
بسم الله الرحمن الرحيم
وَأَمَّا مَا يَنفَعُ ٱلنَّاسَ فَيَمْكُثُ فِى ٱلْأَرْضِ
but as for that which benefits the people, it remains on the earth.
Quran 13:17 (Surah ar-Ra'd)

MOTTO AND VISION

- To impart evidence-based research-oriented medical education
- To provide the best possible patient care
- To inculcate the values of mutual respect and ethical practice of medicine

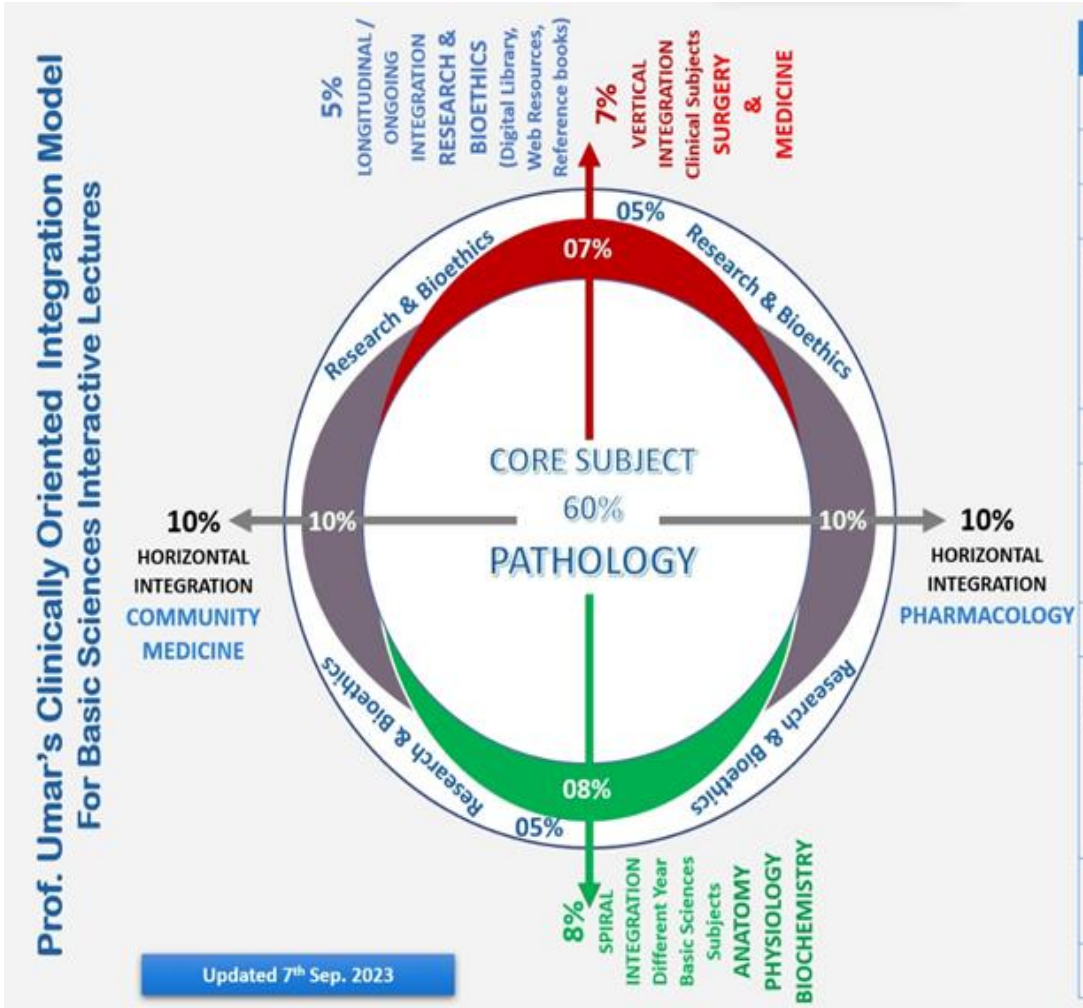
EXCRETION OF DRUGS
&
DRUG CLEARANCE

3rd Year MBBS

LGIS

Sources:

1. **Bertram G. Katzung Basic & Clinical Pharmacology 16th Edition**
2. **Goodman and Gilman's The Pharmacological Basis of Therapeutics 13th edition.**



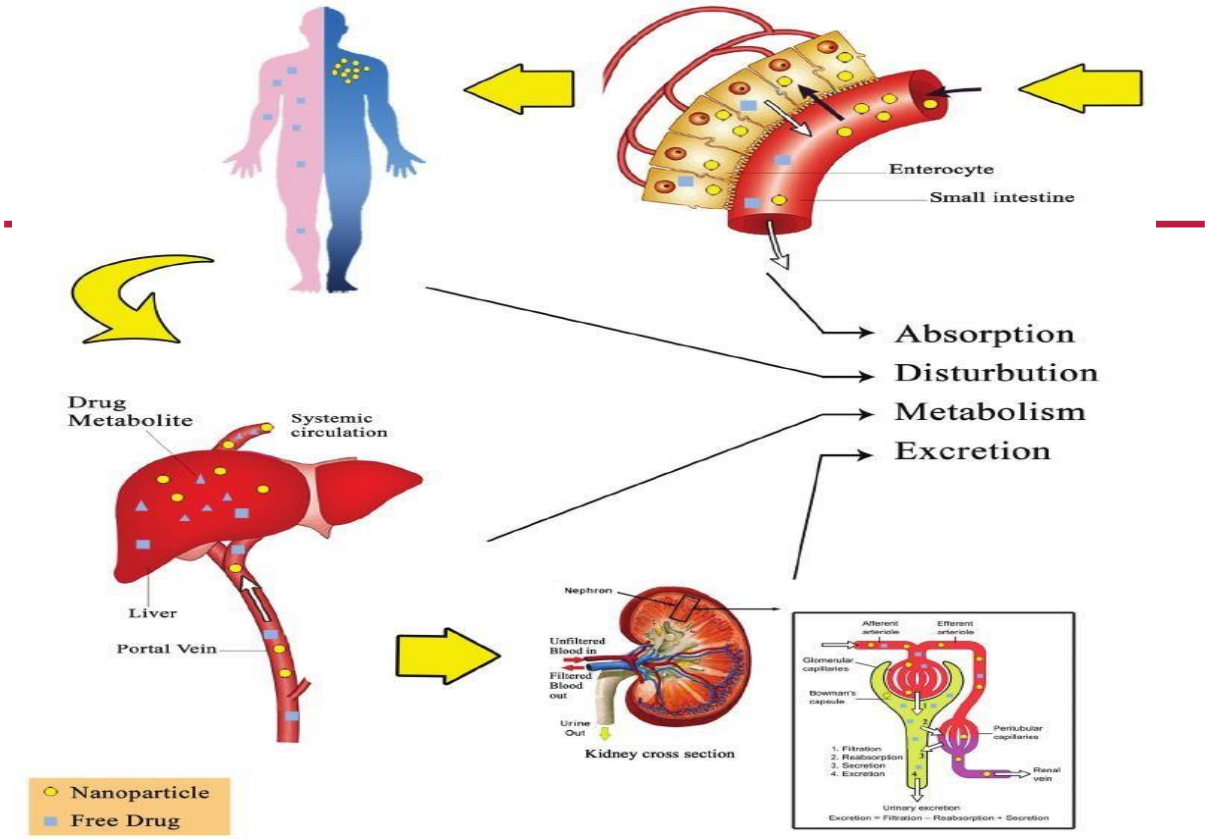
Model 3rd Year Pathology LGIS (≈30 slides)	
Core Subject – 60% (≈ 18-20 slides)	
Pathology (≈ 18-20 slides)	
Horizontal Integration – 20% (≈ 5-6 slides)	
Same Year Subjects	• Pharmacology (10%) (≈ 2-3 slides) • Community Medicine (10%) (≈ 2-3 slides)
Vertical Integration – 07% (≈ 2-3 slides)	
Clinical Subjects	• Medicine (3-5%) (≈ 1-2 slides) • Surgery (3-5%) (≈ 1-2 slides)
Spiral Integration – 08% (≈ 2-3 slides)	
Different Year Basic Sciences Subjects	• Anatomy (1-3%) (≈ 1-2 slides) • Physiology (1-3%) (≈ 1-2 slides) • Biochemistry (1-3%) (≈ 1-2 slides)
Longitudinal / Ongoing Integration – 05% (≈ 1-2 slides)	
Research & Bioethics (≈ 1-2 slides)	

LEARNING OBJECTIVES

1. Drug elimination
2. Sites of excretion
3. Various processes involved in excretion
4. Excretion of acidic and basic drugs
5. Concept of clearance
6. Significance of clearance

PHARMACOKINETIC PROCESSES

1. Absorption
2. Distribution
3. Metabolism
4. Excretion



SITES OF EXCRETION

1. Kidneys
2. Bile & feces
3. Other routes:
    a) Lungs
    b) Saliva, sweat, tears
    c) Hair & Skin
    d) Breast milk

RENAL EXCRETION

1. KIDNEY
   a) Glomerular filtration
   b) Active tubular secretion
   c) Passive tubular reabsorption

RENAL EXCRETION

1.Glomerular Filtration

- Free drug
- Smaller molecular size
- Lipid solubility
- pH
- Plasma protein binding

GFR decreases in:

- In Cardiogenic Shock
- Heart Failure
- In Neonates
- In old age

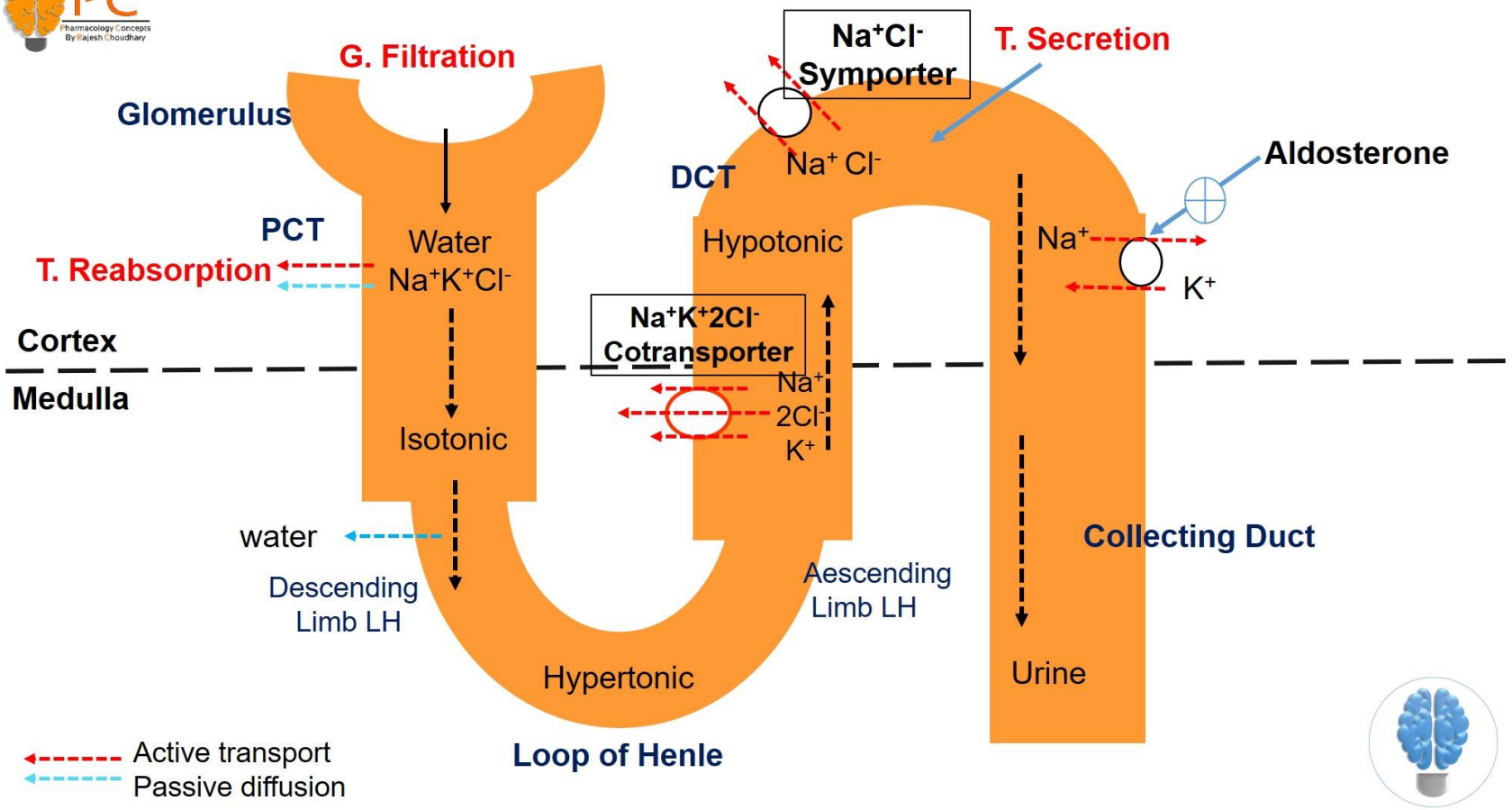
2. Active tubular Secretion

By two carrier systems

- For acids(Penicillin, Furosemide)
- For bases(Amiloride, Quinine)

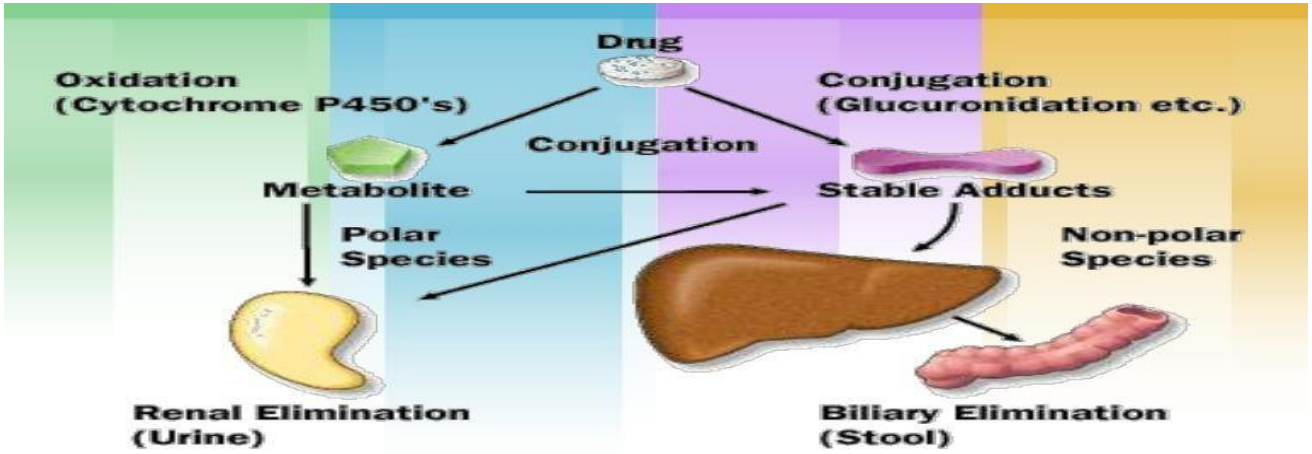
3. Passive tubular reabsorption

- Lipophilic
- Concentration gradient
- Unionized form(Ion trapping)


G. Filtration
Glomerulus
PCT
T. Reabsorption
Water
Na⁺K⁺Cl⁻
Isotonic
Cortex
Medulla
water
Descending
Limb LH
Hypertonic
Loop of Henle
Na⁺Cl⁻
Symporter
T. Secretion
DCT
Na⁺ Cl⁻
Hypotonic
Aldosterone
Na⁺
K⁺
Na⁺K⁺2Cl⁻
Cotransporter
Na⁺
2Cl⁻
K⁺
Aescending
Limb LH
Collecting Duct
Urine
Active transport
Passive diffusion

BILIARY EXCRETION

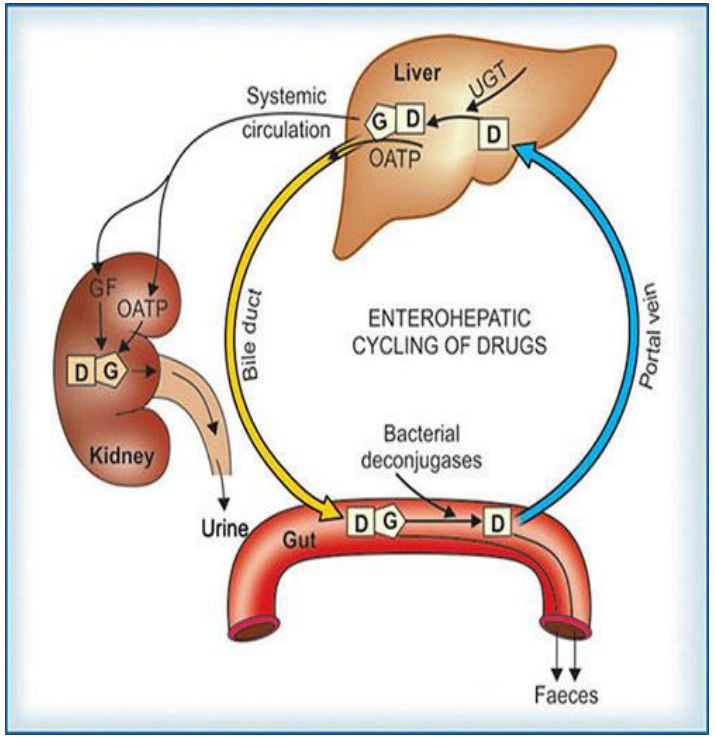
- Bile:
  - Carrier systems
  - Active transport(drugs/metabolites into the bile)



BILIARY EXCRETION

Entero hepatic circulation

- Prolongs the duration of action of drugs e.g. Ezetemibe, Oral contraceptives



FEACAL EXCRETION

Fecal Excretion Of Drugs:

The drugs excreted in feces are

1. Unabsorbed drugs taken orally i.e Neomycin
2. Remainder of drugs(partially absorbed drugs)
3. Drug metabolites in bile. i.e Erythromycin
4. Drugs excreted in the large intestine i.e Anthracene Purgatives, Heavy metals

EXCRETION THROUGH LUNGS

1. Main route for excretion of Volatile GA
2. Alcohol, Paraldehyde(partial excretion with odour)
3. Lipid soluble drug
4. PH dependent
5. Alveolar transfer of gas/vapour
6. Partial pressure in the blood

OTHER ROUTES OF EXCRETION

1. Saliva, Sweat & Tears
   a) Lithium, Iodides & metallic
   b) Rifampicin(orange color to sweat & tears)
   c) Drugs excreted in saliva i.e Lead ,Iodides
2. Skin & Hair:
   a) Forensic significance
   b) Arsenic & mercury
3. Breast milk :
   a) Acidic pH
   b) Non- Electrolytes(Ethanol, Urea)
   c) Beta Blocker(Atenolol)

CLEARANCE

- Definition:

  It is the theoretical volume of plasma from which the drug is completely removed in unit time

CLEARANCE

- Mathematical Expression

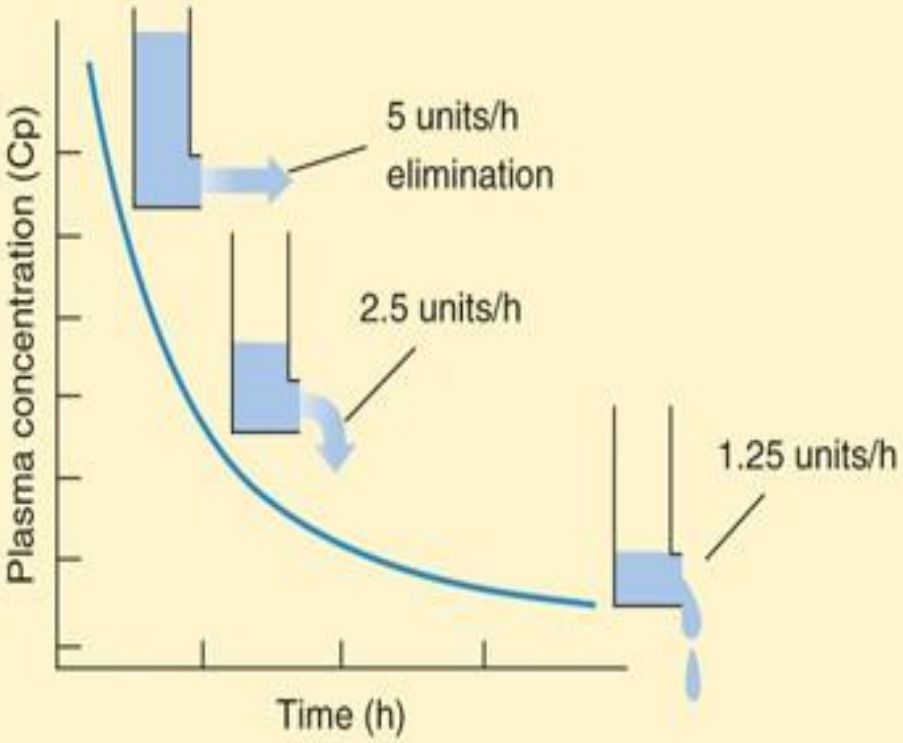
CL= Rate of elimination/ C

Rate of elimination= CL x C

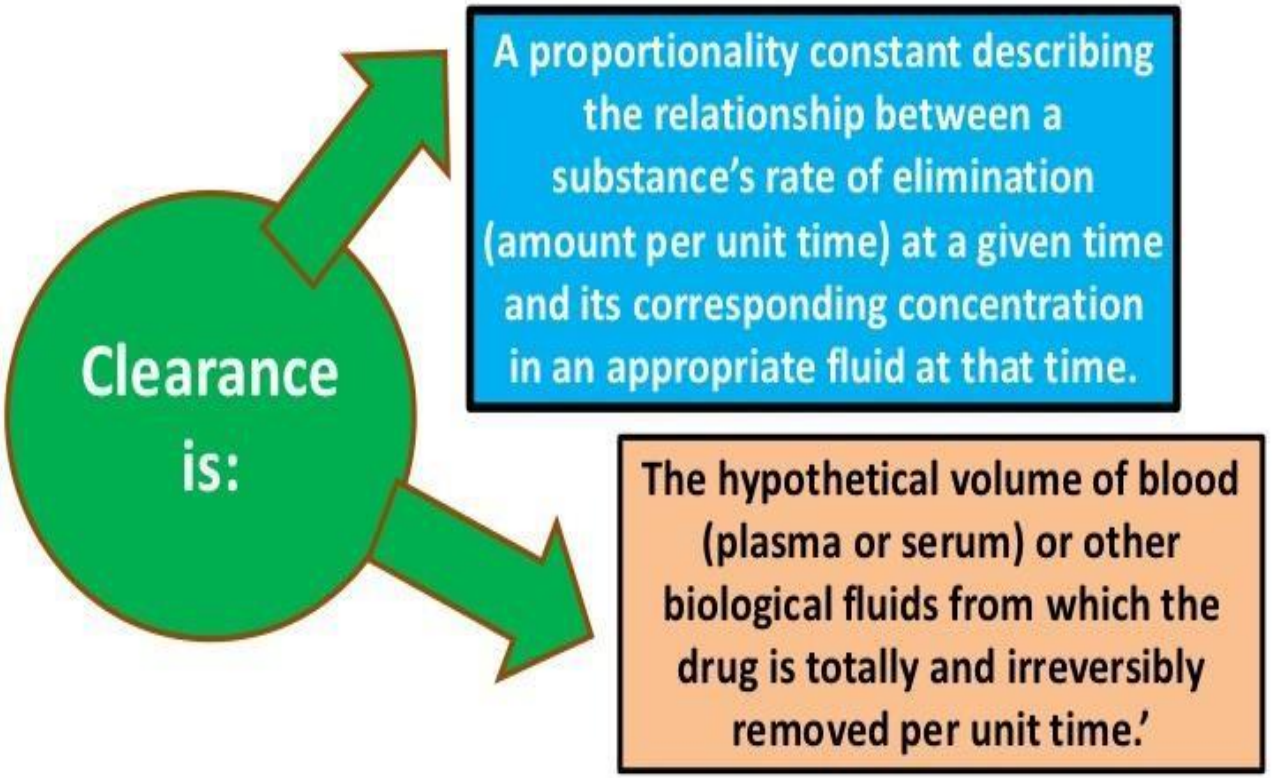
(Drug in blood, plasma or unbound in water)

$$\text{Clearance (CL)} = \frac{\text{Rate of elimination}}{\text{Plasma concentration (Cp)}}$$

Rate of elimination = CL x Cp



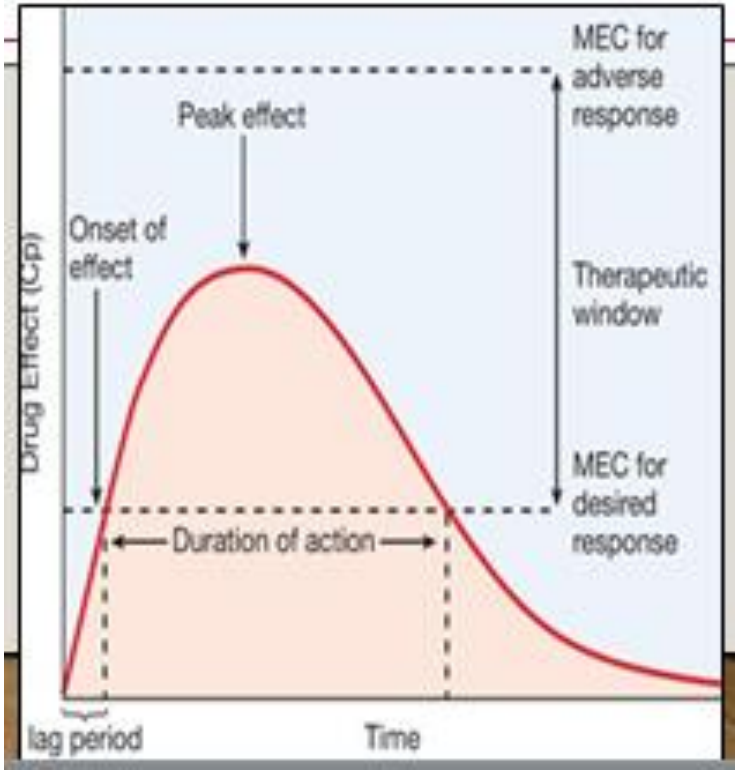
Clearance


Clearance is:
A proportionality constant describing the relationship between a substance's rate of elimination (amount per unit time) at a given time and its corresponding concentration in an appropriate fluid at that time.
The hypothetical volume of blood (plasma or serum) or other biological fluids from which the drug is totally and irreversibly removed per unit time.'

CLEARANCE WITH AUC

1. Single dose
2. Complete bioavailability
3. First-order kinetics of elimination

- Clearance=Dose/AUC



ORGANS INVOLVED IN CLEARANCE

1. Liver
2. Kidney
3. Others

$$CL_{systemic} = Cl_{kidney} + CL_{liver} + CL_{others}$$

FACTORS DETERMINING CLEARANCE

- Capacity-limited Elimination
  - Elimination vary depending on the Concentration achieved
  - High dose ⟶ saturation of Drug elimination pathways e.g Ethanol, Phenytoin
- Flow dependent Elimination
  - Elimination…..depend on the blood supply to the organ
  - High extraction drugs
    - Imipramine, Isoniazid,Lidocaine

Decrease in clearance ↓ **Toxicity**

SIGNIFICANCE OF CLEARANCE

- Dosing rate
  - Dosing rate = Clearance x TC

- Four parameters …..for dose adjustment
  1. Bioavailability
  2. Half life
  3. Volume of distribution
  4. Clearance

DOSING REGIMENS

1. Loading dose
2. Maintenance dose

RESEARCH/ ETHICS/ AI

1. [09:28, 22/02/2023] ASMA KHAN: Jusko, W.J. and Li, X., 2022. Assessment of the Kochak-Benet equation for hepatic clearance for the parallel-tube model: Relevance of classic clearance concepts in PK and PBPK. The AAPS journal, 24, pp.1-7.[09:29, 22/02/2023]
2. Todorović, Z., 2022. BIOETHICS AND PHARMACOLOGY: THE PRECLINICAL DRUG DEVELOPMENT. Animal Bioethics: Old Dilemmas and New Challenges, p.84.

FURTHER READING

EOLA

1. Drug clearance is calculated as the rate of drug elimination from the body divided by:

   a) Plasma drug concentration
   b) Rate of drug absorption
   c) Rate of drug metabolism
   d) Rate of drug excretion
   e) Rate of drug distribution

EOLA

2. Renal clearance of a drug is primarily determined by:

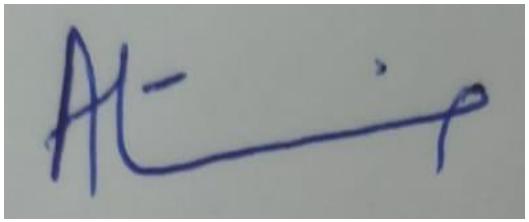
a) Liver enzymes

b) Cardiac output

c) Lung capacity

d) Blood pressure

e) Glomerular filtration rate (GFR)

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