PHARMACOKINETICS

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Pharmacology

The science that deals with drugs.

Drugs

Substances used to prevent and treat diseases.

Drugs

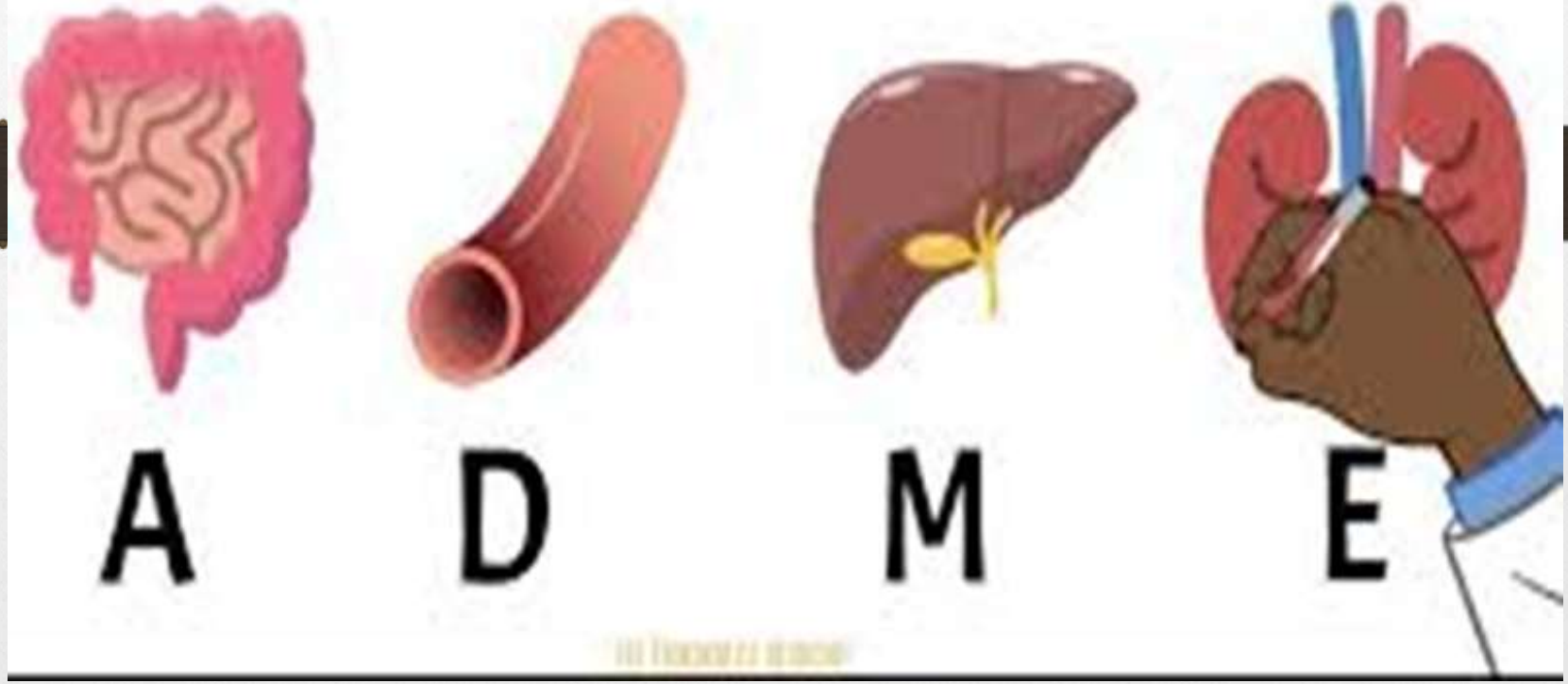
Pharmacokinetics

what the body does to the drug?

Pharmacodynamics

what the drug does in the body?

Pharmacokinetics



Pharmacokinetics

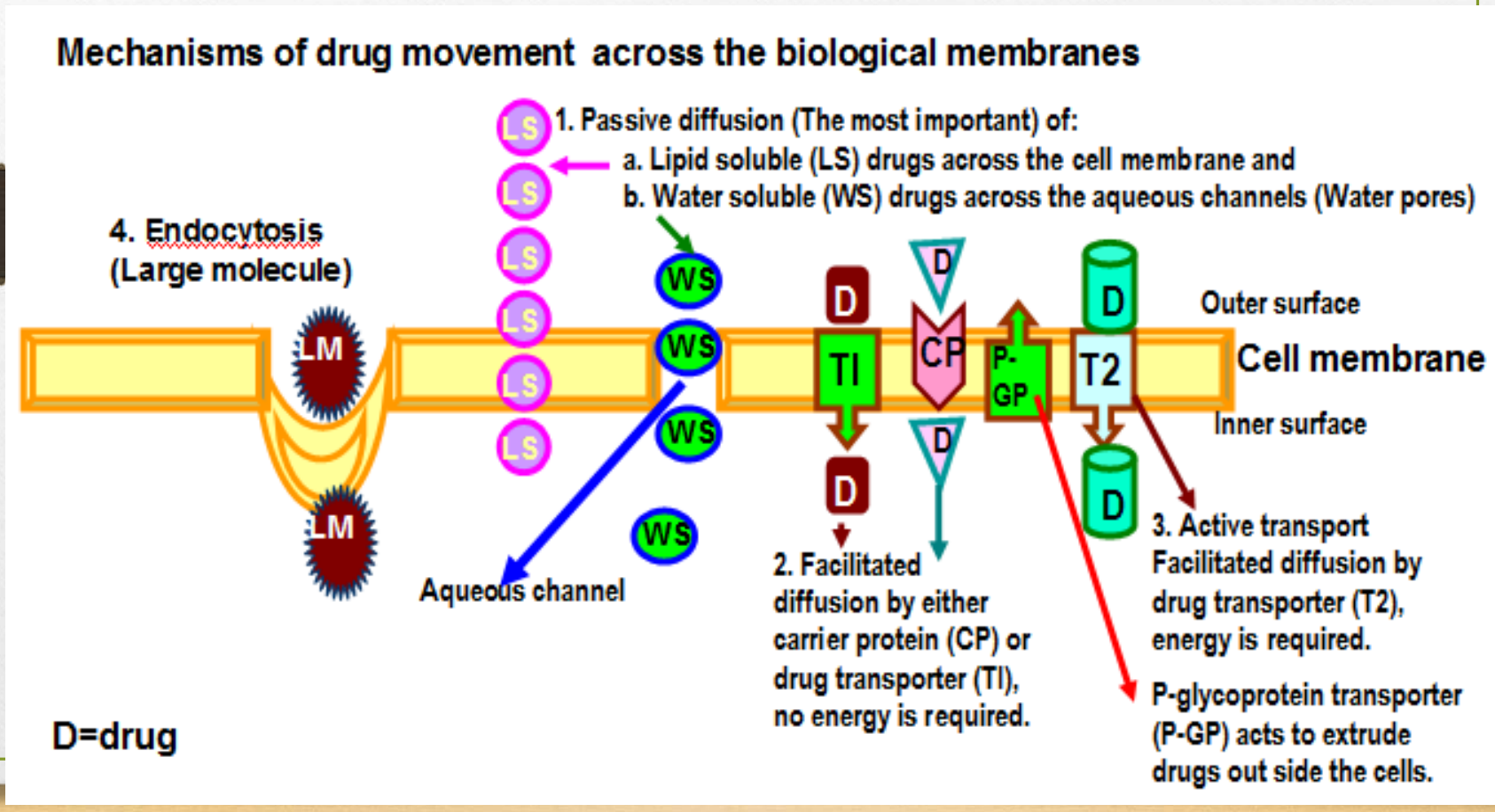
what the body does to the drug?

- Absorption
- Distribution
- Metabolism
- Excretion.

ABSORPTION

PASSAGE OF DRUG FROM SITE OF ADMINISTRATION TO SYSTEMIC CIRCULATION.

Mechanisms of drug absorption (how drugs cross biological membranes)



1. Passive diffusion:

- Rapid movement of lipid soluble drugs across the cell membrane.
- Movement of the water soluble drugs across the aqueous channels(water pores).
- No energy needed and with concentration gradient.

2. Facilitated diffusion

- The drugs are carried into inside the cell by **carrier** or **transporter**.
- **No** energy is required and according to the concentration gradient

3. Active transport

- The drug movement may be **against** the concentration gradient by drug carrier or transporter.
- Energy is required

4. Endocytosis

- Drugs of high molecular weight, the drug binds to the cell membrane, dips in and enveloped by the cell membrane.

Factors affecting absorption:

- Route of Administration
- Absorbing surface
- Co Administration of food or drugs
- Systemic circulation
- Specific factors

- 1-Water & lipid solubility
- 2- Pharmaceutical preparation
- 3- Ionization of the drugs

A. Factors related to the patient

Route of Administration

I.V. and inhalation > I.M. > S.C. > Oral >Topical

Absorbing surface

- **Vascularity:** (Alveoli > S.C. tissue).
- **Surface area:** (Alveoli > Intestine > Stomach).
- **Pathological conditions**: Diarrhea decrease oral absorption

Systemic *circulation*

- **Shock** decrease absorption; oral and subcutaneous routes are not suitable.

Specific factors

Intrinsic factor is essential for vitamin B12 absorption.

Co Administration of other drugs& food

- **S.C. adrenaline (added to local anesthetics) → V.C. absorption of local anesthetics → longer duration of action of local anesthetics.**
- **Ca+2 (e.g. in milk) ▼ oral absorption of tetracyclines (antibiotics).**

B. Factors related to the drug

1- Water and lipid solubility

- **Completely water-insoluble compounds are** not absorbed (e.g. barium chloride).
- **increase lipid solubility** lead to increase absorption (lipid/water partition coefficient).

2- Pharmaceutical preparation

- **Dosage form**: Solution > Suspension > tablet.
- **Shape, size of particles and rate** of dissolution of tablets.
- **Excepient (filler)** containing Ca+2 decreases oral absorption of tetracyclines.

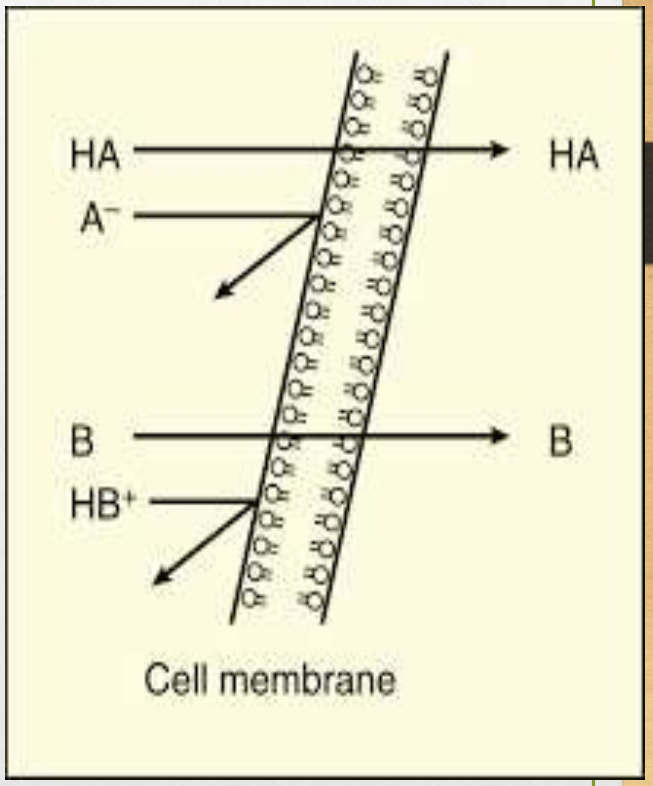
3- Ionization of the drug:

- Ionization decreases lipid solubility and absorption of drugs.
- Non-ionized (uncharged) → better absorption.
- Depends on pKa of the drug and pH of the medium .
- Quaternary ammonium compounds → ionized poor absorption.
- Streptomycin has high pKa → always ionized not absorbed orally.

The effect of pH on drug absorption

When drugs bind hydrogen,

- weak acids become unionized (A-+HA)
- while weak base are ionized (B+BH+)



At low pH weak acids become unionized while the weak bases become ionized.

At high pH weak base drugs become unionized while weak acids become ionized.

- Accordingly, weak acid are more absorbed in acidic media while weak bases are more absorbed in alkaline media.

- **The pH at which the concentrations of the ionized and unionized forms of the drug are equal is termed pKa.**
- **Each drug has its own pKa.**

Clinical importance of pKa

1- GIT: Aspirin (acidic drug) has low pKa.

Drug molecules become unionized in the empty stomach (low pH) and can enter gastric mucosal cells. In gastric mucosal cells (high pH) aspirin becomes ionized and trapped in gastric mucosal cell "peptic ulceration"

2- Kidney: In drug poisoning,

renal elimination could be enhanced by changing urinary pH to increase ionization of drug and inhibit tubular reabsorption of the drug.

• Alkalinization of urine by sodium bicarbonate (to increase urine pH above drug pKa) is useful in acidic drug poisoning e.g. Aspirin and phenobarbital.

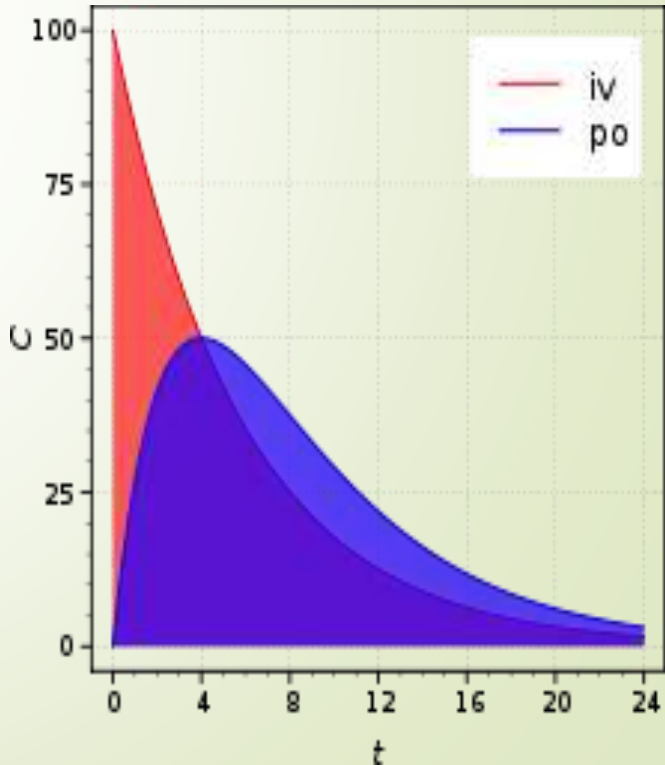
• Acidification of urine by ascorbic acid (to decrease urine pH below drug pKa) is used in basic drug poisoning e.g. amphetamine.

BIOAVAILABILITY

- It is the percentage of drug that reaches the systemic circulation and becomes available for biological effect.

Bioavailability =

$$\frac{\text{Area under the curve (AUC) after oral route}}{\text{Area under the curve (AUC) after L.V. route}} \times 100$$



FACTORS AFFECTING BIOAVAILABILITY:

1-The extent of drug absorption.

2- 1st pass effect (1st pass metabolism):

It is the metabolism of some drugs in a single passage through gut wall, liver or lungs before reaching systemic circulation.

A. Hepatic 1st pass effect:

- Nitroglycerin and propranolol pass from GIT to liver where they are extensively metabolized in their 1st pass through liver before reaching systemic circulation.

B. Intestinal 1st pass effect:

- Estrogens are extensively metabolized in their 1st pass through intestinal wall.

C. Pulmonary metabolism:

- After inhalation, nicotine is partially metabolized in the lung.


TO BE
CONTINUED