Pharmacology – Exam 1
Study Guide

As with all things Mandyam, this will likely change from term to term. Good luck with that.

- **Historical U.S. Drug Laws and Dates**

  1906 – Food and Drug Act.
  Prohibits interstate commerce in misbranded/adulterated foods, drugs, drinks. No more snake-oil!

  1914 – Harrison Narcotic Act.
  Defined “narcotic” and said prescriptions needed for them. Requires docs/pharmacists to keep records on dispensing.

  Controls over therapeutic devices, cosmetics; Drugs have to be safe and defined what that meant and what the tolerances were; Factory inspections.

  1951 – Durham-Humphrey Amendment
  What’s OTC, what’s not.

  1962 – Kefauver-Harris Drug Amendments
  (Response to Thalidomide babies) Drug makers have to prove efficacy of products to FDA.

  1962 – Kennedy’s Consumer Bill of Rights
  Right to safety, to be informed, to choose, to be heard.

  1970 – Comprehensive Drug Abuse Prevention and Control Act
  Establishes [CSA Schedules](CSA = Controlled Substances Act), categorizing drugs by abuse and addiction potential compared to therapeutic value. DEA and DOJ get the power to enforce. (Step 1 of the War on Drugs…Nixon’s “HA! Take that, ya dirty hippies.”)
  Overrides all other drug laws.

  1983 – Orphan Drug Act
  Funding to promote research for drugs needed for rare diseases. (If there are less than about 200k sufferers then drug companies claim there isn’t enough return on the investment to bother…)

  1994 – Dietary Supplement Health and Education Act
  Regulation for manufacturing of dietary supp’s, definition of dietary supps and dietary ingredients, classification of them as food.

  2002 - Public Health Security and Bioterrorism Preparedness and Response Act
  FDA regs to control imports and domestically produced commodities

  2004 – Project Bioshield Act
  Expedite FDA review for rapid distribution of counter measures against terrorist bio-attack
Areas of Pharmacology – from page 3

- **Pharmacodynamics**
  study of drugs fx on living tissues, involves chemical effects of drugs on the body. What a drug does to the body.

- **Pharmacokinetics**
  study of processes of biotransformation: drug absorption, distribution, metabolism, and elimination. Alteration of the chemical structure of drugs occurs here. What the body does to a drug.

- **Pharmacotherapeutics**
  study of use of drugs in treating disease

- **Pharmacy**
  prep/dispensing of medicinals

- **Posology**
  study of amount of drug required for therapeutic effect

- **Toxicology**
  study of harmful fx of drugs on living tissues

Dose-Response and Time-Response Curves (pg 6)
You’ll just have to look at that one on your own.

1. Shows the dose-response curve, a graph of the dose compared to the % of response.

2. Shows the time-response curve, a graph comparing the time a drug is in the system to the concentration of the drug in the blood plasma. Note that there is a period between onset and termination of action in which the drug is in the plasma but isn’t doing squat for you.

CSA (Controlled Substances Act) Categories of Drugs (pg 9)
Know some examples for each class.

<table>
<thead>
<tr>
<th>Schedule</th>
<th>Definition</th>
<th>Controlled drugs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schedule I</td>
<td>High abuse potential, no accepted medical use</td>
<td>Heroine, hallucinogens, marijuana. Illegal to prescribe.</td>
</tr>
<tr>
<td>Schedule II</td>
<td>High abuse potential, accepted medical use.</td>
<td>Narcotics such as morphine and codeine. Cocaine, amphetamines, short acting barbituates. Scrip required. No refills w/o new script each time.</td>
</tr>
<tr>
<td>Schedule III</td>
<td>Moderate abuse potential, accepted medical use</td>
<td>Mod/intermed acting barbituates, preps containing codeine plus other drug, glutethimide (hypnotic sedative, alt to barbituates for sleep). Scrip required. Can refill 5 times in 6 mo w/o doc reauthorization.</td>
</tr>
<tr>
<td>Schedule IV</td>
<td>Low abuse potential, accepted medical use</td>
<td>Phenobarbitol, chloral hydrate (sedative), antianxieties (Librium, valium).</td>
</tr>
</tbody>
</table>
Scrip required. Can refill 5 times in 6 mo w/o doc reauthorization.

| Schedule V | Limited abuse potential, accepted medical use. | Narcotic drugs used in lim quantities for antitussive/atidiarrheal properties. Sold by registered pharmacist. Buyer must be 18 or older, show ID. |

- **Drug Nomenclature/Naming** (pg 8)

  All drugs have 3 names:
  1. **Chemical name**
     The mile-long chemical mix name.
     Non-proprietary.
  2. **Generic name**
     Some shortened version of the chemical name. Important to know this since all companies that make/market drugs have their own trade names.
     Non-proprietary.
  3. **Trade name**
     The marketing name of a drug compound used by the company that manufactures and markets it.
     Proprietary.

- **Drug Formulations** (pg 15-18)

  Drugs have to be in some sort of solution prior to being absorbed. Tablets and caps require time for dissolution. How much time depends on particle size, ionization and more. Here are some to know.
  - Water based solutions such as syrups – water and sugar plus coloring and flavoring.
  - Alcohol based solutions such as elixirs, spirits, tinctures, fluid extracts dissolved in various concentrations of alcohol – 5 – 20%
  - Solids and semi-solids
    - Powders – fine particles
    - Tablets – compressed powders. Some are coated for delayed release or are enteric coated so they pass through the stomach and dissolve in the small intestine.
    - Capsules – gelatin coated caps around powders or liquids. Dissolve in the stomach.
    - Troches/lozenges – flattened tabs you dissolve in the mouth. Common for colds/sore throats
    - Suppositories – drug + substance that melts at body temp. Used for rectum, urethra, vagina.
    - Ointments/salves
    - Transdermal products - bandage or patch releasing drug in measured dose. Keeps the level even in the bloodstream.
## Routes of administration (pg 18) from fastest to slowest.

<table>
<thead>
<tr>
<th>Route</th>
<th>Time</th>
<th>Indication</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intravenous (IV)</td>
<td>W/in 1 minute</td>
<td>➢ Emergency&lt;br&gt;➢ When immed fx needed&lt;br&gt;➢ When meds administered by infusion</td>
<td>➢ IV fluids (saline, dextrose&lt;br&gt;➢ Nutrient supp’s&lt;br&gt;➢ Antibiotics</td>
</tr>
<tr>
<td>Intra-arterial</td>
<td>W/in 1 minute</td>
<td>➢ Local fx w/in an internal organ</td>
<td>Cancer drugs</td>
</tr>
<tr>
<td>Inhalation</td>
<td>W/in 1 minute</td>
<td>➢ Local fx in the resp tract</td>
<td>➢ Antiasthmatic meds (like epinephrine)&lt;br&gt;➢ Asthmatic prevention such as steroid inhalers</td>
</tr>
<tr>
<td>Sublingual</td>
<td>Several minutes</td>
<td>➢ Rapid fx needed</td>
<td>Nitroglycerine for angina pectoris</td>
</tr>
<tr>
<td>Buccal</td>
<td>Several minutes</td>
<td>➢ Convenient for some drugs</td>
<td>➢ Androgenic drugs (male sex hormones)</td>
</tr>
<tr>
<td>Subcutaneous (SC)</td>
<td>Several minutes</td>
<td>➢ Drugs inactiv’d by GI tract</td>
<td>Insulin&lt;br&gt;➢ Allergy shots</td>
</tr>
<tr>
<td>Intramuscular (IM)</td>
<td>Several minutes</td>
<td>➢ Drugs with poor oral absorp&lt;br&gt;➢ When high blood levels are required&lt;br&gt;➢ When want rapid fx</td>
<td>Narcotic analgesics&lt;br&gt;➢ Antibiotics</td>
</tr>
<tr>
<td>Intrathecal</td>
<td>Several minutes</td>
<td>➢ Local fx w/in spinal cord</td>
<td>Spinal anesthesia with lidocaine</td>
</tr>
<tr>
<td>Rectal</td>
<td>15-30 minutes</td>
<td>➢ When pt can’t take oral meds and parenteral not indicated&lt;br&gt;➢ Local fx</td>
<td>Analgesics&lt;br&gt;➢ Laxatives</td>
</tr>
<tr>
<td>Vaginal</td>
<td>15 – 30 minutes</td>
<td>➢ Local fx</td>
<td>Creams&lt;br&gt;➢ Foams&lt;br&gt;➢ Suppositories</td>
</tr>
<tr>
<td>Oral</td>
<td>30 – 60 minutes</td>
<td>➢ Whenever possible. Safest, most convenient route</td>
<td>➢ Aspirin&lt;br&gt;➢ Sedatives&lt;br&gt;➢ Hypnotics&lt;br&gt;➢ Antibiotics&lt;br&gt;➢ Most meds</td>
</tr>
<tr>
<td>Transdermal</td>
<td>30 – 60 minutes</td>
<td>➢ Provides continuous absorption and systemic fx over</td>
<td>Nitroglycerin&lt;br&gt;➢ Estrogen&lt;br&gt;➢ Nicotine (to help)</td>
</tr>
</tbody>
</table>
o **Therapeutic Range (pg 21 diagram 2.2)**

Therapeutic range is the level at which a drug has the desired effect. Going past the therapeutic range increases side effects and toxic reaction. Absorption and distribution move the drug through the system and increase plasma levels while metabolism and excretion decrease plasma levels and move the drug out of the system.

There is often a “loading dose” which is high-ish to raise the plasma drug levels to the therapeutic range then smaller maintenance doses to keep the levels as even as possible and within therapeutic range.

The percentage of a dose that is actually absorbed into the bloodstream is referred to as being bioavailable.

o **FDA Pregnancy Categories (pg 23)**

A drug has to be evaluated for possible risk to the fetus. **Teratogenic drugs** cause birth defects. The categories below rate teratogenicity.

<table>
<thead>
<tr>
<th>Pregnancy Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Safest. Drug studies in preggers have not yet demonstrated risk to fetus</td>
</tr>
<tr>
<td>B</td>
<td>Studies not performed in preggers, animal studies haven’t demonstrated risk.</td>
</tr>
<tr>
<td>C</td>
<td>1) Studies not performed in preggers or animals or 2) animal studies have revealed some teratogenic potential, but risk to fetus = unknown. (“C” as in “could”)</td>
</tr>
<tr>
<td>D</td>
<td>Studies show <strong>adverse risk to fetus</strong>. Benefit-to-risk ratio must be est’d before use in preggers. (“D” as in “don’t”)</td>
</tr>
<tr>
<td>X</td>
<td>Studies show teratogenic fx in women and/or animals. Fetal risk outweighs benefit. Drug <strong>contraindicated in preggers.</strong></td>
</tr>
<tr>
<td>NR</td>
<td>Not rated by FDA.</td>
</tr>
</tbody>
</table>
### Teratogenic drugs (pg 24)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Explanation</th>
<th>Teratogenic fx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Androgens</td>
<td>Male hormones</td>
<td>Masculinization of female fetus</td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>Anticonvulsant used in mood stabilization for bipolar, in epilepsy</td>
<td>Craniofacial and fingernail deformities.</td>
</tr>
<tr>
<td>Diethylstilbestrol</td>
<td>Synthetic estrogen. Used in medicine, but also in feed for poultry and livestock.</td>
<td>Vaginal tumors, genital malformation in female offspring</td>
</tr>
<tr>
<td>Estrogen</td>
<td>Female hormone</td>
<td>Feminization of male fetus</td>
</tr>
<tr>
<td>Lithium</td>
<td>Lithium carbonate and lithium citrate are both used as mood stabilizers for manic-depressive and bipolar disorders</td>
<td>Cardiac defects</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>Anticonvulsant, anti-arrhythmic, muscle relaxant</td>
<td>Craniofacial and limb deformities, growth retardation</td>
</tr>
<tr>
<td>Retinoic acid</td>
<td>Oxidized form of Vitamin A. The active ingredient in Retin-A. Used to treat acne. Can also be used in treating acute promyelocytic leukemia</td>
<td>Craniofacial, cardiac and CNS defects</td>
</tr>
<tr>
<td>Thalidomide</td>
<td>Sedative and hypnotic</td>
<td>Phocomelia (limb deformities – causes severe defects because it inhibits antiogenesis)</td>
</tr>
<tr>
<td>Warfarin (Coumadin)</td>
<td>Anticoagulant/vitamin K antagonist used to treat a thrombus or embolus</td>
<td>Facial, cartilage and CNS defects</td>
</tr>
</tbody>
</table>

### Compounds which cross through to breast milk (pg 24)

Can appear in the breast milk in varying degrees. Infant experiences the same pharmacological fx as the mother. Laxatives for instance can cause infant diarrhea. Some drugs such as anti-cancer agents are contraindicated unless the benefit to the mother outweighs the risk to the fetus. (That’s where breast milk banks and pumping/freezing prior to treatment comes in handy.)

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Explanation (when needed)</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics</td>
<td></td>
<td>ampicillin, erythromycin, penicillin, streptomycin, sulfas, tetracyclines</td>
</tr>
<tr>
<td>Antiepileptics</td>
<td>Anti-seizure meds also</td>
<td>Phenytoin, primidone</td>
</tr>
<tr>
<td>Antithyroid agents</td>
<td>Hormone antagonist that acts on thyroid hormones</td>
<td>Thiouracil</td>
</tr>
<tr>
<td>CNS stimulants</td>
<td></td>
<td>Nicotine</td>
</tr>
<tr>
<td>Laxatives</td>
<td></td>
<td>Cascara, danthron</td>
</tr>
<tr>
<td>Narcotic analgesics</td>
<td></td>
<td>Codeine, heroin, methadone, morphine</td>
</tr>
<tr>
<td>Nonnarcotic anti-</td>
<td>Meds that reduce</td>
<td>Phenybutazone (also an analgesic, treats arthritis and gout as well.)</td>
</tr>
<tr>
<td>inflammatory agents</td>
<td>inflammation</td>
<td></td>
</tr>
<tr>
<td>Sedative-hypnotic</td>
<td>depresses activity of CNS, reduces anxiety, induces sleep</td>
<td>Barbituates, chloral hydrate (treats insomnia)</td>
</tr>
<tr>
<td>Tranquilizers/anti-</td>
<td></td>
<td>Chlorpromazine (aka, Thorazine), lithium</td>
</tr>
<tr>
<td>psychotropic agents</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Drug Interaction Terminology (pg 25)

- Incompatibility
  Physical alteration of drug occurring before administration when different drugs mixed in syringe/container.

- Additive fx
  Combining effects of 2 drugs which have the same mechanism of action. Action is equal to the sum of the individual drug fx.

- Summation
  Combining effects of 2 drugs with different mechanisms of action. Action is equal to the sum of the individual drug fx.

- Synergism
  Combining effects of 2 drugs is greater than the sum of their individual fx.

- Antagonism
  Two definitions to be aware of, depending on context!
  1. Combining effects of 2 drugs is less than the sum of their individual fx.
  2. A drug that is an antagonist binds to specific receptors but does not produce any drug action.

- Agonism
  A drug that is an agonist binds to specific receptors and produces a drug action.

Addiction vs Dependence (pg 26)

- Dependence
  Drug is required for an individual's well-being. Usually psychological and/or physical. Can have tolerance (body accommodates and more is needed for fx) and withdrawal symptoms.

- Addiction
  Severe drug dependence in which compulsive drug behavior dominates all other activities. Also, a behavior disorder characterized by continued compulsive use of drugs in spite of adverse health or social consequences.

Pharmacokinetics vs Pharmacodynamics

- Pharmacodynamics
  Study of drugs' effects on living tissues, involves chemical effects of drugs on the body. What a drug does to the body.

- Pharmacokinetics
  Study of processes of biotransformation: drug absorption, distribution, metabolism, and
elimination. Alteration of the chemical structure of drugs occurs here. What the body does to a drug.

- **First pass effect**

  Drug metabolism that occurs following oral absorption from the GI tract. This refers to the biotransformation and/or excretion of a drug by intestinal and hepatic/biliary (liver/gallbladder) systems after a drug is absorbed from the GI tract but before it gets access to the systemic circulation.

  All things absorbed from the GI tract go immediately to the portal vein enroute to the liver for filtering. The Liver assumes anything coming in is a poison so it gets filtered there first.

- **CYP450**

  CYP450 is Cytochrome P450, a big bunch of hemoproteins/enzymes found in all domains of life. It applies to pharmacology and pharmacokinetics/biotransformation in that it helps to metabolize and eliminate drugs. This group of enzymes in the liver chemically alters lipid soluble compounds so they are water soluble and can be excreted through the kidneys.

  They metabolize 50-70% of all drugs. They can be inhibited (thus allowing more of a drug to be bioavailable and maintaining it’s percentage in the bloodstream) by antifungal drugs, antibiotics, and grapefruit juice. They can also be induced (so that they metabolize more of a drug out more quickly thus lowering it’s effect in the body) by anticonvulsants, steroids, HIV drugs and antibiotics.

- **Major routes of excretion**

  - Renal excretion
    A drug must be water soluble and preferably in an ionized form in order to be excreted via the urine.

  - GI excretion
    Passing through the GI tract, excreted via the feces.

  - Respiratory
    OK, not really a major route. Alcohol and anesthetic gasses are excreted, at least partially, this way.

  - Other routes:
    Sweat, saliva, breast milk. Another way is the enterohepatic pathway. Certain fat soluble drugs can enter the intestines through the biliary tract were it can be absorbed into the blood again. This greatly prolongs a drugs action as it can cycle through again and again (liver → bile → intestines → blood → liver….)

- **Half life of a drug**

  Time required for blood or plasma concentration of a drug to fall to half of it’s original level. This is important when determining frequency of drug administration. Look back at [Therapeutic Drug Range](#) and at the [Dose-Response and Time-Response Curves](#).
Effects of age and drug response (pg 33)

- Drug absorption
  decreased intestinal blood flow, surface area, motility delay absorption and slow onset.

- Drug distribution
  Decreased body water, lean body mass, plasma proteins and increased fat content increase drug concentrations and fx.

- Drug metabolism
  Decreased liver blood flow, liver organ size, enzyme concentration decrease rate of drug metab, increase duration and intensity of action.

- Drug excretion
  Age related decreases in renal fnx and blood flow slow the rate of drug excretion and increase duration/intensity of drug action.

Nutritional status and presence of disease both affect ADME.

Protein binding of a drug, name 2 high protein binders.

Plasma proteins such as albumin and globulins circulate in a protein pool in the blood stream and help regulate osmotic pressure. Many drugs area also attracted to proteins in the plasma. Albumin, the largest transport protein in the blood stream, is a crazy binding fool. Note that only the unbound or free drug molecules actually have a pharmacological function. Albumin and other plasma proteins act as a reservoir or storage depot for drug compounds and slowly release it in an unbound form.

One high protein binder is Warfarin/Coumadin. Mandyam said “gimme 2” but I can only find 1.

It would behoove you to review Mandyam’s Unit One handout starting at page 68.