PHARMACOLOGY-1 PHL-313

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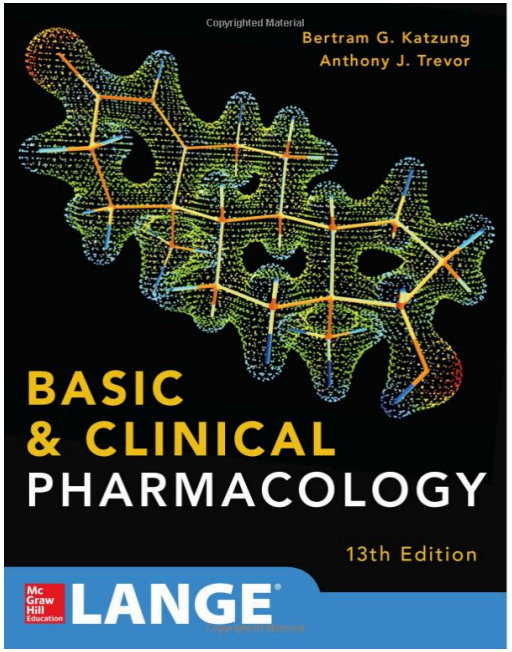
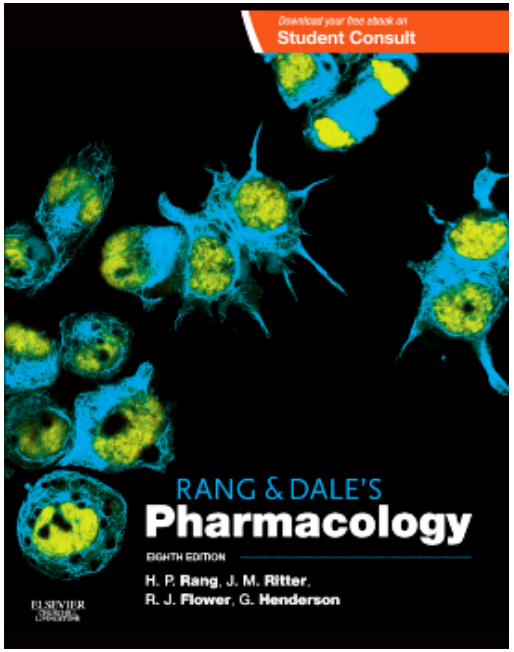
General rules

- Reference:



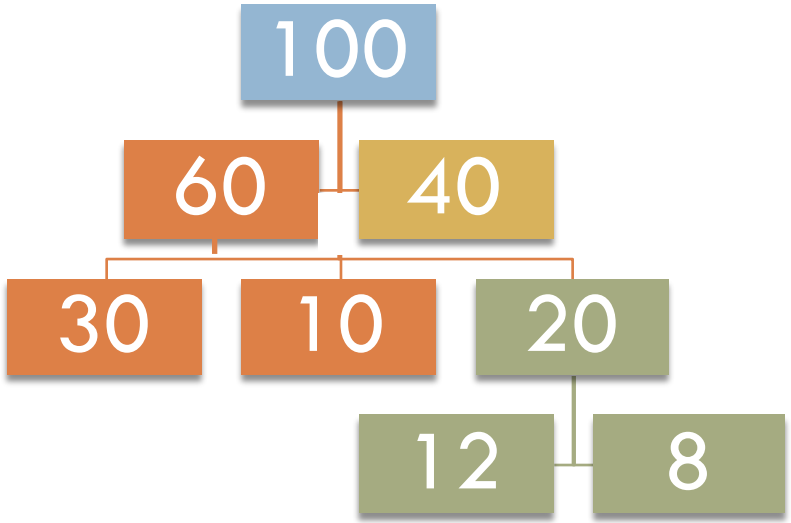


General rules

- Email [PHL313-1st Semester 38-39] Student ID- Question
  - Example :

General rules

- Office hours : Sun Tue Thu 9-10 am
- Course coordinator : Dr.Othman Alshabanah
  - Email: shabanah@ksu.edu.sa
- Grades:

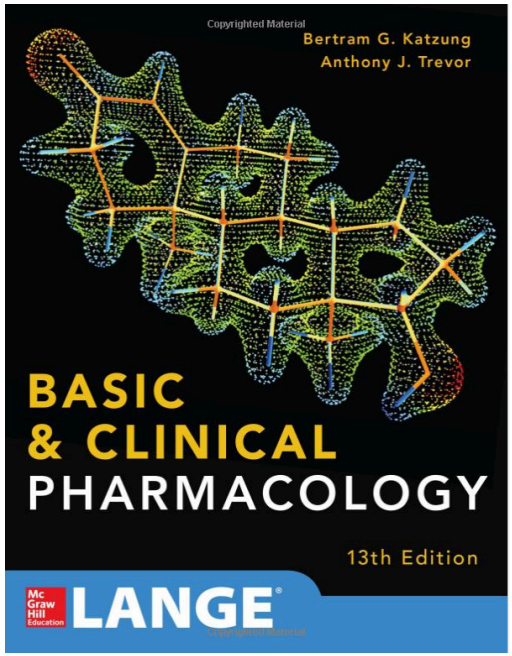


Objectives

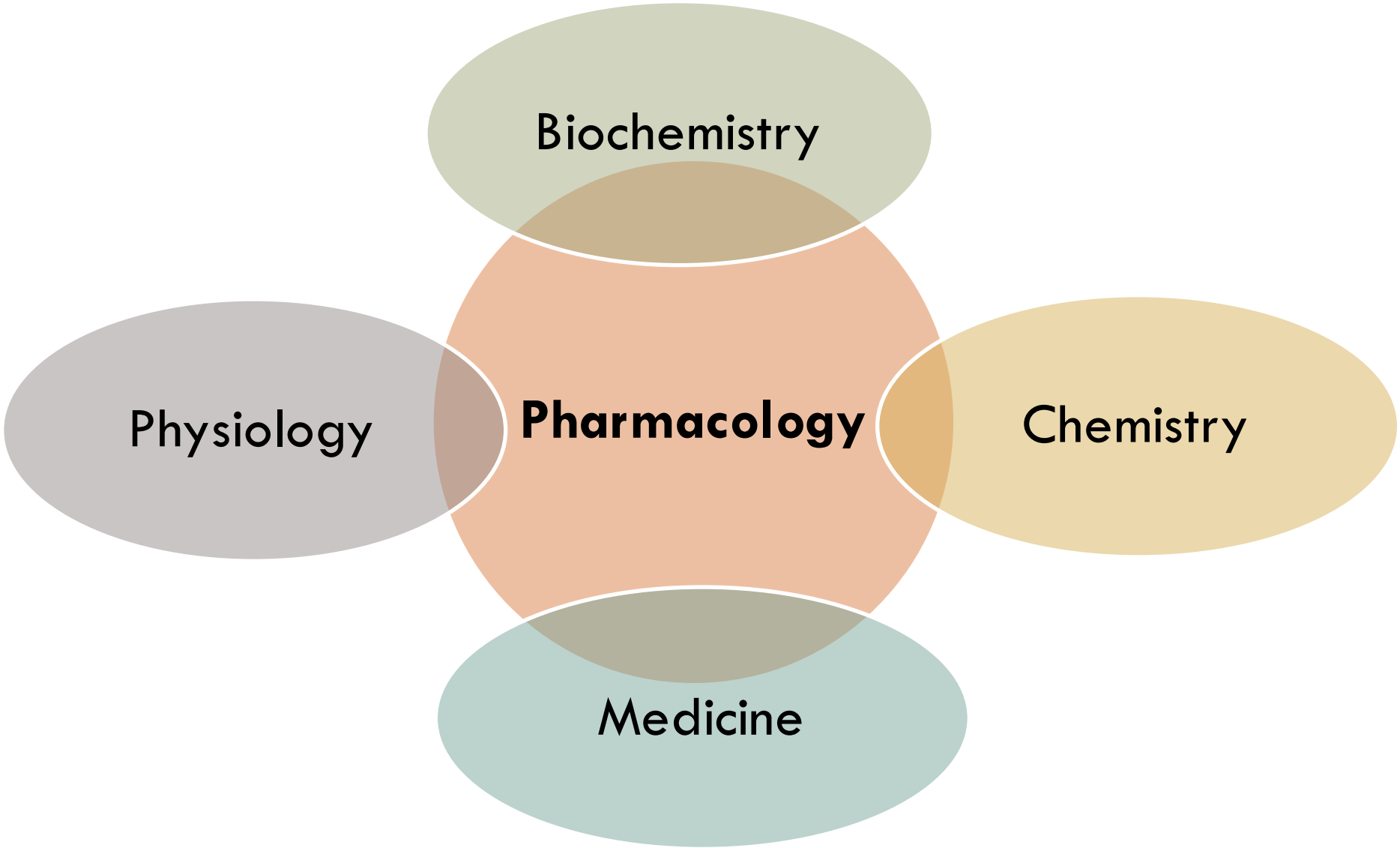
- Know the basic principles of pharmacology including drug discovery and development.
- Understand the pharmacodynamics and pharmacokinetics of drug.
- Understand the mechanism of action of drugs in various categories.
- Acquire knowledge of different therapeutic uses, adverse effects, contraindications and various interactions of autonomic acting drugs, local anaesthetic agents, cardiovascular acting drugs and autacoids.

Pharmacology-1

- Introduction of basic principles of pharmacology and the pharmacological actions, therapeutic uses, mechanisms of actions, adverse effects, contraindications and drug interactions of: autonomic drugs, Local anaesthetics, cardiovascular drugs and autacoids.



Pharmacology



What is Pharmacology

- *Pharmakon* (drug/remedy)
- **Pharmacology** "can be defined as the area of the study of drug that interact with living systems through chemical processes"
  - For regulation
- **Some of the main questions addressed by pharmacologist are:**
  - How do drugs produce their effects on specific body systems such as the cardiovascular or central nervous systems?
  - How do drugs act at the cellular and molecular level?
  - How can we avoid their toxic effects?
  - How does the body protect itself against drugs and other foreign chemicals?
  - Why do many drugs work better in some patients than in others?

http://www.studyat.uwa.edu.au/courses/pharmacology

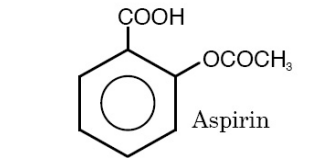
Pharmacology Language

- Drug: is any **Substance** interact with regulatory molecule
- Substance: Endogenous or Exogenous
  - Hormones
  - Neurotransmitters
  - Growth factors
  - Drugs (Pharmaceuticals)
  - Toxic agents in the environment
- Receptor:-
  - "Any cellular macromolecule in either the plasma membrane or interior of a target cell with which a drug/ligand binds to initiate its effect"
    - Macromolecules= Proteins/Nucleic acid

Pharmacology Language

- Dose:
  - "The amount of a substance to be administered at one time"
- Indication:
  - "The reasons for administering a medication or performing a treatment"
- Mechanism of action:
  - "How the substance exerts its action"
- Therapeutic Effects:
  - "The desired results"
- Adverse effect:
  - "Effects that are harmful and undesired, and that occur in addition to the desired therapeutic effects"
    - What about Side effect?
- Drug-X interaction: X= Drug, Diseases, Food..etc
  - "A situation in which a substance (X) affects the activity of a drug when both are administered together"
- Contra-Indication
  - "Factors that prevent the use of a medication or treatment (e.g., Pregnancy)"

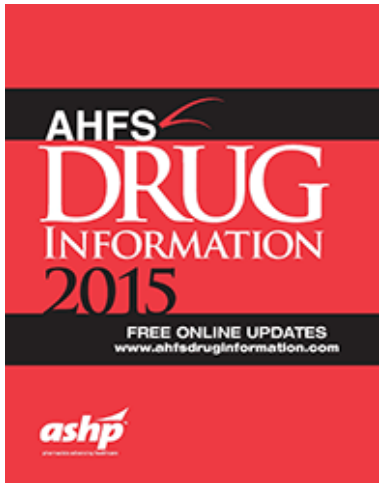
Pharmacology Language (example)

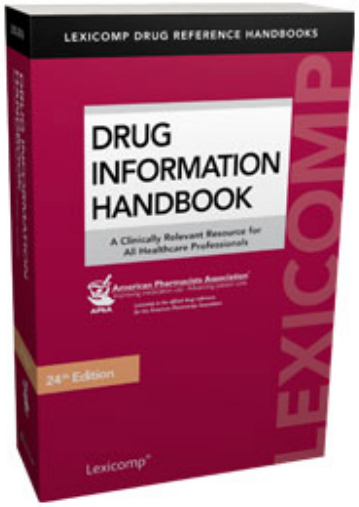


- Acetylsalicylic acid (ASA)-Aspirin
  - Names (Generic, Trade name)
- Indication:
  - mild to moderate pain; fever; various inflammatory
- Mechanism of action :
  - inhibit the action of a human cell membrane enzyme known as cyclooxygenase, which is responsible for the synthesis of a number of inflammatory mediators
- Therapeutic effects:
  - reduce inflammation, pain and fever
- Adverse effect :
  - rash, gastrointestinal ulcerations, abdominal pain, cramping, nausea, gastritis, and bleeding
- Drug-X interaction: X= Drug, Diseases, Food..etc
  - Antacids, corticosteroids "May decrease aspirin levels"
  - Carbonic anhydrase inhibitors (eg, acetohexamide), methotrexate "May increase levels of these drugs.

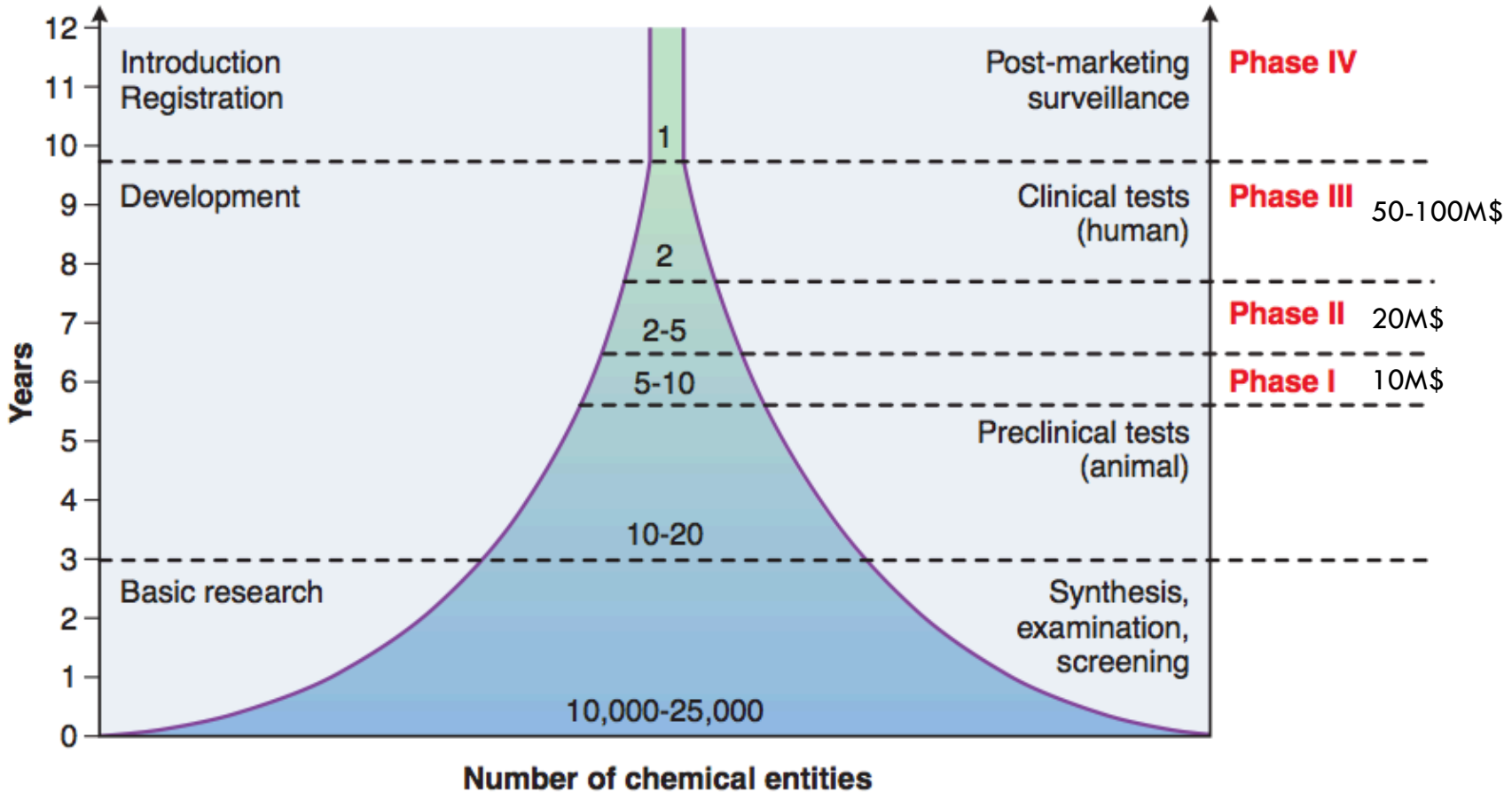
Medical Use

- Formularies



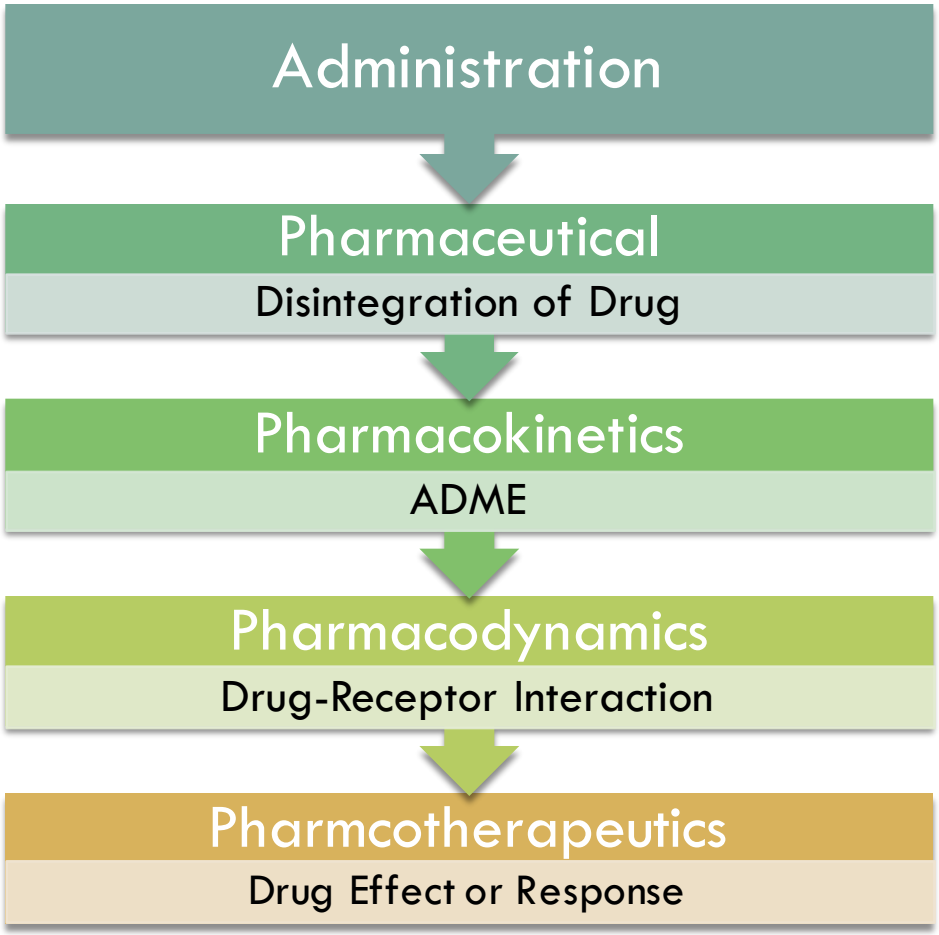


From Discovery to the Market

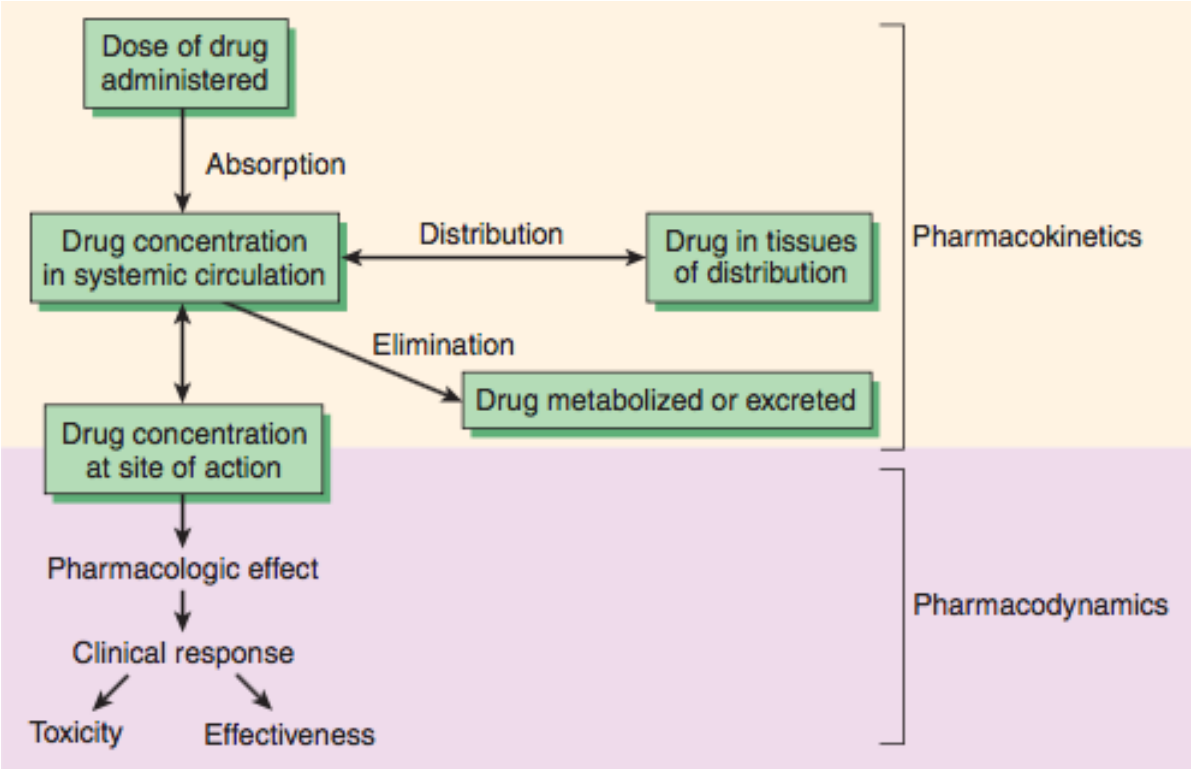


How do we study Pharmacology

General Concept



Relationship between pharmacokinetics and pharmacodynamics.



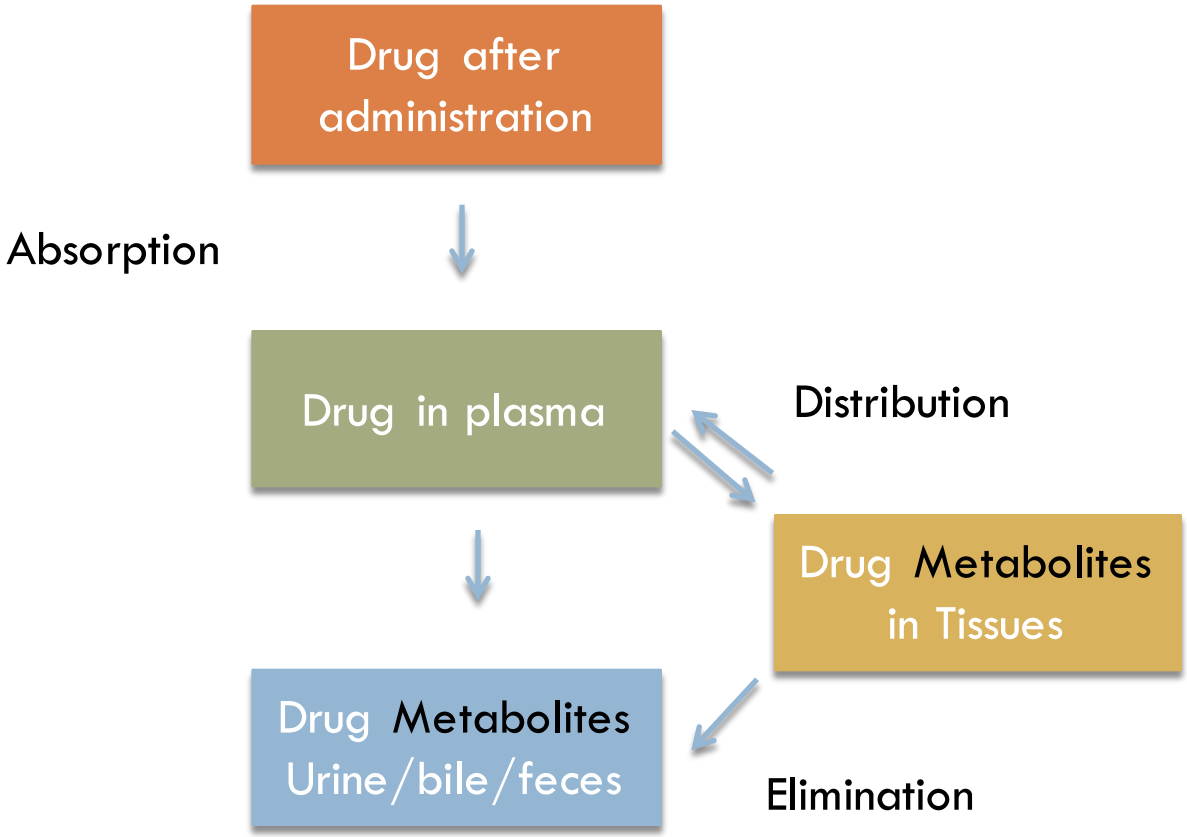
Relationship between pharmacokinetics and pharmacodynamics.

- Pharmacokinetics:
  - "as the study of the time course of drug absorption, distribution, metabolism, and excretion"
  - "Primary goals of pharmacokinetics include enhancing **efficacy** and decreasing **toxicity** of a patient's drug therapy"
- Pharmacodynamics:
  - "relationship between drug concentration at the site of action and the resulting effect"

Pharmacokinetics

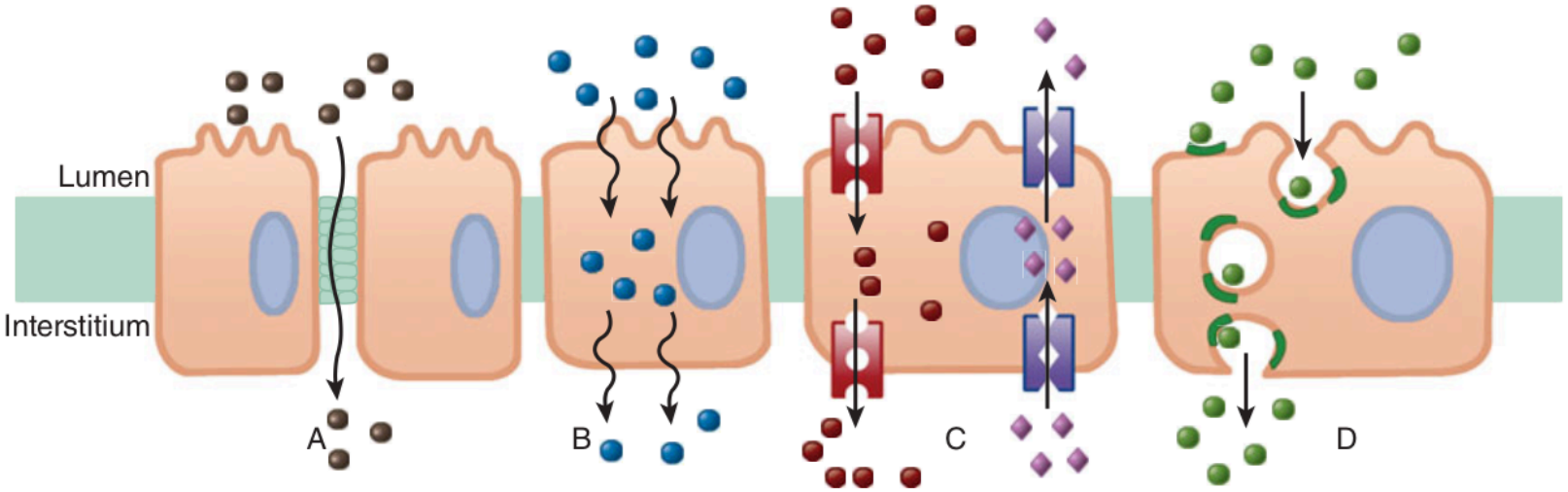
- Absorption:
  - The process of movement of unchanged drug from the site of administration to systemic circulation to reach the site of action.
- Distribution:
  - Transfer the drug from one location to another within the body
- Metabolism:
  - Process by which the drug is altered and broken down into smaller substances (metabolites).
- Elimination (Excretion):
  - Excretion is the removal of drug from body fluids
    - Urine, bile, sweat, saliva, tears, feces, breast, milk ..etc

After Drug Administration?



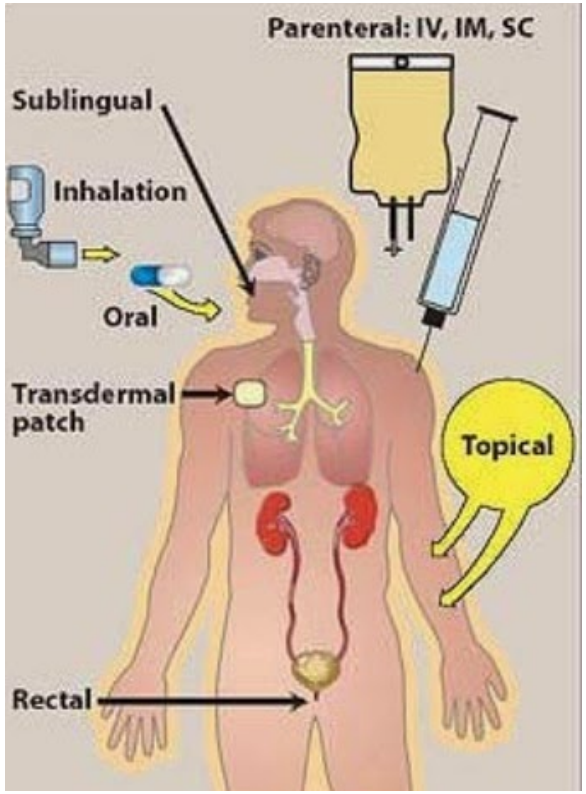
Pharmacokinetics

- Absorption:
  - The process of movement of unchanged drug from the site of administration to systemic circulation to reach the site of action.
- Movement of Drugs
  - Bilayer of amphipathic lipids
  - Q: properties of drugs



Pharmacokinetics

- Bioavailability:
  - "To indicate the fractional extent to which a dose of drug reaches its site of action."
  - First-pass effect
  - Effective dose
- Half life
  - The time required to change the amount of drug in the body by one-half during elimination.
- Routes of administration



Pharmacokinetics

- Distribution:
  - Transfer the drug from one location to another within the body
- Factors affecting drug delivery from the plasma:
  - blood flow: kidney and liver higher than skeletal muscles and adipose tissues.
  - capillary permeability
    - capillary structure: blood brain barrier
    - drug structure
  - binding of drugs to plasma proteins and tissue proteins

Pharmacokinetics

- Metabolism:
  - Process by which the drug is altered and broken down into smaller substances (metabolites)
  - Mainly in liver- Two phases
    - **Phase I :** *Phase I* metabolite may be active or inactive
      - Oxidation, Reduction, Hydrolysis.
      - Pro-Drug (ex: levodopa to Dopamin
    - **Phase II:** metabolites are inactive
      - Conjugation reactions
  - Others including kidney , lung, skin

Pharmacokinetics

- Elimination (Excretion):
  - Excretion is the removal of drug from body fluids
- Major Routes of Excretion
  - Renal Excretion
  - Biliary Excretion
- Minor Routes of Excretion
  - Pulmonary excretion.
  - Salivary excretion.
  - Mammary excretion via milk.
  - Skin / Dermal excretion via sweat.
  - Tears

Pharmacokinetics

- Excretory system is made up from
  - two kidneys ,ureters, bladder, urethra
- The structure unit of kidney is nephron
- Drug excretion
  - Glomerular filtration: small drug and metabolite molecules
  - Tubular secretion: most drugs enter the kidney tubule by tubule secretion. (active transport against Conc)
  - Tubule reabsorption: Some drugs and metabolites (It is passive transport)

Pharmacodynamics (Drug- receptor)

- General principle about drugs:
  - Few drugs act by simple mechanism- chemical/ physical properties
    - Antacid,
  - Most drugs bind to receptor
- Drug (D) + receptor-effector (R) → drug-receptor-effector complex → effect
- D + R → drug-receptor complex → effector molecule → effect
- D + R → D-R complex → activation of coupling molecule → effector molecule → effect

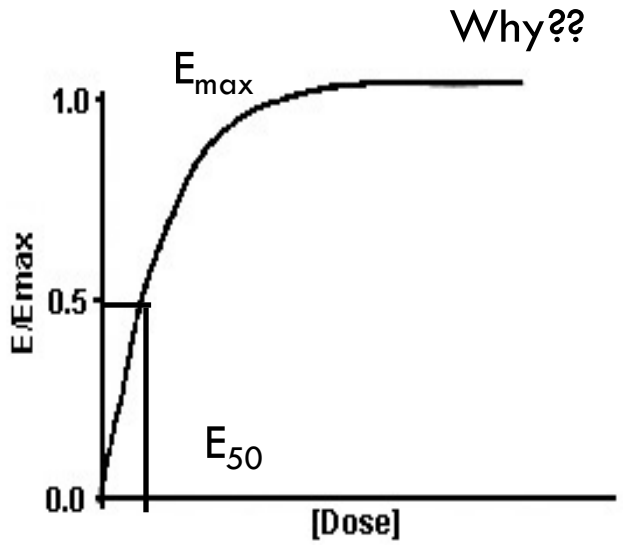
"final change in function is accomplished by an **effector** mechanism"

Dose Response curve

- Dose-response relationships are a common way to portray data in both basic and clinical science
- A. Graded Response
  - Dose gives response (Magnitude of the drug) = action is continues (heart rate)
  - Single organs (Intestine and Acetylcholine)
- B. Quantal Response
  - All or none (not Magnitude of the drug)= action is not continues (convulsions)
  - Population of subjects

Dose Response curve

- Relation between drug concentration and effect" hyperbolic curve
- A. Graded Response

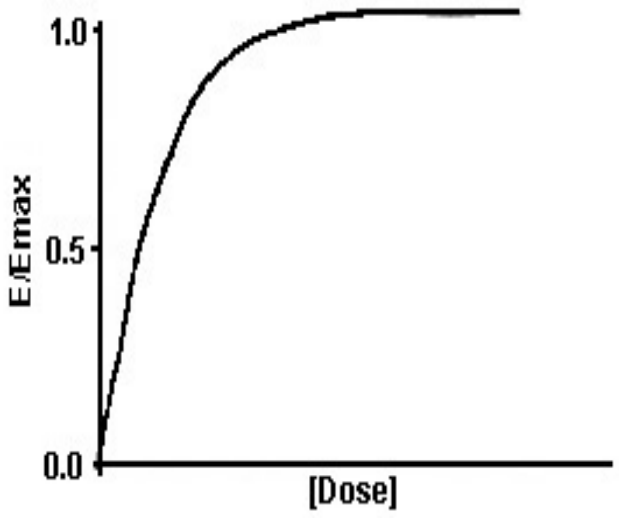


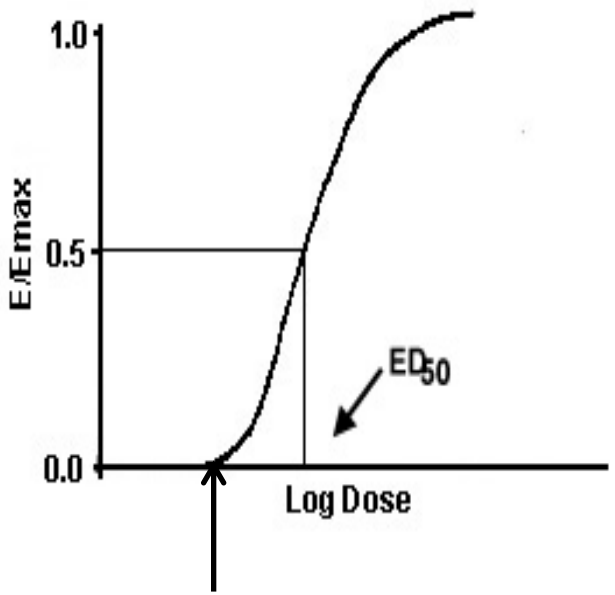
$$E = \frac{E_{max} \times C}{C + EC_{50}}$$

- E = the effect
- C= concentration
- Emax = the maximal response

Dose Response curve

- Can be plotted using log EC_{50} = Sigmoidal curve

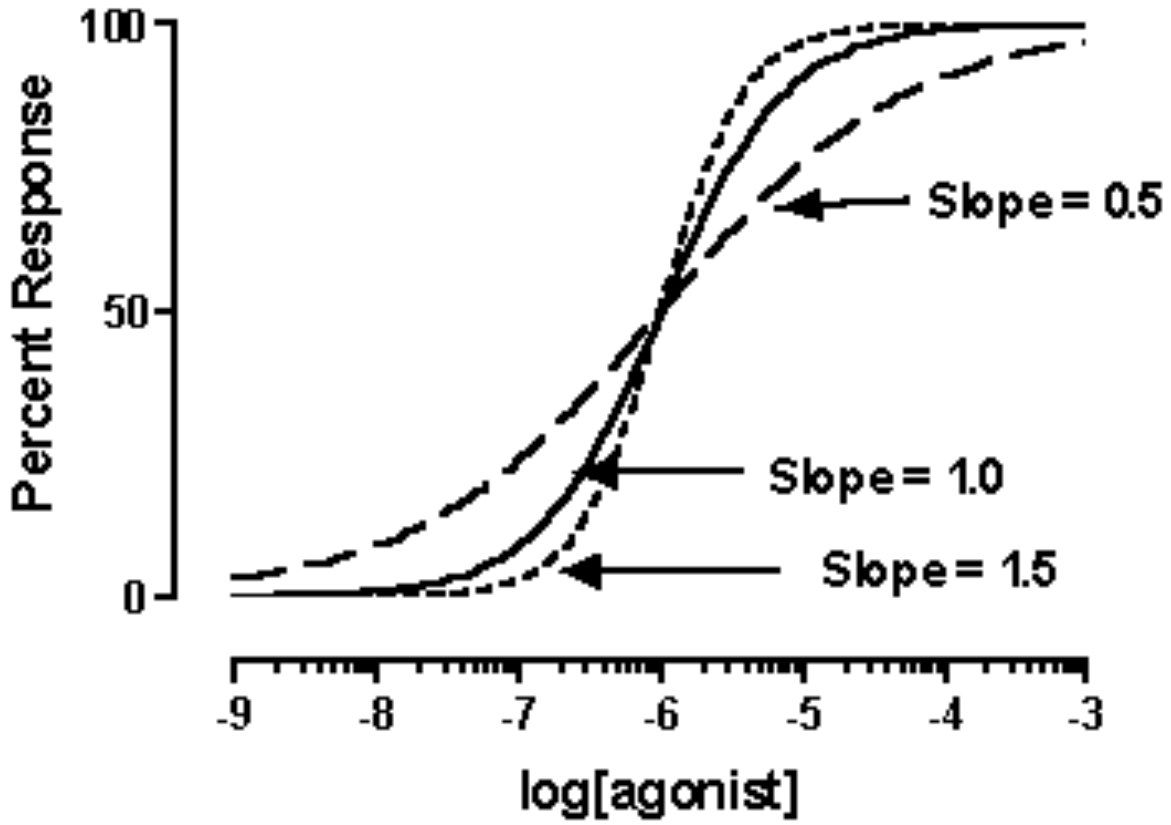




Threshold: Minimal dose needed to produce response.

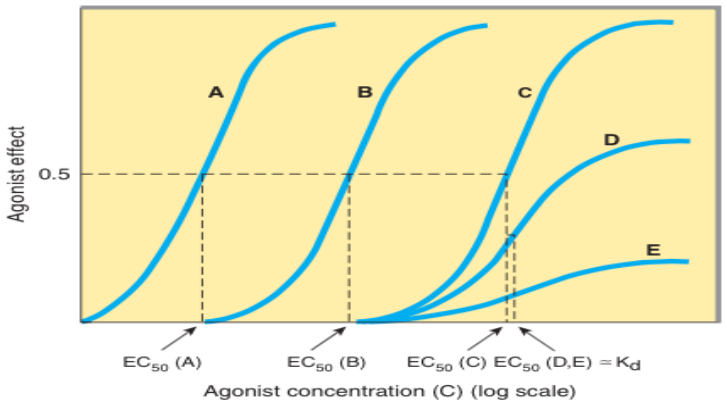
Dose Response curve

- Steepness of the curve ” compare to the standard “



Dose Response curve

- Used to measure :
  - **Potency:** refers to the amount of drug required to achieve a defined biological effect (EC50)
  - **Efficacy:** The maximum biological of effect that can be produced by a drug
  - **Drug Safety: T.I.**
- Compare two or more drugs:
  - **Affinity** of a drug for a receptor is a measure of how strongly that drug binds to the receptor
    - K_d= represent the affinity of the molecule



Dose Response curve

- Isopropanol, Epinephrine ,Norepinephrine = Efficacy
- Isopropanol, Epinephrine, Norepinephrine ≠ Potency