
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

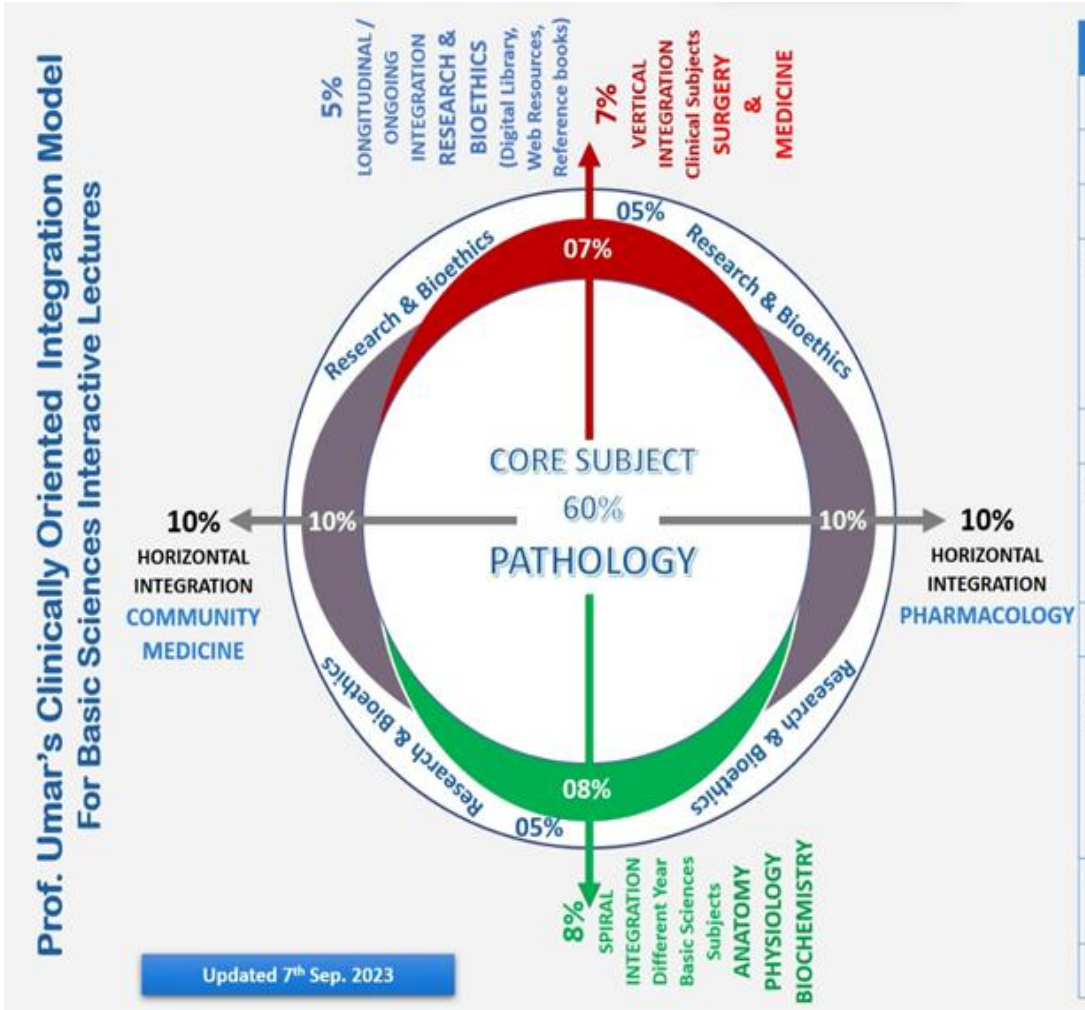
EXCRETION OF DRUGS
&
DRUG CLEARANCE

3rd Year MBBS

LGIS

Sources:

1. **Bertram G. Katzung Basic & Clinical Pharmacology 15th 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. Define excretion of drugs
2. Identify Sites of drug excretion
3. Various processes involved in excretion
4. Concept of clearance of a drug and its mathematical representation.
5. Define extraction ratio
6. Factors effecting Cl.
7. Significance of clearance

SDL Assessment program

MCQs-1 Which of the following Is not a major process involved in renal drug elimination?

a. Glomerular filtration
b. Tubular secretion
c. Tubular reabsorption
d. glucuronidation

MCQs-2 Lipophilic drugs are primarily excreted through

a. Liver
b. Bile
c. Sweat
d. Lungs

MCQ-3 Which type of drugs are mostly reabsorbed in renal tubules

a. Ionized drugs
b. Polar drugs
c. Lipophilic drugs
d. Hydrophilic drugs

SDL Assessment program

MCQ-4 Basic drugs are more readily excreted in

a. Acidic medium
b. Basic medium
c. Neutral medium
d. Plasma

MCQ-5 Which of the following drugs readily excreted by the lungs

a. Penicillin
b. Alcohols
c. Aspirin
d. morphine

MCQ-6 In patients with kidney disease, drug excretion is

a. Decreased
b. Increased
c. Unaffected
d. random

SDL Assessment program

MCQ-7 Which factors effect the renal drug excretion?

a. Protein binding of a drug
b. Renal blood flow
c. Urine PH
d. All of the above

MCQ-8 Drug clearance refers to?

a. The rate at which a drug is metabolized
b. The volume of plasma cleared of a drug per unit of time
c. The amount of drug excreted per minute
d. The bioavailability of a drug.

MCQ-9 A drug that is completely filtered by the kidneys without reabsorption or secretion will have a clearance equal to:

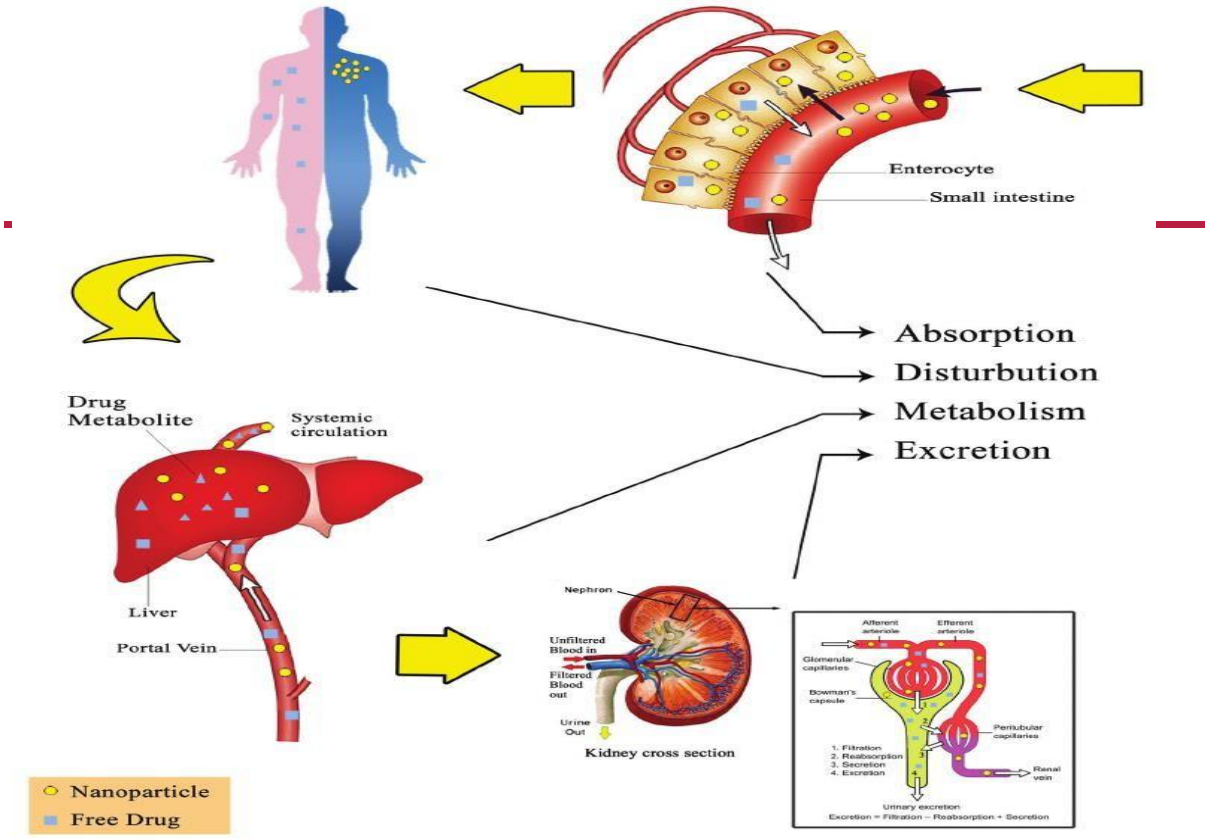
a. GFR
b. RPF
c. Cardiac output
d. Hepatic clearance

MCQ-10 the renal clearance of a drug that is actively secreted will be:

a. Less than GFR
b. Equal to GFR
c. Greater than GFR
d. Independent of renal function.

PHARMACOKINETIC PROCESSES

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



Define excretion

- EXCRETION IS THE PROCESS BY WHICH DRUGS AND THEIR METABOLITES ARE ELIMINATED FROM THE BODY.

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

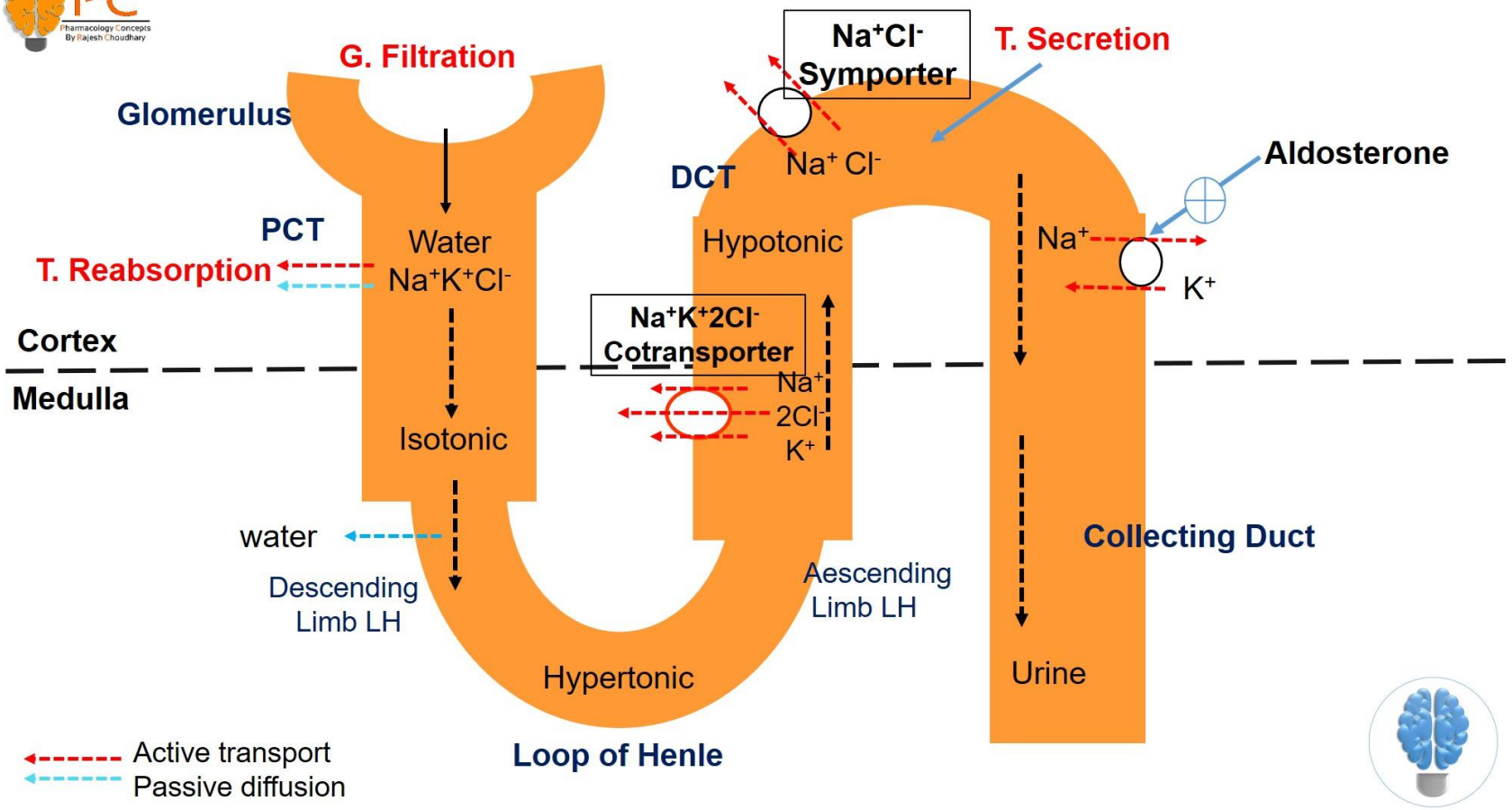
2. Active tubular Secretion

By two carrier systems

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

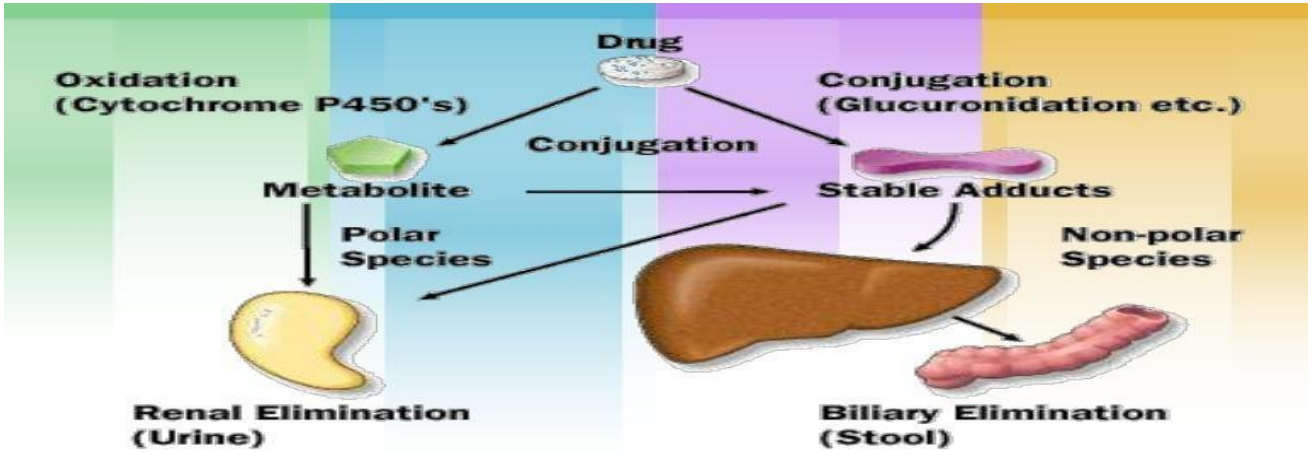
3. Passive tubular reabsorption

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


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

BILIARY EXCRETION

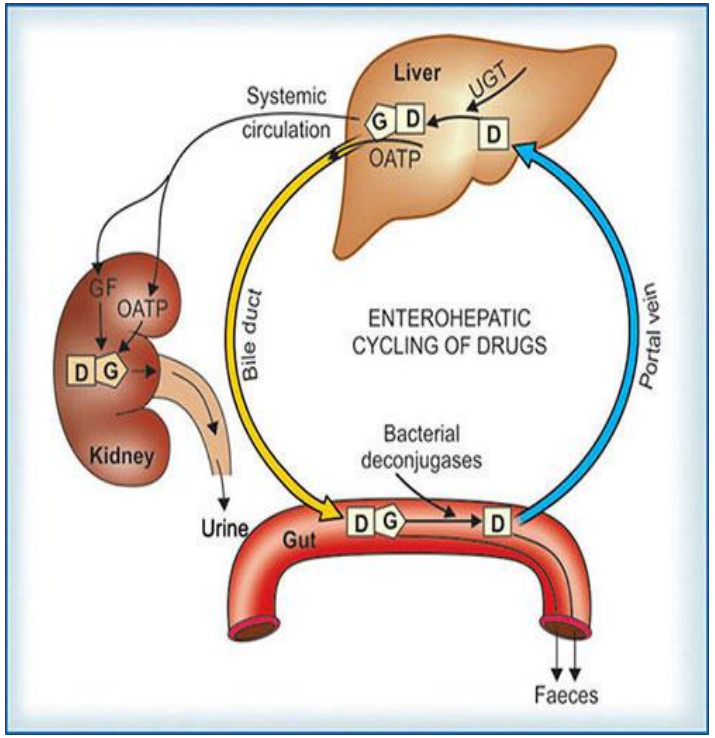
- Bile:
  - Carrier systems
  - Active transport(drugs/metabolites into the bile)



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

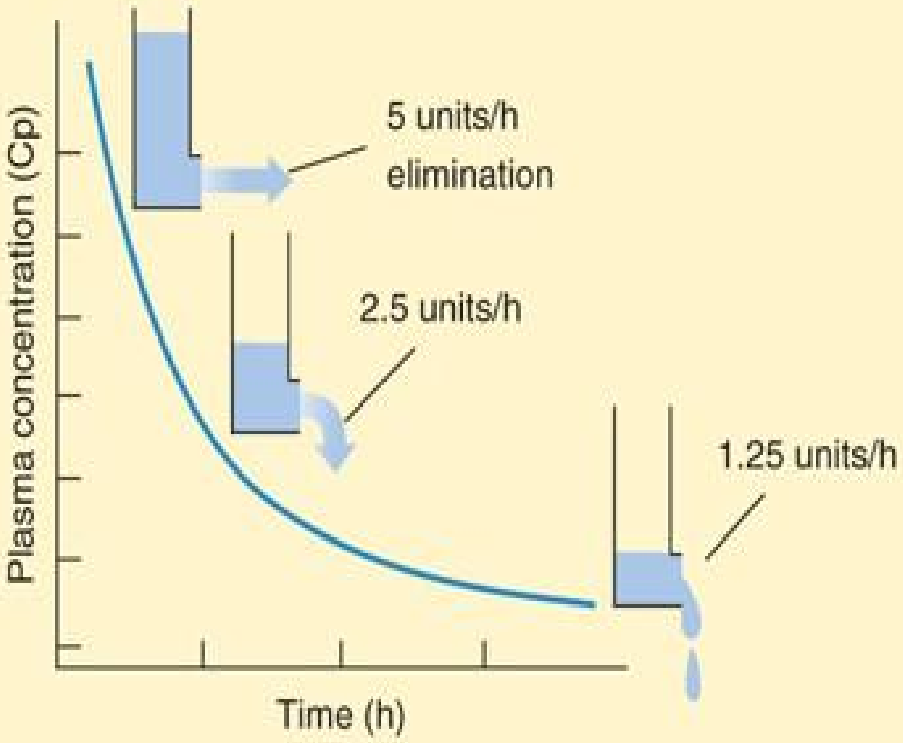
CL= Rate of elimination/ C

Rate of elimination= CL x C

(Drug in blood, plasma or unbound in water)

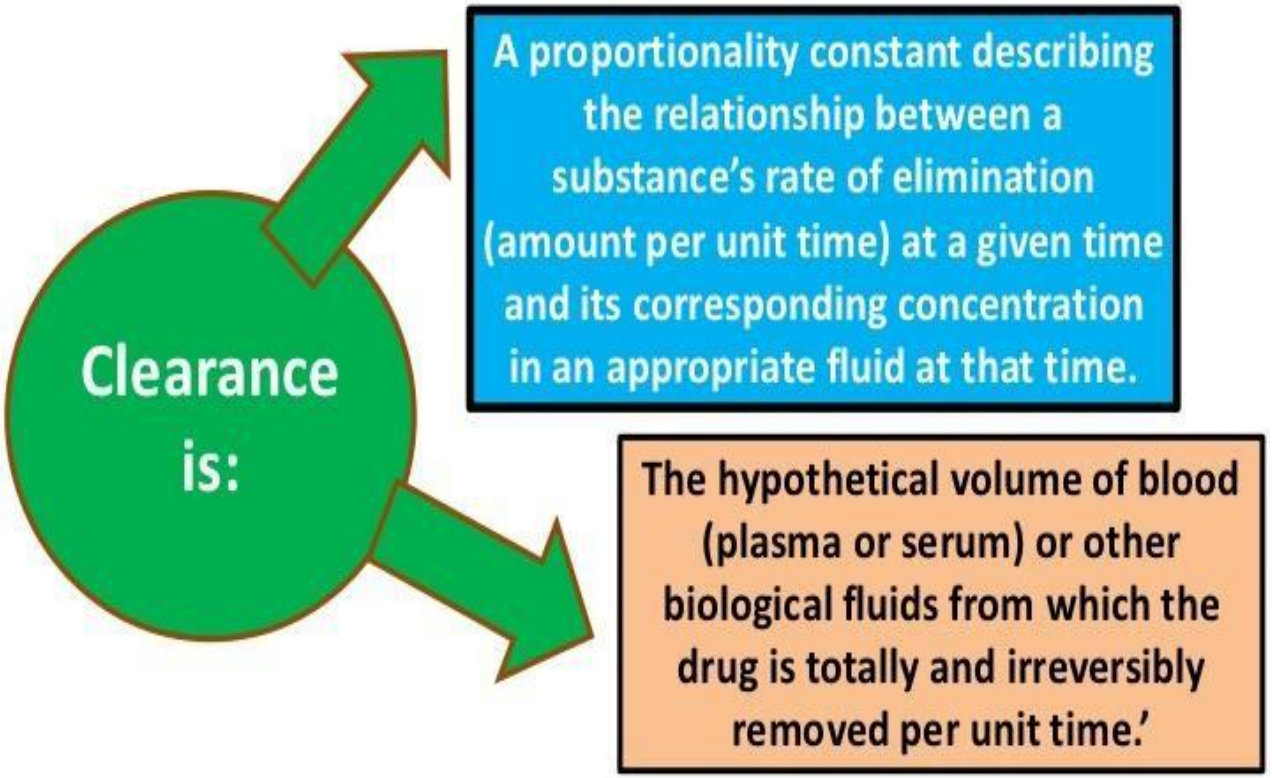
$$\text{Clearance (CL)} = \frac{\text{Rate of elimination}}{\text{Plasma concentration (Cp)}}$$

Rate of elimination = CL x Cp



CORE SUBJECT

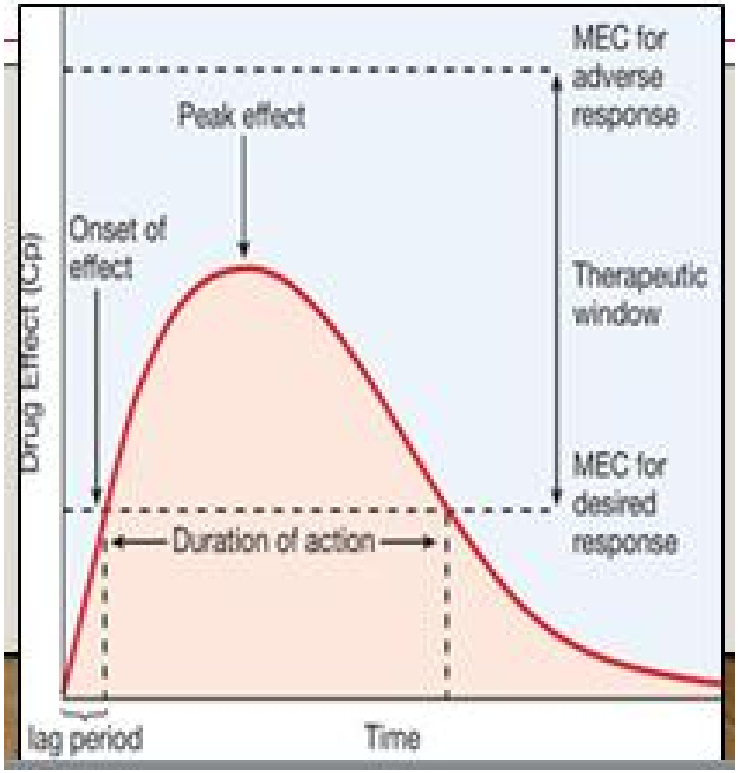
Clearance


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

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.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