Lab. 3

Drug Absorption and Excretion

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Contents

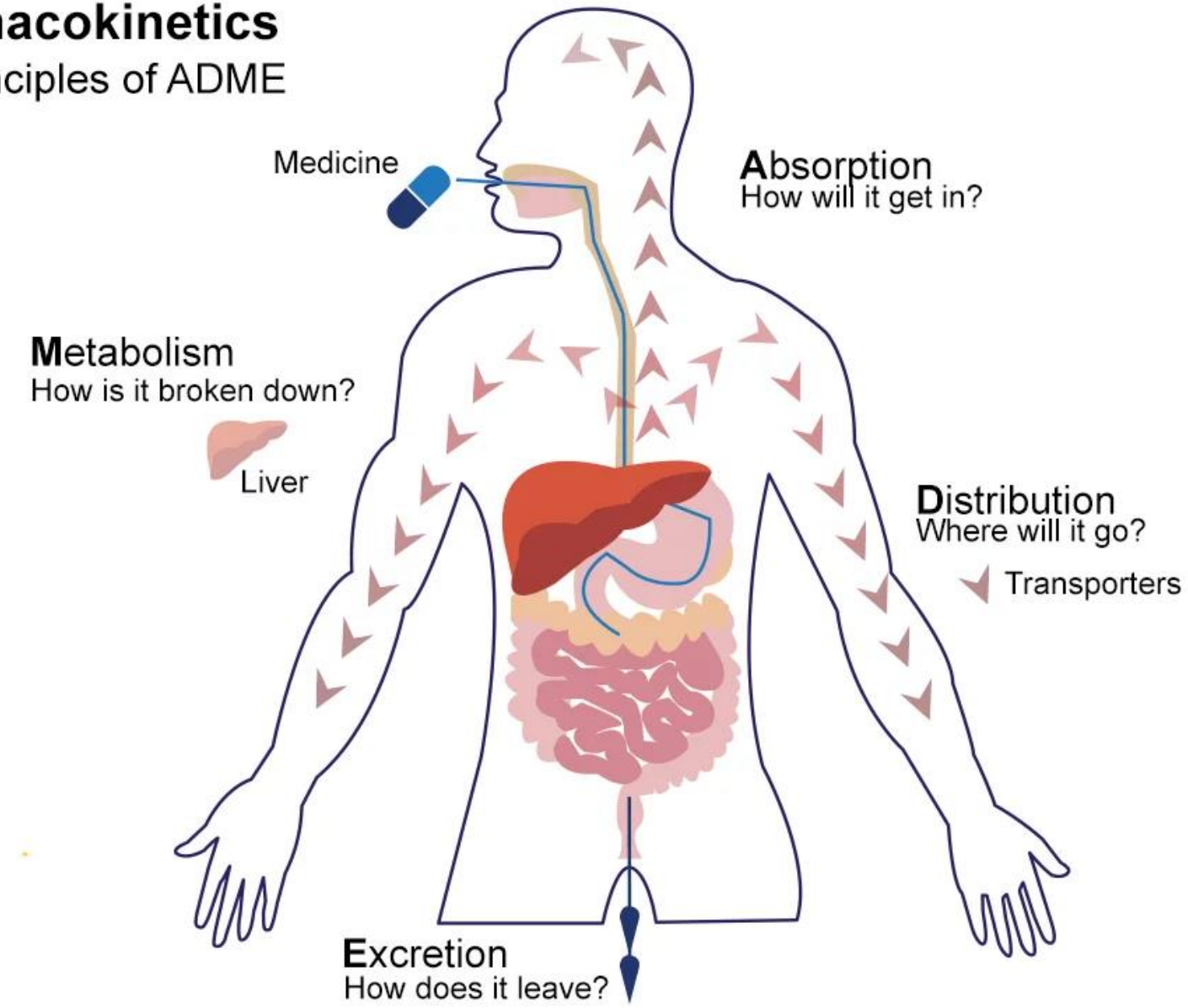
Pharmacokinetics & Pharmacodynamics

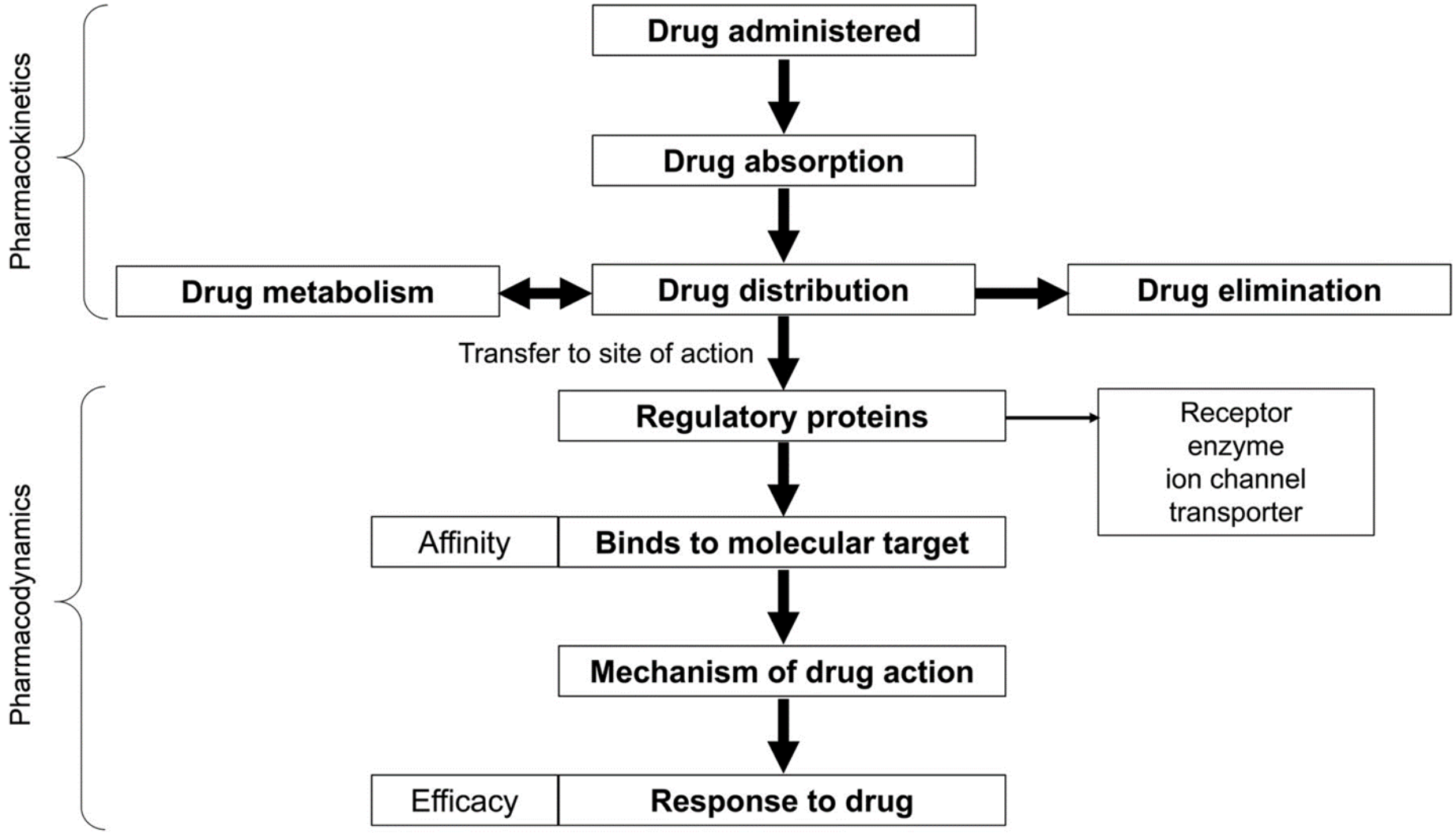
Pharmacokinetics: is the science of the kinetics of drug absorption, distribution, metabolism and excretion

Pharmacodynamics: refers to the relationship between the drug concentration at the site of action (receptors) and pharmacologic response

Pharmacokinetics

The principles of ADME




Pharmacokinetics
Drug administered
Drug absorption
Drug metabolism
Drug distribution
Drug elimination
Transfer to site of action
Pharmacodynamics
Regulatory proteins
Receptor
enzyme
ion channel
transporter
Affinity
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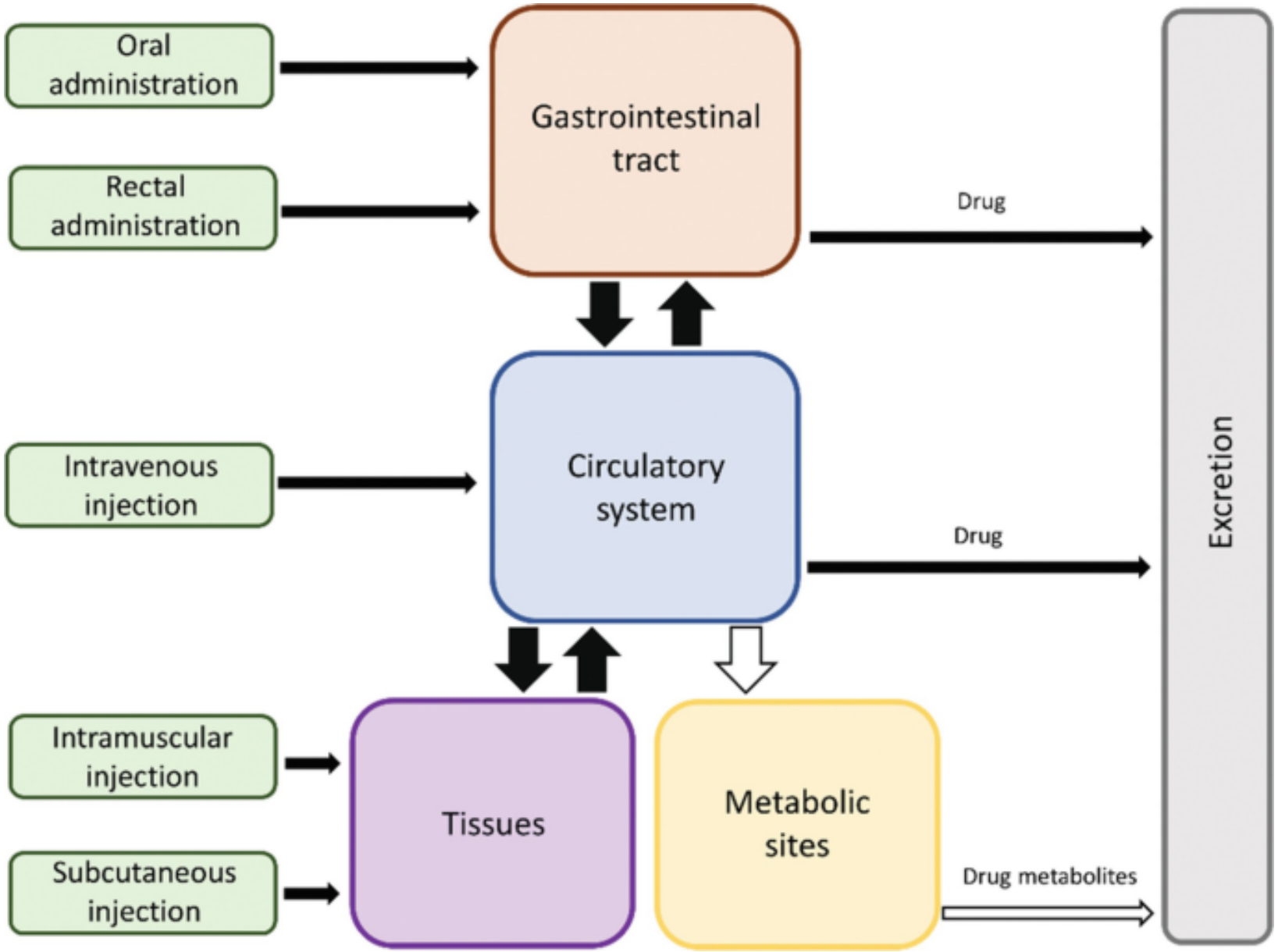
Mechanism of drug action
Efficacy
Response to drug

Absorption of Drugs

- **Absorption**: is the process of movement of unchanged drug from the site of administration to systemic circulation.

- The rate and extent of absorption depend on the environment where the drug is absorbed, chemical characteristics of the drug, and the route of administration (which influences bioavailability). Routes of administration other than intravenous may result in partial absorption and lower bioavailability.


Oral administration
Rectal administration
Gastrointestinal tract
Drug
Intravenous injection
Circulatory system
Drug
Excretion
Intramuscular injection
Subcutaneous injection
Tissues
Metabolic sites
Drug metabolites

Mechanisms of absorption of drugs from the GI tract

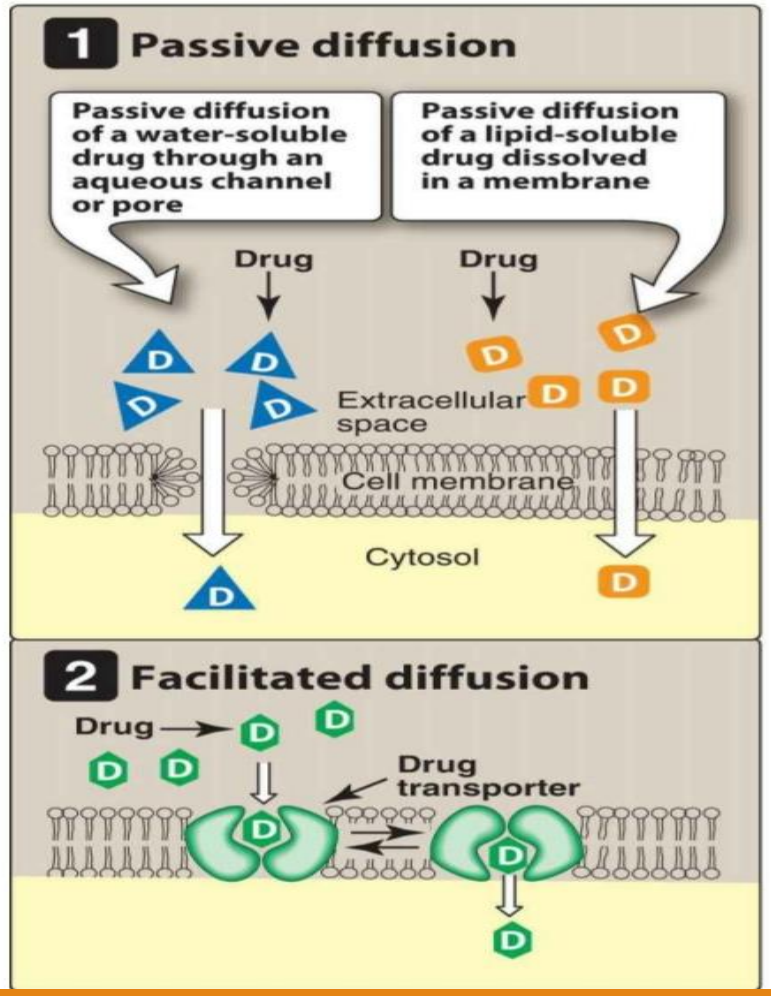
Depending on their chemical properties, drugs may be absorbed from the GI tract by

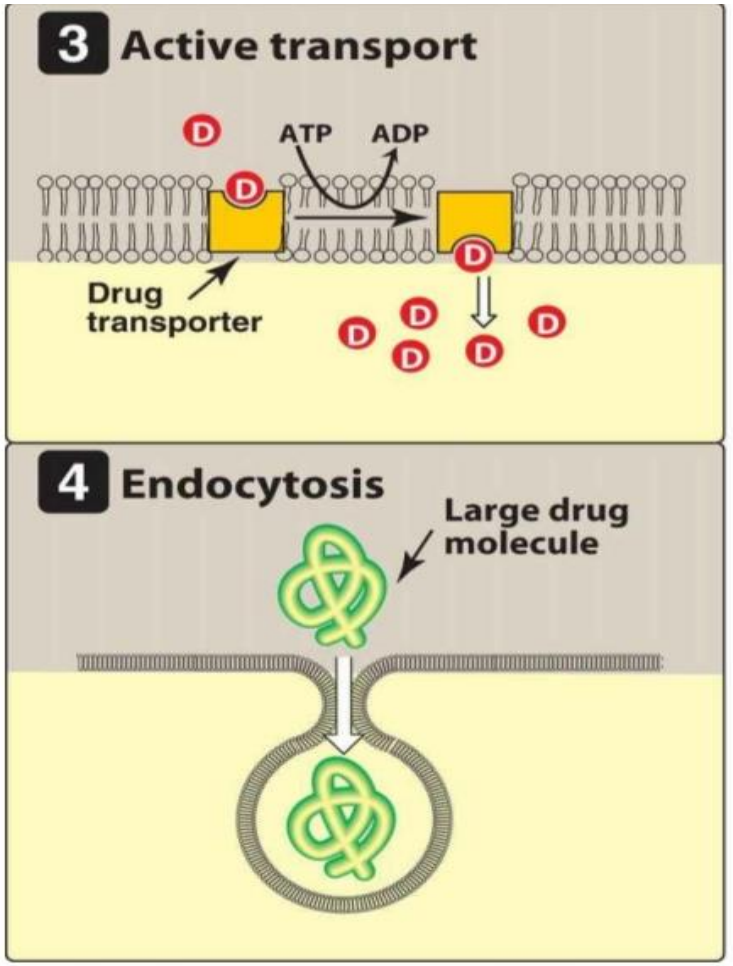
1- passive diffusion,

2- facilitated diffusion

3- active transport

4- endocytosis





1- Passive diffusion

- The driving force for passive diffusion of a drug is the concentration gradient across a membrane separating two body compartments.
- In other words, the drug moves from an area of high concentration to one of lower concentration.
- Passive diffusion does not involve a carrier, is not saturable, and shows low structural specificity
- The vast majority of drugs are absorbed by this mechanism.
- Water-soluble drugs penetrate the cell membrane through aqueous channels or pores, whereas lipid-soluble drugs readily move across most biologic membranes due to solubility in the membrane lipid bilayers.

2- Facilitated diffusion

- Other agents can enter the cell through specialized transmembrane carrier proteins that facilitate the passage of large molecules. These carrier proteins undergo conformational changes, allowing the passage of drugs or endogenous molecules into the interior of cells. This process is known as facilitated diffusion.

- It does not require energy, can be saturated, and may be inhibited by compounds that compete for the carrier.

3- Active transport

- This mode of drug entry also involves specific carrier proteins that span the membrane
- However, active transport is energy dependent, driven by the hydrolysis of adenosine triphosphate (ATP). It is capable of moving drugs against a concentration gradient, from a region of low drug concentration to one of higher concentration.
- The process is saturable.
- Active transport systems are selective and may be competitively inhibited by other cotransported substances.

4- Endocytosis and exocytosis

- This type of absorption is used to transport drugs of exceptionally large size across the cell membrane.

- Endocytosis involves engulfment of a drug by the cell membrane and transport into the cell by pinching off the drug-filled vesicle.
- Exocytosis is the reverse of endocytosis. Many cells use exocytosis to secrete substances out of the cell through a similar process of vesicle formation.

- Vitamin B is transported across the gut wall by endocytosis, whereas certain neurotransmitters (for example, norepinephrine) are stored in intracellular vesicles in the nerve terminal and released by exocytosis.

Factors affecting Absorption

A- Factors related to drugs:

-Lipid , water solubility

-Molecular size

-Patrice size

-Degree of ionization

-Chemical nature

-Dosage forms

-Formulation

-concentration

B- Factors related to body:

- Area of absorptive surface

-Vascularity

-PH

-presence of other substances

-GI motility

-Functional integrity of absorptive surface

-Diseases

Drug Excretion

- **Passage out of systemically absorbed drug**

- Drugs excreted in :

1- Urine

2- Feces

3- Exhaled air

4- Saliva & sweat

5- Milk

Excretion: Urine

- Most important channel for excretion of drugs
- Its eliminates water soluble substances
- Amount of drug or its metabolites depend on :

-Glomerular filteration rate (GFR)

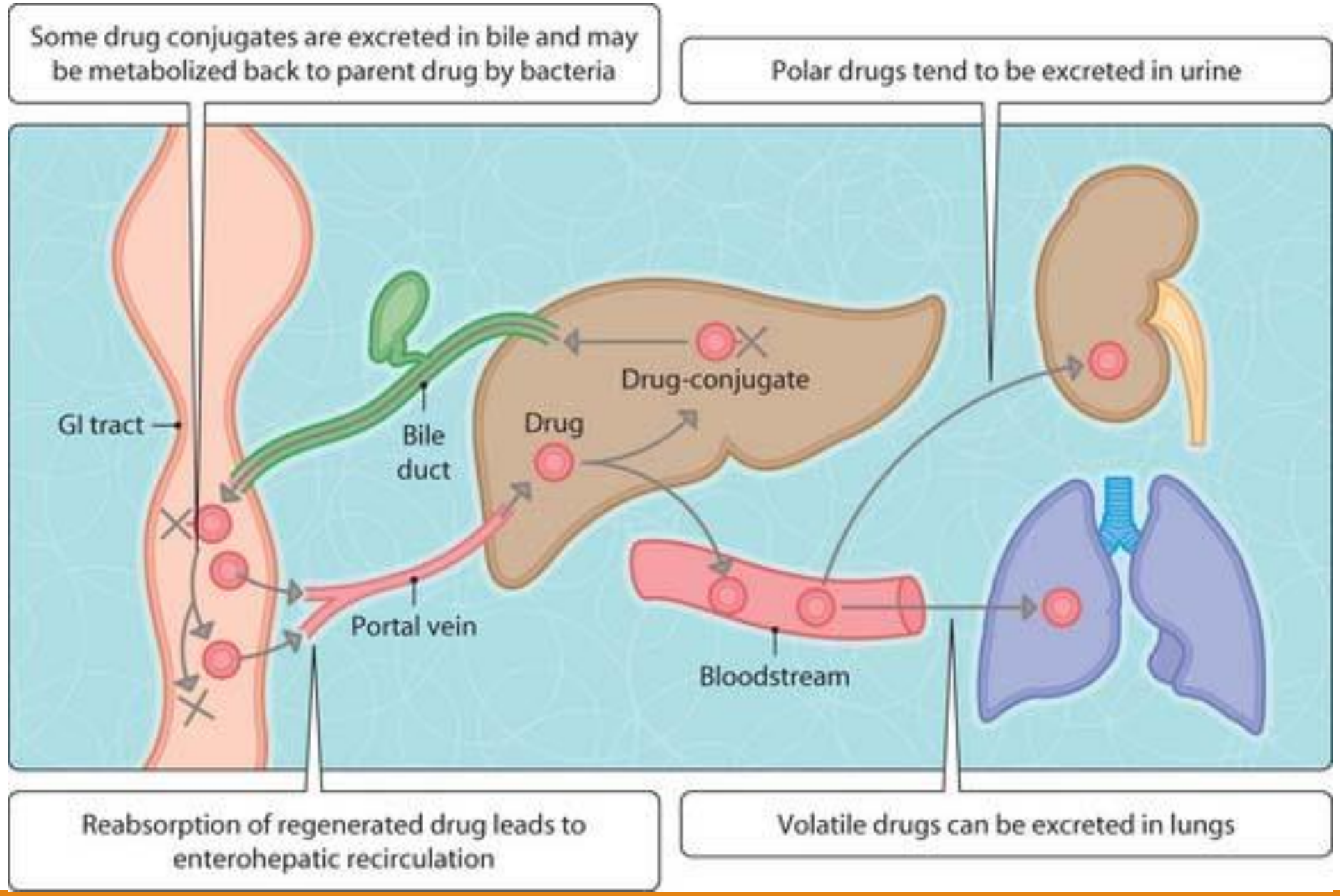
-Tubular Resorption (TR)

-Tubular Secretion (TS)

- **Net Renal Excretion= (GFR + TS)-TR**

Excretion by Other Routes

- Drug excretion may also occur via the intestines, bile, lungs, and breast milk, among others.
- Drugs that are not absorbed after oral administration or drugs that are secreted directly into the intestines or into bile are excreted in the feces.
- The lungs are primarily involved in the elimination of anesthetic gases (for example, *desflurane).*
- *Elimination* of drugs in breast milk may expose the breast-feeding infant to medications and/or metabolites being taken by the mother and is a potential source of undesirable side effects to the infant.
- Excretion of most drugs into sweat, saliva, tears, hair, and skin occurs only to a small extent. Total body clearance and drug half-life are important measures of drug clearance that are used to optimize drug therapy and minimize toxicity.


Some drug conjugates are excreted in bile and may be metabolized back to parent drug by bacteria
Polar drugs tend to be excreted in urine
GI tract
Bile duct
Drug-conjugate
Drug
Portal vein
Bloodstream
Reabsorption of regenerated drug leads to enterohepatic recirculation
Volatile drugs can be excreted in lungs

THANK YOU FOR YOUR ATTENTION