Pharmacokinetics 4

By

Dr. Lamiaa Meghawery

Associate professor of pharmacology
Faculty of Dentistry
Mutah university

Intended learning outcomes (ILOS):

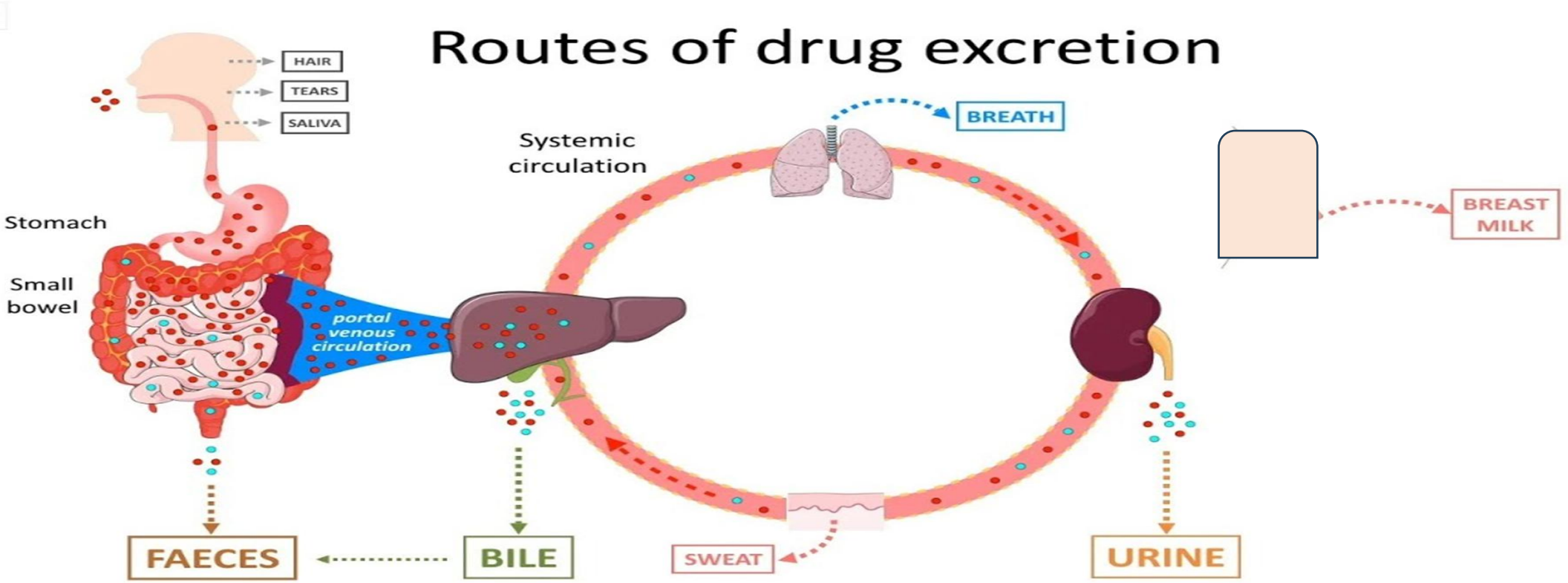
- **Recognize** basics of Excretion.
- **Discuss** factors affecting excretion processes.
- **Interpret** the fundamental principles of pharmacokinetics.
- Identify importance of t1/2.

EXCRETION

Removal of a drug from the body may occur via a few routes, the **most important** being through the **kidney** into the urine.

Other routes include:

GIT, skin glands, lung.

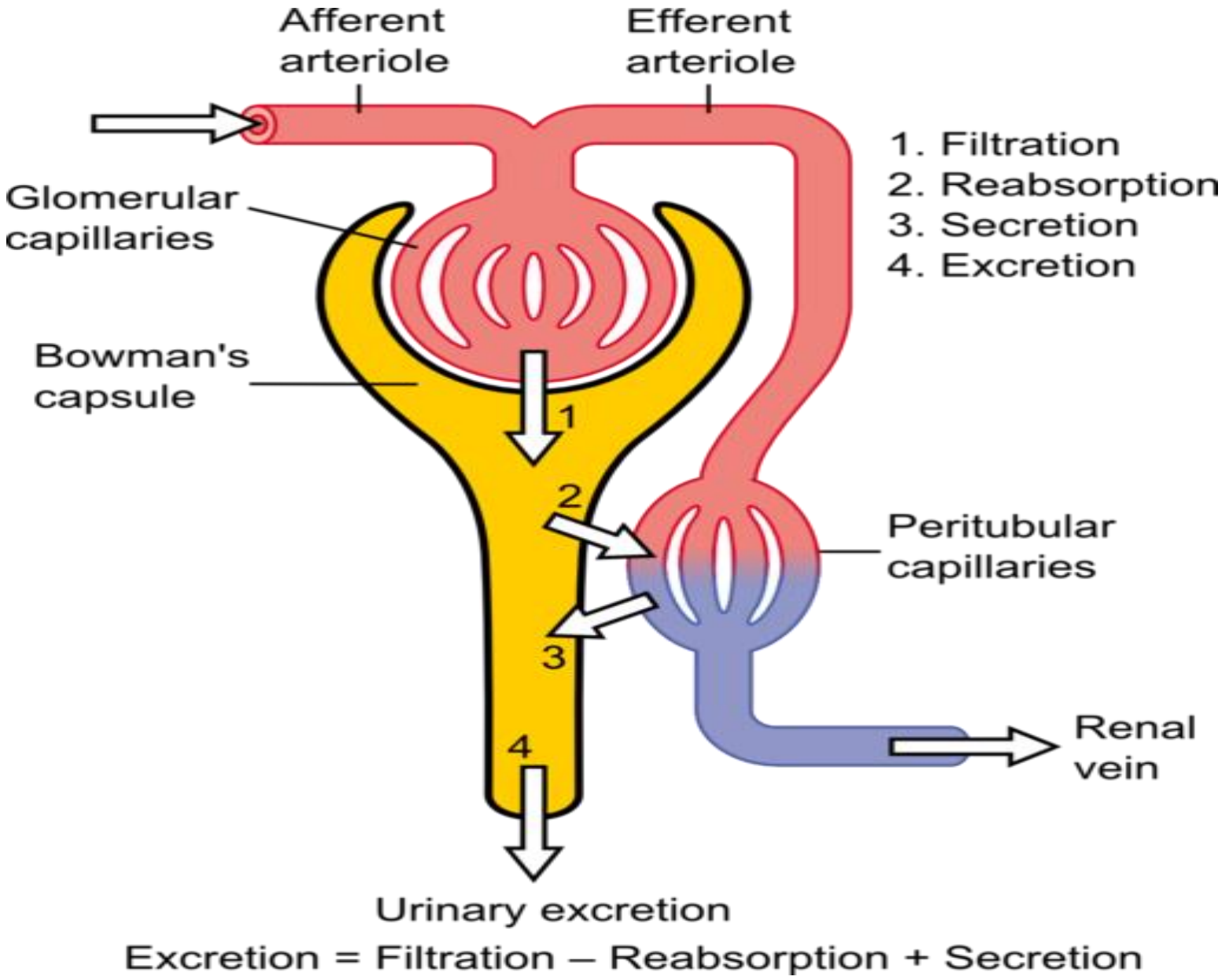


EXCRETION

Renal excretion:

Occurs through 3 different processes:

1. **Glomerular filtration.**
2. **Passive reabsorption.**
3. **Active secretion.**



EXCRETION

Renal excretion: Occurs through 3 different processes:

1. Glomerular filtration.

2. Active secretion.

3. Passive reabsorption.

1. Glomerular filtration:

The drug must be free (not bound to plasma proteins) and water soluble with M.W. < 500 e.g. Mannitol.

Glomerular filtrate =125 ml/min

EXCRETION

Renal excretion: Occurs through 3 different processes:

2. Active secretion:

Occurs in the proximal tubules.

-By active transport systems requiring a carrier:

-(Saturable & Site for competition & Drug Interaction):

- **Weak acid drugs e.g. Penicillin**
- **Weak base drugs e.g. Digoxin**

Probenecid competes with penicillin leading to decreasing tubular secretion of penicillin.

EXCRETION

Renal excretion: Occurs through 3 different processes:

3. Passive reabsorption:

- **Concentration of the drug ↑ as it moves towards the distal tubules, if lipid soluble and unionized reabsorption occurs.**

****The **clearance** of some drugs depends mainly on renal excretion (Little or no metabolism) e.g. Atenolol → **Caution in Renal patients.**

EXCRETION

Changes of pH of the urine affect excretion of drugs:

- **Alkalization of urine by (Na or K Acetate, Bicarbonate or Citrate)→↑ excretion of acid drugs e.g. aspirin.**

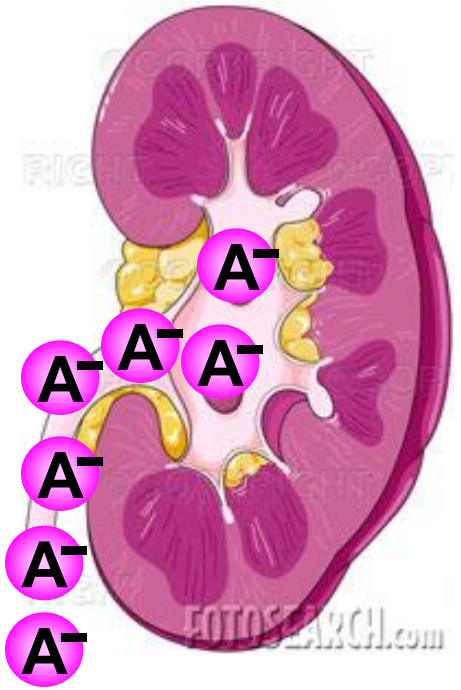
- **Acidification of urine by (NH4Cl or Ascorbic acid "Vit C") → ↑ excretion of base drug as ephedrine.**

This process is called "ion trapping"

Alkalinization of urine

$NaHCO_3$

Excretion



weak **Acidic** drugs

Ionized

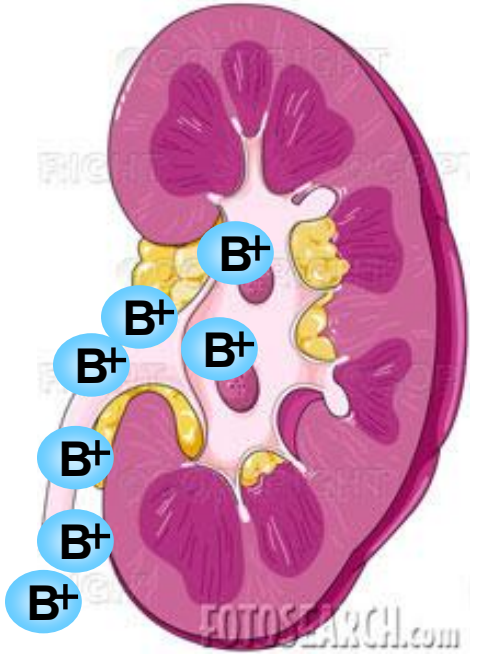
In **Alkaline** medium

e.g. aspirin

Acidification of urine

↑↑ Excretion

- vitamin C
- NH_4Cl



weak **base** drugs

↑↑ **Ionized**

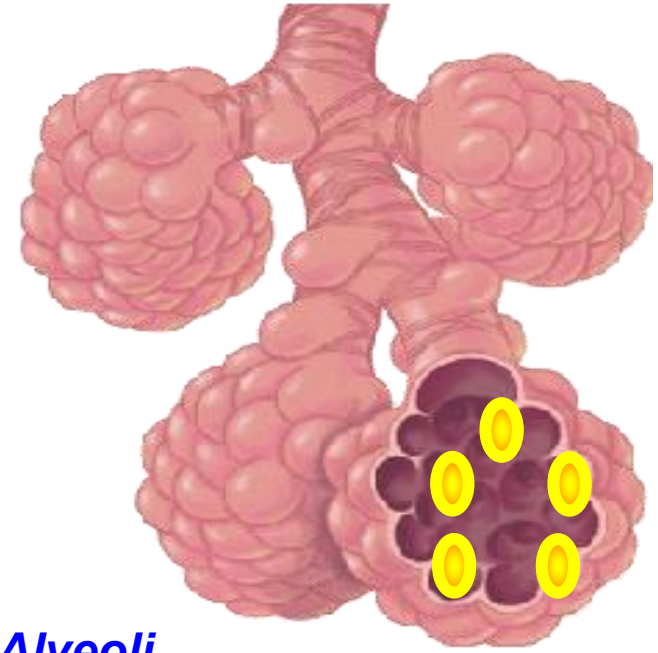
In **Acidic** medium

e.g. Ephedrine

Other routes of excretion:

* Lung:

Gaseous and volatile drugs e.g. halothane .



Alveoli

* Skin glands:

- Sweat: e.g. rifampicin → red sweat.

-Mammary g. (milk)

* Most of drugs administered to lactating women are detectable in breast milk.

*pH of milk (7) is more acidic than plasma (7.4) → Ion trapping for basic drugs.

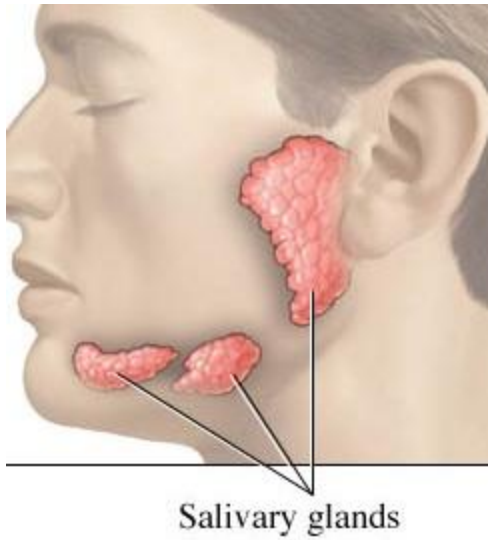
*Milk is rich in fat → Retention of lipid soluble drugs.

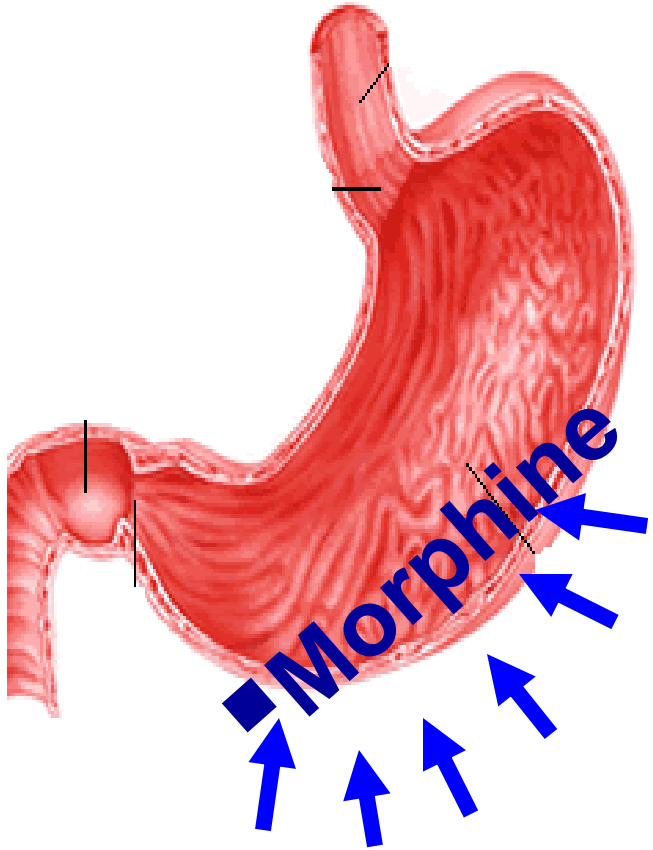
*May affect suckling baby e.g. purgatives

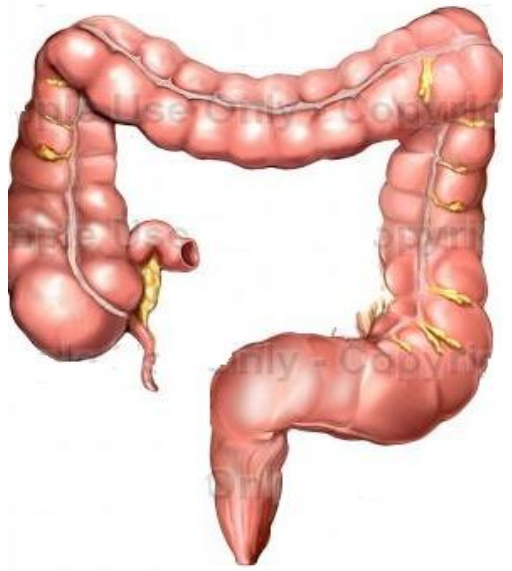
*G.I.T. (Alimentary Tract) :

- Saliva(pH = 8): e.g iodide and morphine
- Stomach: e.g. morphine.
- Colon: either via the bile or unabsorbed oral drugs.

- Iodides
- Rifampicin

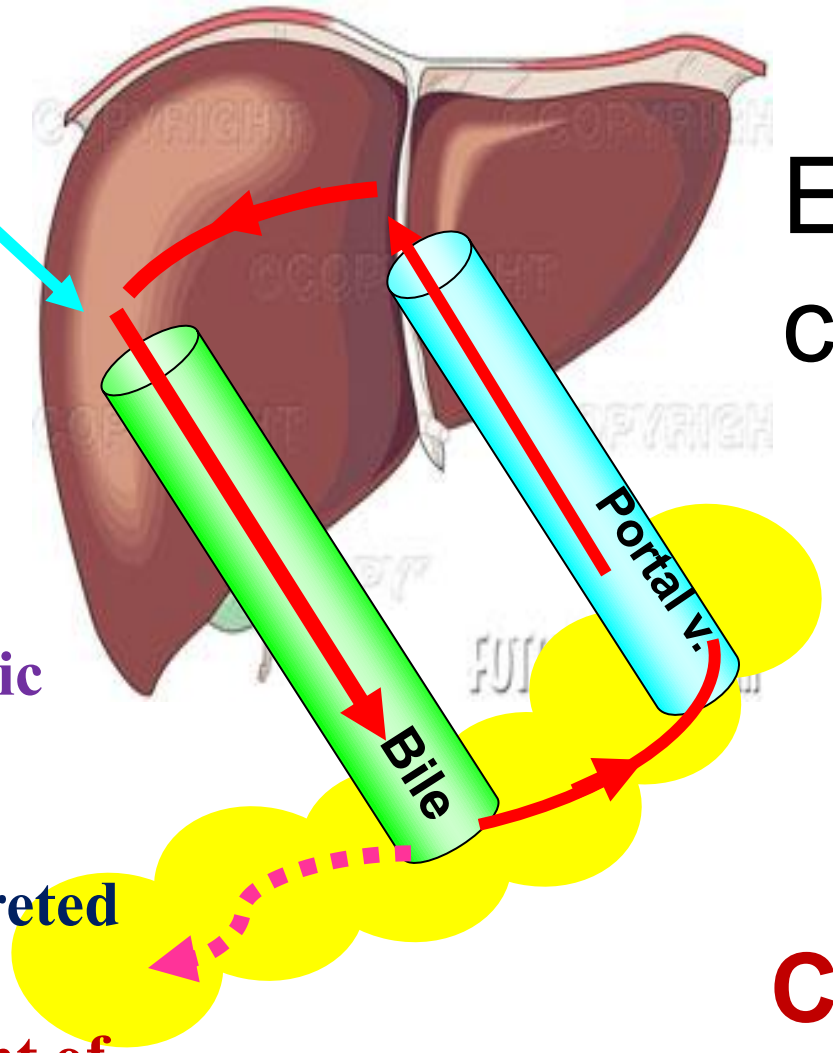






✓ Streptomycin

Rifampicin



Enterohepatic circulation

***Bile:** Intestine → Either:

a- Excreted in large intestine

b- Reabsorbed → Entero-Hepatic Circulation e.g., **Rifampicin.**

c- Some anti-microbials are excreted in bile in an active form e.g. **Ampicillin** → Useful in treatment of Cholecystitis & Typhoid carrier.

Colchicine

Clearance

**Includes the processes that terminate drug action e.g. metabolic inactivation renal excretion.

- **It is expressed as the volume of body fluid from which drug is removed in unit time**

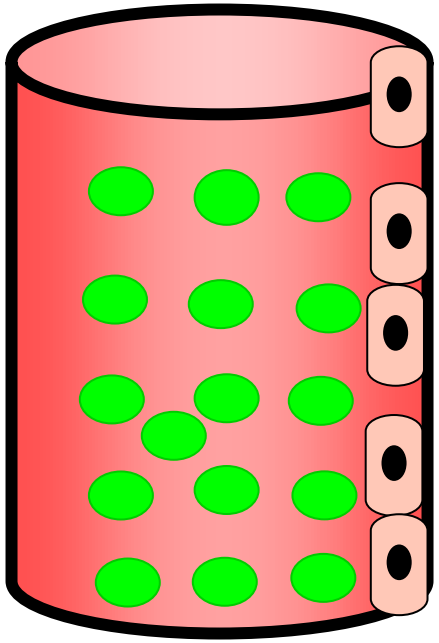
$$\text{Clearance } C = Kel \times Vd = \frac{0.693}{t\ 1/2} \times Vd$$

- **Kel** is the rate constant of elimination per hour and has a formula of **0.693 /t½**
- **Vd = $A_{(mg)}/C_{(mg/ml)}$**
- **t1/2 = Plasma half-life of the drug.**

Plasma half life (t ½)

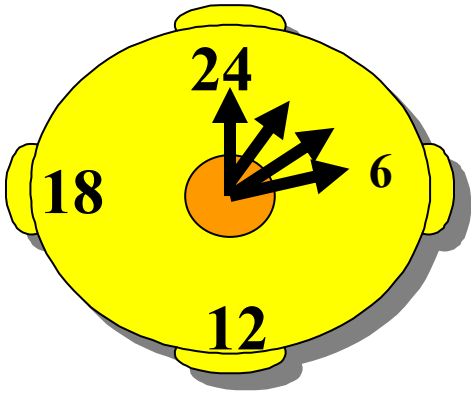
- **Time** required by the body to **decrease plasma concentration of a drug by 50%**

- It depends upon **kinetics of drug elimination (clearance)** e.g. **metabolism and excretion and volume of distribution (Vd).**



Drug concentration in Plasma

Decline by one half

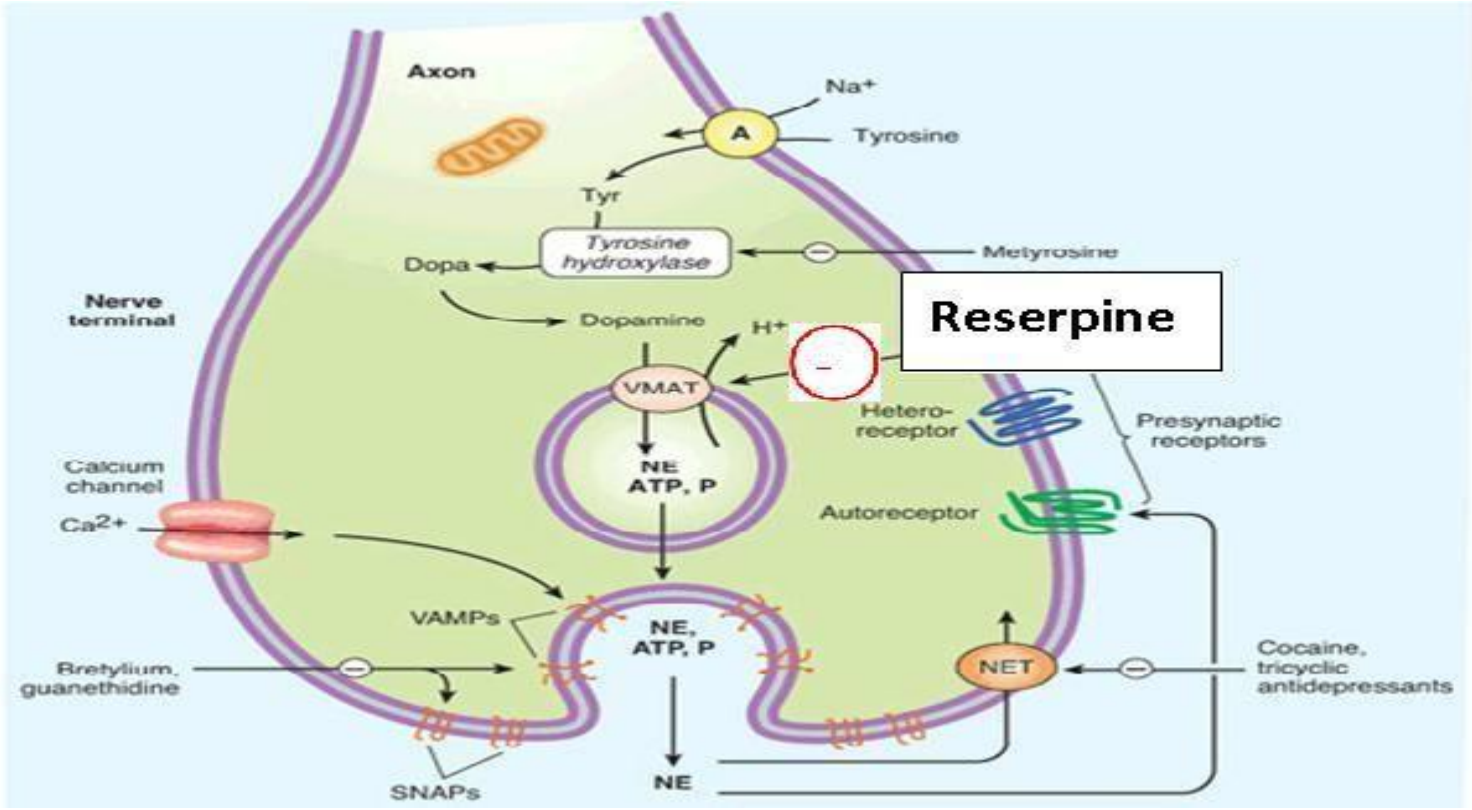


Time

Plasma half life (t ½)

❑ For some drugs, their **Biological t1/2> Plasma t1/2**

e.g. **Reserpine** :Irreversible ↓ of vesicular enzymes **(Hit & Run).**Its effect does not depend on its presence in plasma & ends by resynthesis of new vesicles.



Plasma half life (t ½)

- t ½ is useful to determine **the frequency & route of drug administration.**

Questions

1.Explain :
All cases of Morphine toxicity can be treated by stomach wash.

2.What is t1/2 and its significance?

Thank You