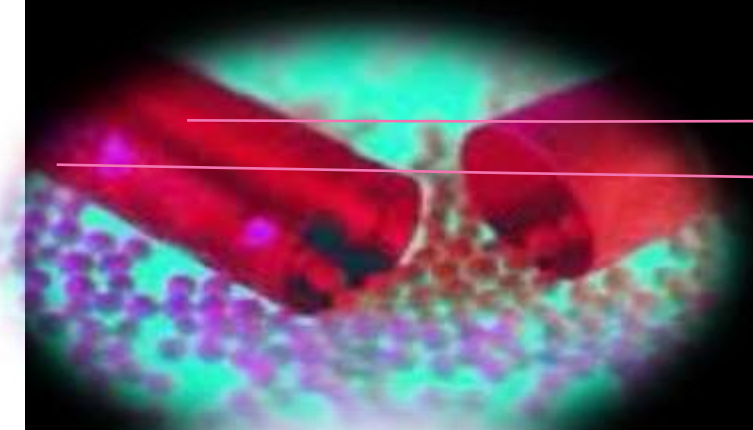
PHARMACOKINETICS



MERLYN A. BARACLAN, RN, RMT

pharmacokinetics

- Definition:

- refers on **how the body acts on the drug**

- involves the study of ***absorption, distribution, metabolism (biotransformation) and drug excretion***

I. Overview

- **Aim of drug therapy**

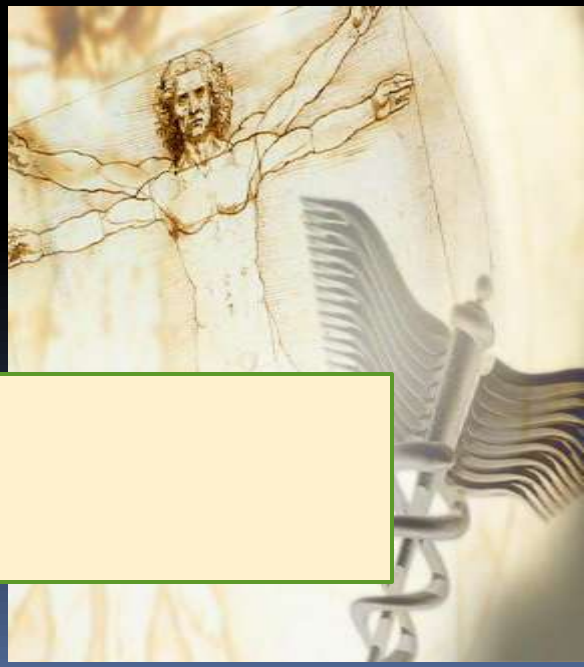
- To prevent, cure or control various disease states

adequate drug doses must be delivered to the target tissues

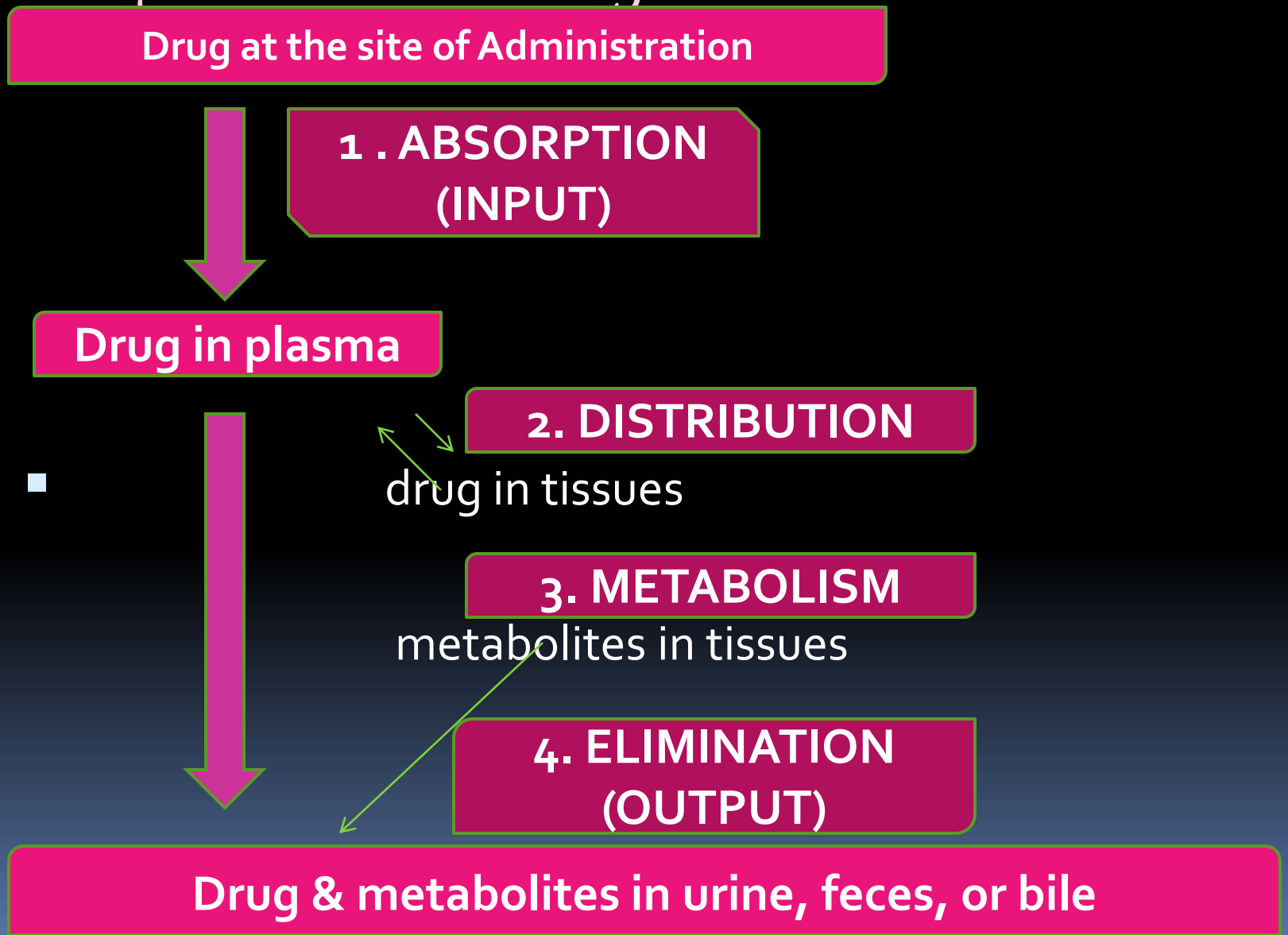
so that **therapeutic yet NON – toxic levels are obtained**

Overview

- Too much of a drug will result into toxic effects & too little will not result into the desired therapeutic effects.



4 Fundamental Pathways of Drug Movement & Modification in the Body

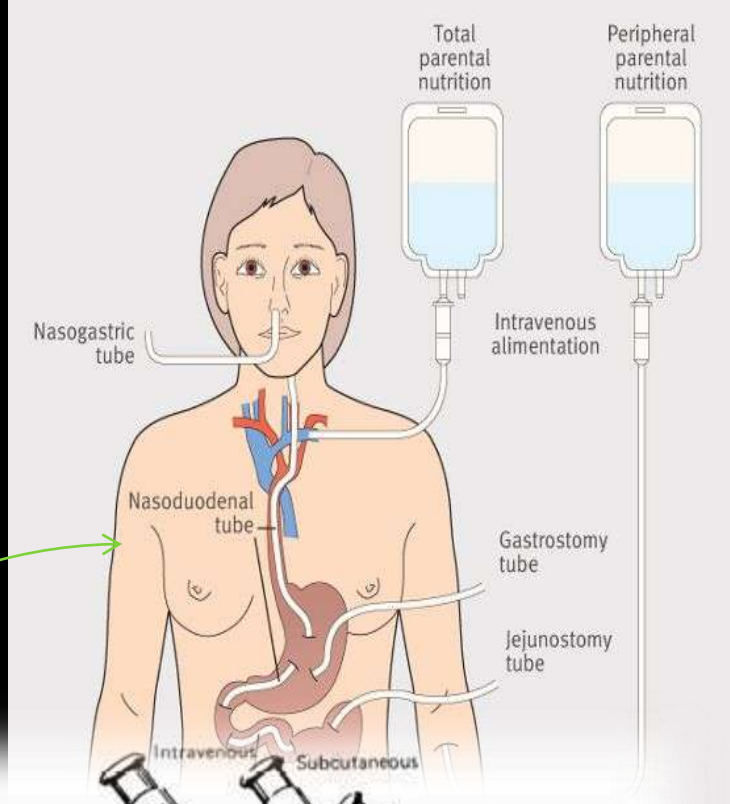


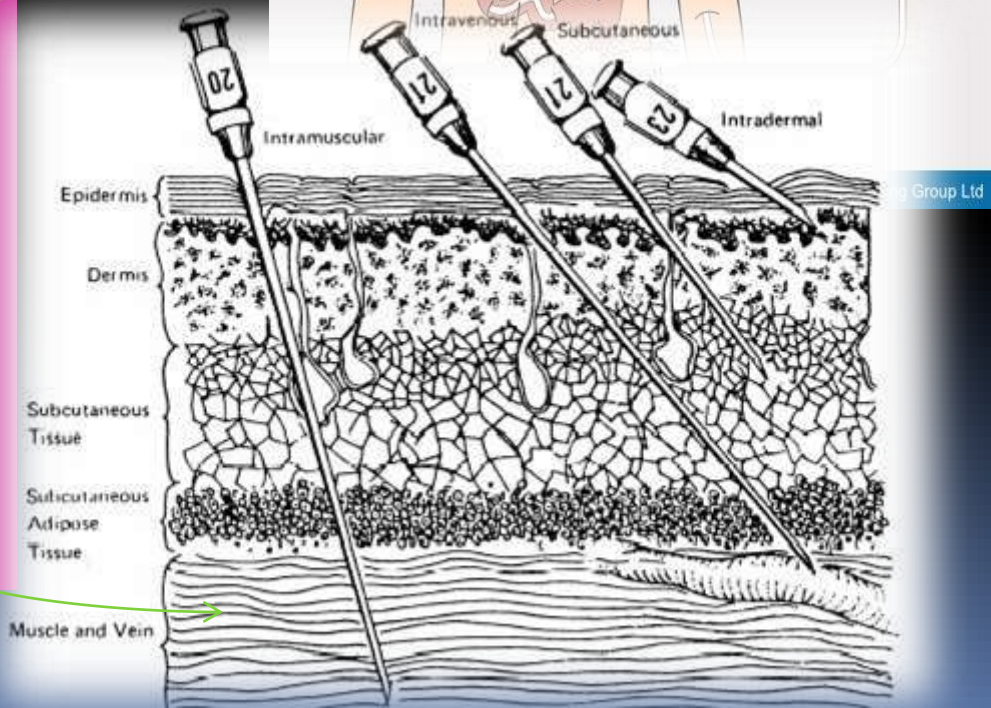
II. Routes of Drug Administration

- Determined primarily by the properties of the drug

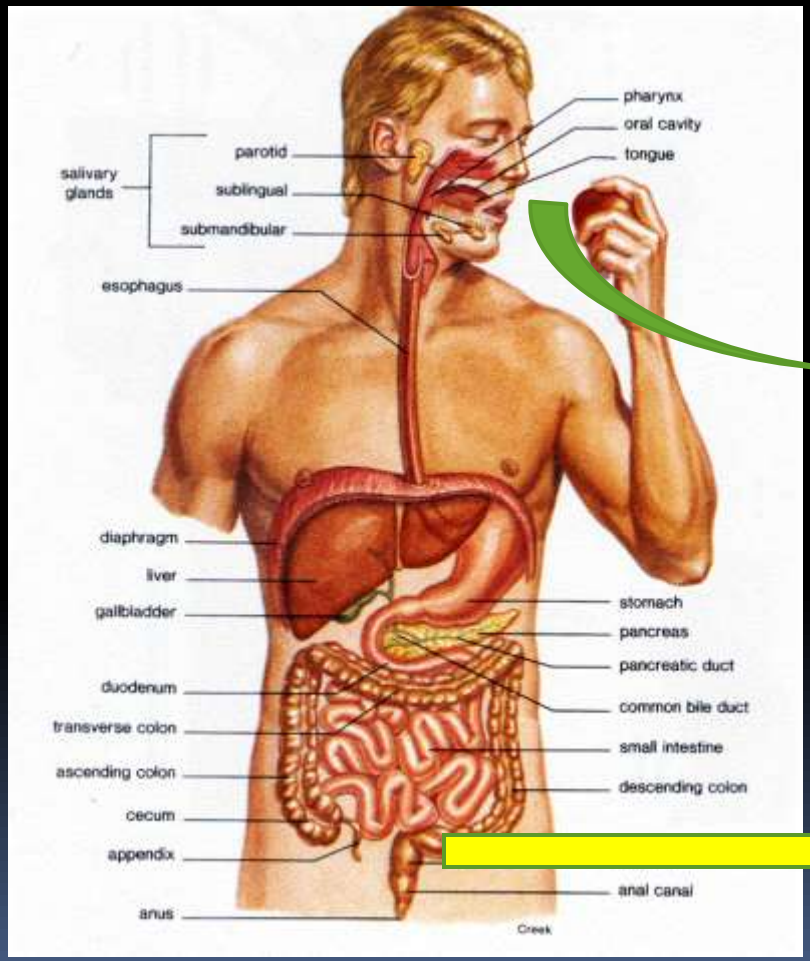
2 MAJOR ROUTES OF DRUG ADMINISTRATION

1. **Enteral**
2. **Parenteral**





ENTERAL routes



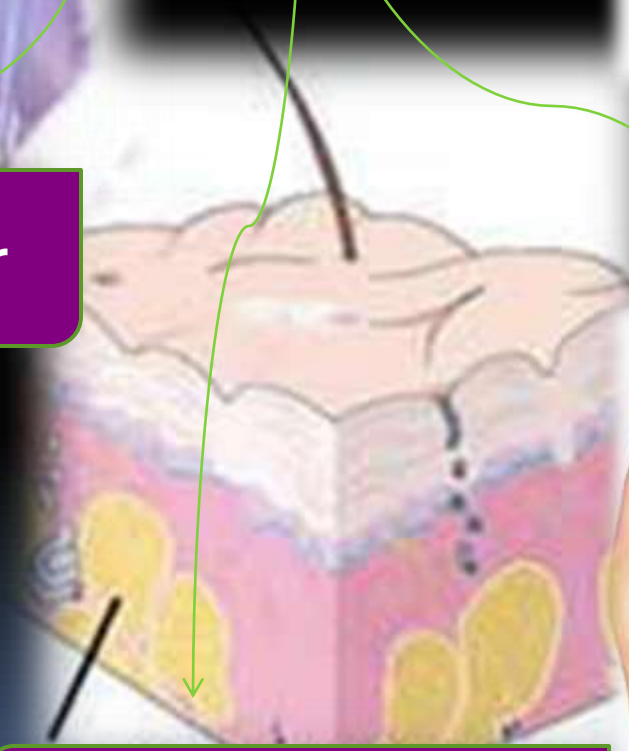
A. ORAL

B. SUBLINGUAL

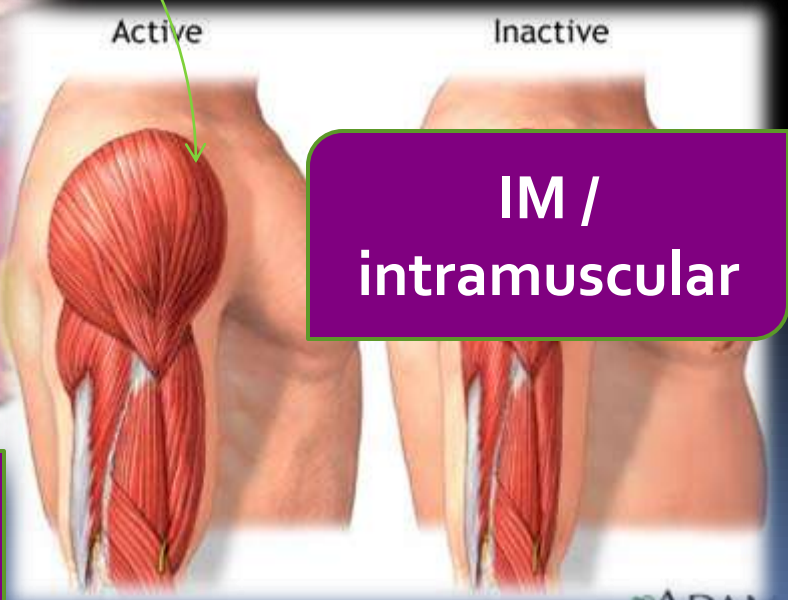
C. RECTAL

PARENTERAL routes

IV / intravascular



SC / subcutaneous



IM / intramuscular

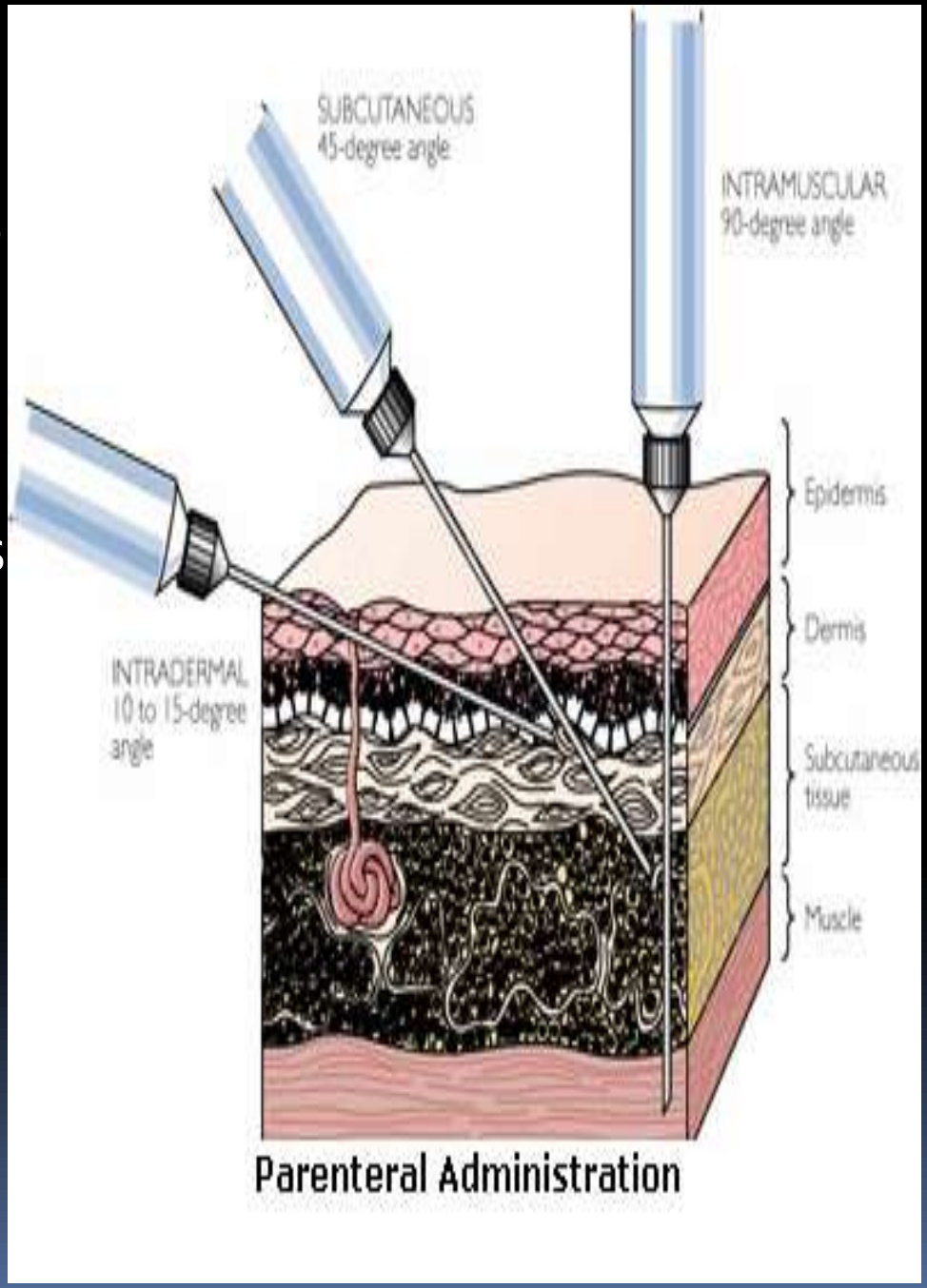
parenteral

- **Advantages**
- Fast: 15–30 seconds for IV, 3–5 minutes for IM and subcutaneous (SC)
- 100% bioavailability
- suitable for drugs not absorbed by the gut or those that are too irritant (anti-cancer)
- IV can deliver continuous medication, e.g., morphine for patients in continuous pain, or saline drip for people needing fluids

- **Disadvantages**
- more risk of addiction when it comes to injecting drugs of abuse
- Belonephobia, the fear of needles and injection.
- If needles are shared, there is risk of HIV and other infectious diseases
- It is the most dangerous route of administration
- If not done properly, potentially fatal air boluses (bubbles) can occur.
- Need for strict asepsis

Parenteral

- Used for drugs which are poorly absorbed in the GIT
- Unstable drugs
- For unconscious patients
- Circumstances that require a rapid onset of action
- Provides the most control over the actual dose delivered to the body



Routes of Drug Administration

- **1. ENTERAL**

A. ORAL

- most common route of administration
- Most variable
- most complicated pathway
- Cheapest
- Non - invasive

[NOTE: most drugs are absorbed in the GIT & encounter the liver before they are distributed into the general circulation]

Routes of Drug Administration

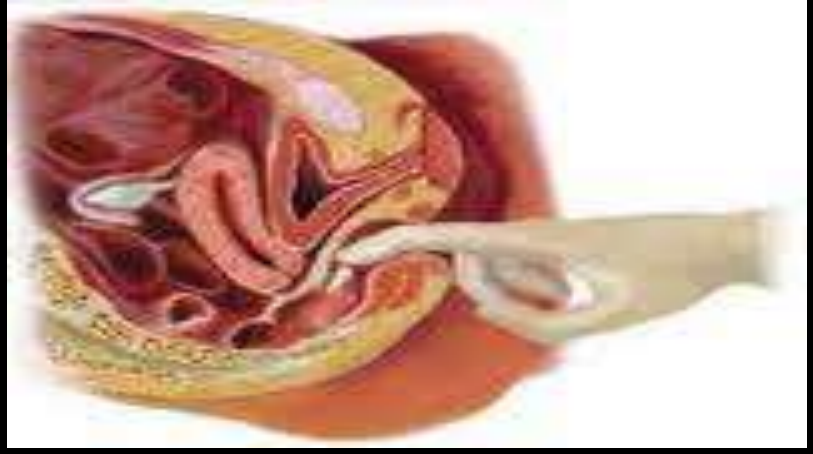
- 1. Enteral

B. SUBLINGUAL

- Placement **under the tongue**
- Allows the drug to diffuse into the capillaries & therefore to enter the systemic circulation

Advantage: the drug bypasses the intestine & liver & thus **avoids 1st pass metabolism**

Routes of Drug Administration



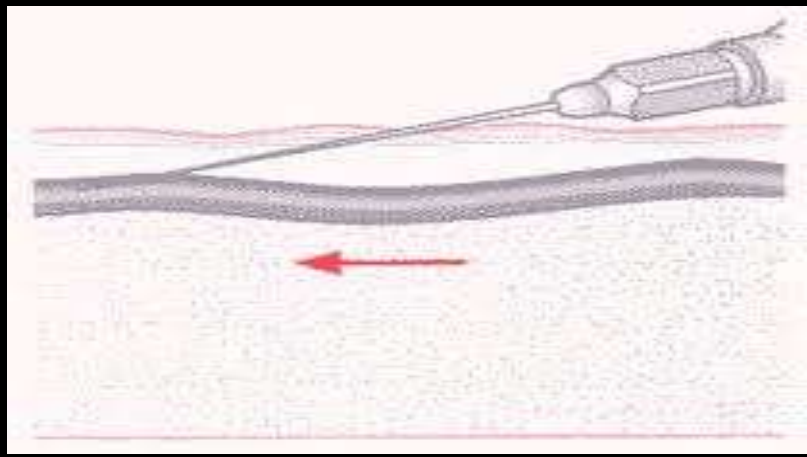
1. Enteral

c. Rectal

- Useful if the drug induces vomiting if given orally or if the patient is already vomiting
- Drainage of the rectal region bypasses the portal circulation
- Similar to the sublingual route, it prevents the destruction of the drug by intestinal enzymes or by the low pH in the stomach

[note: commonly used to administer anti – emetic agents]

Routes of Drug Administration



2. Parenteral

a. IV / intravascular

- IV injection is the **most** common parenteral route
- For drugs which are not absorbed orally
- Bypasses the liver
- Permits a rapid effect and a maximal degree of control over the circulating levels of the drug
- Can introduce bacterial contamination at the site
- Can cause hemolysis

Routes of Drug Administration

2. **Parenteral**

b. IM / intramuscular

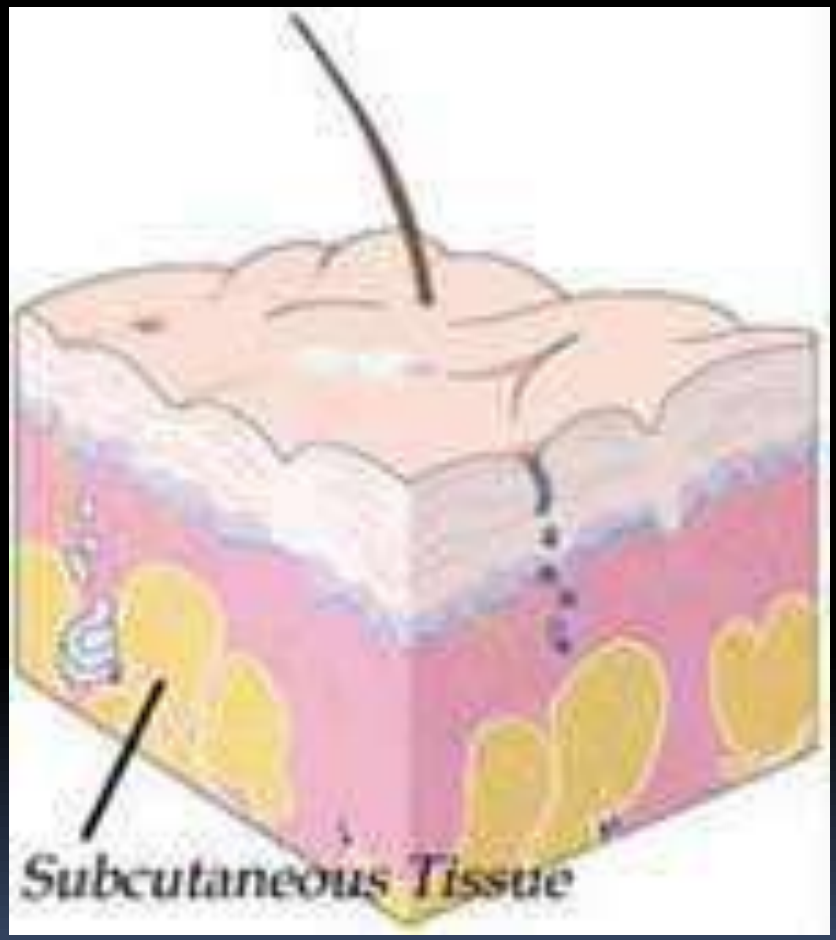
Drugs administered
- aqueous sol'n
- specialized depot preparations

Routes of Drug Administration

2. Parenteral

c. SC / subcutaneous

- This route of administration like IM requires absorption & somewhat slower than the IV route



Routes of Drug Administration

3. **Others**

a. **Inhalation**

- Provides a ***rapid delivery*** of a drug across a large surface area of the ***mucus membranes of the respiratory and the pulmonary epithelium***
- Effect is as rapid as IV injection
- For gaseous drugs

- **Advantages**
- Fastest method, 7–10 seconds for the drug to reach the brain

- **Disadvantages**
- Typically a more addictive route of administration because it is the fastest, leading to instant gratification.
- Difficulties in regulating the exact amount of dosage
- Patient having difficulties administering a drug via inhaler

Routes of Drug Administration

3. **Others**

b. Intranasal

- Through the nose

eg. : desmopressin, salmon calcitonin, cocaine

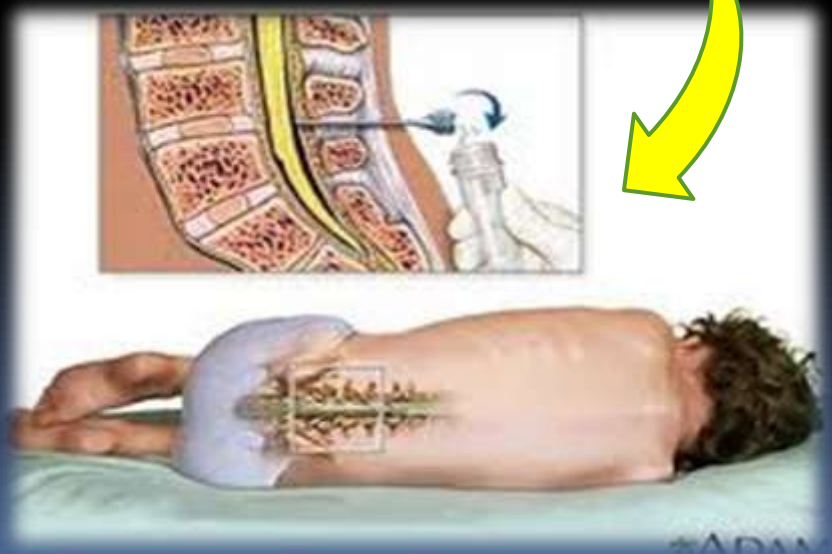
Routes of Drug Administration

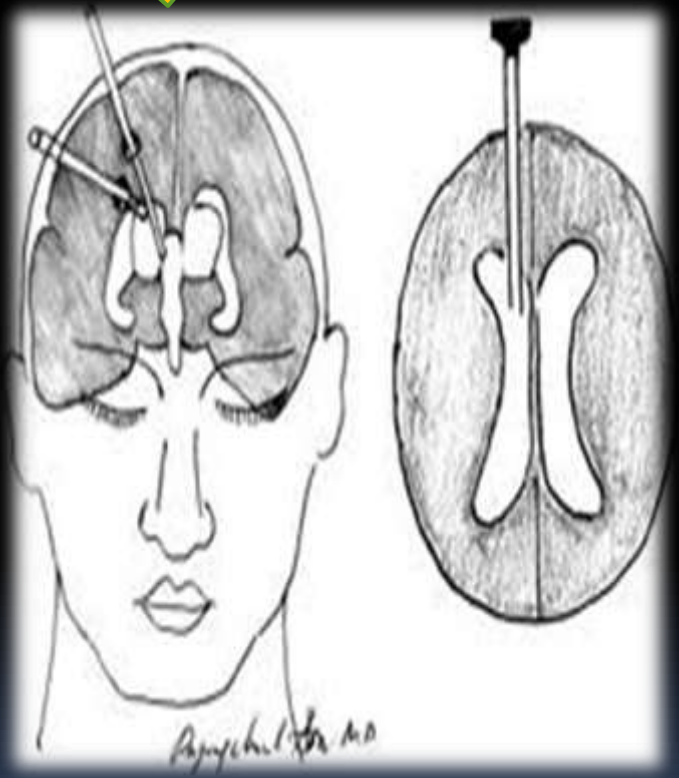
. **Others**

c. Intrathecal, intraventricular

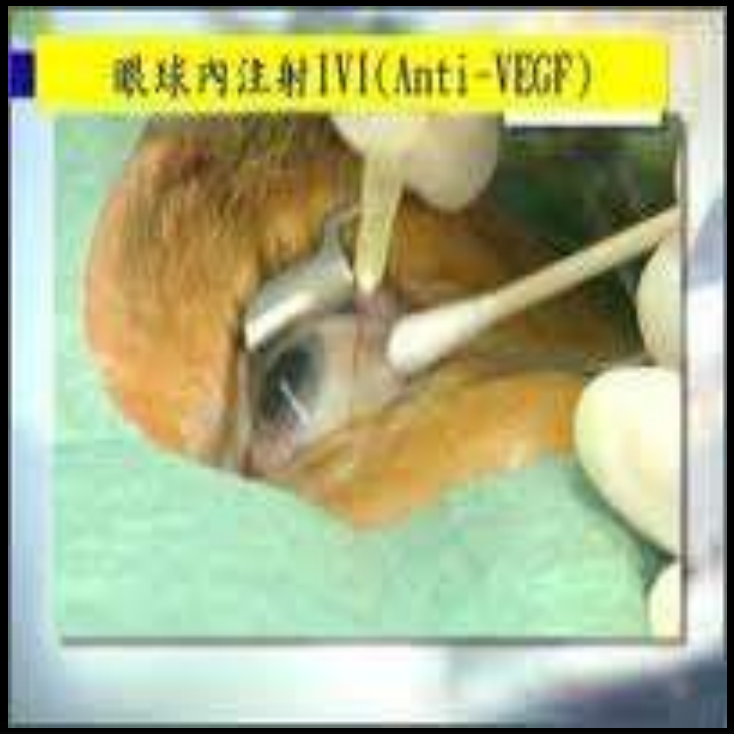
- Introducing drugs directly into the cerebrospinal fluid / CSF

Eg., amphotericin B





Routes of Drug Administration



- 3. **Others**

d. Topical

- Is used when a local effect of a drug is required

- Eg., clotrimazole, atropine

Routes of Drug Administration

3. **Others**

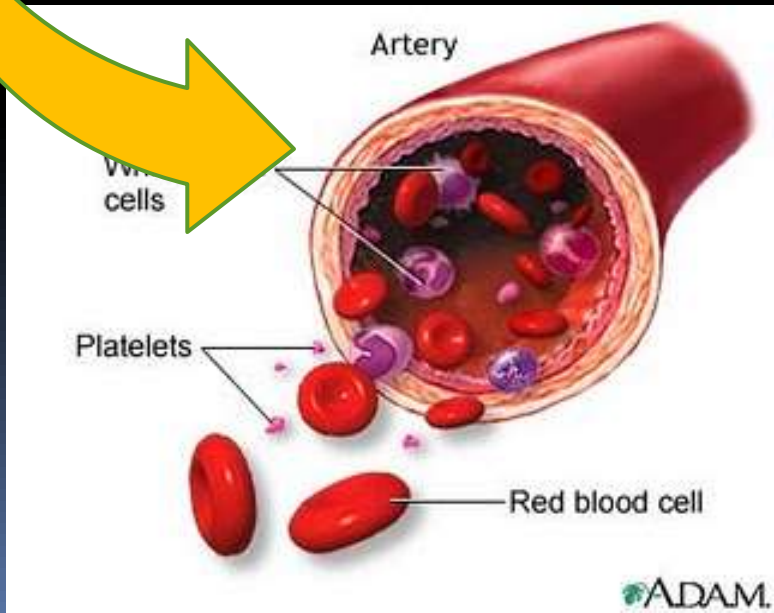
e. Transdermal

- This route of administration achieves systemic effects by application of drugs to the ***skin***, usually by using a transdermal patch.
- Rate of absorption varies markedly
- Eg., nitroglycerin

III. ABSORPTION OF DRUGS

- Is the transfer of a drug from its site of administration to the bloodstream

- IV delivery – absorption is complete



III. ABSORPTION OF DRUGS

- **A. Transport of Drug from the GIT**

1. **PASSIVE DIFFUSION**

- The driving force for passive absorption of a drug is the concentration gradient
- The drug moves from a region ***of high concentration to one of a lower concentration***
- Does not involve a carrier
- Vast majority of drugs gain access to the body by this mechanism

III. ABSORPTION OF DRUGS

2. Active Transport

- Involves a specific carrier protein

- Is "energy dependent" & is driven by the hydrolysis of ATP

- Also capable of moving a drug against a concentration gradient

III. ABSORPTION OF DRUGS

B. Physical Factors Influencing Absorption

1. Blood flow to the absorption site

2. Total surface area available for absorption

3. Contact time at the absorption surface

IV. Bioavailability

- Refers to the fraction of an administered drug that reaches the systemic circulation

V. Drug Distribution

- Is the process by which a drug reversibly leaves the bloodstream & enters the interstitium (extracellular fluid) and / or the cells of the tissues.

- **Affected by the following factors:**

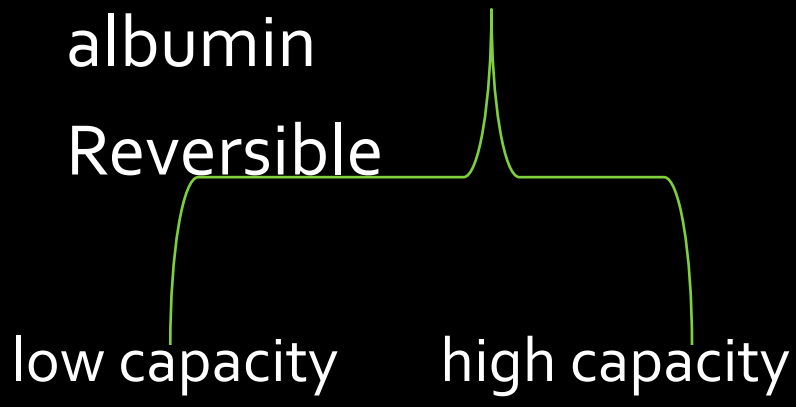
- **1. Blood Flow**
- **2. Capillary permeability**
  - **capillary structure**
  - **blood brain barrier**
- **3. Binding of Drugs to proteins**

VI. Binding of Drugs to Plasma Proteins

- Bound drugs are pharmacologically INACTIVE, only the FREE, UNBOUND drug can act on target sites in the tissues, elicit a biologic response & be available to the processes of elimination

A. Binding capacity of albumin

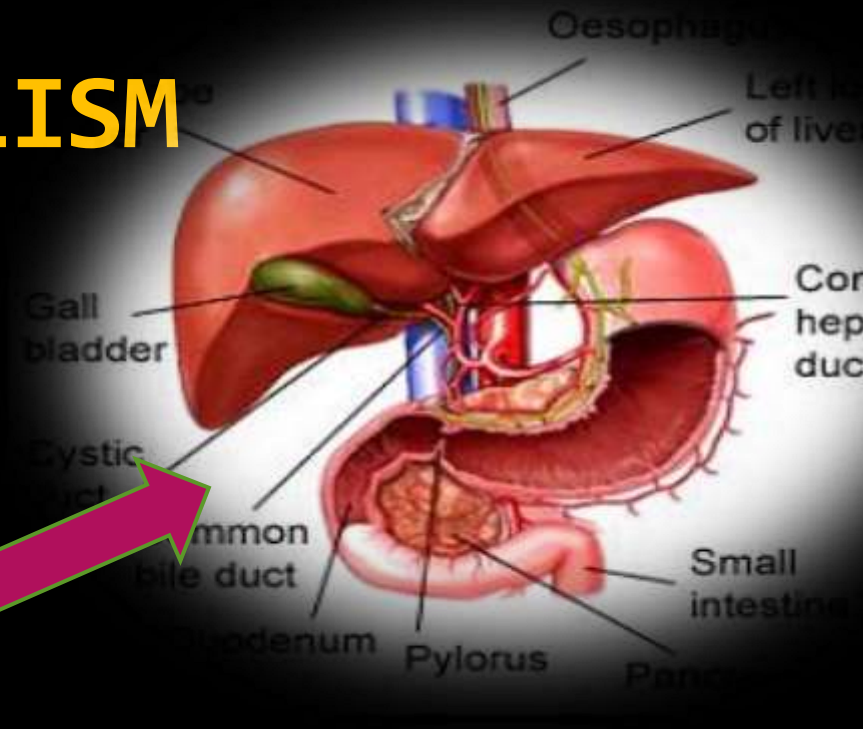
- Reversible



Note **: ALBUMIN** has the strongest affinity for ANIONIC DRUGS & HYDROPHOBIC DRUGS.

VII. DRUG METABOLISM

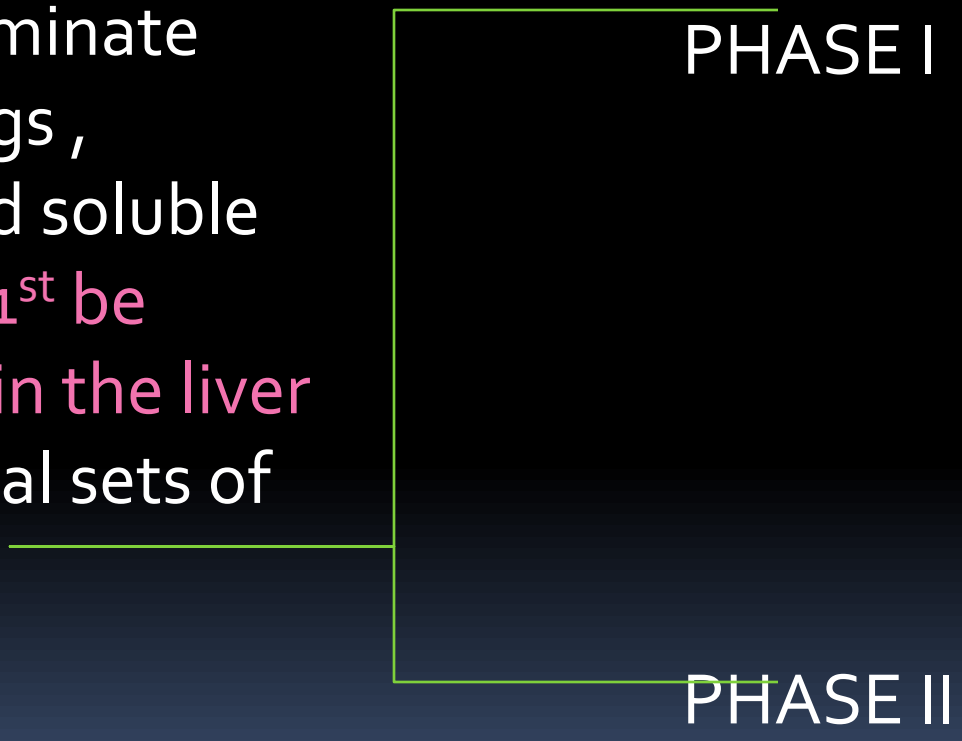
- Drugs are often eliminated by biotransformation and or excretion into the URINE OR BILE.



- **LIVER** – the MAJOR SITE FOR DRUG METABOLISM

Reactions of Drug Metabolism

- The kidney cannot efficiently eliminate lipophilic drugs , therefore lipid soluble agents must 1st be metabolized in the liver using 2 general sets of reactions



Phase I

- Converts lipophilic molecules into more polar molecules

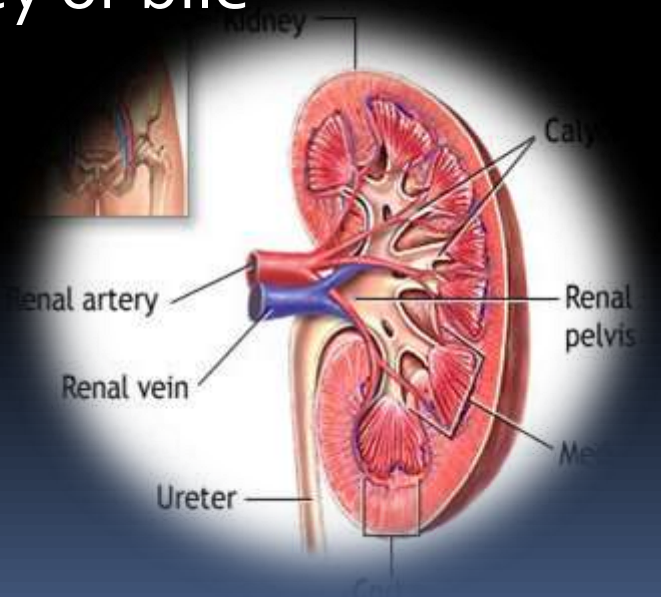
- Phase I metabolism may increase, decrease, or leave unaltered the drug's pharmacologic activity.

Often uses the P 450 system

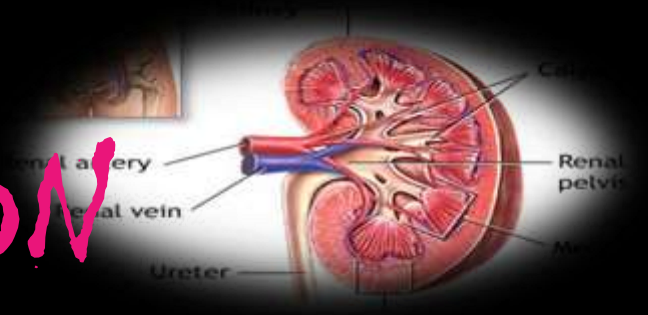
Phase II

- Consists of conjugation reactions
- Uses substrates like glucuronic acid, sulfuric acid, acetic acid, or an amino acid
- Renders the metabolites INACTIVE and more water soluble

- The highly polar drug conjugates may then be excreted by the kidney or bile



DRUG ELIMINATION



- Removal of a drug from the body may occur via a number of routes, **the most important** being the kidney or urine
- Other routes:

- bile, intestine, lung, milk,

- Drugs that have been made water soluble in the liver are often readily excreted in the kidneys.
- Kidney dysfunction can lead to toxic levels of the drug in the body because the drug cannot be excreted.

Thank you for listening!!!

- Self-respect is the fruit of discipline; the sense of dignity grows with the ability to say no to oneself.