzumab.

13.6 Immune Checkpoint Inhibitors And T-Cell-Redirecting Agents			
Recommended Curriculum Equivalent: 0.5 hr			
Drug Classes and Drugs			
Anti-CTLA-4 Antibodies	**Anti-PD1/PD-L1 Antibodies**	**LAG-3 Inhibitors**	**CD3-Directed Bispecific Antibodies**
IPILIMUMAB	PEMBROLIZUMAB atezolizumab cemiplimab durvalumab nivolumab	relatlimab	EPCORITAMAB blinatumomab mosunetuzumab

Learning Objectives

13.6.1 Mechanism of Action and Effects

1. Compare and contrast the mechanisms of action and downstream immunologic effects of CTLA-4 inhibitors, PD-1/PD-L1 inhibitors, LAG-3 inhibitors, and bispecific T-cell engagers.
2. Identify their molecular targets and describe how their site of action (i.e., lymph node vs peripheral tissue vs tumor microenvironment) influences therapeutic efficacy, peripheral tolerance, and adverse drug effects.

13.6.2 Pharmacokinetics

1. Describe the pharmacokinetic properties of monoclonal antibody therapeutics, including route of administration, half-life, catabolism via reticuloendothelial pathways, and implications for dosing schedules and delayed toxicity.

13.6.3 Therapeutic Uses

1. Contrast the use of immune checkpoint inhibitors and T-cell-redirecting therapies in solid tumors versus hematologic malignancies.
2. Identify common clinical scenarios in which non-oncologists may encounter patients receiving these agents.

13.6.4 Adverse Effects, Contraindications, and Drug Interactions

1. Differentiate immune-related adverse events from conventional chemotherapy toxicities, including life-threatening complications and common immune-related toxicities affecting the skin, gastrointestinal tract, endocrine organs, liver, lungs, and heart.
2. Outline the stepwise management of immune-mediated reactions, including the use of corticosteroids, immunosuppressive agents, and drug discontinuation.
3. Discuss the management of potential severe reactions due to over-activation of the immune system (e.g., apply knowledge of immune checkpoint inhibition to evaluating a patient on immunotherapy who presents with diarrhea, dyspnea, fatigue, rash, or chest pain).

13.7 Miscellaneous Agents		
Recommended Curriculum Equivalent: 1.0 hr		
Drug Classes and Drugs		
Immune Globulin Intravenous	**Anti-integrin Antibodies**	**Toll-like Receptor Activators**
IGIV	NATALIZUMAB VEDOLIZUMAB	IMIQUIMOD
CTLA-4-Ig	**B Cell Depletion**	**Immunizing Agents**
ABATACEPT BELATACEPT	ocrelizumab	rho(D) immune globulin
Anti-IL-17	**Anti-IL-23**	**Anti IL-12/IL-23**
brodalumab ixekizumab secukinumab	brodalumab ixekizumab secukinumab	ustekinumab

Learning Objectives

13.7.1 Mechanism of Action and Effects

1. Distinguish mechanisms of action for each drug class and resulting immunologic effects of each drug class (e.g., anti-LFA-3, anti-IL-17, anti-IL-23, anti-integrin, CTLA-4-Ig, TLR activators, B-cell depletion, immunizing agent, and Toll-like receptor activator).
2. Discuss the mechanisms by which intravenous immune globulin (IGIV) modulates immune function and explain its resulting immunologic and therapeutic effects in different pathological states, including autoimmune, inflammatory, and immunodeficiency disorders.
3. Compare the pathophysiologic pathway targeted by these agents and the immunologic and therapeutic effects in diseases such as psoriasis, Crohn's disease, genital warts, myeloma, multiple sclerosis, and autoimmune disorders.
4. Illustrate how drug-induced modulation of specific immune pathways alters cellular and humoral immune responses and contributes to disease improvement or immune suppression at the cellular level.

13.7.2 Pharmacokinetics

1. Specify key pharmacokinetic parameters of agents within a drug class, including the route of administration, catabolism and elimination.
2. Interpret PK profiles to justify dosing intervals and therapeutic choices (e.g., monoclonal antibodies vs IVIG).

13.7.3 Therapeutic Uses

1. Delineate pharmacologic treatment options for organ-specific immune-
2. mediated disorders (e.g., psoriasis, MS, Crohn's disease).
3. Apply guideline-based principles to select appropriate therapy for a given clinical scenario.

13.7.4 Adverse Effects, Drug Interactions, and Contraindications

1. List the major acute and chronic toxicity associated with each agent and/or class such as infusion reaction and immune-related adverse events.
2. List major acute and chronic toxicities (e.g., infusion reactions, immune-related adverse events).

3. Evaluate clinically significant drug interactions and contraindications for each class.
4. Develop strategies to mitigate infusion-related hypersensitivity reactions.

13.8 Drugs for the Treatment of Rheumatic Diseases		
Recommended Curriculum Equivalent: 1.0 hr		
Drug Classes and Drugs		
DMARDS (Disease Modifying Antirheumatic Drugs)		
Biologics (TNF Inhibitors & Non-TNF Inhibitors)	**JAK Inhibitors**	**Conventional Therapies**
ADALIMUMAB ETANERCEPT RITUXIMAB abatacept certolizumab golimumab infliximab sarilumab tocilizumab	TOFACITINIB baricitinib filgotinib upadacitinib	METHOTREXATE hydroxychloroquine leflunomide sulfasalazine
Adjunct Therapies		
CELECOXIB IBUPROFEN glucocorticoids		
Learning Objectives		
13.8.1 Mechanism of Action and Effects 1. Explain the molecular mechanism of action common to all nonsteroidal anti-inflammatory drugs (NSAIDs) and the resulting pharmacologic effects on prostaglandin synthesis, inflammation, pain, and fever. 2. Describe the mechanisms of action of conventional and targeted DMARDs and relate their therapeutic targets to the pathophysiologic processes involved in rheumatoid arthritis, including chronic synovial inflammation, pannus formation, and joint destruction. 3. Correlate the roles of inflammatory mediators, particularly TNF-α and IL-6, in rheumatoid arthritis pathogenesis with the mechanisms and therapeutic effects of biologic and targeted DMARD therapies. 4. Analyze how modulation of immune pathways by DMARDs and biologic agents influence autoantibody-mediated disease processes, including those involving rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA), and their effects on disease progression and joint damage. 5. Illustrate how biologic DMARD therapies modulate immune pathways and the resulting effects on cytokine production, immune cell activity, immune-mediated inflammation, and clinical outcomes in autoimmune diseases. 6. Differentiate reference biologic DMARDs from biosimilars and explain how biosimilars achieve comparable mechanisms of action, immunologic effects, therapeutic outcomes, and safety profiles in the treatment of rheumatoid arthritis and other immune-mediated diseases.		
13.8.2 Pharmacokinetics 1. Recognize the delayed onset of action of DMARDs and relate this pharmacokinetic characteristic to the clinical management of rheumatoid arthritis,		

including early treatment initiation, individualized therapy, and the use of NSAIDs or low-dose corticosteroids as bridging therapy.
13.8.3 Therapeutic Uses 1. Justify the role of DMARDs in the management of rheumatic diseases considering their pathophysiology. 2. List the other inflammatory conditions for which DMARDs have demonstrated utility.
13.8.4 Adverse Effects, Drug Interactions, and Contraindications 1. Describe the main adverse effects of the drugs of each class. 2. Describe the clinically important drug interactions of the drugs of each class. 3. Describe the principal contraindications or precautions of the drugs of each class. 4. Identify the agents contraindicated in pregnant patients and those with preexisting liver disease. 5. Identify the symptoms of the rituximab hypersensitivity reaction, discuss the underlying pathology, and develop a plan to treat the patient undergoing this reaction.

13.9 Drugs Used for Treatment of Multiple Sclerosis		
Recommended Curriculum Equivalent: 0.25 hr		
Drug Classes and Drugs		
Monoclonal Antibodies	**Pyrimidine Synthesis Inhibitor**	**Class II MHC Suppression**
NATALIZUMAB OCRELIZUMAB alemtuzumab	leflunomide teriflunomide	interferon-beta 1a

MBP Decoy	Anti-inflammatory
glatiramer	dimethyl fumarate fingolimod

Learning Objectives

13.9.1 Mechanism of Action and effects

1. Discuss the pathology involved in myelin destruction in multiple sclerosis and targets where it can be reduced
2. Differentiate the mechanism of action of each drug class.
3. Elucidate the effects of each drug on the immune system and/or on myelin with respect to efficacy in suppressing inflammation and demyelination.

13.9.2 Pharmacokinetics

1. Identify routes of administration and factors affecting metabolism and elimination for each drug.

13.9.3 Therapeutic uses

1. Identify drugs of first choice based on effectiveness and minimal serious side effects.
2. Describe patient characteristics that would affect the choice of drug to be used.

13.9.4 Adverse Effects, Drug Interactions, and Contraindications

1. Identify the agents most likely to induce progressive multifocal leukoencephalopathy (PML) and patient characteristics which heighten this risk.
2. Recognize that natalizumab cannot be used in patients with a history of John Cunningham virus due to the risk of PML, and that patients with this virus must be monitored closely.
3. Describe other drug-specific adverse effects that may occur and specify patients most at risk for these effects, or in which the drugs are contraindicated.
4. Identify drugs that are teratogenic.

SECTION 14

VITAMINS, NATURAL PRODUCTS, AND HERBALS

Pamela Potter (section chair), Douglas Jones

14.1 Natural Products to Consider	
Dugs Classes and Drugs	
Botanicals/Herbals	**Other Supplements**
GARCINIA CAMBOGIA GINGER GINKGO BILOBA MILK THISTLE SAW PALMETTO ST. JOHN'S WORT TURMERIC/CURCUMIN YOHIMBINE ashwagandha Asian ginseng bitter orange chamomile cinnamon echinacea elderberry evening primrose garlic green tea extract guarana kava valerian	BIOTIN/COLLAGEN CALCIUM CREATINE FOLIC ACID MAGNESIUM GLYCINATE VITAMIN B12 VITAMIN D FISH OIL/OMEGA 3 FATTY ACIDS glucosamine chondroitin *Lactobacillus*/probiotics melatonin

Learning Objectives

14.1.1 Mechanism of Action and Effects

1. Analyze what is known about the mechanism of action and effects of each product.
2. Apply this knowledge to the probable use of each product and evaluate the likelihood of efficacy for each of them.

14.1.2 Pharmacokinetics

1. Identify any known mechanisms of absorption and elimination for each compound and how that affects their probable use and effects.

14.1.3 Therapeutic Uses

1. Given what is known about the effects of each of these products, summarize the uses for them.
2. Evaluate which products are considered to be effective for their proposed use based on the mechanism of action and clinical studies which have shown benefits. Some examples include:
    a. Saw palmetto for benign prostatic hyperplasia.
    b. Melatonin for jet lag.
    c. St. Johns' Wort for mild depression.
    d. Glucosamine chondroitin for knee pain.
    e. Curcumin as an anti-inflammatory.
    f. Ginger for nausea.

14.1.4 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions

1. Identify toxicity on specific organ systems, including
    a. Liver: Asian ginseng, black cohosh, concentrated green tea, garcinia cambogia, kava, valerian
    b. Kidney: Bitter orange, echinacea
    c. Cardiovascular system: Bitter orange, green tea extract, guarana
2. Evaluate potential adverse effects of these products, such as allergic reactions (chamomile, echinacea, milk thistle, feverfew, ginkgo), increased blood pressure and possible stroke (bitter orange), and excess accumulation (vitamin D, magnesium glycinate).
3. Predict potential drug interactions based on mechanism of action and effects, e.g.,
    a. Bitter orange, St. Johns' Wort with MAOIs
    b. Biotin interference with TSH, troponin, vitamin D measurement
    c. Ginkgo with anticoagulants
    d. St. John's Wort with protease inhibitors, calcineurin inhibitors, oral contraceptives, antidepressants, general anesthetics, digoxin, warfarin, phenytoin
    e. Yohimbine with clonidine, MAOIs, tricyclic antidepressants and phenothiazines
    f. Garcinia cambogia with hypoglycemic medications, statins, and warfarin
4. Analyze the concerns resulting from interference of biotin with blood tests using specific immunoassays, such as TSH and troponin measurements.
5. Predict products that are contraindicated in pregnancy based on their known mechanism and compare with products that are recommended.

14.1.5 Notes

Historical/Toxicology Context

- There is little FDA oversight for herbal products and supplements. The purity and quantity may vary widely. Herbal products have been contaminated with prescription drugs as well as heavy metals and drugs banned in the US. Although FDA does try to remove fraudulent and unsafe products, there is no guarantee that the labelling is accurate. Products with a USP seal on the label are more likely to contain the stated ingredients.

SECTION 15: TOXICOLOGY AND THERAPY OF INTOXICATION

Brooks McPhail (section chair), Jayne S. Reuben, Selina F. Darling-Reed, Precious Pringle, Jim Beardsley, Jaime Matta

15.1. Priority Toxic Chemicals	
Recommended Curriculum Equivalent: 2.0 hr	
Xenobiotics and Antidotes	
Drug(s)/Chemical Toxicant(s)	**Antidote(s)/Therapy**
Opioids (heroin, morphine, fentanyl analogs, synthetic opioids)	NALOXONE; nalmefene; BUPRENORPHINE (maintenance)
Tricyclic Antidepressants (TCAs)	SODIUM BICARBONATE
Benzodiazepines	FLUMAZENIL
Anticholinergic / Antimuscarinic Agents	PHYSOSTIGMINE
Acetylcholinesterase Inhibitors (organophosphates)	ATROPINE; PRALIDOXIME (2-PAM)
Acetaminophen	N-ACETYL-L-CYSTEINE (NAC)
Salicylates	SODIUM BICARBONATE (urinary alkalinization); hemodialysis
Beta-Blockers	ATROPINE; GLUCAGON; HIGH-DOSE INSULIN; LIPID EMULSION
Calcium Channel Blockers	CALCIUM CHLORIDE; HIGH-DOSE INSULIN (HIET); GLUCAGON; LIPID EMULSION
Digoxin / Cardiac Glycosides	DIGOXIN-SPECIFIC ANTIBODY FRAGMENTS (Fab)
Warfarin	PCC (prothrombin complex concentrate); FFP; VITAMIN K1
Direct Thrombin Inhibitor (dabigatran)	IDARUCIZUMAB
Direct Factor Xa Inhibitors (rivaroxaban, apixaban)	ANDEXANET ALFA; 4-factor PCC
Heparin / LMWH	PROTAMINE SULFATE
Methanol / Ethylene Glycol	FOMEPIZOLE > ethanol; HEMODIALYSIS
Ethanol (alcohol use disorder)	DISULFIRAM; ACAMPROSATE; naltrexone
Cyanide	HYDROXOCOBALAMIN; sodium nitrite + SODIUM THIOSULFATE

Methemoglobin-Forming agents	METHYLENE BLUE
Lithium	HEMODIALYSIS; saline diuresis
Methotrexate	LEUCOVORIN; GLUCARPIDASE
Valproic acid	L-CARNITINE

Learning Objectives

15.1.1 Mechanism of Action and Effects

1. Elucidate the molecular mechanisms by which drugs produce toxicity at excessive doses, including receptor over-activation or blockade, enzyme inhibition, disruption of ion transport, and reactive metabolite formation.
2. Relate the mechanism of toxicity of a given drug to its expected clinical presentation, predicting the signs and symptoms that result from the underlying pathophysiological process.
3. Differentiate among toxidromes, including cholinergic, anticholinergic, opioid, sedative-hypnotic, and sympathomimetic, based on their pharmacological mechanisms and distinguish their clinical features across autonomic, CNS, and vital sign domains.
4. Explain the mechanism of action of each antidote and justify its use by linking it directly to the mechanism of toxicity of the causative drug.

15.1.2 Pharmacokinetics

1. Apply pharmacokinetic principles, including volume of distribution, protein binding, and elimination half-life, to predict the severity and time course of drug toxicity and to justify antidote dosing strategies.
2. Justify the use of enhanced elimination strategies, including urinary pH manipulation, activated charcoal, hemodialysis, and hemoperfusion, based on the pharmacokinetic properties of the toxicant.
3. Evaluate how route of exposure, rate of absorption, and metabolic activation influence the onset, duration, and severity of drug toxicity.

15.1.3 Pharmacogenomics

1. Evaluate how genetic polymorphisms in drug-metabolizing enzymes alter individual susceptibility to drug toxicity and influence the clinical response to antidotal therapy.
2. Differentiate the clinical implications of pharmacogenomic variation in the context of drug-induced toxicity, providing examples of genotype-phenotype relationships relevant to toxicological management.

15.1.4 Therapeutic Uses

1. Integrate the pathophysiology of each toxidrome to guide toxidrome-based selection of antidotal and supportive pharmacotherapy.
2. Develop a structured management plan for acute drug toxicity, applying a decision-tree framework that incorporates clinical assessment, antidote selection, decontamination strategies, and monitoring parameters.

3. Evaluate evidence-based indications and limitations for GI decontamination strategies — activated charcoal, whole-bowel irrigation, and gastric lavage — and apply current guidelines to patient-specific scenarios.
4. Analyze a clinical vignette of drug overdose and justify a prioritized, stepwise approach to antidotal and supportive care management.

15.1.5 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions

1. Predict the adverse effects associated with antidotal therapy and justify the risk-benefit rationale for their use in acute toxicity management.
2. Determine contraindications to specific antidotes based on patient-specific factors, co-ingestions, and underlying comorbidities.
3. Evaluate clinically significant drug interactions that alter the toxicity profile of a drug or reduce the effectiveness of its antidote.
4. Justify the role of laboratory and clinical monitoring parameters in guiding antidote dosing, determining therapeutic endpoints, and detecting complications during management of acute drug toxicity.

15.1.7 Notes

Cross-References

- Content on cholinergic and anticholinergic pharmacology are covered in the Autonomic Nervous System section.
- Anticoagulant reversal agents are covered in the Hemostasis and Blood-Forming Organs section.

Clinical Guidelines

- Evidence-based GI decontamination guidelines: American Academy of Clinical Toxicology (AACT): https://www.acmt.net

Historical/Toxicology Context

- National Poison Data System (NPDS) annual reports provide current data on the leading categories of toxicological emergencies in the US: https://www.poisoncenters.org/annualreports
- Poison Control Center (US): 1-800-222-1222 | https://www.poisoncenters.org

15.2. Management of Heavy Metals and Chelating Agents	
Recommended Curriculum Equivalent: 1.0 hr	
Metals and Chelators	
Metal(s) / Metalloid(s)	**Chelating Agent(s)**
Arsenic (As)	DIMERCAPROL (BAL); DMSA (succimer); DMPS (unithiol)
Iron (Fe)	DEFEROXAMINE; deferasirox; deferiprone
Lead (Pb)	DIMERCAPROL with EDTA, succimer
Mercury	DIMERCAPROL; DMPS (unithiol); DMSA (succimer)
Copper (Cu)	PENICILLAMINE; ZINC (maintenance); trientine;
(Abbreviations) EDTA: Ethylenediamine tetraacetic acid, edetate; DMPS: Dimercaptopropanesulfonic acid; DMSA: Dimercaptosuccinic Acid.	

Learning Objectives

15.2.1 Mechanism of Action and Effects

1. Compare and contrast the mechanisms of toxicity produced by the major toxic metals, identifying their primary molecular targets — including sulfhydryl group binding, enzyme inhibition, mitochondrial dysfunction, and oxidative stress — and the resulting target organ injury.
2. Relate the specific molecular and cellular mechanisms of metal toxicity to the clinical signs and symptoms of acute versus chronic metal poisoning.
3. Explain how chelating agents form stable coordination complexes with metal ions to facilitate their elimination, and differentiate agents based on route of elimination, metal selectivity, and route of administration.
4. Evaluate the mechanism of action and clinical rationale for each chelating agent listed in the drug table, justifying its selection for a given metal based on the mechanism and target organ of toxicity.

15.2.2 Pharmacokinetics

1. Apply pharmacokinetic principles, including multi-compartment distribution, tissue redistribution, and elimination half-life, to predict the expected response to chelation therapy and the risk of metal redistribution during treatment.
2. Justify chelating agent selection and route of administration based on the pharmacokinetic profiles of both the metal toxicant and the chelating agent.

15.2.3 Pharmacogenomics

1. Evaluate how genetic variation in metal transporter proteins and metabolic enzymes alters individual susceptibility to metal toxicity and response to chelation therapy.

15.2.4 Therapeutic Uses

1. Integrate the pathophysiology of metal toxicity when selecting appropriate chelation pharmacotherapy, accounting for metal-specific toxicokinetics, organ-targeted injury, and patient-specific factors.
2. Propose a chelation management plan for a patient presenting with metal toxicity, justifying agent selection, route and duration of administration, and monitoring plan based on current clinical guidelines.
3. Distinguish between acute and chronic metal poisoning presentations and determine when chelation therapy is clinically indicated versus contraindicated.
4. Analyze a clinical vignette involving metal toxicity and formulate a pharmacological management strategy, justifying each decision in the context of the metal's mechanism of toxicity.

15.2.5 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions

1. Predict the major adverse effects of each chelating agent and specify contraindications based on the metal involved, route of toxicity, and patient-specific factors.
2. Compare the adverse effect profiles of chelating agents used for similar metal toxicities and justify agent selection based on the risk-benefit profile.
3. Determine appropriate laboratory and clinical monitoring parameters throughout chelation therapy, specifying endpoints that define successful treatment and criteria for therapy discontinuation.

15.2.6 Notes

Cross-References

- Content on iron metabolism and heme synthesis is covered in the Hemostasis and Blood-Forming Organs section.

Clinical Guidelines

- CDC guidelines for chelation therapy in lead poisoning: https://www.cdc.gov/niosh
- EASL Clinical Practice Guidelines for Wilson's disease: https://www.easl.eu

Historical/Toxicology Context

- Some chelating agents (e.g., unithiol/DMPS) are not FDA-approved in the US but are used internationally; educators may include these for comparative purposes.

15.3 Environmental Toxicology/Risk Assessment		
Recommended Curriculum Equivalent: 1.0 hr		
Agricultural and Environmental Pollutants		
Pesticides	**Herbicides**	**Environmental Pollutants**
2,4-dichlorophenoxyacetic acid atrazine botanical pesticides carbamates glyphosate organochlorines (e.g., DDT, BHCs, Cyclodienes, Toxaphene) organophosphates sodium bicarbonate	bipyridyl herbicides (PARAQUAT) chlorophenoxy herbicides (2,4-D & 2,4,5-T) cyanide glyphosate	asbestos dioxins endocrine disruptors perfluorinated compounds (PFAS) polychlorinated & polybrominated biphenyls (PCBs/PBBs)

Air Pollutants/Gases	Solvents
carbon monoxide (CO) hydrogen sulfide (H_2S) lead (Pb) nitrogen dioxide (NO_2) oxidizing agents (e.g., nitrogen oxides) ozone (O_3) particulate matter (PM) sulfur dioxide (SO_2)	aromatic hydrocarbons halogenated aliphatic hydrocarbons (HAC) hydrocarbons PCBs

(Abbreviations) DDT: Dichlorodiphenyltrichloroethane; BHC: Benzene hexachloride; 2,4-D: 2,4-Dichlorophenoxyacetic acid; 2,4,5-T: 2,4,5-trichlorophenoxyacetic acid

Learning Objectives

15.3.1 Mechanism of Action and Effects

1. Explain how exposure to agricultural and environmental toxicants can occur, identifying relevant routes of exposure (inhalation, dermal absorption, ingestion, and transplacental) and the factors that influence the degree of systemic uptake.
2. Describe the signs and symptoms of toxic exposure for each major class of agricultural and environmental chemical toxicant listed in the drug table.
3. Elucidate the mechanism of toxicity for each class of agricultural and environmental chemical toxicant, identifying the primary molecular targets and affected organ systems.
4. Compare and contrast the toxicity induced by the neurotoxic pesticide classes, distinguishing their mechanisms of action, clinical presentations, and management strategies.
5. Compare and contrast the toxicity induced by the listed herbicide classes, differentiating target organs, mechanisms of injury, and the availability of specific antidotes.
6. Compare and contrast the toxicity induced by the listed environmental pollutant classes, including persistent organic pollutants, endocrine disruptors, and air pollutants, and predict the acute versus chronic health consequences of each.
7. Compare and contrast the toxicity induced by the listed solvents, identifying class-specific target organs and mechanisms of injury for each chemical category.

15.3.2 Pharmacokinetics

1. Apply pharmacokinetic principles to predict how route of exposure, lipophilicity, and metabolic activation influence the tissue distribution, bioaccumulation, and elimination of agricultural and environmental toxicants.
2. Evaluate the pharmacokinetic basis for the environmental persistence and biological half-life of lipophilic pollutants and relate long-term tissue storage to delayed or chronic toxicity.
3. Justify the use and timing of decontamination and enhanced elimination strategies for specific agricultural or environmental chemical poisonings based on the toxicokinetic properties of the agent.

15.3.3 Pharmacogenomics

1. Evaluate how genetic polymorphisms in metabolic enzymes and receptor proteins modify individual susceptibility to agricultural and environmental chemical toxicity, with examples relevant to occupational and environmental exposure risk stratification.

15.3.4 Therapeutic Uses

1. Describe the antidote and/or treatment for each class of agricultural and environmental chemical toxicant listed in the drug table, specifying the mechanism by which each intervention counteracts the toxicological process.
2. Integrate the pathophysiology of agricultural or environmental chemical toxicity when designing a pharmacological management plan, specifying antidotal therapy, decontamination strategy, supportive care measures, and monitoring parameters.
3. Develop a management algorithm for a patient presenting with acute chemical toxicity from an agricultural or environmental source, applying a toxidrome-based approach to identify the causative agent class and guide treatment selection.
4. Evaluate the indications and limitations of specific antidotes for agricultural and environmental chemical toxicants, including scenarios in which no specific antidote is available and supportive care is the primary management strategy.

15.3.5 Adverse Effects, Drug Monitoring, Contraindications, and Drug Interactions

1. Predict the adverse effects associated with antidotal therapy for agricultural and environmental chemical toxicants and justify the risk-benefit rationale for their use.
2. Evaluate monitoring parameters for the management of agricultural and environmental chemical toxicity, identifying clinical and laboratory endpoints that guide treatment intensity and duration.
3. Determine contraindications to specific antidotes or treatment strategies based on the mechanism of toxicity of the causative agent and patient-specific clinical factors.

15.3.6 Notes

Cross-References

- Content on organophosphate and carbamate AChE inhibition is also covered in the Autonomic Nervous System section.

Clinical Guidelines

- CDC/NIOSH pesticide poisoning guidelines: https://www.cdc.gov/niosh/topics/pesticides
- EPA resources on environmental pollutants and PFAS: https://www.epa.gov/pfas

- IARC Monographs on carcinogenic risk of environmental chemicals: https://monographs.iarc.fr
- UHMS hyperbaric oxygen therapy guidelines: https://www.uhms.org
- AACT/EAPCCT GI decontamination position statements: https://www.acmt.net

15.4 Supplementary Materials

15.4.1 Describe and discuss the top 10 toxicological emergencies in the US from 2022-2024.

1. According to the National Poison Data System (NPDS) Annual Reports (2022-2024) from America's Poison Center, name some of the top 10 toxicological medical emergencies in the US in the last 3 years. These reports compile near real-time data from all US poison centers (covering approximately 2.0–2.1 million human exposure cases per year from 2022 to 2024). They track substance categories involved in exposure, many of which result in emergency department (ED) visits, hospitalizations, or serious outcomes. Data for 2025 are not yet available.
2. Consistent top substance categories (by frequency of involvement in all human exposures) across 2022–2024 (some of the top 10, with minor year-to-year shifts in ranking/percentages):
    a. Analgesics (e.g., acetaminophen, opioids, NSAIDs; ~10.5–11.5% of cases) — consistently #1; includes many overdoses requiring medical intervention.
    b. Household cleaning substances (~6.9–7.2%) — often unintentional pediatric exposures but can cause serious respiratory/GI effects.
    c. Antidepressants (~5.5–5.6%) — frequently intentional; high risk of serious outcomes.
    d. Cardiovascular drugs (~5.0–5.1%; rose to top 5 in 2023–2024) — includes beta blockers and calcium channel blockers, common in older adults with severe effects.
    e. Cosmetics/personal care products (~5.0%) — mostly mild/unintentional but high volume in young children.
    f. Other frequent categories rounding out the top 10 (based on reports and data snapshots): antihistamines, sedatives/hypnotics/antipsychotics, foreign bodies/toys/miscellaneous, stimulants and street drugs (rising in serious outcomes), and dietary supplements/herbals/homeopathic
3. Key notes on medical emergencies/severity (2022–2024 trends).
    a. Approximately 30% of cases originate from or are referred to healthcare facilities (true medical emergencies).
    b. Serious outcomes (moderate/major effects or death) have been increasing (~4% per year since 2000), even as total exposures are stable or slightly decreasing.
    c. Leading categories of deaths/fatalities were analgesics (including opioids and acetaminophen), stimulants/street drugs, sedatives/hypnotics/antipsychotics, cardiovascular drugs, and alcohols.
    d. Pediatric (<5–6 years) exposure (nearly half of all cases) is dominated by cleaners, analgesics, cosmetics, and foreign bodies (mostly unintentional/mild).
    e. Adult exposure shifted toward analgesics, cardiovascular drugs, antidepressants, and sedatives (higher intentional/serious proportion).
4. The NPDS data represent the most comprehensive national surveillance of toxicological emergencies. Full reports (with exact tables) are available at poisoncenters.org/annual reports. Trends were very stable over the last 3 years, with analgesics and cleaners remaining dominant overall, while stimulants and certain pharmaceuticals drove increases in severe cases.

15.4.2 Name some newer antidotes developed in the last decade for management of the acute poisoned patient and explain their main uses.

1. Antidotes are used in a minority of poisonings (<2-10%) of cases, and most management relies on supportive care, decontamination, and enhanced elimination.

2. Nalmefene (Opioid antagonist, FDA-approved 2023 for injection and intranasal spray) (Trade name: Opvee, Zurnai)
    a. Main use: Reversal of opioid overdose, including respiratory depression from potent synthetic opioids (e.g., fentanyl analogs and nitazenes). It has a longer duration of action than naloxone (hours vs shorter), reducing the need for repeated dosing or infusions in some cases, and lacks opioid agonist activity.
    b. Advantages: Useful in community and hospital settings for known or suspected overdose; intranasal form supports layperson use. It may provide a more sustained reversal against long-acting or high-potency opioids.
    c. Note: Naloxone remains the first-line and most widely available opioid reversal agent, and nalmefene is an alternative with pharmacokinetic benefits.
3. Glucarpidase (Carboxypeptidase enzyme, FDA-2022 updates/clarifications on use; more data and guideline integration in recent years) (Trade name: Vistogard)
    a. Main use: Rapid reduction of methotrexate (MTX) levels in cases of high-dose MTX toxicity or delayed clearance (e.g., in cancer patients with renal impairment, leading to severe myelosuppression, mucositis, or renal failure). It enzymatically cleaves MTX into an inactive metabolite.
    b. Advantages: Dramatically lowers serum MTX concentrations within hours when combined with leucovorin. Its role is clearer in severe or intrathecal overdose scenarios, though evidence for routine high-dose therapeutic toxicity is still evolving
4. Other Developments or Refinements (Not Strictly "New")
    a. Hydroxocobalamin (Cyanokit) is the preferred first-line treatment for cyanide poisoning (especially smoke inhalation) and is emphasized in the 2023 AHA guidelines for immediate use without waiting for laboratory confirmation. It binds cyanide to form a non-toxic cyanocobalamin.
5. The AHA guidelines refer to the American Heart Association (AHA) Guidelines for Cardiopulmonary Resuscitation (CPR) and Emergency Cardiovascular Care (ECC). These are comprehensive, evidence-based recommendations that are updated periodically (typically every 5 years for the full set, with focused updates in between) to guide healthcare providers in managing cardiac arrest, life-threatening emergencies, and related conditions.
    a. Fomepizole is the standard treatment (preferred over ethanol) for toxic alcohol (methanol and ethylene glycol) poisoning. It inhibits alcohol dehydrogenase to prevent the formation of toxic metabolites. Wider availability and guideline support are also needed. (Trade name: Antizol)
    b. High-dose insulin euglycemic therapy (HIET) and intravenous lipid emulsion (ILE) are strongly recommended in the 2023 AHA toxicology guidelines for refractory shock from calcium channel blockers, beta-blockers, or local anesthetic systemic toxicity (LAST). These act via metabolic support and lipid partitioning ("lipid sink"), respectively.
    c. L-carnitine — Increasing use/evidence of valproic acid toxicity (hyperammonemia/hepatic dysfunction) via mechanistic repurposing.

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All drugs are listed by generic (nonproprietary) name, and drugs capitalized in the document are also capitalized here.

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