Drugs and the Body

Pharmacokinetics - The study of the movement of drugs through the body.

This includes:
- Absorption
- Distribution
- Metabolism
- Elimination

The pharmacokinetics of a drug...
- determine effective routes of administration.
- largely determine the duration/intensity of a drug effect.
Drug Absorption - How does the drug get into the bloodstream?

- Most routes require crossing cell membranes.
  - Influenced by:
    - Diffusion
    - Lipid Solubility

Ways to cross cell membranes:
- Channels
- Active Transport
- Diffusion through the lipid bilayer.
  - Drug must be lipid soluble.
Lipid solubility of a compound is greatly influenced by its state of ionization.

- Ionization - the presence of an electrical charge.

Atoms are comprised of
- Positively charged protons.
- Neutrally charged neutrons.
- Negatively charged electrons.

Usually an atom has an equal number of protons and electrons.
- Electrically neutral

Ionized atoms or molecules (ions) have an unequal number of protons and electrons.
- Ionized compounds tend to be more water soluble.
- Nonionized compounds tend to be more lipid soluble.

Routes of Administration
- Oral Administration (P. O.)
  - The drug is swallowed.
  - The stomach dissolves the drug.
  - The drug is passed into the small intestine.
  - Drug is absorbed through mucous membranes and enters the blood capillaries.
Oral administration continued...

- Factors determining rate of absorption
  - Food in G.I. Tract.
  - Lipid Solubility of the Drug
    - Drug and environment pH can affect lipid solubility.

pH - 14 point scale indicating concentration of free H+ ions.

- pH of 7 is “neutral”.
- pH of < 7 is acidic.
- pH of > 7 is basic (alkaline).

Ionization Rule

- Basic drugs tend to be ionized in acidic environments.
- Acid drugs tend to be ionized in basic environments.

- The stomach environment is very acidic, so ________ drugs aren’t absorbed very well.
Orally administered drugs reach the liver before the brain.
• First-pass metabolism.

Advantages of oral drug administration:
• Easy

Disadvantages of oral drug administration:
• Slow Absorption
• Drug Depot
• Acidic GI environment.
• First-Pass Metabolism
• GI Irritation

Administration through injection (IV, IM, SC)
• Advantages
  • No harsh GI environment.
  • Controlled onset of effects.
    • Rapid onset (IV).
    • Less rapid (IM, SC).
• Disadvantages
  • Risk of overdose (IV).
  • Risk of infectious disease.
  • Tissue Damage.
Administration through inhalation

- Advantages
  - Most rapid effect.
- Disadvantages
  - Overdose Potential
  - Throat and lung irritation.
  - Potential dose variability.

Other routes of administration:

- Topical application to the skin.
- Application to nasal, oral, or rectal membranes.

Differences in release profiles of medications.

- Most medications are “Immediate Release”.
- “Delayed Release” oral meds prevent stomach irritation.
- “Extended Release” preparations are a newer phenomenon.
  - New formulations of an old product often have a suffix of: XR, SR, LA, TR, SA, CR
  - Most common oral mechanism is multiple layers of dissolvable medication.
  - Extended release also found in non oral meds.
Drug Distribution

• Heart pumps the blood throughout the body.
• Drugs diffuse out of capillaries into surrounding tissue.

Barriers to drug distribution.

• Protein Binding

Affinity - The potential for one molecule to attach to another.

Barriers to Drug Distribution continued...

• Blood-Brain Barrier
  • Capillary walls form tight junctions.
Because of the Blood-Brain Barrier, drugs must be lipid-soluble…

…while inside the bloodstream (pH 7.4)…

...in order to be psychoactive.

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**But the blood-brain barrier isn’t perfect.**

- A few areas of the brain have a “leaky” blood-brain barrier.
  - E.g., the Area Postrema
- The blood-brain barrier is incomplete in infants.
- Injuries or infections can disrupt the blood-brain barrier.

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Barriers to Drug Distribution continued...

- Very lipid-soluble drugs bind to fat tissue in the body.
  - removes the drug from circulation.

- How would this influence the effective duration of a psychoactive drug?
Drug Metabolism

• Metabolism - Changing a substance from one form to another while inside the body.

Drug metabolism is usually accomplished by the liver.
• Hepatic Microsomal Enzymes
• Typically involves several steps.
• Products of metabolism are called metabolites.

In many cases the metabolite is:
• Less Lipid Soluble
• Less psychoactive

• But not always…
  • Codeine -> Morphine -> Norcodeine
Factors affecting drug metabolism

- Enzyme availability
- Experience dependent.
- Individual differences.
- Drug Interactions
  - Metabolic interference
  - Shared metabolic pathways.

Ethanol → Alcohol dehydrogenase → Acetaldehyde → Aldehyde dehydrogenase → Acetic Acid → Citric Acid Cycle

Elimination - The drug and/or metabolites are removed from the body.

- Kidneys filter out water and dissolved substances.
- Some substances are reabsorbed into bloodstream by active and passive processes.
- Substances not reabsorbed are excreted in urine.
- Fat solubility increases reabsorption.
- How can urine pH affect drug elimination?

In many cases the active drug can be removed by the kidneys along with the metabolite.

- Amphetamine
- Amanita muscaria

Urine drug screens usually look for the drug metabolite.
Other routes of elimination (less significant)

• feces
• breath,
• Perspiration
• breast milk.

Drug Half-Life

• The time it takes to remove 50% of the drug from the bloodstream.
• Determined by rate of metabolism and elimination.
• Half-lives vary across different drugs.

Drugs and the Fetus

• Substances pass between the fetus and mother through the placenta.
• Does the placenta act as a barrier to psychoactive drugs?
  NO!
Risks of drug exposure to the fetus:

- Acute Toxicity
- Teratogenic Effects - abnormal development (e.g., fetal alcohol syndrome).
- Fetal Addiction
  - Neonatal Abstinence Syndrome

Liver of newborn is not fully functional.
- Childbirth concerns.