

NBDE II Review

The Exam: Test logistics

- 2 days
 - **Day 1:** 400 Multiple Choice Questions (200 a.m. + 200 p.m.)
 - General dental and specialty topics admixed
 - Diagnosis, treatment planning and management emphasis
 - Image booklet to supplement some of the questions

The Exam: Test logistics

- **Day 2:** 200 multiple choice questions a.m.
 - 10-13 cases with 9-14 multiple choice questions each
- *Scores* are shown as low, average, or high for each section → but only one overall percentile is given at the end
- *Study* with the dental decks, supplemental review material, and old exams...but learn the *concepts* behind the questions! Questions change, but the concepts they test are similar over the years. The more you look over the material, the more comfortable you will be.

Pharmacology I

Why or When do we use drugs (clinically)?

- To control, cure, or prevent disease

Who can prescribe drugs, and Where?

- Licensed doctors, requires *DEA registration* and is *state specific*
- DEA regulates drug laws (legal R_x and illegal) in this country

What can you Rx?

- Drugs within the scope of your practice
- Must be cognizant of Controlled Substances Act
 - Drug Schedules I-V

DEA Schedules

- Schedule I
[Use illegal/restricted to research; high abuse potential; no accepted medicinal use in US]
Examples: hallucinogens, heroin, marijuana
- Schedule II
[Requires prescription; high abuse potential; no refills or verbal orders allowed; some states require triplicate Rx]
Examples: amphetamines, barbiturates, opiates (single entity, some combos)
- Schedule III
[Requires prescription; moderate abuse potential; max 5 refills/6mo; verbal orders allowed]
Examples: anabolic steroids, dronabinol, ketamine, opiates (some combos)
- Schedule IV
[Requires prescription; low/moderate abuse potential; max 5 refills/6mo; verbal orders allowed]
Examples: appetite suppressants, benzodiazepines, sedative/hypnotics
- Schedule V
[Requires prescription or may be OTC with restrictions in some states; limited abuse potential; max 5 refills/6mo; verbal orders allowed]
Examples: opiate or opiate-derivative antidiarrheals and antitussives

How do we use drugs?

- **Enteral** – GI tract route of administration
 - » *Oral* → stomach → intestines → liver (portal circulation) → heart → general circulation → target tissues
 - » *Sublingual or Rectal* → straight into general circulation and bypasses first-pass liver metabolism
- **Parenteral** – Non-GI route of administration
 - » *Intravascular, intramuscular, subcutaneous* → straight into general circulation and bypasses first-pass liver metabolism

How else do we use drugs?

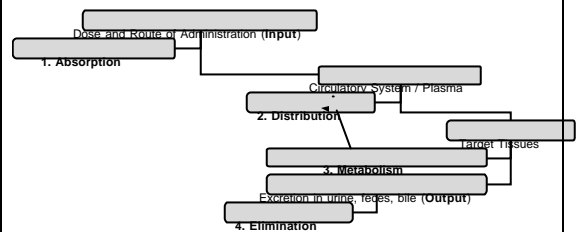
- **Other** –
 - Inhalation*
 - i.e. anesthetics, sterols for asthma
 - Intra-nasal*
 - i.e. calcitonin for osteoporosis, cocaine
 - Intra-thecal*
 - i.e. analgesics, anti-neoplastics
 - Topical*
 - i.e. anesthetics, antibiotics, antifungals

Key Concepts of Drug Activity

- **Pharmacokinetics**
 - The body's effect on a drug
- **Pharmacodynamics**
 - The drug's effect on the body

Pharmacokinetics

- The body's effect on a drug



1. Absorption

- The *onset of action* of a drug is *primarily* determined by the rate of **absorption**
- 4 factors that affect the *absorption* of drugs into the bloodstream:
 1. *Bioavailability*
 - The amount (quantity or %) that reaches the blood or plasma. Usually, a drug's major effect is produced by the amount of drug that is *free in plasma*.
 2. *Stability*
 - Insulin is unstable in the GI tract, hence the injections for Diabetics to bypass the enteral route

1. Absorption

3. Permeability

- pH (acid-base interactions, protonation, pKa, Hendersson-Hasselbach)
 - Coated tabs (buffered)
- Gastric Emptying
 - Parasympathetic vs. Sympathetic
 - Food in the stomach delays gastric emptying and increases acid production to allow for proper digestion; drugs destroyed by acid should be taken without food when possible
- Lipid solubility (hydrophobic, non-ionized, i.e. sterols)
- Water solubility (hydrophilic, ionized or charged)
- Transport mechanisms (passive, active, or facilitated)
- Contact time, surface area, blood supply

1. Absorption

4. First-pass hepatic metabolism

- For enteral drugs, some are inactivated by the liver before reaching systemic circulation, thus decreasing bioavailability; others drugs are activated by the liver, increasing bioavailability
- IV (intravenous) route of administration bypasses first-pass liver metabolism, also increasing bioavailability

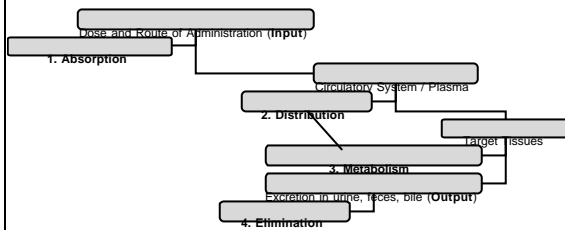
Can stress effect drug absorption from an enteral route?

Would you tell your patients to take Penicillin on an empty or full stomach?

Hint: Penicillin is inactivated by stomach acid. What if patient has nausea when taking it on an empty stomach?

Pharmacokinetics

- The body's effect on a drug



2. Distribution

- In circulation, drugs bind to plasma proteins (mainly **albumin**) relatively non-specifically
- Competition for plasma protein binding sites (affinity) explains some drug-drug interactions
 - i.e. sulfonamide antibiotics and warfarin anti-coagulants are highly bound to plasma proteins, so if you give a sulfonamide to a patient on chronic warfarin therapy, the sulfonamide can displace warfarin and cause dangerously high free warfarin concentrations in the blood

Test Question?

A patient is treated with drug A, which has a high affinity for albumin and is administered in amounts that do not exceed the binding capacity of albumin. A second drug, drug B, is added to the treatment regimen. Drug B also has a high affinity for albumin and is administered in amounts that are 100 times the binding capacity of albumin. Which of the following might occur after administration of drug B?

- A. An decrease in tissue concentration of drug A
- B. An increase in tissue concentration of drug A
- C. A decrease in the half-life of drug A
- D. A decrease in the volume of distribution (V_d) of Drug A

2. Distribution

- Other factors affecting drug distribution:
 - Blood flow
 - Capillary permeability
 - Drug structure
 - Affinity
 - Half-life of drug (t_{1/2})
 - Drug volume of distribution (V_d)
 - Hydrophobic or Hydrophilic nature of drug...

2. Distribution

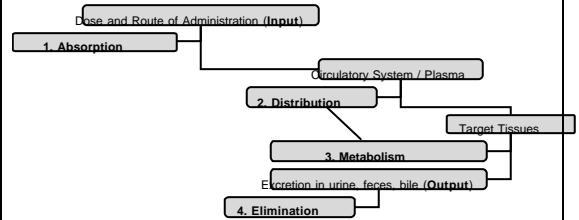
Example: *Blood-Brain Barrier*

- Water-soluble molecules require carrier or transport mechanisms, or they must travel through gap junctions of cells if possible
- Lipid-soluble molecules pass more readily through cell membranes, but are also more likely to be distributed to fat cells

Can obesity be a factor in causing *unequal drug distribution*?

Pharmacokinetics

- The body's effect on a drug



3. Metabolism

- Most drugs are metabolized in the **liver** or other tissues in a process called *biotransformation*, which occurs for two main reasons :
 - **Inactivation** of the drug for future excretion or elimination
 - **Activation** of the drug for desired effect
- The **liver** does this through:
 - Phase I reactions (*cytochrome p450 red-ox, hydrolysis...*) mainly activate
 - Phase II reactions (*conjugation*) mainly inactivate

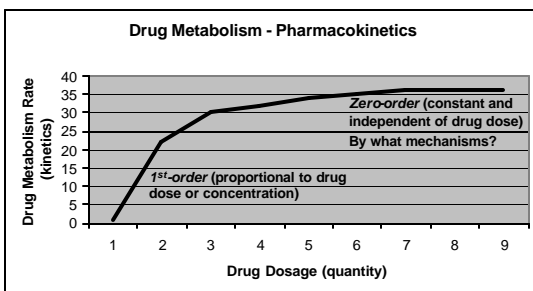
Note: Neonates are deficient in conjugating enzymes. What implications does this have with respect to drug metabolism?

Test Question?

The conjugation of glucuronic acid to a drug by the liver is an example of a:

- Cytochrome P450 reaction
- Amination reaction
- Phase I activation reaction
- Phase II inactivation reaction

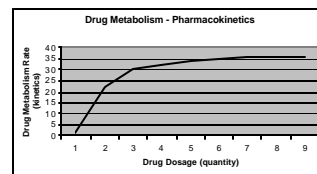
3. Metabolism



Test Question?

Drugs showing zero-order kinetics of elimination:

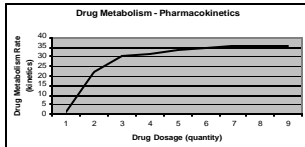
- Are more common than those showing first-order kinetics
- Decrease in concentration exponentially in time
- Have a half-life that is independent of dose
- Show a plot of drug concentration versus time that is linear



Test Question?

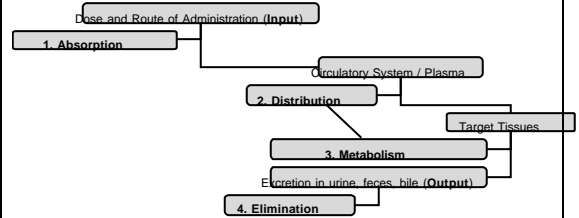
Which one of the following is TRUE for a drug whose metabolism or elimination from plasma shows first-order kinetics?

- The half-life of the drug is proportional to drug concentration in plasma
- The amount eliminated per unit time is constant
- The amount eliminated per unit time is proportional to the plasma concentration
- A plot of drug concentration versus time is sigmoidal



Pharmacokinetics

- The body's effect on a drug



4. Elimination

- Excretion of drug
 - Changed (metabolized by liver)
 - Unchanged (not metabolized by liver)
- The **Kidney** is the primary site of drug excretion and clearance through the urine
- Lungs
 - Gases
 - Garlic
- GI
 - Emesis (i.e. alcohol), Bile, Feces
- Body fluids
 - Sweat, Saliva, Tears and Breast Milk

Test Question?

Which of the following combination of diseases would have the most deleterious effects on drug metabolism and excretion?

- CNS degeneration and Cerebral Palsy
- Hepatic failure and adrenal insufficiency
- Renal failure and hepatic insufficiency
- Hepatic insufficiency and GI malabsorption

What lab tests or values could you use to help you clinically if prescribing medications to this population?

For kidney, creatinine clearance is a good measure of excretory function, or lack thereof. For liver, AST/ALT, although not really reliable clinically.

Pharmacodynamics

- The drug's effect on the body
- Drug-receptor interactions (forces) and biochemical cascades (G-protein, cAMP)
- Non-receptor acting drugs
 - i.e. *Antacids* are bases that just neutralize stomach acid (what can you treat with these?)
 - i.e. *Chelating* drugs just bind metallic ions (what can you treat with these?)

Pharmacodynamics

Receptor Interactions:

- Agonists (inducers)
 - *Efficacy*
 - The maximum response that an agonistic drug can produce
 - *Potency*
 - The measure of how much drug is required to produce a desired effect

Pharmacodynamics

Receptor Interactions:

- Antagonists (competitors)
 - Competitive antagonists are reversible
 - Non-competitive antagonists are irreversible

Receptor interactions are key to understanding drug effects on the **systems** of the body!

Pharmacodynamics

- Dose-response curves give us an idea of what minimum drug dose or quantity will produce a predetermined response in a population:
 - **ED₅₀** (Effective Dose) is the dose of drug that will produce the desired effect in 50% of the population
 - **TD₅₀** (Toxic Dose) is the minimum dose that produces a specific toxic effect in 50% of the population
 - **LD₅₀** (Lethal Dose) is the minimum dose that kills 50% of the population
 - **TI** (Therapeutic Index) is a measure of *drug safety* and is expressed as the following ratio:
 - $TI = TD_{50}/ED_{50}$ or LD_{50}/ED_{50}
 - Higher TI is better, lower is worse (value >2 is okay, less requires patient monitoring)

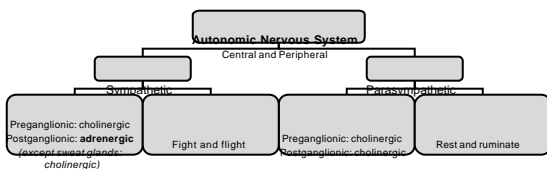
Test Question?

Which of the following combinations derived from dose-response curves makes for the safest drug, or the best Therapeutic Index?

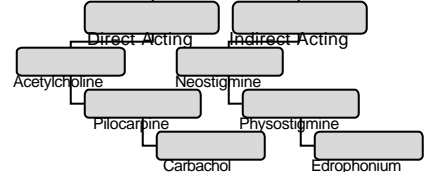
- Low ED₅₀ and Low TD₅₀
- High ED₅₀ and High LD₅₀
- Low LD₅₀ and High ED₅₀
- Low ED₅₀ and High LD₅₀

THE DRUGS!

Autonomic Nervous System Drugs

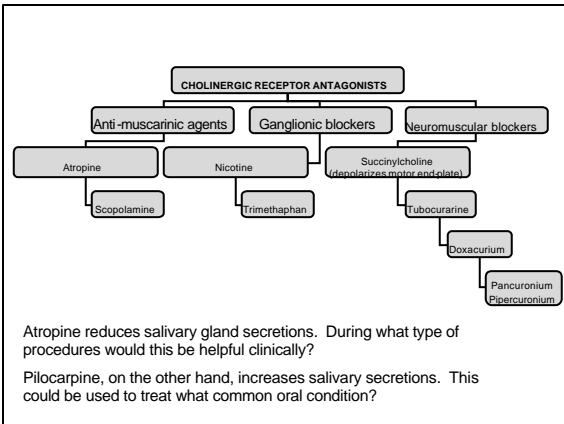


CHOLINERGIC RECEPTOR AGONISTS



Many of these drugs are used to treat *glaucoma*. Anti-cholinergic drugs are *contraindicated* in patients with *glaucoma*.

Sweat glands are innervated by acetylcholine (cholinergic), but uniquely by *sympathetic* post-ganglionic cholinergic receptors as opposed to *parasympathetic* post-ganglionic cholinergic receptors.



Atropine reduces salivary gland secretions. During what type of procedures would this be helpful clinically?
 Pilocarpine, on the other hand, increases salivary secretions. This could be used to treat what common oral condition?

Test Question?

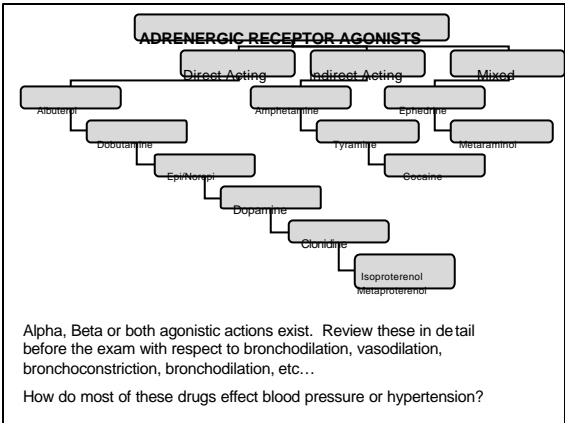
Which ONE of the following drugs most closely resembles atropine in its pharmacologic actions?

- Trimethaphan
- Scopolamine
- Physostigmine
- Acetylcholine

Test Question?

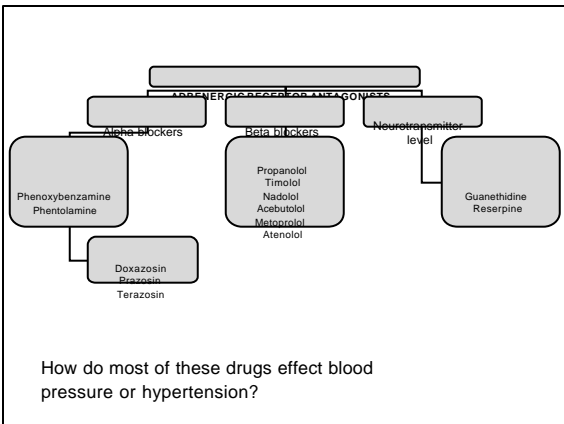
Which of the following drugs would be the most effective in treating Myasthenia Gravis?

- Atropine
- Scopolamine
- Neostigmine
- Nifedipine



Alpha, Beta or both agonistic actions exist. Review these in detail before the exam with respect to bronchodilation, vasodilation, bronchoconstriction, bronchodilation, etc...

How do most of these drugs effect blood pressure or hypertension?



How do most of these drugs effect blood pressure or hypertension?

Test Question?

Which one of the following drugs is useful in treating tachycardia?

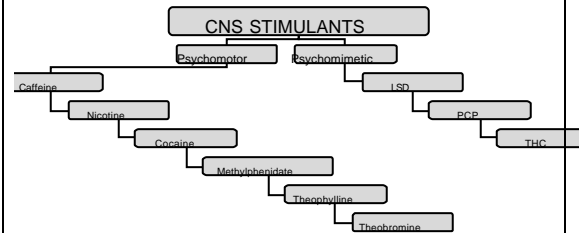
- Clonidine
- Tyramine
- Propranolol
- Reserpine

Test Question?

Systolic blood pressure is decreased after the injection of which of the following drugs?

- A. Reserpine
- B. Tyramine
- C. Dopamine
- D. Clonidine

CNS Stimulants



CNS Depressants

To treat Anxiety (sympathetic overflow)

– *Benzodiazepines* (GABA receptor-like activity, RAS) have largely replaced *barbiturates*

- Clonazepam
- Diazepam (Valium®)
- Lorazepam
- Midazolam
- Triazolam
- Alprazolam
- Buspirone
- Hydroxyzine
- Zolpidem

CNS Depressants

To treat Epilepsy (over-activity)

– Antiepileptic drugs:

- Carbamazepine
- Clonazepam
- Diazepam
- Gabapentin
- Phenobarbitol
- Phenytoin (Gingival Hyperplasia side-effect)
- Primidone
- Valproic Acid

CNS Depressants

- To treat Schizophrenia and some Psychoses

– *Neuroleptic* drugs

– Block dopamine and serotonin receptors

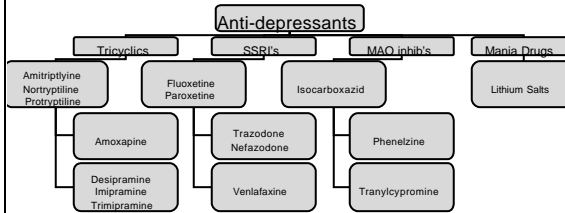
- Butyrophenones
 - Haloperidol
- Benzisoxazoles
 - Risperidone
- Phenothiazines
 - Chlorpromazine
 - Promethazine

Test Question?

Besides being a good anxiolytic, benzodiazepines are also very useful for:

- A. Myasthenia gravis
- B. General anesthesia
- C. Parkinson's disease
- D. Hypothermia

Anti-depressants



Test Question?

The tricyclic anti-depressants work by which of the following mechanisms?

- GABA agonist
- GABA antagonist
- releasing norepinephrine
- blocking norepinephrine reuptake

CNS

Parkinson's disease

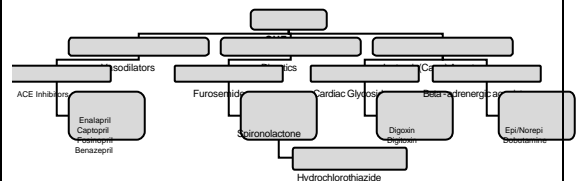
- Levodopa (dopamine) and carbidopa are used to treat Parkinson's to compensate for lack of endogenous dopamine in the substantia nigra
- Dopamine alone does not cross the Blood-Brain Barrier, but it can as Levodopa

Pharmacology II

Cardiovascular System Drugs

- Congestive Heart Failure (CHF)**
 - Heart is unable to meet the needs of the body
 - Starling's law: $CO=CR$, in CHF either output or return is impaired
 - "Congestive" because symptoms include pulmonary edema with left sided heart failure, and peripheral edema with right sided heart failure
 - Therapeutic goal is to increase cardiac output

Drugs used to treat CHF



Test Question?

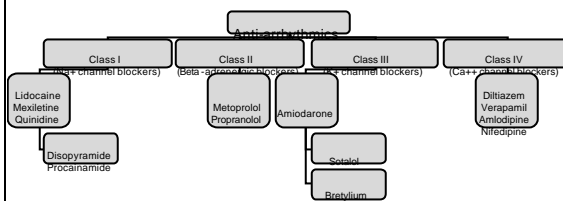
All of the following classes of drugs are used to treat CHF *except* the following:

- A. Beta-adrenergic antagonists
- B. Beta-adrenergic agonists
- C. Vasodilators
- D. Diuretics

Anti-arrhythmic Drugs

- In arrhythmia, the heart beats too rapidly (tachycardia), too slowly (bradycardia), or responds to impulses originating from sites or pathways other than the SA node (pacemaker)
- Therapeutic goal is to normalize impulse conduction

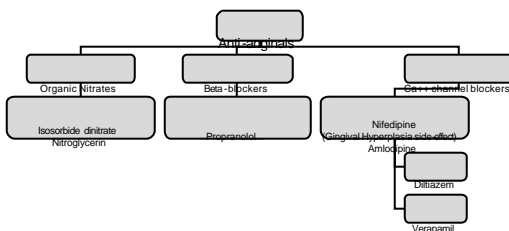
Anti-arrhythmic Drugs



Anti-anginal Drugs

- Angina pectoris results from coronary blood flow that is insufficient to meet the oxygen demands of the body
- Therapeutic goal is to increase perfusion to the heart (vasodilating nitrates and Ca⁺⁺ channel blockers) or decrease the demand (Beta-blockers)
- Significant first-pass hepatic metabolism occurs with the nitrates

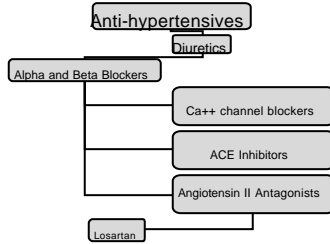
Anti-anginal Drugs



Anti-hypertensive Drugs

- HTN defined as >140/90 mmHg, affects 15% of the US population (60 million)
- Therapeutic goal is to lower BP and prevent disease sequelae, being cognizant of concomitant disease
- Multi-drug regimen may be warranted
- Compliance is the most common reason for therapy failure
 - Dentists can play an important role here

Anti-hypertensive Drugs



Test Question?

Which of the following class of drugs is NOT used to treat hypertension?

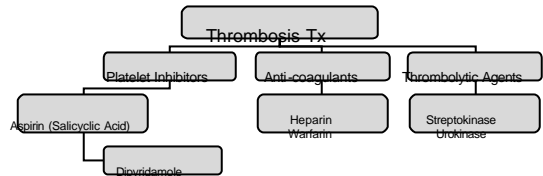
- A. Diuretics
- B. ACE inhibitors
- C. Alpha agonists
- D. Beta antagonists

Drugs affecting Blood

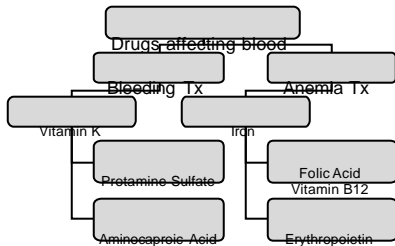
- The drugs useful in treating blood dyscrasias cover 3 important dysfunctions:
 - Thrombosis
 - Bleeding
 - Anemia

What could you use to treat each of these abnormalities based on your knowledge of physiology?

Drugs affecting Blood



Drugs affecting Blood



Note: *Hydroxyurea* is used to treat Sickle Cell Anemia!

Drugs affecting the Respiratory System

- What do the lungs do?
- What type of drugs can affect that?

Drugs affecting the Respiratory System

- Drugs used to treat Allergic Rhinitis
 - Anti-histamines (H₁)
 - Corticosteroids
 - Alpha-adrenergic agonists (vasoconstricts)
- Drugs used to treat Asthma:
 - Beta-adrenergic agonists (bronchodilates)
 - Corticosteroids
 - Theophylline (coffee, tea)

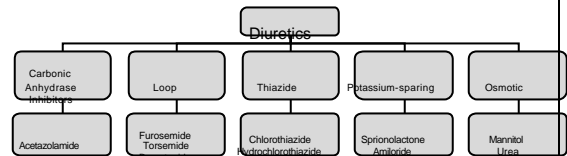
Drugs affecting the Respiratory System

- Drugs used to treat COPD:
 - Corticosteroids
 - Beta-adrenergic agonists
- Drugs used to treat Cough:
 - Opiates (suppress CNS cough centers)

Drugs affecting the Kidney

- What do the kidneys do?
- What type of drugs can affect that?

Drugs affecting the Kidney



Drugs affecting the GI System

- Drugs used to treat Peptic Ulcer
 - Proton pump inhibitors
 - Omeprazole
 - Lansoprazole
 - H₂-receptor antagonists
 - Cimetidine
 - Ranitidine
 - Famotidine
 - Antimicrobial
 - Amoxicillin
 - Tetracycline
 - Metronidazole

Drugs affecting the GI System

- Drugs used to treat Peptic Ulcer
 - Antacids
 - Magnesium hydroxide (milk of magnesia)
 - Calcium carbonate (Tums®, Rolaids®)
 - Aluminum hydroxide
 - Sodium bicarbonate
 - Anti-muscarinic agents
 - Hyoscyamine
 - Pirenzepine

Drugs affecting the GI System

- Drugs used to treat Diarrhea:
 - Anti-diarrheals
 - Kaolin
 - Pectin
 - Methylcellulose
- Drugs used to treat Constipation:
 - Laxatives
 - Castor oil
 - Senna
 - Aloe
 - Glycerine

Compensatory Drugs

Normal physiology is key to understanding these drug effects:

- Thyroid?
- Pancreas?
- Pituitary?
- Adrenals? (all 3 layers)

Anti-inflammatory Drugs

NSAID's are less dangerous than chronic steroidal anti-inflammatory drugs:

- Aspirin (Bayer®)
 - Diclofenac
 - Etodolac
 - Fenoprofen
 - Ibuprofen (Advil®)
 - Indomethacin
 - Naproxin
 - Sulindac
 - Tolmetin
- Non-narcotic analgesics:*
- Acetaminophen (Tylenol®)
 - Phenacetin

Test Question?

Which of the following NSAID's is not anti-inflammatory?

- A. ASA (salicylic acid)
- B. Ibuprofen
- C. Naproxen
- D. Acetaminophen

Anti-microbial Drugs

- Antimycobacterials
 - INH, Rifampin, Ethambutol, Dapsone
- Antivirals
 - Acyclovir, Famciclovir, Ganciclovir
 - Vidarabine, Rimantadine, Amantadine, Ribavirin
 - Interferon (Hepatitis)
 - Zidovudine, Zalcitabine, Stavudine, Didanosine (HIV)
- Antiprotozoals
 - Quinolones, Metronidazole

Test Question?

Which of the following drugs is useful for treating Hepatitis C?

- A. Ganciclovir
- B. Interferon
- C. Acyclovir
- D. Famciclovir

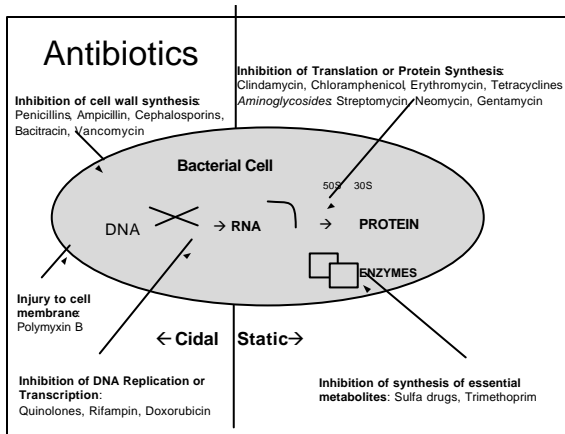
Anti-microbial Drugs

- Antifungals
 - Polyenes:
 - Amphotericin B (systemic)
 - Nystatin (topical)
 - Imidazoles:
 - Ketoconazole (systemic)
 - Clotrimazole (systemic or topical, Mycelex®)
 - Miconazole
 - Itraconazole
 - Fluconazole
 - Griseofulvin
 - Disrupts fungal mitotic spindle formation
 - Used to treat *dermatophytic* infections

Test Question?

A significant difference between nystatin and amphotericin B is that:

- They are different types of antifungals
- One is effective against candidiasis and one is not
- One is administered topically and the other systemically
- Only one of them acts on the fungal cell membrane



Local Anesthetics

Amides:

[aniline derivatives]

articaine, bupivacaine, dibucaine, levobupivacaine, lidocaine, mepivacaine, prilocaine, ropivacaine

Esters:

[PABA derivatives]

benzocaine, butamben, chlorprocaine, cocaine, procaine, proparacaine, tetracaine

• Hypersensitivity info:

Ester allergy more common; cross-sensitivity between classes rare; consider paraben or bisulfite sensitivity if apparent allergy to both classes

General Anesthetics

- 3 stages:
 - Induction, Maintenance, Recovery
- Induction and Pre-anesthetic medication regimens can use:
 - Benzodiazepines
 - Opioids
 - Anticholinergics
 - Antiemetics
 - Antihistamines

General Anesthetics

• Maintenance:

- Today mainly volatile inhalation gases
 - Enflurane
 - Halothane
 - Isoflurane
 - Methoxyflurane
 - NO

• Recovery:

- Reverse of induction, withdrawal of drugs for redistribution, counter-acting med's prn

Antibiotic Premedication (Endocarditis Prophylaxis-Adult)

[timing of administration]
unless otherwise noted, give all PO doses 1h before procedure; a II IM/IV doses within 30min of procedure

for orodental , resp , esoph

[standard regimen]
Dose: amoxicillin 2 g PO; Alt: ampicillin 2 g IM/IV

[PCN allergy]
Dose: clindamycin 600 mg PO/IV; Alt: cephalexin 2 g PO; cefazolin 1 g IM/IV; azithromycin 500 mg PO; clarithromycin 500 mg PO

for GI, GI (not esoph)

[high risk]
Dose: ampicillin 2 g IM/IV and gentamicin 1.5 mg/kg within 30min before procedure, then ampicillin 1 g IM/IV or amoxicillin 1 g PO 6h later

Info: prosthetic, bioprosthetic , homograft valves; previous endocarditis ; complex cyanotic congenital heart disease; surgical pulmonary shunts

[high risk, PCN allergy]
Dose: vancomycin 1 g IV and gentamicin 1.5 mg/kg IM/IV

[moderate risk]
Dose: amoxicillin 2 g PO; Alt: ampicillin 2 g IM/IV

Info: other congenital cardiac malformation; acquired defects, r rheumatic heart disease; hypertrophic cardiomyopathy; MVP with regurgitation and/or thickened leaflets

[moderate risk, PCN allergy]
Dose: vancomycin 1 g IV

Antibiotic Premedication (Endocarditis Prophylaxis-Child)

[timing of administration]
unless otherwise noted, give all PO doses 1h before procedure; a II IM/IV doses within 30min of procedure

for orodental , resp , esoph

[standard regimen]
Dose: amoxicillin 50 mg/kg (max 2 g) PO; Alt: ampicillin 50 mg/kg (max 2 g) IM/IV

[PCN allergy]
Dose: clindamycin 20 mg/kg (max 600 mg) PO/IV; Alt: cephalexin 50 mg/kg (max 2 g) PO; cefazolin 25 mg/kg (max 1 g) IM/IV; azithromycin 15 mg/kg (max 500 mg) PO; clarithromycin 15 mg/kg (max 500 mg) PO

for GI, GI (not esoph)

[high risk]
Dose: ampicillin 50 mg/kg (max 2 g) IM/IV and gentamicin 1.5 mg/kg (max 120 mg) within 30min before procedure, then ampicillin 25 mg/kg (max 2 g) IM/IV or amoxicillin 25 mg/kg (max 2 g) PO 6 h later

Info: prosthetic, bioprosthetic , homograft valves; previous endocarditis ; complex cyanotic congenital heart disease; surgical pulmonary shunts

[high risk, PCN allergy]
Dose: vancomycin 20 mg/kg (max 1 g) IV and gentamicin 1.5 mg/kg (max 120 mg) IM/IV

[moderate risk]
Dose: amoxicillin 50 mg/kg (max 2 g) PO; Alt: ampicillin 50 mg/kg (max 2 g) IM/IV

Info: other congenital cardiac malformation; acquired defects, r rheumatic heart disease; hypertrophic cardiomyopathy; MVP with regurgitation and/or thickened leaflets

[moderate risk, PCN allergy]
Dose: vancomycin 20 mg/kg (max 1 g) IV

GOOD LUCK!