

PHARMACOLOGY: Core Concepts and Learning Objectives

I. MEDICAL KNOWLEDGE

After each of the following specific lecture topics students will be expected to be able to understand, discuss and explain each of the following pharmacological concepts. Where appropriate a list of the relevant drugs is provided for each topic. In these cases, students should be able to identify which specific drugs belong to each major drug class, as well as have an understanding of the indications, clinical effect, mechanism of action and adverse effects of each of the major drug classes.

A. BASIC CONCEPTS IN PHARMACOLOGY

A1. PRINCIPLES OF PHARMACOLOGY

1. The different types of drugs formulations and their respective advantages and disadvantages.
2. The various routes of drug administration and their respective advantages and disadvantages for specific therapeutic indications.
3. The various factors that affect drug absorption, drug distribution and drug excretion.
4. The role of receptors as targets for drug action and their role in the mediation of drug responses.
5. The fundamental difference between an agonist and antagonist.
6. The relationship between generic versions of drugs and their branded product.
7. The differences in the chemical equivalence, biological equivalence and therapeutic equivalence of a drug product as related to generic drug substitution.
8. The concept of drug bioavailability.
9. The essentials of the drug approval process.
10. The concept that in addition to beneficial clinical effects the use of drugs can also lead to toxic side effects

A2. PHARMACODYNAMICS

1. The relationship between drug dose (or concentration), receptor occupation and biological response.
2. The concepts of drug selectivity, potency, efficacy, full and partial agonism and neutral and negative antagonism.
3. The different types of pharmacologic antagonism and the difference between pharmacological and non-pharmacological types of drug antagonism.
4. The concept of spare receptors, how it can be experimentally demonstrated, and how it may be reflected in the shape of the dose-response curve.
5. The difference between graded and quantal dose response relationships and the information that can be provided by each of these relationships.
6. How drugs can produce beneficial versus toxic effects via the same receptor or different receptors, and how toxic effects may be managed in each of these situations.
7. The key aspects of the 5 major types of receptor signaling mechanisms and the similarities and differences between the adenylyl cyclase and the phosphoinositide signal transduction systems.

8. The different types of altered responsiveness to drugs, the concepts of supersensitivity and desensitization and how these will affect the dose response curve.
9. The differences between homologous and heterologous desensitization, the mechanisms that contribute to each of these phenomena and the clinical implications of these phenomena.

A3. PHARMACOKINETICS

1. The definition of pharmacokinetics according to the acronym ADME (Absorption, Distribution, Metabolism and Elimination).
2. The mechanisms by which drugs are absorbed in the body to reach their sites of action (e.g. aqueous & lipid diffusion, active transport, etc.).
3. The chemical characteristics of drugs (e.g. solubility, pKa) and other factors (e.g. regional differences in blood flow, transporters, non-specific binding) that influence drug absorption.
4. The one-compartment and two-compartment model of drug distribution and elimination
5. The concept of Volume of Distribution and the effect of plasma protein binding on drug distribution.
6. How differential drug distribution can create drug reservoirs that affect the time course and magnitude of a drug's effect.
7. The difference between first-order, zero-order and dose-dependent kinetics of drug elimination and examples of commonly prescribed drugs that typically display these kinetic profiles.
8. The concept of steady-state with regard to plasma drug concentrations.
9. The importance of different pharmacokinetic parameters on the time course of drug action.
10. The concept that Volume of Distribution (V_d) and Clearance of Elimination (CL) are the primary pharmacokinetic parameters and that elimination half-life and elimination rate constants are dependent on V_d and CL.
11. The use of pharmacokinetic parameters to determine the loading dose and maintenance dose of specific drug regimens.
12. An understanding of how repetitive drug administration or continuous drug infusion can attain steady-state therapeutic drug concentrations.
13. The roles of the kidney and liver in the elimination of drugs from the body and the factors that affect hepatic clearance (hepatic blood flow, protein binding, intrinsic clearance).

A4. DRUG METABOLISM AND DRUG INTERACTIONS

1. The different types of metabolic transformations that drugs undergo and their physiological consequences.
2. The potential changes in the chemical properties of a drug metabolite versus the properties of the parent drug.
3. The concept that the effects of one drug can be modified by the prior, or simultaneous, administration of a second drug.
4. The major mechanisms that can lead to drug-drug interactions
5. The role that drug metabolism plays in mediating drug-drug interactions.
6. The role that enzyme induction and inhibition of metabolic enzymes play in drug metabolism.

A6. DRUG DISCOVERY AND CLINICAL TRIALS

1. An understanding of the different phases of clinical trials.
2. The differences between single and double blind designs for clinical trials.
3. The definition of an IND and a NDA.
4. The ways in which a clinical drug study is evaluated.

A7. PHARMACOGENOMICS

1. The concept of variability in drug responses among the general population.
2. The major phase I and II isozymes associated with adverse drug reactions.
3. The role of polymorphisms in CYP2D6, N-Acetyltransferase 2, CYP2C9, CYP3A4 and VKORC1 in drug actions and the patient response to drugs.
4. The application of pharmacogenomic techniques to clinical trials and clinical practice and how pharmacogenomic DNA-based diagnosis can be coupled to the use of innovative personalized patient-specific therapy.
5. The use of recombinant proteins and antibody-based therapy in the treatment of disease- their advantages and disadvantages.
6. The molecular basis of gene silencing and how this technology can potentially be applied to treat disease.

A8. TOXICOLOGY

1. The dose-response relationships that define toxicological effects.
2. The major toxic endpoints.
3. The most common types of toxic agents, routes of exposure and types of exposure.
4. The categories of teratogens and their classification.
5. The common toxic syndromes including:
 - a) cholinergic and anticholinergic syndrome,
 - b) hemoglobinopathies
 - c) sympathomimetic excess
 - d) narcotic overdose and narcotic withdrawal syndromes.

B. AUTONOMIC PHARMACOLOGY

B1. DRUG ACTION AT THE SYNAPSE: AN INTRODUCTION

1. The five essential steps involved in neurotransmission
2. The major pre-synaptic and post-synaptic mechanisms by which drugs act enhance or decrease synaptic transmission.
3. The five major classes of neurotransmitters and specific examples of each (e.g. biogenic amino acids, amino acids, peptides, nucleotides and gases)
4. The unique features of classic and peptidergic neurotransmission.
5. The major differences between indirect and direct acting agonists
6. The major mechanisms by which synaptic transmission of adrenergic neurons can be altered pharmacologically.
7. The major side effects that can occur by combining indirect acting agonists of the sympathetic nervous system with other drugs that influence sympathetic neurotransmission.

B2. ADRENERGIC AGONISTS AND ANTAGONISTS

1. The distinctive anatomical and chemical characteristics of the sympathetic and parasympathetic nervous systems.
2. The visceral organs that are innervated by the sympathetic and parasympathetic systems and the functional responses of the organs to activation of either system.
3. The main subtypes of adrenergic receptors and the most common second messenger systems to which they are coupled, and how these second messenger mediate their biological effect.
4. The distribution of the adrenergic receptor subtypes in the visceral organs.
5. Understand how the activation of adrenergic receptors normally expressed on the pre-synaptic membrane is able to influence neurotransmitter release.
6. The relative affinities of epinephrine, norepinephrine and the prototypical β -adrenergic receptor agonist isoproterenol for the different adrenergic receptors.
7. How a drug's affinity for a particular receptor influences its potency in mediating arterial contraction, bronchial smooth muscle relaxation and cardiac contractility.
8. How the different catecholamines influence cardiovascular and bronchial function and what receptors mediate these responses.
9. How the prototypical synthetic adrenergic agonists influence cardiovascular and bronchial function and what receptors mediate these responses.
10. The most common toxic side effects of the endogenous and synthetic adrenergic agonists and an understanding of why they occur.
11. The most important therapeutic uses for the endogenous and synthetic adrenergic agonists.
12. The most common indirect acting sympathomimetics and their most prominent effects.
13. The most important toxic side effects and therapeutic uses of adrenergic agonists.
14. Identify which adrenergic agonists have the most important therapeutic value in the treatment of the following disorders:
 - a) Shock
 - b) Hypotension
 - c) Nasal congestion
 - d) Asthma
 - e) Anaphylaxis
 - f) Attention-deficit disorder
15. The major α -adrenergic receptor antagonists currently used in clinical practice and their principal indications
16. The most serious side effects caused by α -adrenergic receptor antagonists
17. Why selective α_1 -adrenergic receptor antagonists are preferable for the treatment of hypertension as compared to non-selective α -adrenergic receptor antagonists
18. The major β -adrenergic receptor antagonists that are most commonly used in clinical practice and their principal indications
19. Understand the differences between the different β -adrenergic receptor antagonists with regard to their selectivity and duration of action.
20. Understand the relationship between the selectivity of the different β -adrenergic receptor antagonists and their toxic side effects.
21. Understand how differences in the selectivity of the β -adrenergic receptor antagonists helps determine which agent is most suitable for a particular condition in a specific patient population.
22. Identify the major indications for β -adrenergic receptor antagonists and the mechanisms by which they mediate their clinical effects.

Relevant DrugsA. Adrenergic Agonists*I. Direct acting Sympathomimetics*

Epinephrine
Norepinephrine
Dopamine

II. Non-selective β -adrenergic agonists

Isoproterenol

III. Selective β_1 -adrenergic receptor agonist

Dobutamine

IV. Selective β_2 -adrenergic receptor agonists

Terbutaline
Albuterol

V. Selective α_1 -adrenergic agonist

Phenylephrine

VI. Selective α_2 -adrenergic agonist

Clonidine

VII. Indirectly acting Sympathomimetics

Amphetamine
Metamphetamine
Methylphenidate
Ephedrine
Pseudoephedrine
Tyramine

B. β -adrenergic antagonists*I. Non-selective β -blockers*

Propranolol
Timolol
Nadolol

II. Cardioselective β_1 -blockers

Metoprolol
Atenolol
Esmolol

III. Partial β -adrenergic receptor agonist

Pindolol

C. α -adrenergic receptor antagonists*I. Non-selective α -receptor antagonists*

Phenoxybenzaine (irreversible)
Phentolamine (reversible)

II. Selective α_1 receptor antagonists

Prazosin
Doxazosin
Terazosin

B3. CHOLINERGIC AGONISTS AND ANTAGONISTS

1. The distinctive anatomical and chemical characteristics of the parasympathetic system.
2. The visceral organs that are innervated by the parasympathetic system and the functional responses of the organs to parasympathetic activation.
3. The main structural and functional differences between nicotinic and muscarinic receptors, their mechanisms of action, and their location in the body.
4. The differences between parasympathetic and nicotinic effects in the body.
5. The mechanisms behind directly and indirectly acting cholinergic agonists.
6. The differences in the pharmacological activity of key quaternary nitrogen analogs of choline.
7. The mechanism by which pilocarpine exerts its therapeutic effect in the treatment of glaucoma
8. The two different types of cholinesterase in the body, their location, and their mechanism of action.
9. The key representative reversible cholinesterase inhibitors, their clinical applications, and pharmacological effects.
10. The mechanism of action of the irreversible cholinesterase inhibitors, and the reason behind the success of 2-PAM as an antidote to irreversible cholinesterase inhibition.
11. The toxic pharmacologic effects caused by exposure to organophosphates and its pharmacological treatment
12. The major clinical applications for atropinic agents
13. The dose-dependent pharmacological effects of atropine.
14. The symptoms of acute atropine poisoning, and its treatment.

Relevant Drugs

A. Nicotinic agonists

Nicotine

Succinylcholine

B. Muscarinic Agonists

Quaternary Nitrogen analogs of Choline

Acetylcholine

Methacholine

Carbachol

Bethanechol

C. Naturally occurring Tertiary Amines

Muscarine

Pilocarpine

D. Cholinesterase inhibitors

Reversible

Neostigmine

Edrophonium

Physostigmine

Donepezil

Irreversible

Pralidoxime (2-PAM)

Echothiophate

E. Muscarinic Antagonists

Atropine

Scopolamine

Glycopyrrolate

B4. NEUROMUSCULAR RELAXANTS

1. The mechanisms by which skeletal muscle nicotinic receptor activation stimulates skeletal muscle contraction including the agonists, receptors, and post-synaptic signaling mechanisms that initiate contraction.
2. The difference in mechanism of action between depolarizing and non-depolarizing neuromuscular blockers
3. The major pharmacokinetic features of the two classes of neuromuscular blockers.
4. How cholinesterase inhibition affects the paralysis produced by depolarizing and non-depolarizing neuromuscular blockers.
5. The mechanisms by which the action of neuromuscular blockers are terminated and how these mechanisms are exploited clinically.
6. The major characteristics of non-depolarizing or depolarizing neuromuscular blockers that make them suitable for specific clinical uses
7. The prominent side effects of each class of skeletal muscle relaxant.
8. The antidote for either class of neuromuscular blockers.
9. The characteristics of phase I and phase II block with depolarizing neuromuscular blockers and why phase II should be avoided.
10. The characteristics of the non-depolarizing neuromuscular blockers pancuronium, rocuronium, mivacurium and vecuronium and why these characteristics make a given agent preferable over another for use in the long-term ventilation/intubation of either a healthy patient or patient with renal failure.
11. The mechanisms by which baclofen and benzodiazepines alter somatic motor neuron excitation.
12. The mode of administration and major side effects of baclofen and benzodiazepines when used as neuromuscular relaxants.
13. The mechanisms by which tizanidine and dantrolene reduce muscle spasticity and recognize the major side effects of both drugs.
14. The important alternative use of dantrolene in clinical practice.

Relevant DrugsA. Non-depolarizing blocking drugs-competitive antagonists

Pancuronium

D-tubocurarine

Vecuronium

Rocuronium

Mivacurium

B. Depolarizing blocking drugs-Agonists

Succinylcholine

C. Spasmolytic drugs

Baclofen

Benzodiazepines (e.g. Diazepam, Clonazepam)

Tizanidine

Dantrolene

C. ANESTHETICS AND ANALGESICS

C1. LOCAL ANESTHETICS

1. The mechanisms by which local anesthetics block nerve conduction.
2. An understanding of how the physiochemical properties of local anesthetics influence the pharmacodynamics and pharmacokinetics of these drugs.
3. What undesirable side effects may occur with the use of local anesthetics and why these side effects happen.
4. The unique characteristics and the common clinical use for each prototypical local anesthetic.
5. The common uses of the local anesthetics with particular emphasis on spinal and epidural anesthesia.
6. The most commonly caused severe complications of local anesthetics when they are systemically absorbed or injected intravenously.

Relevant Drugs

A. Esters:

Procaine

Cocaine

Tetracaine

Benzocaine

B. Amides:

Lidocaine

Mepivacaine

Bupivacaine

L-Bupivacaine

Ropivacaine

C2. GENERAL ANESTHETICS

1. The definition of general anesthesia and how it can be achieved.
2. A working understanding of the pharmacokinetics for inhalational anesthetics.
3. The various stages of anesthesia.
4. How the blood:gas coefficient influences the onset of action (and termination of anesthesia) for inhaled anesthetics.
5. How the ventilation rate and pulmonary blood flow influence the onset of action for inhalation anesthetics.
6. How blood flow to a tissue influences the tension of an anesthetics gas in that tissue.
7. The definition of minimum alveolar concentration (MAC) and what information it provides about a volatile anesthetic.
8. The pharmacokinetic properties of the ultrashort-acting hypnotics and how these properties make this class of drugs popular general anesthetic agents.
9. The advantages and disadvantages for clinically used inhaled and intravenously administered general anesthetics. When they should be used and when they are contraindicated.
10. The concept that inhalational and intravenous anesthetics cause varying degrees of respiratory depression with an exception being ketamine.

Relevant Drugs

A. Halogenated Hydrocarbons:

Isoflurane
Sevoflurane
Desflurane

B. Inert Gas
Nitrous Oxide

C. Ultrashort-Acting Barbiturates
Thiopental
Methohexital

D. Sedative-Hypnotics
Ketamine
Etomidate
Propofol

E. Opioids
Morphine
Fentanyl

F. Benzodiazepines
Midazolam

C3. TREATMENT OF HEADACHES

1. Recognition of the primary headache disorders, including migraine, cluster headache, and tension headache
2. The major differences between primary and secondary headache disorders
3. The current concepts in migraine pathophysiology
4. Identification of the treatment strategies for the various headache disorders
5. The indications for the various abortive migraine-specific medications and headache preventive medications.
6. The mechanisms of action and adverse effects of the various abortive migraine-specific medications and headache preventive medications.

Relevant Drugs

(A) Triptans
Sumatriptan
Naratriptan
Rizatriptan
Sumatriptan
Zolmitriptan
Almotriptan
Frovatriptan

(B) Ergot Alkaloids
Ergotamine
Dihydroergotamine

(C) Migraine preventative agents
Propranolol
Topiramate
Divalproic acid
Amitriptyline
Flunarizine

Verapamil
Methysergide

C4. NON-STEROIDAL ANTI-INFLAMMATORY DRUGS

1. The role of cyclooxygenase enzymes and prostaglandins in the etiology of inflammation, pain and fever.
2. The role of prostaglandins in the homeostatic regulation of:
 - a) gastric function,
 - b) kidney function
 - c) regulation of vasoconstriction and platelet activation
3. The indications, mechanism of action, adverse effects, contraindications and potential drug interactions of:
 - a) Aspirin and the salicylates
 - b) Traditional NSAIDs e.g. ibuprofen and naproxen
 - c) Celecoxib
 - d) Acetaminophen
4. The rationale behind the unique indication for low dose aspirin as a prophylactic treatment in the prevention of platelet aggregation and the development of cardiovascular heart disease.
5. The pharmacokinetics of aspirin and the mechanisms that lead to the development of salicylate toxicity
6. The mechanisms underlying acetaminophen poisoning and its treatment

Relevant Drugs

A. Aspirin and Salicylic Acids

Aspirin (Bayer™)
Diflusal (Dolobid™)
Salsalate (Disalcid™)

B. Non-Selective and traditional NSAIDs

Ibuprofen (Advil™/Motrin™/Nuprin™)
Naproxen (Aleve™/Anaprox™/Naprosyn™)
Oxaprozin (Daypro™)
Ketoprofen (Actron™)
Indomethacin (Indocin™)
Diclofenac (Cataflam™)
Sulindac (Clinoril™)
Ketorolac (Toradol™)
Tolmetin (Tolectin™)
Meloxicam (Mobic™)
Piroxicam (Feldene™/Fexicam™)
Meclofenamate (Meclomen™)
Mefenamic acid (Ponstel™)
Nabumetone (Relafen™)
Etodolac (Lodine™)

C. Coxibs: COX-2 specific inhibitors

Celecoxib (Celebrex™)

D. Non-NSAID Related Analgesic

Acetaminophen (Tylenol™/Paracetamol™)

C5. OPIOID ANALGESICS

1. Familiarity with the brain's opioid system. In particular the major opioid receptors, their principal endogenous ligands and the signal transduction pathways that they utilize.
2. The role of opioid transmission in the pain experience and how opioid agonists induce analgesia.
3. The concepts of opioid-induced tolerance, physical dependence, addiction and pseudo-addiction, and how to recognize each.
4. The indications, mechanism of action, clinical effects, adverse effects and contraindications of the major classes of opioid analgesics used in the management of pain.

Relevant Drugs

A. Analgesics

Morphine

Hydromorphone

Methadone

Meperidine

Fentanyl

Codeine

Oxydocone

Hydrocodone

Propoxyphene

B. Mixed Receptor Agonist-Antagonists.

Pentazocine

Nalbuphine

Buprenorphine

Butorphanol

C. Opioid Antagonists.

Naloxone

Naltrexone

C6. ACUPUNCTURE

1. The role of the spinal cord, midbrain, hypothalamus and cortex in the regulation of pain pathways through endogenous opioids and neurotransmitters
2. The effects of High and Low frequency acupuncture stimulation on the endogenous opioids and neurotransmitters in the pain pathway
3. The appropriate conditions for treatment with acupuncture.

D. CARDIOVASCULAR PHARMACOLOGY

D1. TREATMENT OF THROMBOSIS: HEPARIN, LOW MOLECULAR WEIGHT HEPARIN AND ANTITHROMBIN AGENTS

1. The mechanism of action of heparin and low molecular weight heparins.
2. The role of the APTT in heparin monitoring and that knowledge that therapeutic anticoagulation is achieved when the APTT is 2.5 times the patient's baseline level.
3. The differences between heparin and low molecular weight heparins.
4. The mechanism of action of direct thrombin inhibitors and how it differs from the mechanism of heparin and low molecular weight heparin

Relevant Drugs*Heparin (systemic anticoagulant)**Low molecular weight heparin (enoxaparin, dalteparin, tinzaparin)**Pentasaccharide (Arixtra®)**Danaparoid (Orgaran®)**Protamine sulfate**Antithrombin-III**Hirudin (Refludan®)**Argatroban (Novastan®, Acova)**Bivalirudin (Angiomax®)***D2. PROPHYLAXIS AND TREATMENT OF THROMBOSIS: ORAL ANTICOAGULANTS**

1. The mechanism of action of warfarin.
2. The drugs that interact with warfarin and the underlying mechanisms involved
3. The concept of using INR in the management of warfarin therapy

Relevant Drugs*Warfarin (oral anticoagulant).**Vitamin K**Fresh frozen plasma**Recombinant factor VIIa**Anti-Xa agents- Rivaroxaban, Apixaban**Anti-IIa agents- Dabigatran***D3. ANTIPLATELET DRUGS AND EICOSANOIDS**

1. The basic structure of platelets with particular reference to light and dense granules and their respective composition.
2. The major antiplatelet drugs and their sites of actions.
3. The mechanism of action of aspirin and related inhibitors of cyclooxygenases.
4. The use of antiplatelet drugs for the treatment of arterial thrombosis.
5. The mechanism of antiplatelet action of dipyridamole.
6. The laboratory tests useful in the monitoring of antiplatelet drugs.
7. The main pathways of arachidonic acid metabolism and their physiological significance.
8. The cyclooxygenase pathway and the main inhibitors of this pathway.
9. The role of thromboxane and prostacyclin in the regulation of vascular tone, platelet function and endothelium.
10. The lipooxygenase pathway and the main regulator of this pathway.
11. The main leukotrienes and their physiological function.
12. The role of platelet-activating factor in various pathological processes.
13. The mechanism of the antiplatelet action of omega-3 fatty acids.
14. The mechanisms of action of the glycoprotein IIb/IIIa inhibitors (GPIIb/IIIa inhibitors).
15. The rationale for use of aspirin in the management of acute coronary syndromes
16. The mechanism of action of clopidogrel (Plavix®)
17. The major drug interactions between antiplatelet agents and other anticoagulant drugs

Relevant Drugs*A. Eicosanoids, Prostaglandins and Leukotrienes**Aloprostadiil (prostaglandin E 1)*

Carboprost (PGF 2 α analogue)
Dinoprostone (PGE 2)
Epoprostenol (Prostacyclin)
Misoprostol (PGE 1 analogue)
Monteleukast
Zafirleukast
Zileuton

B. Antiplatelet drugs

Aspirin
Clopidogrel
NSAIDS
Dipyridamole
Cilostazol
Abciximab
Eptifibatide
Tirofiban

D4. PHARMACOLOGY OF NITRIC OXIDE

1. The physiologic processes that can generate endogenous nitric oxide.
2. The role of arginine as the main endogenous source of nitric oxide.
3. The isoforms of the enzymes responsible for the synthesis of nitric oxide.
4. The beneficial effects and toxic effects of nitric oxide.
5. The drugs that can increase the levels of endogenous nitric oxide.
6. The principal biological effects of nitric oxide relevant to its mechanism of action
7. The therapeutic uses of nitrates.

Relevant Drugs

Nitroglycerine
Iso-sorbide dinitrite
Amyl nitrate
Nitroprusside
Hydralazine (vasodilator)
Nitric oxide (INOmax)
Furoxans (Furazolidone, antiprotozoal)
L-Arginine

D5. PHARMACOLOGY OF VASOACTIVE PEPTIDE

1. The enzyme responsible for the conversion of angiotensinogen to angiotensin I.
2. The effects of angiotensin converting enzyme (ACE).
3. The drugs that are known as angiotensin converting enzyme inhibitors (ACE Inhibitors).
4. The pharmacologic actions of bradykinin.
5. The major actions of Atrial Natriuretic Peptide.
6. The actions of kallikreins.
7. The actions of endothelins.
8. The functions of vasoactive intestinal peptide (VIP), substance P and calcitonin gene-related peptide (CGRP).
9. The effect of desmopressin on endothelial cells.
10. The effects of aprotonin on the actions of kallikrein.

Relevant Drugs

Captopril (ACE inhibitor)
Enalapril (ACE inhibitor)
Losartan (Angiotensin receptor inhibitor)
Valsartan (Angiotensin receptor inhibitor)
Icatibant (Bradykinin receptor inhibitor)
Aprotonin (Kallikrein inhibitor)
Desmopressin (Vasopressin analogues, release vW factor)
Bosentan (ETA-ETB receptor inhibitor)

D6. PHARMACOLOGY OF THROMBOLYTIC AGENTS

1. The different components of the fibrinolytic system in terms of inhibitors, activators and zymogens.
2. The differences between the plasmin-mediated degradation of fibrinogen and fibrin.
3. The role of plasminogen in fibrinolysis.
4. The physiologic activators of plasminogen with particular reference to the role of endothelial t-PA in physiologic thrombolysis.
5. The site of action of different thrombolytic agents.
6. The main side effects of thrombolytic therapy.
7. The antagonists that can be used for neutralizing the actions of thrombolytic agents.
8. The possible interactions of thrombolytic agents with aspirin and heparin
9. The laboratory tests that can be used for the monitoring of thrombolytic agents.

Relevant Drugs

Urokinase
Streptokinase
Streptokinase Plasminogen Complex (Anistreplase, Eminase)
Tissue plasminogen activators (Alteplase, Reteplase, Tenecteplase)
Pro-urokinase
Epsilon amino caproic acid
Tranexamic acid
Ancrod
Aprotinin

D7. DRUGS TO TREAT HYPERLIPIDEMIA

1. The role that elevated serum levels of LDL-C play in promoting the risk of developing cardiovascular disease.
2. The protective role that increased serum levels of HDL-C play in decreasing the risk of developing cardiovascular disease.
3. The presently accepted values for desirable serum LDL-C, HDL-C and triglycerides in normal individuals and the treatment goals for those individuals with hyperlipidemia.
4. The benefit of diet and lifestyle changes in the initial treatment of hyperlipidemia
5. The indications, mechanism of action, clinical effects, adverse effects and contraindications of the major drug classes used in the treatment of hyperlipidemia including:
 - a) the statins
 - b) bile-acid resins
 - c) cholesterol absorption inhibitors
 - d) Niacin
 - e) the fibrates
 - f) omega-3 fatty acids
6. The symptoms of rhabdomyolysis and the factors that can influence the risk of developing Rhabdomyolysis when on statin therapy

7. The role of combination drug therapy in treating complex hyperlipidemias

Relevant DrugsA. The STATINS*Atorvastatin (Lipitor®)**Fluvastatin (Lescol®)**Lovastatin (Mevacor®)**Simvastatin (Zocor®)**Pravastatin (Pravachol®)**Rosuvastatin (Crestor®)*B. Bile Acid-binding resins*Cholestyramine (Questran®)**Colestipol (Colestid®)**Colesevelam (Welchol®)*C. Cholesterol Absorption Inhibitor*Ezetimibe (Zetia®)*D. NiacinE. The Fibrates*Fenofibrate (Tricor®, Lofibra®)**Gemfibrozil (Lopid®)*F. Omega-3 fatty acids*Eicosapentaenoic acid: Docosahexaenoic acid (Lorvaza®)***D8. DIURETICS**

1. An understanding of the transepithelial movement of bicarbonate, H₂O, H⁺, sodium, chloride, potassium, calcium, and magnesium in the different segments of the nephron.
2. An understanding of where the secretion of substances into the nephron occurs, and by what mechanisms;
3. The importance of the organic anion transport system and protein binding to the renal action of diuretics.
4. The sites of action, the mechanisms of action, and the common adverse effects of the six classes of diuretics:
 - a) carbonic anhydrase Inhibitors
 - b) osmotic diuretics
 - c) loop diuretics
 - d) thiazides
 - e) potassium-sparing diuretics
 - f) ADH antagonists.
5. The effects of the different diuretics on electrolyte excretion patterns.
6. The therapeutic applications of diuretics including: a) edema, b) kidney disease, c) hepatic cirrhosis, d) congestive heart failure, e) left heart failure, f) hyponatremia, g) hypertension, h) nephrogenic diabetes insipidus, i) nephrolithiasis and j) hypercalcemia.
7. The conditions and/or drug interactions that interfere with or contraindicate diuretic use.

Relevant DrugsA. Carbonic Anhydrase Inhibitors*Acetazolamide**dichlorphenamide*

methazolamide
dorzolamide

B. Osmotic Diuretics
mannitol

C. Loop Diuretics
furosemide
bumetanide
toremide
ethacrynic acid

D. Thiazides
chlorthalidone
chlorothiazide
hydrochlorothiazide
metolazone
indapamide

E. Potassium-sparing diuretics
spironolactone
eplerenone
triamterene
amiloride

F. ADH antagonists
demeclocycline
lithium
lixivaptan
tolvaptan
OPC-31260
conivaptan.

D9. DRUGS TO TREAT HYPERTENSION

1. The current definition of hypertension and the currently accepted criteria for staging of hypertension.
2. How the stage of hypertension at diagnosis influences management of the disease.
3. The mechanism of action of each class of anti-hypertensive agent.
4. The prototypical drug for each class and additional drugs used currently that have particular advantages compared to the prototypes.
5. The major side effects of each class of anti-hypertensive drug, as well as conditions in which the class of drug is contraindicated.
6. The dangerous drug interactions associated with each class of anti-hypertensive agent.
7. The most commonly used anti-hypertensive drug combinations and why these drug combinations are more effective than either of the compounds alone.
8. Potentially dangerous or ineffective combinations of anti-hypertensive medications and why they should be avoided.
9. The stepped-care approach in the treatment of hypertension and the underlying logic behind the algorithm.
10. The exceptions to the stepped-care approach in the treatment of hypertension and what drug regimen should be substituted in cases of other pathologies e.g., heart failure, diabetes, myocardial infarction etc.

Relevant DrugsA. Diuretics

Hydrochlorothiazide

Chlorthalidone

Furosemide

Spironolactone

Eplerenone

B. Calcium Channel Antagonists

Nifedipine

Verapamil

Diltiazem

C. Sympatholytic Drugs

Clonidine

Methyldopa

Reserpine

D. Alpha-Adrenergic Antagonists

Phentolamine

Prazosin

Terazosin

E. Beta-Adrenergic Antagonists

Propranolol

Atenolol

Nadolol

Pindolol

Metoprolol

Labetolol

Carvedilol

F. Vasodilators

Hydralazine

Minoxidil

Nitroprusside

G. ACE inhibitors

Captopril

Enalapril

Lisinopril

H. Angiotensin II receptor Antagonists

Losartan

Doxazosin

D10. ANTI-ANGINAL DRUGS

1. The pathophysiological basis for the development of angina pectoris and other ischemic coronary syndromes.
2. The indications, mechanisms of action, adverse effects and contraindications of drugs commonly used in the treatment of angina.
3. How pharmacological therapies are used along with non-pharmacological approaches to the relief of angina and other ischemic coronary syndromes.

Relevant DrugsA. Organic Nitrates

Nitroglycerin
Isosorbide dinitrate
Erythryl tetranitrate

B. Calcium Channel Blockers

Nifedipine
Nicardipine
Amlodipine
Verapamil
Diltiazem

C. Beta Receptor Antagonists

Propranolol
Nadolol
Atenolol
Metoprolol
Carvedilol

D. pFOX Inhibitor

Ranolazine

D11. DRUGS TO TREAT CONGESTIVE HEART FAILURE

1. The pathophysiological basis for the development of both acute and chronic congestive heart failure.
2. The rationale for the use of inotropic drugs, vasodilators, beta-blockers, and diuretics in the treatment of congestive heart failure.
3. How pharmacological therapies are used along with non-pharmacological approaches for the treatment of congestive heart failure.

Relevant DrugsA. Inotropic Agents

Isoproterenol
Dopamine
Dobutamine
digoxin

B. Phosphodiesterase Inhibitors

Amrinone
milrinone

C. Diuretics

Thiazides
Furosemide
Spironolactone
eplerenone

D. Angiotensin Converting Enzyme (ACE) Inhibitors

Captopril
Enalapril
lisinopril

E. Angiotensin Receptor Blockers (ARB)

Losartan
Valsartan
Irbesartan
candesartan

F. Other vasodilators

Nitroprusside
Nitroglycerin
Hydralazine

G. Beta-blockers

Metoprolol
Carvedilol
Bucindolol

D12. ANTI-ARRHYTHMIC DRUGS

1. The concept that anti-arrhythmic drugs act at the level of ion channels, which act to determine the cardiac action potential configuration and function
2. The concept that anti-arrhythmic drugs are classified by their predominant effect on the cardiac action potential or by their cellular mechanism of action.
3. The concept that anti-arrhythmic drugs suppress cardiac arrhythmias by reducing ectopic pacemaker activity and/or by modifying conduction characteristics and that each class of drugs possesses different mechanisms of action.
4. The indications and therapeutic use, mechanism of action, route of administration, adverse effects and contraindications of each class of anti-arrhythmic drugs.
5. The concept that because anti-arrhythmic drugs exert significant untoward side effects and are not always effective against certain types of lethal arrhythmias, other non-pharmacological approaches to the treatment of cardiac arrhythmias are becoming more prevalent.
6. The different non-pharmacological methods of anti-arrhythmic treatment, which types of arrhythmias can be treated with each method, and the mechanisms by which each method acts.

Relevant Drugs

A. Class I

Quinidine
Lidocaine
Flecainide

B. Class II

Propranolol
Atenolol

C. Class III

Amiodarone
Ibutilide

D. Class IV

Verapamil
Diltiazem

E. Others

Adenosine
Magnesium

Potassium
Digitalis

D13. PHARMACOTHERAPY OF ANEMIAS AND HEMATOPOIETIC GROWTH FACTORS

1. The basic pharmacology, clinical indications, mechanism of action, adverse effects and contraindications of the agents used in the treatment of anemia including a) iron, b) vitamin B12, and c) Folic Acid
2. The basic pharmacology, clinical indication, mechanism of action, adverse effects and contraindications of the growth factors used in the treatment of cytopenias, including a) erythropoietin, b) G-CSF, c) GM-CSF, and d) IL-11.

Relevant Drugs

A. Drugs used in the treatment of anemia

Iron
Vitamin B12
Folic Acid

B. Growth factors used in the treatment of cytopenias

Erythropoietin
G-CSF
GM-CSF
IL-11

E. THE PHARMACOLOGY OF INFECTIOUS DISEASE

E1. ANTIBIOTICS I: AN INTRODUCTION

1. The identification of bacteria according to characteristics observed on gram-stain including cell wall staining results (gram-positive vs. gram-negative), morphology (cocci vs. bacilli), and growth characteristics (aerobic vs. anaerobic).
2. Description of the normal flora, including the identification of the anatomic sites where normal flora are commonly present and body sites that are usually “sterile” and the identification of the bacteria that are considered to be normal flora in each of the sites that are normally colonized.
3. The differences between contamination, colonization, and infection.
4. The typical clinical, laboratory and radiologic signs and symptoms of infection (fever, white blood cell count, infiltrate on chest x-ray, etc), and how the results of these tests may impact the process of antibiotic selection.
5. The most likely pathogens associated with infection at a particular anatomic site of infection.
6. The definition of the terms MIC, MBC, and MIC susceptibility breakpoints and the differences between the antimicrobial susceptibility testing methods.
7. The definition of the common pharmacodynamic terminology used to describe the effects of antimicrobial therapy such as bacteriostatic, bactericidal, concentration-dependent, and time-dependent bactericidal activity. Know examples of antibiotics that display each of these properties.
8. The factors that should be considered in the antibiotic selection process for each patient in the treatment of infection.

E2. ANTIBIOTICS II: PENICILLINS

1. The differences in the chemical structure between the penicillins, cephalosporins, carbapenems, and monobactams.
2. The general characteristics of β -lactam antibiotics including their mechanism of action, bactericidal vs. bacteriostatic activity, elimination half-life, route of elimination, and potential for cross-allergenicity.
3. The differences in the spectrum of activity between the natural penicillins, the penicillinase-resistant penicillins, the aminopenicillins, the carboxypenicillins, the ureidopenicillins, and the β -lactamase inhibitor combinations with special attention to the specific agents that have activity against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Bacteroides fragilis*.
4. The distribution characteristics of the penicillins into the cerebrospinal fluid, urinary tract, lungs, skin/soft tissue, and bone.
5. The indications, mechanism of action, adverse effects and contraindications of each group of penicillins
6. The mechanisms by which bacteria develop resistance to the penicillins.

Relevant Drugs

A. Natural Penicillins:

Penicillin G
Benzathine Penicillin
Procaine Penicillin G
Penicillin VK

B. Penicillinase-Resistant Penicillins:

Nafcillin
Oxacillin
Dicloxacillin

C. Aminopenicillins:

Ampicillin, Amoxicillin

D. Carboxypenicillins:

Ticarcillin

E. Ureidopenicillins:

Piperacillin

F. Beta-Lactamase Inhibitor Combinations:

Ampicillin-Sulbactam (Unasyn®)
Amoxicillin-Clavulanate (Augmentin®)
Piperacillin-Tazobactam (Zosyn®)

E3. ANTIBIOTICS III: CEPHALOSPORINS, CARBAPENEMS, and MONOBACTAMS

1. The differences in the spectrum of activity between the four generations of cephalosporins, as well as the carbapenems and aztreonam
2. The indications, mechanism of action, adverse effects and contraindications of the cephalosporins, carbapenems and aztreonam.
3. The mechanisms by which bacteria develop resistance to cephalosporins, carbapenems and aztreonam.

4. The pharmacokinetics of the cephalosporins, carbapenems and aztreonam, particularly those drugs able to penetrate the CNS and those drugs that require dosage adjustment in the presence of renal impairment.
5. The risk of cross-reactivity between penicillins and cephalosporins, carbapenems and aztreonam
6. The major clinical uses of representative agents within each generation of cephalosporins, carbapenems, and aztreonam.

Relevant Drugs**A. 1st Generation Cephalosporins***Cefazolin**Cephalexin***B. 2nd Generation Cephalosporins***Cefuroxime**Cefoxitin**Cefotetan**Cefprozil***C. 3rd Generation Cephalosporins***Ceftriaxone**Ceftazidime***D. 4th Generation Cephalosporins***Cefepime***E. Carbapenems:***Imipenem**Meropenem**Ertapenem**Doripenem***F. Monobactams:***Aztreonam***E4. ANTIBIOTICS IV: FLUOROQUINOLONES**

1. The spectrum of activity of the older and respiratory fluoroquinolones, particularly, the fluoroquinolones that have the best activity against *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Pseudomonas aeruginosa*, atypical bacteria, and anaerobes.
2. The indications, mechanism of action, adverse effects, contraindications and major drug interactions of the fluoroquinolones
3. The mechanisms by which bacteria develop resistance to the fluoroquinolone antibiotics.
4. The major pharmacokinetic differences between the fluoroquinolones in terms of oral bioavailability, half-life, dosing interval, penetration into the CSF, route of excretion, necessity for dosage adjustment in renal insufficiency, and removal by hemodialysis.

Relevant Drugs*Ciprofloxacin**Levofloxacin**Moxifloxacin*

Gemifloxacin

E5. ANTIBIOTICS V: AMINOGLYCOSIDES

1. The spectrum of activity of the aminoglycoside antibiotics, with special attention to those agents that display activity against *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and tuberculosis.
2. The indications, mechanism of action, adverse effects and contraindications for the aminoglycosides
3. The mechanisms by which bacteria become resistant to the aminoglycosides.
4. The major pharmacokinetic characteristics of the aminoglycosides (absorption, distribution, metabolism, elimination) including an understanding of the patient characteristics that may alter the pharmacokinetic parameters of volume of distribution and clearance, as well as how these alterations may influence dosing of aminoglycosides.

Relevant Drugs

Gentamicin

Tobramycin

Amikacin

Streptomycin

E6. ANTIBIOTICS VI: VANCOMYCIN AND OTHER AGENTS WITH ACTIVITY AGAINST GRAM-POSITIVE AEROBES

1. The general spectrum of activity of vancomycin, quinupristin-dalfopristin, linezolid, and daptomycin.
2. The indications, mechanism of action, adverse effects and contraindications for vancomycin, quinupristin-dalfopristin, linezolid, and daptomycin.
3. The mechanisms by which bacteria become resistant to vancomycin, quinupristin-dalfopristin, linezolid, and daptomycin.
4. The major pharmacokinetic characteristics of vancomycin, quinupristin-dalfopristin, linezolid and daptomycin including bioavailability, half-life, CSF penetration, route of elimination, necessity for dosage adjustment in renal insufficiency, and removal by hemodialysis.

Relevant Drugs

A. Glycopeptides

Vancomycin

B. Streptogramins

Quinupristin-dalfopristin (Synercid®)

C. Oxazolidinones

Linezolid (Zyvox®)

D. Lipopeptides

Daptomycin (Cubicin®)

E7. ANTIBIOTICS VII: TETRACYCLINES and SULFONAMIDES

1. The spectrum of activity of the tetracyclines and sulfonamides.

2. The indications, mechanism of action, adverse effects, contraindications and major drug interactions of the tetracyclines and sulfonamides.
3. The pharmacokinetic characteristics of the tetracyclines and sulfonamides with respect to oral bioavailability, distribution into the central nervous system, route of elimination, removal by hemodialysis, and dosage adjustment in end-organ dysfunction.
4. The potential therapeutic advantages of the glycylycylcline antibiotics.
5. The mechanisms by which bacteria develop resistance to the tetracyclines.
6. The mechanisms by which bacteria develop resistance to the sulfonamides.

Relevant Drugs

A. Tetracyclines

Tetracycline

Doxycycline

Minocycline

B. Glycylycylclines

Tigecycline (Tygacil®)

C. Sulfonamides

Sulfadiazine

Sulfisoxazole

Trimethoprim-Sulfamethoxazole

E8. ANTIBIOTICS VIII: CLINDAMYCIN and METRONIDAZOLE

1. The spectrum of activity of clindamycin and metronidazole, with special emphasis on their activity against anaerobes and *Clostridium difficile*.
2. The indications, mechanism of action, adverse effects, contraindications and major drug interactions of clindamycin and metronidazole
3. The mechanisms of resistance to clindamycin and metronidazole.
4. The pharmacokinetic characteristics of clindamycin and metronidazole with respect to oral bioavailability, distribution into the central nervous system, route of elimination, removal by hemodialysis, and dosage adjustment in end-organ dysfunction.

Relevant Drugs

Clindamycin

Metronidazole

E9. ANTIBIOTICS IX: ANTIMYCOBACTERIAL DRUGS

1. The indications, mechanism of action, adverse effects and contraindications of the first line antituberculosis therapeutic agents,
2. The treatment principals that should be followed when treating patients infected with *M. tuberculosis*.
3. The therapeutic indications of rifampin.
4. The mechanisms of primary and secondary resistance in *M. tuberculosis* infections.
5. The reasons for resurgence of tuberculosis and ways to stop the TB epidemic.
6. The major determinant of outcome of treatment for tuberculosis and the ways to improve this determinant.

Relevant Drugs

Isoniazid, Isonicotinic Acid Hydrazide, INH

*Rifampin,
Rifampicin
Rifabutin
Rifapentine
Ethambutol
Pyrazinamide
Streptomycin*

E10. ANTI-PARASITIC AGENTS

1. The distinction between protozoal and helminth infections
2. The general approaches to antiparasitic chemotherapy
3. The general strategies and relevant drugs used to treat the following protozoal infections: a) Malaria, b) Amebiasis, c) African trypanosomiasis, d) American trypanosomiasis, e) Cryptosporidiosis, and f) Toxoplasmosis
4. The general strategies and relevant drugs used to treat the major Helminth Infections
5. The principal indications, mechanism of action, adverse effects and contraindications for the major drugs used in the treatment of protozoal and helminth infections

Relevant Drugs

A. Anti-malarial drugs

*Chloroquine
Quinine and Quinidine
Mefloquine
Primaquine
Proguanil
Atovaquone
Amodiaquone
Pyrimethamine
Halofantrine
Artemisinin
Antibiotics: tetracycline, doxycycline, azithromycin, clindamycin*

B. Antiamebic Drugs

*Metronidazole
Emetine
Iodoquinol
Paromomycin*

C. Drugs to treat African Trypanosomiasis

*Pentamidine
Suramin
Melarsoprol
Eflornithine*

D. Drugs to treat American Trypanosomiasis

*Nifurtimox
Benznidazole*

E. Drugs to treat Leishmaniasis

Sodium Stibogluconate

F. Drugs to treat cryptosporidiosis

Nitazoxanide

Paromomycin

G Drugs to treat Giardiasis

Metronidazole

Nitazoxanide

H. Drugs to treat Toxoplasmosis

Pyrimethamine

Folinic acid

sulfadiazine

clindamycin

I. Drugs to treat Helminths

Albendazole

Diethylcarbamazine citrate

Ivermectin

Mebendazole

Praziquantel

Pyrantel Pamoate

E11. ANTIMYCOTIC AGENTS

1. The indications, mechanism of action, adverse effects and contraindications for the most commonly used anti-mycotic agents.

Relevant Drugs

A. Polyene Antifungal agents

Amphotericin B

Nystatin

B. Azole antifungal agents

Imidazoles: miconazole, clotrimazole, ketoconazole

Triazoles: fluconazole, itraconazole, voriconazole, terconazole

Posaconazole,

C. Echinocandins

Caspofungin

Micafungin

Anidulofungin

D. Other anti-mycotic drugs

5-Flucytosine

Griseofulvin

Terbinafine

E12. ANTIVIRAL DRUGS

1. Understand the mechanism of action of the major nucleoside analogs
2. Identify the viruses targeted by the major nucleoside analogs and the relative benefits of each agent.
3. Understand the mechanism of action of the antiviral non-nucleoside analogs
4. Identify the viruses targeted by the antiviral non-nucleoside analogs
5. Understand the indications, mechanism of action and clinical efficacy of the principal inhibitors of viral entry or dissemination.
6. Understand mechanisms leading to the development of antiviral resistance

7. Understand how drugs targeting different virus infection stages can be synergistic when administered simultaneously.

Relevant Drugs

A. The nucleoside analogs

Acyclovir

Ganciclovir

Idoxuridine

Vidarabine

Azidothymidine

Dideoxyinosine

dideoxycytosine

B. Non-nucleoside analogs

Ribavirin

Foscarnet

C. Inhibitors of virus entry or dissemination

Amantadine

Neuraminidase inhibitors

Pleconoril

Interferons

Passive antibody transfer

E13. THERAPEUTICS OF HIV INFECTION

1. How distinct antiretroviral agent classes target different phases of the HIV replication cycle.
2. The diagnostic criteria and therapeutic goals for the treatment of HIV infection.
3. The indications, clinical use, major adverse effects, contraindications and significant drug interactions for each of the major classes of antiretroviral medications used in the treatment of HIV infection.
4. The utility and effectiveness of combination therapy in the treatment of HIV infection
5. The concept that the presence of co-morbid conditions may require a modified antiviral regimen.

Relevant Drugs

A. NUCLEOSIDE/NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS

Abacavir

Didanosine

Emtracitabine

Lamivudine

Stavudine

Tenofovir

Zalcitabine

Zidovudine

B. NON-NUCLEOTIDE REVERSE TRANSCRIPTASE INHIBITORS

Delavirdine

Efavirenz

Etravirine

Nevirapine

C. PROTEASE INHIBITORS

Fosamprenavir

Atazanavir
 Darunavir
 Indinavir
 Lopinavir
 Nelfinavir
 Ritonavir
 Saquinavir
 Tipranavir

D. VIRAL INTEGRASE INHIBITORS

Raltegravir (Isentress)

E. FUSION INHIBITORS

Enfuvirtide

F. CCR5 ANTAGONISTS

Mariviroc

F. THE PHARMACOLOGY OF THE CENTRAL NERVOUS SYSTEM

F1. DRUGS TO TREAT ANXIETY AND BIPOLAR AFFECTIVE DISORDER

1. The target sites of action of the benzodiazepines and SSRIs and the strategy for using benzodiazepines in combination with SSRIs in the treatment of anxiety disorders.
2. The target sites of action of lithium, its pharmacokinetics, adverse effects and considerations in its use in the treatment of bipolar disorder.
3. The pharmacokinetics, adverse effects and considerations in using the anticonvulsants to treat bipolar affective disorder.
4. The sites of action, adverse effects and considerations in using the atypical antipsychotics to treat bipolar affective disorder.
5. The potential risk of birth defects with the use of lithium, valproate, carbamazepine and lamotrigine in pregnant women.

Relevant Drugs

A. Benzodiazepines

Alprazolam (Xanax®)
 Clonazepam (generic, Klonopin®)
 Diazepam (generic, Valium®)
 Lorazepam (generic; Ativan®)

B. 5-HT_{1A} receptor agonist

Buspirone (Buspar®)

C. Lithium (generic; Eskalith®)

D. Anticonvulsants

Carbamazepine (generic, Tegretol®)
 Lamotrigine (Lamacital®)
 Valproic acid (generic; Depakene®, Depakote®)

E. Atypical Antipsychotics

Aripipazole (Abilify®)

Olanzapine	(Zyprexa®)
Quetiapine	(Seroquel®)
Risperidone	(Risperidal®)
Ziprasidone	(Geodon®)

F2. PHARMACOLOGY OF ANTIDEPRESSANT DRUGS

1. The primary sites of action of the different classes of antidepressant drugs that are responsible for their therapeutic efficacy.
2. The adverse/side effects of the different classes of antidepressant drugs and considerations for their use in certain populations (e.g. in the elderly, in pregnancy, etc).
3. The pharmacologic sites of action of different antidepressant drugs that contribute to the acute and/or side effects of these drugs.
4. The proposed mechanisms underlying the delayed therapeutic effects of antidepressant drugs.
5. The considerations in using irreversible versus reversible MAOIs, the potential adverse effects of MAOIs, and the important considerations in switching between MAOIs and SSRIs or other antidepressant drugs.

Relevant Drugs

A. Tricyclic antidepressants (TCAs)

Imipramine	(generic; Tofranil®)
Amitriptyline	(generic; Elavil®)
Clomipramine	(Anafranil®)
Desipramine	(Nopramin®)
Doxepin	(Sinequan®)

B. Selective-serotonin reuptake inhibitors (SSRIs)

Citalopram	(Celexa®) and
S-Citalopram	(Lexapro®)
Fluoxetine	(generic; Prozac®)
Fluvoxamine	(Luvox®)
Paroxetine	(Paxil®)
Sertraline	(Zoloft®)

C. Atypical antidepressants

Bupropion	(Wellbutrin®, Zyban®)
Mirtazapine	(Remeron®)
Nefazodone	(Serzone®)

D. Norepinephrine/serotonin reuptake inhibitors (SNRIs)

Venlafaxine	(Effexor®)
Desvenlafaxine	(Pristiq®)
Duloxetine	(Cymbalta®)

E. MAOIs (monoamine oxidase inhibitors)

Irreversible:	Phenelzine (generic; Nardil®)
	Tranylcypromine (generic; Parnate®)
	Selegiline (l-deprenyl); Eldepryl®, Emsam®

Reversible (RIMA):	Moclobemide (Manerix®, in Canada)
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F3. ANTIPSYCHOTIC DRUGS

1. The four well-defined dopamine systems in the brain as they relate to antipsychotic drug action and side effects.
2. The distinction between “typical” and “atypical” antipsychotics.
3. The difference in the mechanism(s) of action between a typical antipsychotic, an atypical anti-psychotic and the partial agonist aripiprazole.
4. The common and rare side effects associated with the use of both low potency and high potency typical antipsychotics
5. The common and rare side effects associated with the use of the second-generation atypical anti-psychotics.

Relevant Drugs

A. Typical anti-psychotics

Chlorpromazine (Thorazine®)

Haloperidol (Haldol®)

B. Atypical anti-psychotics

Risperidone (Risperidal®)

Olanzapine (Zyprexa®)

Quetiapine (Seroquel®)

Ziprasidone (Geodon®)

Aripiprazole (Abilify®)

Paliperidone (Invenga®)

C. Clozapine (Clozaril®)

F4. PHARMACOLOGY OF SEDATIVE–HYPNOTIC DRUGS AND THEIR USE IN TREATING ANXIETY AND SLEEP DISORDERS

1. The structural aspects of the GABAA receptor and the receptor components (i.e. binding sites) mediating the effects of drugs that modulate GABAA receptor activity.
2. The differences between benzodiazepines with respect to Phase I only versus Phase I & II pharmacokinetics.
3. The similarities and differences among the benzodiazepines with respect to: a) time of onset, b) potency, c) metabolism and d) elimination half-lives.
4. The similarities and differences between the benzodiazepines and the barbiturates in producing sedative-hypnotic effects.
5. The factors to consider in choosing the most appropriate drug for specific clinical situations and/or individuals.
6. The characteristics of benzodiazepines and other sedative-hypnotics that contribute to different degrees of abuse liability and withdrawal symptoms.
7. The target sites or putative mechanisms of non-benzodiazepine drugs that can be used to treat sleep disorders.

Relevant Drugs

A. Benzodiazepines

Alprazolam (Xanax®)

Clonazepam (generic, Klonopin®)

Diazepam (Valium®)

Estazolam (ProSom®)

Flurazepam (Dalmane®)

Lorazepam (generic; Ativan®)

Oxazepam (Serax®)

Temazepam (Restoril®)
Triazolam (Halcion®)

B. Non-Benzodiazepines
Eszopiclone (Lunestra®)
Zolpidem (Ambien®)
Zaleplon (Sonata®)

C. Tricyclic Antidepressants
Amitriptyline (generic; Elavil®)
Doxepin (Sinequan®)
Imipramine (Tofranil®)

D. Barbiturates
Pentobarbital (generic, Nembutol Sodium®)
Phenobarbital (generic, Luminol Sodium®)
Thiopental Sodium (Pentathal®)

E. Other Sedating Drugs
Mirtazapine (Remeron®)
Nefazodone (Serzone®)
Trazadone (Deseryl)
Diphenhydramine (Benadryl®)
Cyclobenzaprine (Flexeril®)
Hydroxyzine (Atarax®)
Meprobamate (Equinil®, Miltown®)
Ramelteon (Rozerem®)

F5. DRUGS OF ABUSE AND DRUG DEPENDENCY

1. The underlying biological basis of addiction as a disease.
2. The differential diagnostic criteria for drug abuse vs dependence and the difference between them
3. The mechanism of action within the central nervous system of the major drugs of abuse
4. The signs and symptoms of overdose caused by the major drugs of abuse including alcohol, heroin and cocaine.
5. The signs and symptoms of opioid withdrawal
6. The pharmacotherapeutic options for the treatment of opioid abuse and dependence and their relative benefits and side effects.
7. The signs and symptoms of alcohol withdrawal
8. The pharmacotherapeutic options for the treatment of alcohol abuse and their relative benefits and side effects.

Relevant Drugs

Benzodiazepines e.g. lorazepam
Naloxone
Methadone
Buprenorphine
Naltrexone
Disulfiram
Acomprostate

F6. PEDIATRIC PSYCHOPHARMACOLOGY

1. The indications, mechanism of action, adverse effects and contraindications of drugs used in the treatment of attention-deficit hyperactivity disorder (ADHD)
2. The concept that stimulant drugs should not be used in children with structural cardiac abnormalities, cardiomyopathy and serious heart rhythm abnormalities.
3. The current treatment algorithm for the treatment of ADHD

Relevant Drugs

A. Stimulants

Methylphenidate
Dexmethylphenidate
Amphetamine Sulfate

B. SNRIs

Atomoxetine

C. Alpha-2-adrenergic agonists

Clonidine
Guanfacine

F7. ANTIEPILEPTIC DRUGS

1. Recognition of the different seizure types
2. The concept that the seizure type determines the selection of a specific antiepileptic drug
3. The spectrum of action of the most commonly used antiepileptic drugs
4. For a given seizure type, an understanding of the selection process of an antiepileptic drug based on its: a) Mechanism of action, b) Efficacy, c) Clinical pharmacokinetics (ease of use), d) Drug-drug interaction potential, e) Tolerability (common side-effects), f) Serious toxicity (idiosyncratic reactions)
5. The role of co-morbidities in the selection of an antiepileptic drug

Relevant Drugs

A. "Classic" antiepileptic drugs:

Benzodiazepines
Carbamazepine (Tegretol[®])
Ethosuximide (Zarontin[®])
Phenobarbital
Phenytoin (Dilantin[®])
Primidone Mysoline[®]
Valproate (Depakote[®])

B. "Newer" antiepileptic drugs:

Felbamate (Felbatol[®])
Gabapentin (Neurontin[®])
Lamotrigine (Lamictal[®])
Levetiracetam (Keppra[®])
Oxcarbazepine (Trileptal[®])
Pregabalin (Lyrica[®])
Tiagabine (Gabitril[®])
Topiramate (Topamax[®])
Zonisamide (Zonegran[®])

F8. PARKINSONISM & ITS TREATMENT

1. The presentation of Parkinson's disease and its underlying pathophysiology
2. The functional circuitry of the nigrostriatal system.
3. The major classes of pharmacotherapy for Parkinson's Disease and the timeline for their use
4. The indications, mechanism of action, adverse effects and contraindications for the major classes of drugs used in the treatment of Parkinson's Disease
5. The type and mechanisms of alternative treatments for Parkinson's Disease.

Relevant Drugs

Levodopa
Carbidopa
Levodopa/Carbidopa
Bromocriptine
Pramipexole
Ropinirole
Selegiline
Talcapone
Ammantadine
Benzotropine

F9. PHARMACOLOGY OF STROKE AND ALZHEIMER'S DISEASE

1. The laboratory and clinical tests for ruling out reversible forms of dementia in the elderly.
2. The drug treatments for the reversible forms of dementia.
3. The current symptomatic and theoretical preventive drug therapies for Alzheimer's disease.
4. The theoretical drug therapies for Huntington's disease and ALS.
5. The preventive and symptomatic drug treatments for cerebrovascular disease.

Relevant Drugs

Tacrine
Donepezil
Rivastigmine
Cevimeline (AF102B)
Fluoxetine
Indomethacin
Ibuprofen
Celocoxib
Vitamin E
Haloperidol
Creatine (OTC)
Riluzole
Clofibrate
Captopril
Warfarin
Heparin
Atorvastatin
vitamin B₁₂
Levothyroxine

G. ENDOCRINE PHARMACOLOGY

G1. NEUROENDOCRINE PHARMACOLOGY: HYPOTHALAMIC AND PITUITARY HORMONES

1. The physiology of neuroendocrine hormonal regulation, specifically the regulation and function of the:
 - a) Hypothalamus-Pituitary-Growth Hormone Axis
 - b) Hypothalamus-Pituitary-Reproductive Axis
 - c) Hypothalamus-Pituitary-Prolactin Axis
2. The use of specific neuroendocrine agents in the treatment of the following neuroendocrine disorders:
 - a) growth hormone deficiency
 - b) growth hormone excess
 - c) infertility
 - d) hyperprolactinemia
3. The indications, mechanism of action, adverse effects, contraindications and therapeutic considerations for the major neuroendocrine hormones and pharmacological agents.

Relevant Drugs

A. Drugs to treat Growth Hormone Deficiency

Recombinant hGH (Somatropin, Somatrem)

Synthetic GHRH (Sermorelin)

Recombinant IGF-1

B. Drugs to treat Growth Hormone Excess

Octreotide

Pegvisomant

C. Drugs to treat male and female infertility

Human chorionic gonadotropin

Menotropins

Urofollitropin,

Follitropin

Synthetic GHRH (Sermorelin)

Analogs of GnRH

Goserelin,

Histrelin,

Leuprolide,

Nafarelin,

Triptorelin

GnRH antagonists

Ganirelix

Cetrorelix

Abarelix

D. Drugs to treat hyperprolactinemia

Dopamine receptor agonists

Bromocriptine

Cabergoline

Pergolide

G2. PHARMACOLOGY OF GONADAL HORMONES: ESTROGENS AND PROGESTINS

1. The physiological actions and pharmacological effects of estrogens and progestins that are relevant to their clinical uses.
2. The adverse effects and contraindications of estrogens and progestins.
3. The current strategies for the use of estrogens and progestins in oral contraceptives and in hormone replacement therapy in menopause.
4. The pharmacological actions and clinical uses of selective Estrogen Receptor Modulators (SERMs).

Relevant Drugs

A. Estrogens and related

Estradiol

Ethinyl estradiol

Conjugated equine estrogens

Estradiol Transdermal

Diethylstilbestrol/DES

Tamoxifen, Clomiphene, Raloxifene (SERM)

Fulvestrant (ER antagonist)

Anastrozole, Letrozole, Exemestane, Formestane (Aromatase inhibitors)

B. Progesterins and related

Norgestrel

Etonogestrel

Medroxyprogesterone

Levo-norgestrel

Norethindrone

Mifepristone (PR antagonist)

G3. PHARMACOLOGY OF GONADAL HORMONES: ANDROGENS

1. The physiological actions, pharmacological effects, and clinical uses of androgens.
2. The adverse effects and contraindications to use of androgens.
3. The pharmacology and clinical uses of androgen antagonists.

Relevant Drugs

Testosterone

Dihydrotestosterone

Methyltestosterone

17alpha-ethinyltestosterone (Danazol)

Finasteride (inhibitor of DHT conversion)

Flutamide, Spironolactone (AR antagonist)

G4. THYROID AND ANTI-THYROID DRUGS

1. The concept that thyroid hormone plays a major role in regulating development as well as metabolism and calorogenesis.
2. The steps in the synthesis of Tetraiodothyronine (T4) and triiodothyronine (T3)
3. The endocrine regulation of T3 and T4 production and feed-back loops
4. The physiological roles of T3 and T4 and, therefore, the changes associated with hypo- and hyper-thyroidism.

5. The mechanism of action, adverse effects and contraindications of drugs used to treat hyperthyroidism.

Relevant Drugs

Thyroid Agents: Levothyroxine (T₄), Liothyronine (T₃) & Liotrix (T₄:T₃ = 4:1)

Iodide: Diatrizoate Sodium

Iodide (¹³¹I) sodium

Methimazole

Propylthiouracil

Propranolol

Hydrocortisone

G5. PHARMACOLOGY OF CALCIUM METABOLISM

1. The role of the key organs involved in regulation of plasma calcium concentration
2. The endocrine regulation of calcium homeostasis and mechanisms involved
3. The principles underlying the treatment of both hyper- and hypocalcemia.
4. The indications, mechanism of action, adverse effects and contraindications of the drugs used in therapy of hypo- and hyper-calcemia.

Relevant Drugs

1,25- dihydroxy Vitamin D₃, 25-OH Vitamin D₃

Calcitonin

PTH- Teriparatide

Gallium Nitrate

Glucocorticoids

Bisphosphonates

Cinacalcet.

Estrogen

Raloxifene

G6. ADRENOCORTICOSTEROIDS

1. The role of ACTH and the HPA axis in the regulation of corticosteroid synthesis
2. The principal physiological responses to both glucocorticoids and mineralocorticoids, especially the role of cortisol and exogenous glucocorticoids in the negative feedback suppression of the HPA axis.
3. The use of synthetic glucocorticoids and mineralocorticoids drugs in the treatment of adrenal deficiency diseases such as Adrenal insufficiency and Congenital Adrenal Hyperplasia
4. The mechanism of action of glucocorticoid drugs and their pharmacological use in the treatment of non-endocrine diseases e.g. Rheumatoid Arthritis, Asthma, Inflammation and Cancer.
5. The major adverse effects associated with the clinical use of glucocorticoids
6. The concept that abrupt withdrawal of chronic glucocorticoid therapy can lead to acute adrenal crisis due to atrophy of the adrenal cortex and subsequent deficiency in endogenous cortisol production
7. The use of cortical synthesis inhibitors such as ketoconazole, metyrapone, aminoglutethimide and mitotane in the treatment of Cushing's disease.

Relevant Drugs

A. Principal synthetic corticosteroids

Hydrocortisone (Cortisol)

Cortisone

Fludrocortisone
Prednisone
Prednisolone
Dexamethasone

B. Inhaled forms of glucocorticoids used in asthma:

Triamcinolone acetonide
beclometasone
fluticasone

C. Adrenocorticoid synthesis inhibitors

Ketoconazole
Metyrapone
Aminoglutethimide
Mitotane

G7. DRUGS TO TREAT DIABETES

1. The fundamental differences between type 1 and type 2 diabetes
2. Recognition of the diagnostic criteria and therapeutic goals for the treatment of diabetes
3. The pharmacological differences between the various insulin formulations used in the treatment of diabetes especially their duration of action. Specifically, which insulin types are used for the control of post-prandial glucose levels versus those used for the control of fasting glucose levels.
4. The use and clinical benefits of an intensive insulin therapy regimen in the treatment of type 1 diabetes
5. The important role of diet and exercise in the treatment of type-2 diabetes
6. The indications, mechanism of action, clinical effects, adverse effects and contraindications of drugs commonly used in the treatment of type 2 diabetes including:
 - a) metformin
 - b) the sulfonylureas
 - c) the meglitinides
 - d) the thiazolidinediones
 - e) the alpha-glucosidase inhibitors
 - f) modulators of the incretin pathway
 - g) insulin
 - h) pramlintide.
7. An understanding of which of the drugs used for the treatment of type-2 diabetes primarily affect either post-prandial or fasting glucose levels.
8. The concept that effective treatment of type-2 diabetes will likely require combination therapy with one or more oral anti-diabetic agents, as well as potentially the use of insulin therapy.
9. An understanding of the current treatment algorithm approved by the American Diabetes Association for the treatment of type-2 diabetes.
10. The effectiveness of tight glycemic control in the prevention of the macro- and microvascular complications of diabetes

Relevant Drugs

A. INSULIN FORMULATIONS

- (i) Rapid acting insulins*
Insulin aspart (Novolog®)
Insulin lispro (Humalog®)

Insulin glulisine (Apidra®)

(ii) Regular Insulin

Regular Insulin (Humulin R®, Novolin R®)

(iii) Intermediate-acting insulin

NPH Insulin (Humulin N®, Novolin N®)

(iv) Long-lasting insulin

Insulin detmir (Levemir®)

Insulin glargine (Lantus®)

B. ORAL ANTI-DIABETIC DRUGS: INSULIN SECRETAGOGUES

(i) SULFONYLUREAS

Chlorpropamide (Diabinese®),

Tolbutamide

Glimepiride (Amaryl®)

Glyburide (DiaBeta®, Micronase®)

Glipizide (Glucotrol®)

(ii) MEGLITINIDES

Repaglinide (Prandin®)

Nateglinide (Starlix®)

C. ORAL ANTI-DIABETIC DRUGS: INSULIN SENSITIZERS

(i) BIGUANIDES

Metformin (Glucophage®)

(ii) THIAZOLIDINEDIONES

Pioglitazone (Actos®)

Rosiglitazone (Avandia®)

D. ORAL ANTI-DIABETIC DRUGS: ALPHA-GLUCOSIDASE INHIBITORS

Acarbose (Precose®)

Miglitol (Glyset®)

E. Pramlintide and modulators of the Incretin Pathway

Pramlintide (Symlin®)

Exenatide (Byetta®)

Sitagliptin (Januvia®)

H. CANCER PHARMACOLOGY

H1. CHEMOTHERAPY I: OVERVIEW

1. The importance of tumor cell heterogeneity and the development of malignant cell resistance to chemotherapy as critical factors in determining treatment outcome;
2. The process of antineoplastic drug development;
3. The criteria determining the response to antineoplastic agents;
4. The toxicity of cancer chemotherapy.
5. The principles of management of the patient with cancer.
6. The importance of tumor staging in the management of the patient with cancer.
7. The principles of chemotherapy.
8. The rationale for the administration of adjuvant chemotherapy.

H2. CHEMOTHERAPY II: ALKYLATING AGENTS

1. The characteristic indications for the alkylating agents and plant alkaloids commonly used in chemotherapy
2. The mechanism of action and mechanisms of resistance for the alkylating agents and plant alkaloids commonly used in chemotherapy
3. The principal adverse effects of the commonly used alkylating agents and plant alkaloids.

Relevant Drugs

Cyclophosphamide
Ifosfamide
BCNU
Cis-diaminedichloroplatinum (II)
Carboplatin
Oxaliplatin
Vincristine
Vinblastine
Vinorelbine
Paclitaxel
Docetaxel
Etoposide

H3. CHEMOTHERAPY III: ANTIBIOTIC/ANTI-TUMOR AGENTS

1. The characteristic indications, mechanism of action, mechanism of resistance and adverse effects of doxorubicin and the other commonly used antibiotic and anti-tumor agents.
2. The concept of multiple drug resistance and its effects on effective chemotherapy.
3. The concept of cumulative toxicity and schedule independent toxicity.
4. The concept of the hormonally-sensitive neoplasms and their treatment
5. The major side effects associated with antibiotic and anti-tumor agents commonly used in chemotherapy

Relevant Drugs

Doxorubicin
Bleomycin
Prednisone
Progestins
Flutamide
Leuprolide acetate
Anastrozole
Tamoxifen

H4. CHEMOTHERAPY IV: ANTI-METABOLITES

1. The characteristic indications for the use on antimetabolites commonly used in the treatment of cancer.
2. The mechanism of action of the antimetabolites commonly used in the treatment of cancer.
3. The mechanism of resistance to antimetabolites
4. The major adverse effects associated with antimetabolites commonly used in the treatment of cancer.

Relevant Drugs*Methotrexate**Pemetrexed**Cytarabine**Gemcitabine**5-Fluorouracil**Capecitabine***H5. CHEMOTHERAPY V: TARGETED THERAPIES OF CANCER MISCELLANEOUS AGENTS**

1. The concept of “targeted cancer therapy”.
2. The role of tyrosine kinases as targets for cancer therapy
3. The potential benefits and toxicities of the commercially available targeted therapies.
4. The uses and side effects of miscellaneous anti-cancer agents.

Relevant Drugs*Imatinib mesylate (Gleevec)**Erlotinib (Tarceva)**Cetuximab (Erbix)**Trastuzumab (Herceptin)**Bevacizumab (Avastin)**Rituximab (Rituxin)**Asparaginase**Hydroxyurea**All-trans-retinoic acid**Arsenic trioxide***I. MISCELLANEOUS TOPICS****11. DRUGS TO TREAT RHEUMATOID ARTHRITIS AND GOUT**

1. The relative therapeutic benefit of NSAIDs, Analgesics, Glucocorticoids, DMARDs and Biological Response Modifiers in the treatment of Rheumatoid Arthritis.
2. The concept that NSAIDs, Analgesics and Glucocorticoids are used as initial therapy to provide symptomatic relief only and do not affect the overall disease course of RA.
3. The use of the frequently used DMARDs (methotrexate, hydrochloroquine, sulfasalazine and leflunomide) in the treatment of Rheumatoid Arthritis; specifically, their time to effect, potential for use during pregnancy and their major adverse effects.
4. The roles of the distinct classes of Biological Response Modifiers in the treatment of Rheumatoid Arthritis including their mechanism of action, major adverse effects and contraindications
5. The concept that treatment with Biological Response Modifiers can lead to the reactivation of latent bacteria and viruses.
6. The pathophysiology of Gout; the role of uric acid in the etiology of the disease; and the typical disease course including hyperuricemia, acute gouty attack, intercritical phase and chronic gout.
7. The rationale for the use of Colchicine and NSAIDs in the treatment of an acute gouty attack.
8. The concept that aspirin and the salicylates are contraindicated in the treatment of gout due to their effects on uric acid renal excretion at low doses.

9. The indications, mechanism of action, clinical effects, adverse effects and contraindications of uricosuric agents and allopurinol used in the treatment of chronic gout.

Relevant Drugs

A. NSAIDs

B. Acetaminophen (Tylenol[®]/Paracetamol[®])

C. Topical Analgesics e.g. Capsaicin

D. Glucocorticoids (Injectable/Oral)

E. Disease-Modifying anti-Rheumatic Drugs (DMARDs)

(i) Commonly used DMARDs:

Methotrexate (Rheumatrex[®])
 Hydroxychloroquine (Plaquenil[®])
 Sulfasalazine (Azulfidine[®])
 Leflunomide (Arava[®])

(ii) Less frequently used DMARDs:

Azathioprine (Imuran[®])
 D-penicillamine (Depen[®])
 Gold salts
 Cyclosporin A (Sandimmune[®] & Neural[®])
 Cyclophosphamide (Cytosan[®])

F. Biological-response Modifiers

Etanercept (Enbrel[®])
 infliximab (Remicade[®])
 Adalimumab (Humira[®])
 Anakinra (Kineret[®])
 Abatacept (Orenica[®])
 Rituximab (Rituxan[®])

G. Colchicine

H. Uricosuric agents

Probenecid
 Sulfinpyrazone (Anturane[®])

I. Uric Acid Synthesis Inhibitor

Allopurinol (Zyloprim[®])

12. TREATMENT OF ASTHMA

1. The indications, mechanism of action, adverse effects and contraindications for the different anti-asthmatics including the preference for certain drugs in certain situations.
2. The pharmacokinetics of anti-asthmatics and the rapidity of their onset of action.

Relevant Drugs

A. Beta2-adrenergic agonists

Metaproterenol (Metaprel[®])
Albuterol (Proventil[®])
Terbutaline (Brethaire[®])

Bitolterol (Tornalate®)
Salmeterol (Serevent®)

B. Methylxanthines
Theophylline (Theo-Dur®)

C. Muscarinic Receptor Antagonists
Ipratropium bromide (Atrovent®)

D. Adrenal Corticosteroids
Beclomethasone (Vanceril®)
Flunisolide (AeroBid®)
Triamcinolone (Azmacort®)

C. Cromolyn sodium (Intal®)

D. Leukotriene inhibitors
Zafirlukast (Accolate®)
Montelukast sodium (Singulair®)
Zileuton (Zyflo®)

E. Monoclonal antibodies
Omalizumab (Xolair®)

13. HISTAMINE AND ITS ANTAGONISTS

1. The physiological and pathophysiological role of histamine
2. The pharmacology of histamine receptors
3. The mechanisms of histamine release
4. The indications, mechanism of action, adverse effects and contraindications of histamine H1 and H2 receptor antagonists.

Relevant Drugs

Diphenhydramine
Chlorpheniramine
Fexofenadine
Loratidine
Citirizine
Cimetidine
Famotidine
Nizatidine
Ranitidine
Omeprazole
Lansoprazole
Rabeprazole
Carafate

14. PHARMACOLOGY OF THE GI TRACT RELATED TO END OF LIFE

1. The most common causes of constipation.
2. The mechanisms of action, indications, and contraindications for drugs used for the relief of constipation
3. An understanding of an appropriate pharmacologic plan of therapy to palliate the symptom of constipation.

4. The pathophysiology of nausea and vomiting.
5. The mechanisms of action, indications, and contraindications for antiemetics
6. An understanding of an appropriate pharmacologic plan of therapy to palliate the symptoms of nausea and vomiting.

Relevant Drugs

A. Drugs used in the relief of constipation

Bulk laxatives
Osmotic laxatives
Nonabsorbable sugars
Saline and magnesium laxatives
Polyethylene glycol
Stimulant laxatives
Detergent laxatives
Lubricants
Enemas

B. Antiemetics

Dopamine receptor antagonists: Metoclopramide, Prochlorperazine & Haloperidol
Prokinetic agents
Antihistamines
Serotonin antagonists
Anticholinergics
Benzodiazepenes
Corticosteroids

15. IMMUNOMODULATION THERAPY

1. How to predict the type of host immune response based on the type of infection or autoimmune disease and identify potential sites of therapeutic intervention.
2. The potential clinical hazards of blocking pathways or mediators of immune responses and the rationales for diagnosis and treatment of opportunistic pathogens in patients treated with immunomodulators
3. The ability to choose the most appropriate class of drug or biologic treatment required to modulate a particular immune response in a clinically effective way
4. The indications, mechanism of action and potential adverse effects of the major classes of immunomodulatory drugs.
5. The concept that interference with immune responses has the potential to increase the risk of neoplasia.

Relevant Drugs

Corticosteroids
Cyclophosphamide
Azathioprine
Methotrexate
Mycophenolate Mofetil
Leflunomide
Cyclosporine
Tacrolimus
Rapamycin
Monomurab
Basiliximab
Daclizumab
Rituximab

*Pooled IVIg***16. DIETARY SUPPLEMENTS AND HERBAL MEDICATIONS**

1. The role of the Federal Drug Administration (FDA) in the regulation of Dietary Supplements and Herbal Medications.
2. The permitted types of claim that a manufacturer of dietary supplements and herbal medications may make on the packaging of their products.
3. The typical natural sources of the major vitamins and minerals
4. The specific clinical conditions associated with deficiencies of the major vitamins and minerals
5. The typical patient groups that can benefit from vitamin and mineral supplements
6. The specific health risks associated with overconsumption of the major vitamins and minerals
7. The potential indications, adverse effects and drug interactions of the most commonly used herbal medications including: a) Bitter Orange, b) Echinacea c) Gingko, d) Gingseng, e) Horse Chestnut, f) Kava, g) Licorice Root, h) Milk Thistle, i) Saw Palmetto, j) St. John's Wort, k) Valerian, and l) Yohimbe.

Relevant Drugs(A) Dietary Supplements:

Vitamin A
Vitamin B6, B12
Vitamin C
Vitamin D
Vitamin E
Vitamin K
Selenium
Folic Acid/Folate
Co-enzyme Q
Glucosamine
Calcium
Magnesium
Iron
Zinc

(B) Herbal Medications:

Bitter Orange
Echinacea
Gingko
Gingseng
Horse Chestnut
Kava
Licorice Root
Milk Thistle
Saw Palmetto
St. John's Wort
Valerian
Yohimbe

II. INTERPERSONAL AND COMMUNICATION SKILLS

By the end of this course, students must have demonstrated knowledge of the basic principles of effective interpersonal communication, and the skills and attitudes that allow effective interaction with their peers, faculty, and support staff. Students will:

1. Use verbal language effectively.
2. Use effective listening skills and elicit and provide information using effective nonverbal, explanatory, and questioning skills.
3. Use written language effectively.
4. Facilitate the learning of other students, including giving effective feedback.
5. Communicate essential information effectively within their small group and with other students in the class.

III. PROFESSIONALISM, MORAL REASONING AND ETHICAL JUDGEMENT

By the end of this course, students must demonstrate a combination of knowledge, skills, attitudes, and behaviors necessary to function as a respected member of a learning team in both small group and large class settings. Students will:

1. Behave professionally in the context of the small group problem-solving session, including attendance, punctuality, preparedness, and ability to interact effectively with other small group members in the educational setting.
2. Recognize and effectively deal with unethical behavior of other members of the class, if encountered.

IV. LIFELONG LEARNING, PROBLEM SOLVING AND PERSONAL GROWTH

By the end of this course, students must demonstrate a combination of knowledge, skills, attitudes, and behaviors necessary to function as a respected member of a learning team in both small group and large class settings. Students will:

1. Apply acquired knowledge effectively.
2. Demonstrate an investigatory and analytic thinking approach in SGPSS and course projects.
3. Demonstrate a commitment to individual, professional and personal growth.