Definitions

- **Pharmacokinetics**: The process by which a drug is *absorbed, distributed, metabolized, and eliminated* by the body.

- **Pharmacodynamics**: The *interactions* of a drug and the receptors responsible for its action in the body.
Pharmacokinetics, or the Life Cycle of a Drug

- Absorption
- Distribution
- Degradation
- Excretion
Absorption

- Slow
- Faster
- Fastest
- Enteral absorption is through the gastrointestinal tract: oral, sublingual, rectal.
- Parenteral absorption is not within the alimentary canal: inhaled, injected, transdermal.
- Central absorption is directly to the brain.
Slow Absorption

- **Oral: swallowed**
- **Mucous Membrane:**
  - Oral mucosa: sublingual
  - Nasal mucosa: sniffed
- **Topical / Transdermal**
- **Rectal: suppository**
Faster Absorption

- **Injection:**
  - Intravenous, IV
  - Intramuscular, IM
  - Subcutaneous, SC
  - Intraperitoneal, IP (into a body cavity)

- **Inhaled:** lungs
Fastest Absorption

- Directly to brain
  - Intracerebral, into brain tissue
  - Intracerebroventricular, into brain ventricles
General Principal of Absorption

- The faster the absorption, the quicker the onset, the higher the addictiveness, but the shorter the duration.
Absorption

- The solubility of a drug affects the way it permeates and binds to tissue.
  - Water-soluble drugs can move through pores in tiny blood vessels called capillaries, but can’t move through cell membranes. They have an electrical charge.
  - Fat-soluble drugs can cross pores, cell membranes, and the blood-brain barrier. They do NOT have an electrical charge.
Uncharged drug

WATER SOLUBLE drug must be charged to be excreted in urine

LIPID SOLUBLE drug must be uncharged to cross a membrane

\[(\text{water} = \text{H}^+ + \text{-OH})\]

An acidic drug DONATES a H⁺ when dissolved in water

Basic drug

A basic drug ACCEPTS a H⁺ when dissolved in water

(hydroxyl group)

(amine group)
Bioavailability

- The portion of an administered dose of drug that reaches the bloodstream.
- What determines bioavailability?
  - Physical properties of the drug like its charge, and whether it is water- or fat-soluble
  - Drug formulation: immediate release or timed release
  - Drug administered on a full or empty stomach
Bioavailability

What determines bioavailability?

◦ How fast the stomach empties
◦ Day / night patterns (circadian)
◦ Interactions with other drugs
◦ Patient age
◦ Patient diet
◦ Patient gender
◦ Patient disease state
Storing in Tissue Reservoir

- Some drugs can bind to depot sites, and be stored in fat, muscle, bones, organs
- Drug storage in tissue reduces the bioavailability, slows elimination of the drug, and can increase the window of drug detection
- Tissue-stored drugs can be released during sudden weight loss or other metabolic changes. This might account for flashback experiences.
Degradation and Excretion

Liver

- Liver enzymes can transform drugs into more water-soluble metabolites. Drugs undergo biotransformation to become inactive forms called metabolites that can be excreted.
- Repeated drug exposure can increase the liver’s efficiency to transform drugs, and thus can increase tolerance for the drug.
Degradation and Excretion

- Kidneys
  - Kidneys can trap water-soluble compounds.
  - These can be eliminated as urine.
Degradation and Excretion

- Other routes of excretion:
  - Breath
  - Sweat
  - Feces
  - Saliva
  - Skin
  - Breast milk
Metabolism: Half-Life

- Plasma half-life: the amount of time it takes for the blood plasma concentration of a drug to drop to 50% of the initial level
- Whole body half-life: the amount of time it takes to eliminate 50% of the drug from the entire body
- Half-life can be affected by age, kidney function, liver metabolism
Pharmacokinetics

- Describes the interactions of a drug and its receptors responsible for its action in the body.
- First- and zero-order kinetics
- Dose-response
- ED50, LD50, EC50
- Efficacy, tolerance, sensitization
- Drug interactions
Drug Kinetics

- First-order kinetics vs. zero-order kinetics
- First-order kinetics occurs when a constant fraction of the drug is eliminated per hour
Drug Kinetics

- Zero-order kinetics is when the rate of elimination of a drug is constant.
- It’s not dependent upon drug concentration.
- A constant amount (not fraction) is eliminated per hour.
- Example: Alcohol is metabolized around one ounce per hour.
Dose-Response Curve

- The dose-response curve describes the relationship between the dose of the drug and the magnitude of the drug effect.
**ED$$\_50$$**

- **ED$$\_50$$** is the effective dose for 50% of the population.
- At this dose, response will be elicited in half of the people treated.
LD50

- LD50 is the dose at which half of the population dies from the drug.
Therapeutic Index

- This is the relationship between the ED$_{50}$ and the LD$_{50}$.
- The larger the gap between the ED50 and the LD50, the safer the drug is.
Agonists and Antagonists

- An agonist is a chemical that produces a biological response.
- An antagonist blocks the action of an agonist.
Potency and $\text{EC}_{50}$

- Potency is the strength of response to a dose.
- The effective concentration 50 is the concentration that elicits half of the maximum biological response of the agonist.
- More potent drugs show a response at a lower dose.
**Efficacy**

- Efficacy is the maximum possible effect that can be elicited by different drugs.
- A full agonist gives 100% efficacy; a partial agonist gives less efficacy; an antagonist gives no efficacy.
Tolerance

- Tolerance is also called desensitization.
- People exhibit a decreased response to the same dose with repeated exposure.
- More drug is needed to elicit the same response.
Sensitization

- Sensitization is the opposite of tolerance.
- People exhibit an increased response to the same dose with repeated exposure.
- Less drug is needed to achieve the same effect.
Tolerance and Sensitization

- It is possible for people to develop tolerance and sensitization at the same time.
- The may develop tolerance to some side effects of the drug.
- The may also develop sensitization to some side effects of the same drug.
Drug-Drug Interactions

- **Pharmacokinetic drug interactions**: when one drug affects the *absorption, distribution, metabolism* or *excretion* of another drug.

- **Pharmacodynamic drug interactions**: when two drugs have *interactive effects on the brain*.
Types of Drug Interactions

- Additive
- Synergistic
- Antagonistic
- Cumulative
Drug Interactions

- Additive effect: the effect of the two chemicals is equal to the sum of the chemicals taken separately.
- Aspirin and motrin.
Additive Effects

Response

Hi

Lo

Time

A

B

A + B
Drug Interactions

- Synergistic effects: the effect of two chemicals taken together is greater than the sum of their separate doses.
- Alcohol and cocaine.
Synergistic Effects

Response

Hi

Lo

Time

A

B

A + B
Drug Interactions

- Antagonistic effect: the effect of two chemicals taken together is less than the sum of their separate effects, if taken separately.
- Oxycodone and naloxone.
Antagonistic Effects

Response

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Time

A + B
Drug Interactions

- Cumulative effects: repeated administration of a drug produces effects that are more pronounced than the original dose.
Drug A shows no cumulative effects. Drug B shows cumulative effects.
Summation

- Drugs can potentially alter the rate of any bodily or brain function.
- Drugs CAN cause effects outside the normal physiologic range of cells.
- Drugs are not bad. It’s what we do with them that can be bad.