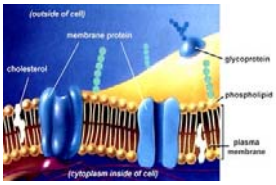
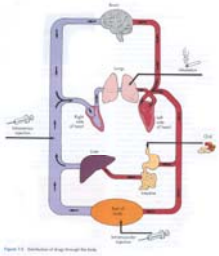
Drugs and the Body





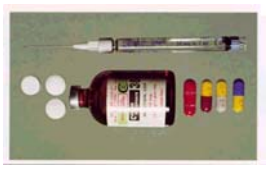
Pharmacokinetics - The study of the movement of drugs through the body.

This includes:

- Absorption
- Distribution
- Metabolism
- Elimination

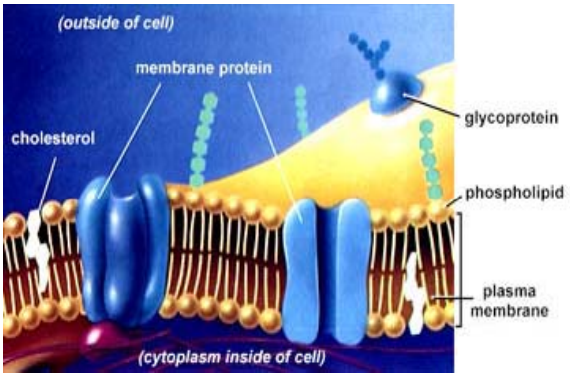
The pharmacokinetics of a drug...

- determine effective routes of administration.
- largely determine the duration/intensity of a drug effect.



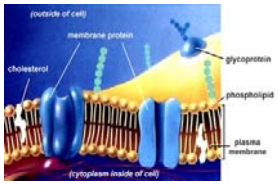
Drug Absorption - How does the drug get into the bloodstream?

- 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.

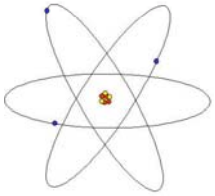


Lipid solubility of a compound is greatly influenced by its state of *ionization.*

- Ionization - the presence of an electrical charge.

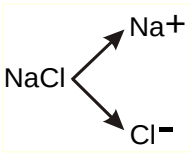
Atoms are comprised of

- Positively charged protons.
- Neutrally charged neutrons.
- Negatively charged electrons.



Usually an atom has an equal number of protons and electrons.

- Electrically neutral

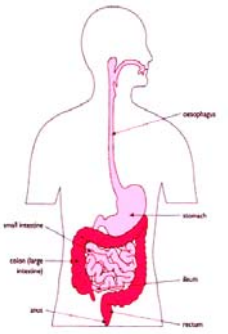


Ionized atoms or molecules (Ions) have an unequal number of protons and electrons.

- 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.

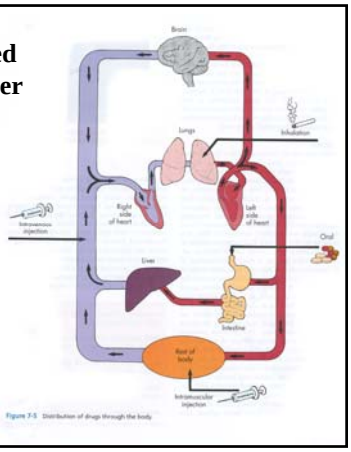
- pH of 7 is “neutral”.
- pH of < 7 is acidic.
- pH of > 7 is basic (alkaline).

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:

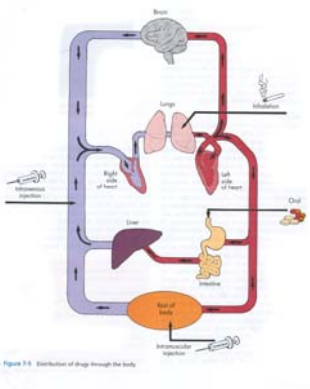
- Slow Absorption
- Drug Depot
- Acidic GI environment.
- First-Pass Metabolism
- GI Irritation

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:

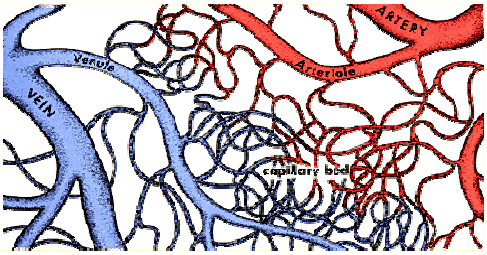
- Topical application to the skin.
- Application to nasal, oral, or rectal membranes.

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.

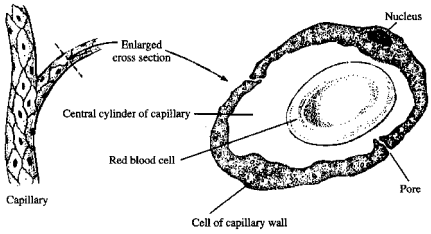
Drug Distribution

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



Barriers to drug distribution.

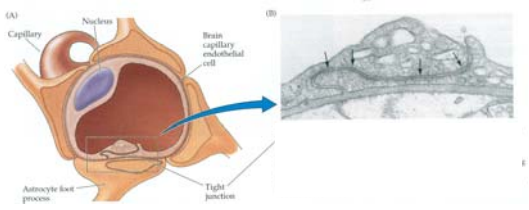
- Protein Binding



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.

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.

Barriers to Drug Distribution continued...

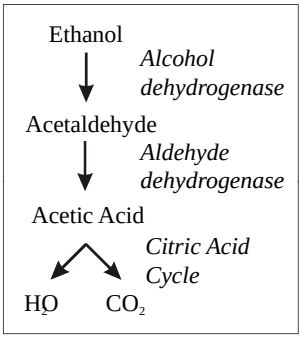
- Very lipid-soluble drugs bind to fat tissue in the body.
  - removes the drug from circulation.
- How would this influence the effective duration of a psychoactive drug?

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*.



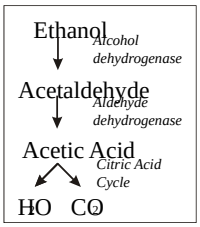
In many cases the metabolite is:

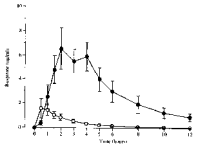
- Less Lipid Soluble
- Less psychoactive

- But not always…
  - Codeine -> Morphine -> Norcodeine

Factors affecting drug metabolism

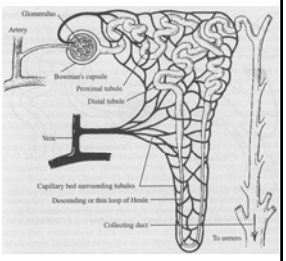
- Enzyme availability
  - Experience dependent.
  - Individual differences.
- Drug Interactions
  - Metabolic interference
  - Shared metabolic pathways.





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*

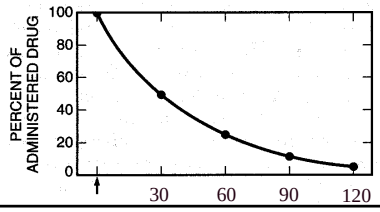
Urine drug screens usually look for the drug metabolite.

Other routes of elimination (less significant)

- feces
- breath,
- Perspiration
- breast milk.

Drug Half-Life

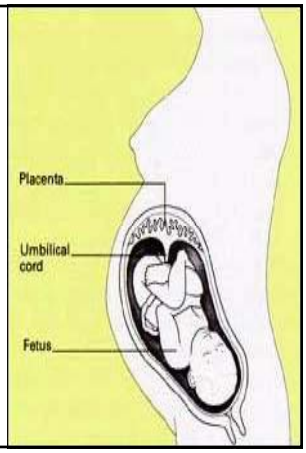
- The time it takes to remove 50% of the drug from the bloodstream.
- Determined by rate of metabolism and elimination.
- Half-lives vary across different drugs.



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**.**