HALF LIFE

Sources:

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

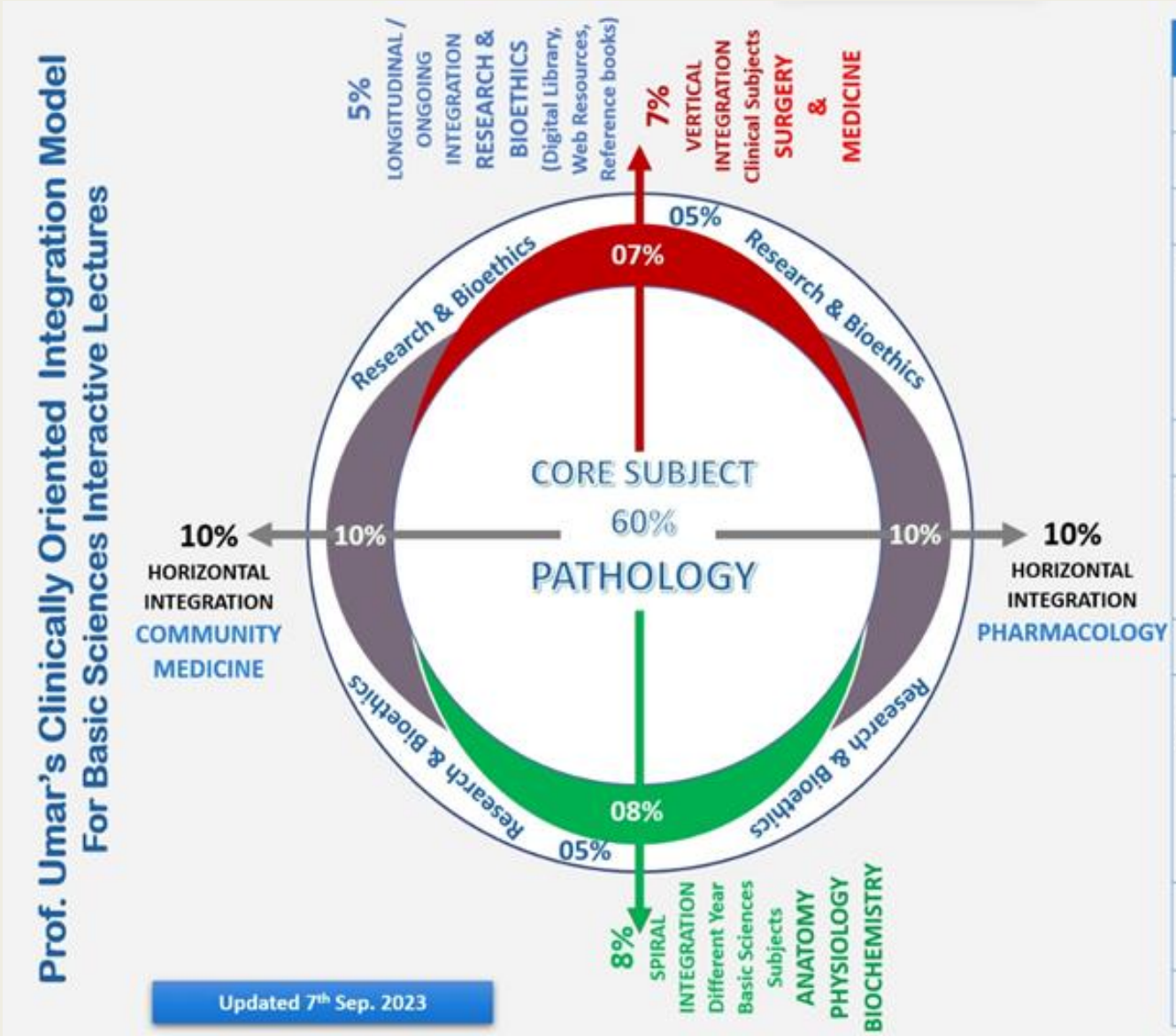
Motto And Vision

To impart evidence based research oriented medical education

To provide best possible patient care

To inculcate the values of mutual respect and ethical practice of medicine

Prof. Umar's Clinically Oriented Integration Model For Basic Sciences Interactive Lectures



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

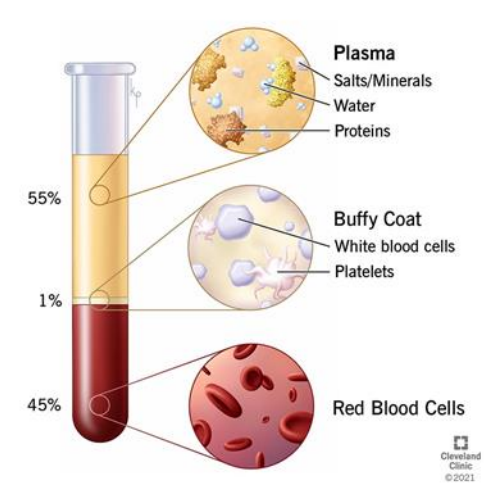
- Definition
- Mathematical expression & Types
- Steady state Concentration
- Accumulation factor
- Factors affecting Plasma half life($t_{1/2}$)
- Clinical significance of Plasma half life ($t_{1/2}$)

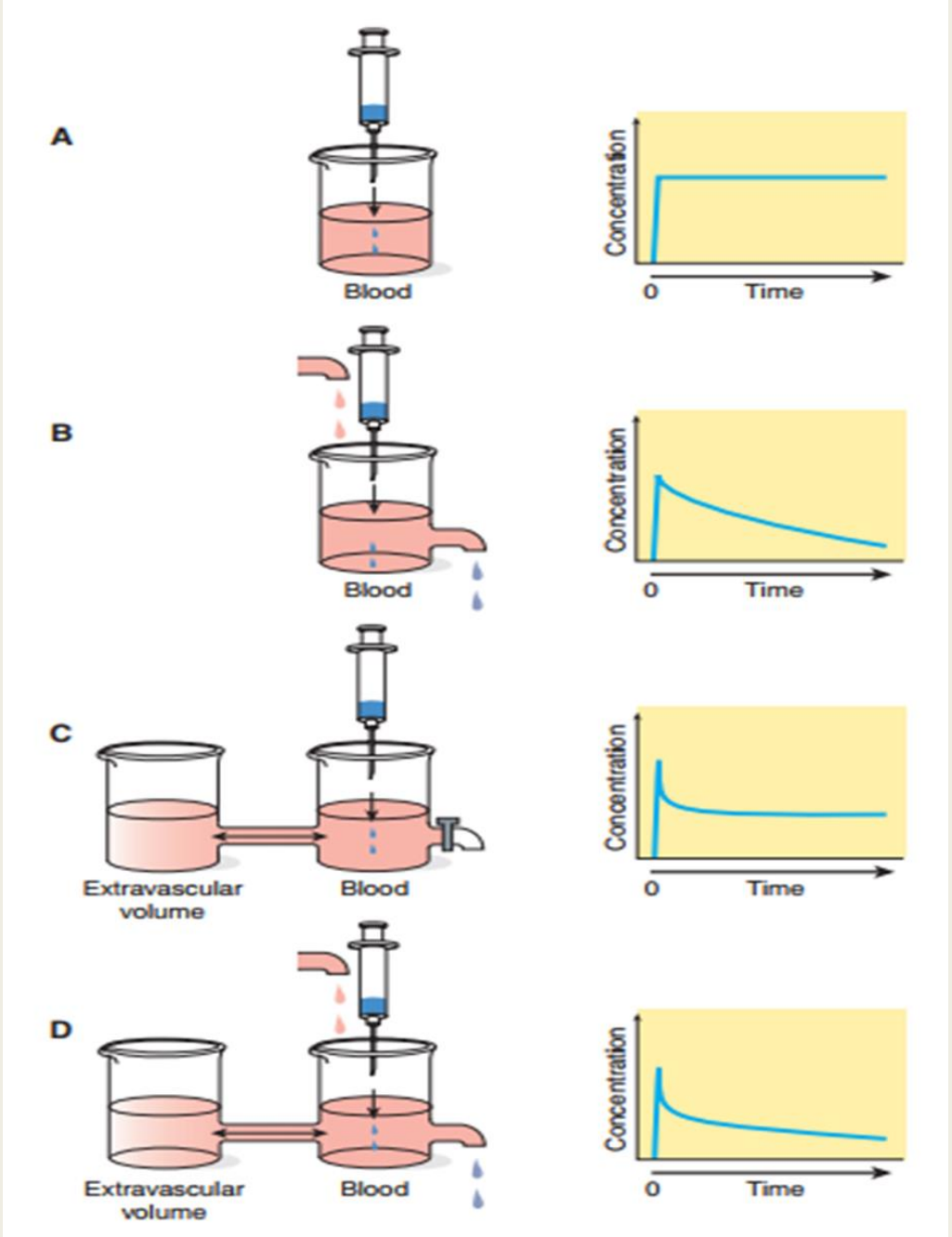
Half life

- Half-life ($t_{1/2}$) is the time required to change the amount of drug in the body by one-half during elimination (or during a constant infusion)
- Time in which plasma concentration of a drug decreases to half of its initial levels after peak has been achieved

Core Subject

Body Compartments





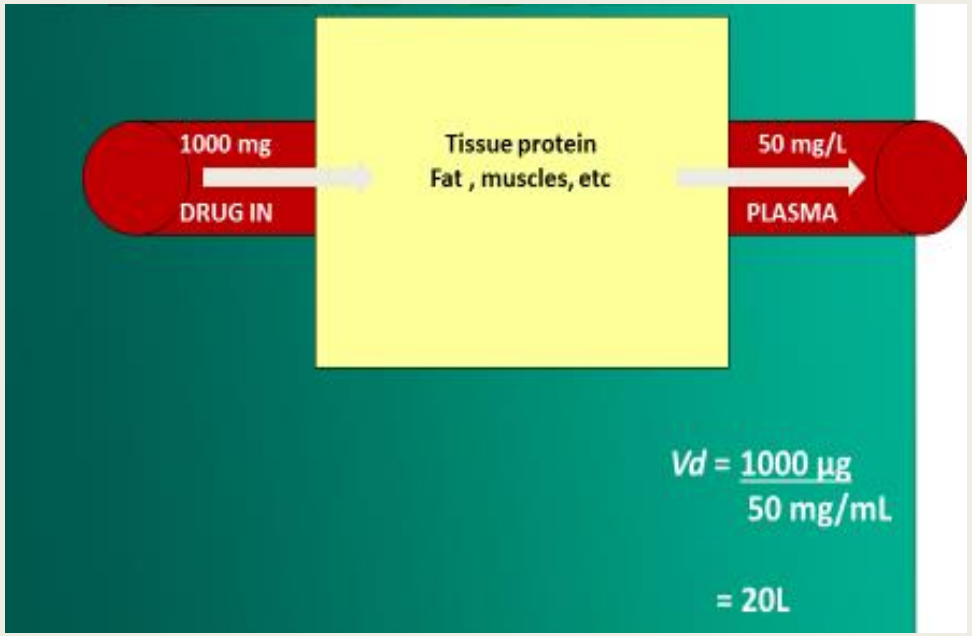
Vertical Integrations

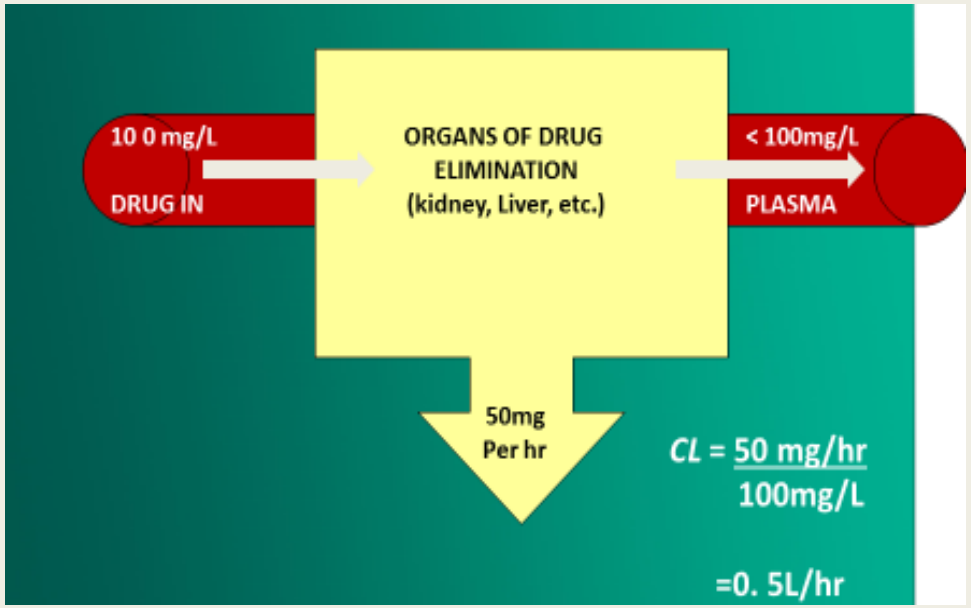
Half life

$t_{1/2}$ is a useful parameter derived from:

- Volume of distribution (Vd)
- Clearance (CL)

- $t_{½} = \frac{0.7 \times Vd}{Cl}$

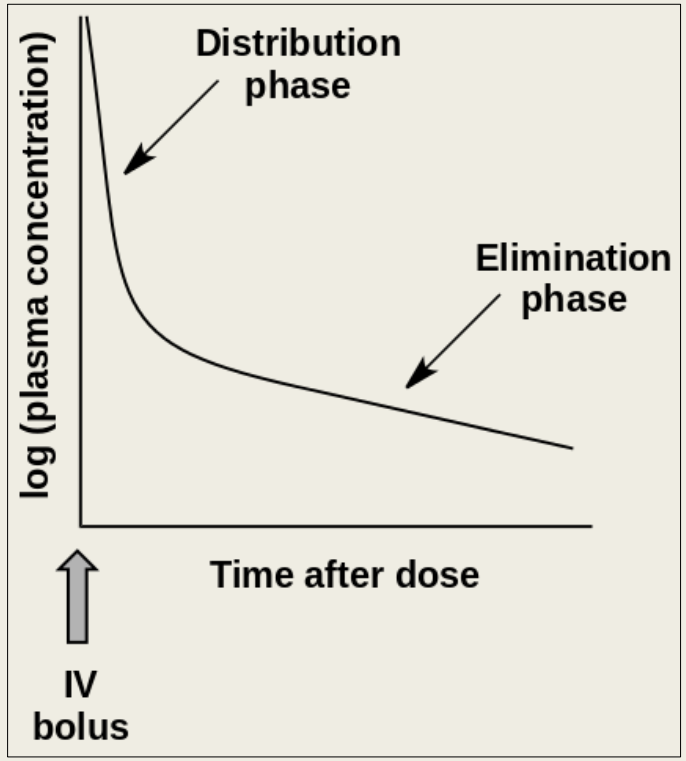




Core Subject

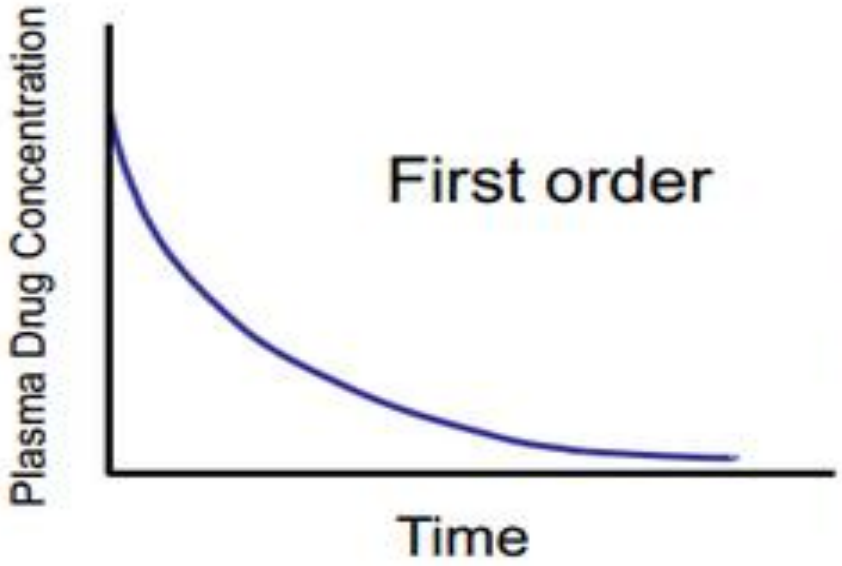
Half life

TYPES:
Steady-state/Alpha.....Distribution phase
Terminal/Beta.....Elimination Phase

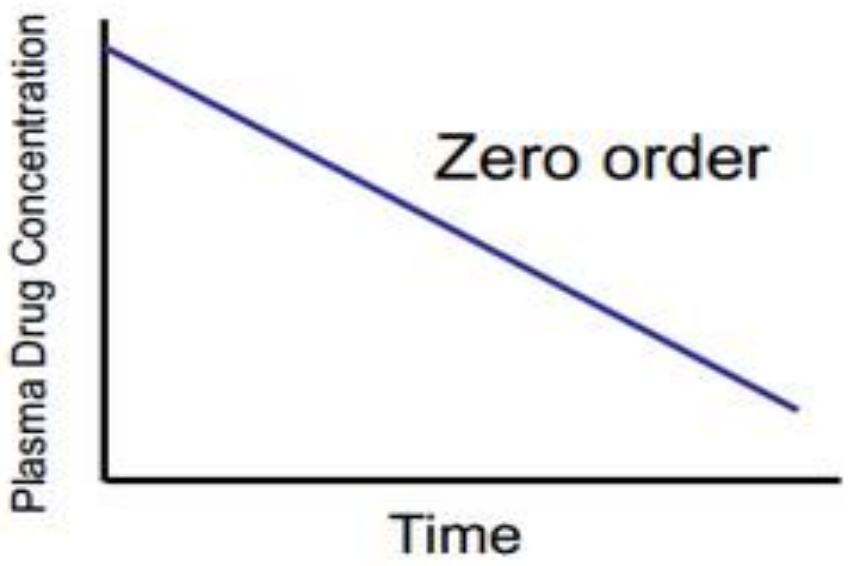


Core Subject

Half life: Pharmacokinetic patterns



- Constant fraction of drug eliminated per unit time
- Rate of drug elimination proportional to drug plasma concentration



- Constant amount of drug eliminated per unit time
- Rate of drug elimination independent of drug plasma concentration

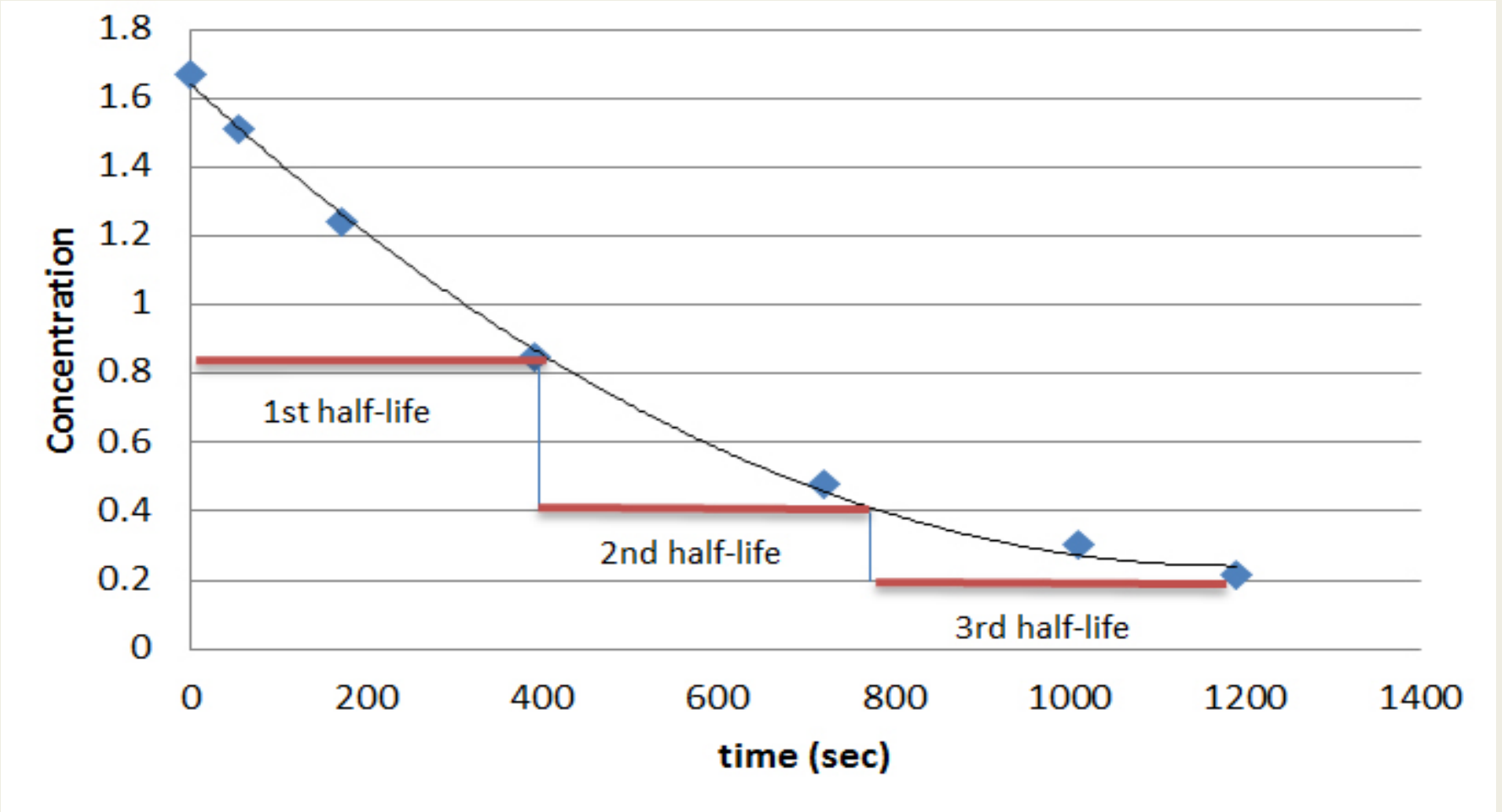
Core Subject

Half life: Pharmacokinetic patterns

- Saturation of Pharmacokinetic Processes in Zero Order Kinetics
- Pharmacokinetic Processes are
  - Absorption
  - Distribution
  - Metabolism
  - Excretion
- Reserve in pharmacokinetic processes is present to deal with higher concentrations in first-order kinetics

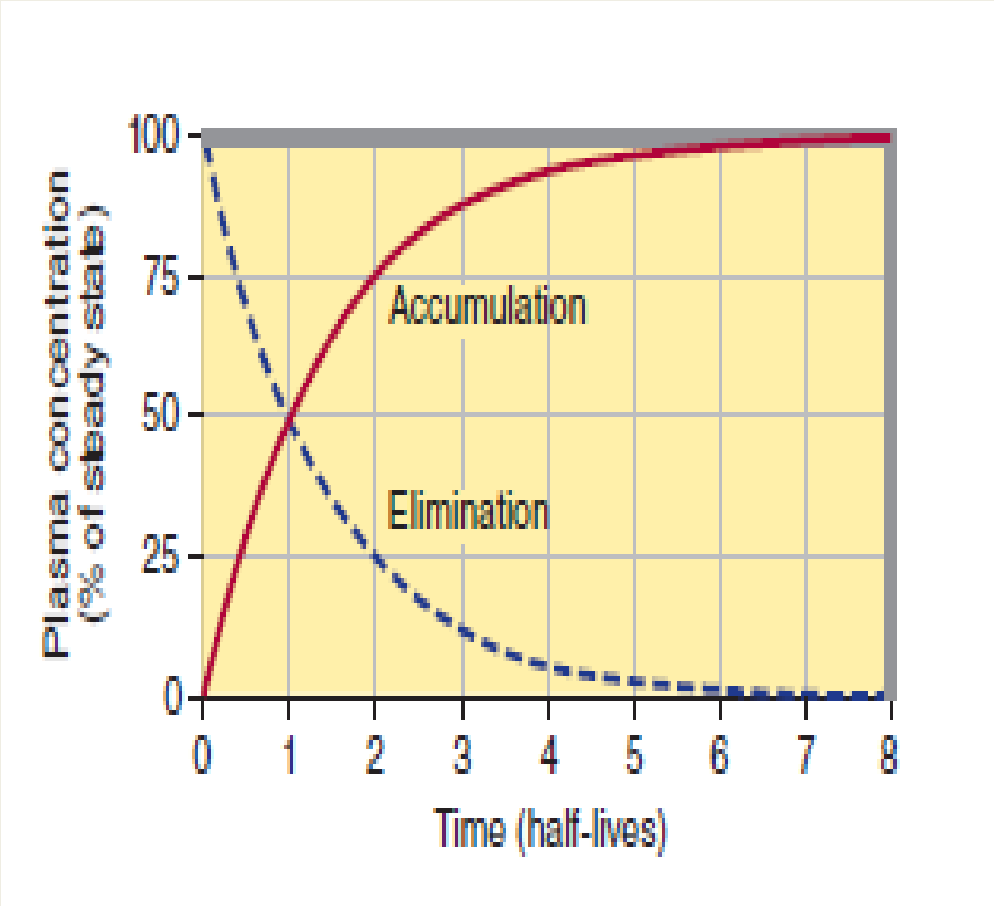
Core Subject

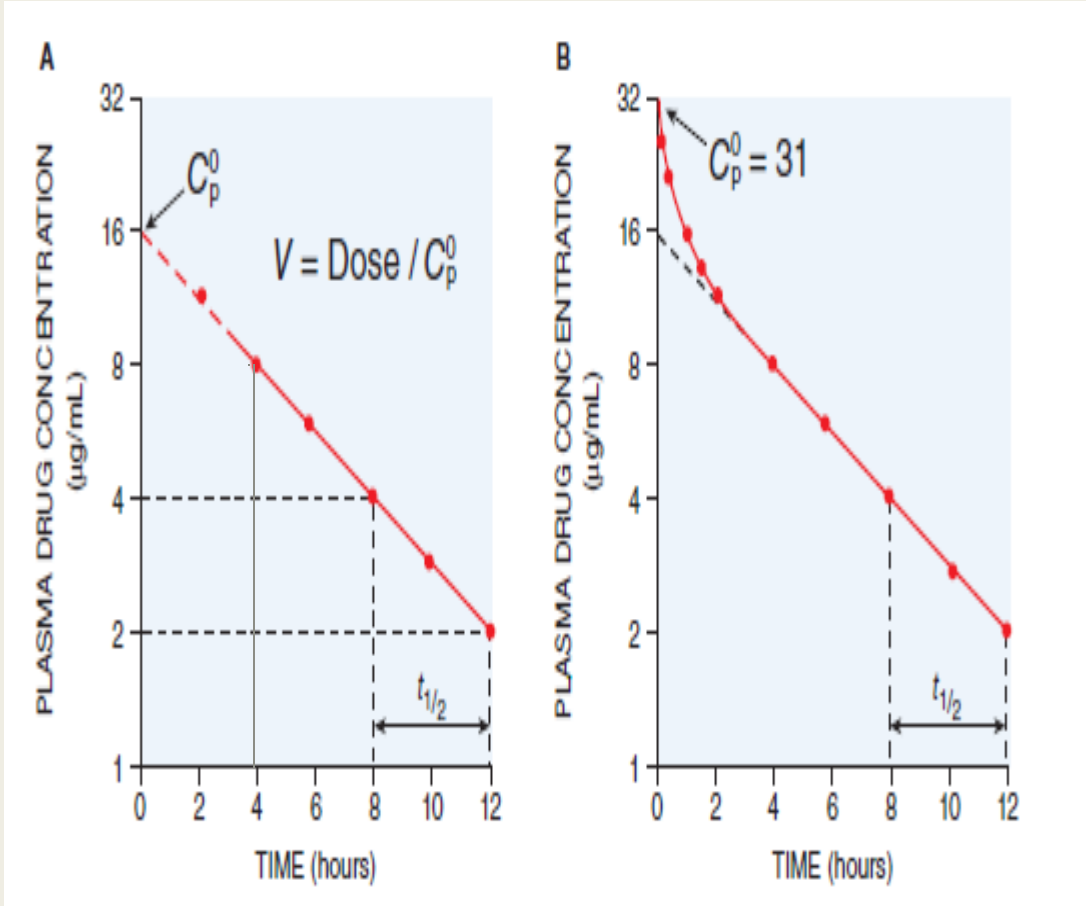
Half Life: First Order Kinetics



Core Subject

Half life





Core Subject

EOLA

- A lady of 33 years was given 200mg of a drug I/V in a single dose; during the first 120 minutes, its 100mg were eliminated. As this drug follows first-order elimination kinetics, after 6 hours the amount of the drug left behind in the blood will be:

a) None
b) 15 mg
c) 25 mg
d) 35 mg
e) 40mg

End of lecture assessment

Half life

- What does half-life predict?
- Half-life predicts the manner in which plasma concentration alters
  - Time to reach steady state
  - Time for elimination/duration of action

Core Subject

Drug Accumulation

- Accumulation is inversely proportional to the fraction of the dose lost in each dosing interval
- The fraction lost is 1 minus the fraction remaining just before the next dose

$$\text{Accumulation factor} = \frac{1}{\text{Fraction lost in one dosing interval}}$$

$$\text{Accumulation factor} = \frac{1}{1 - \text{Fraction remaining}}$$

Core Subject

Half life: Steady State Concentration(Css)

Steady state (SS):

- A condition in which the average total amount of the drug in plasma remains constant.

  Rate of administration = Rate of elimination

  - Plasma & tissue concentration is relatively constant
  - A stable drug effect can be assumed

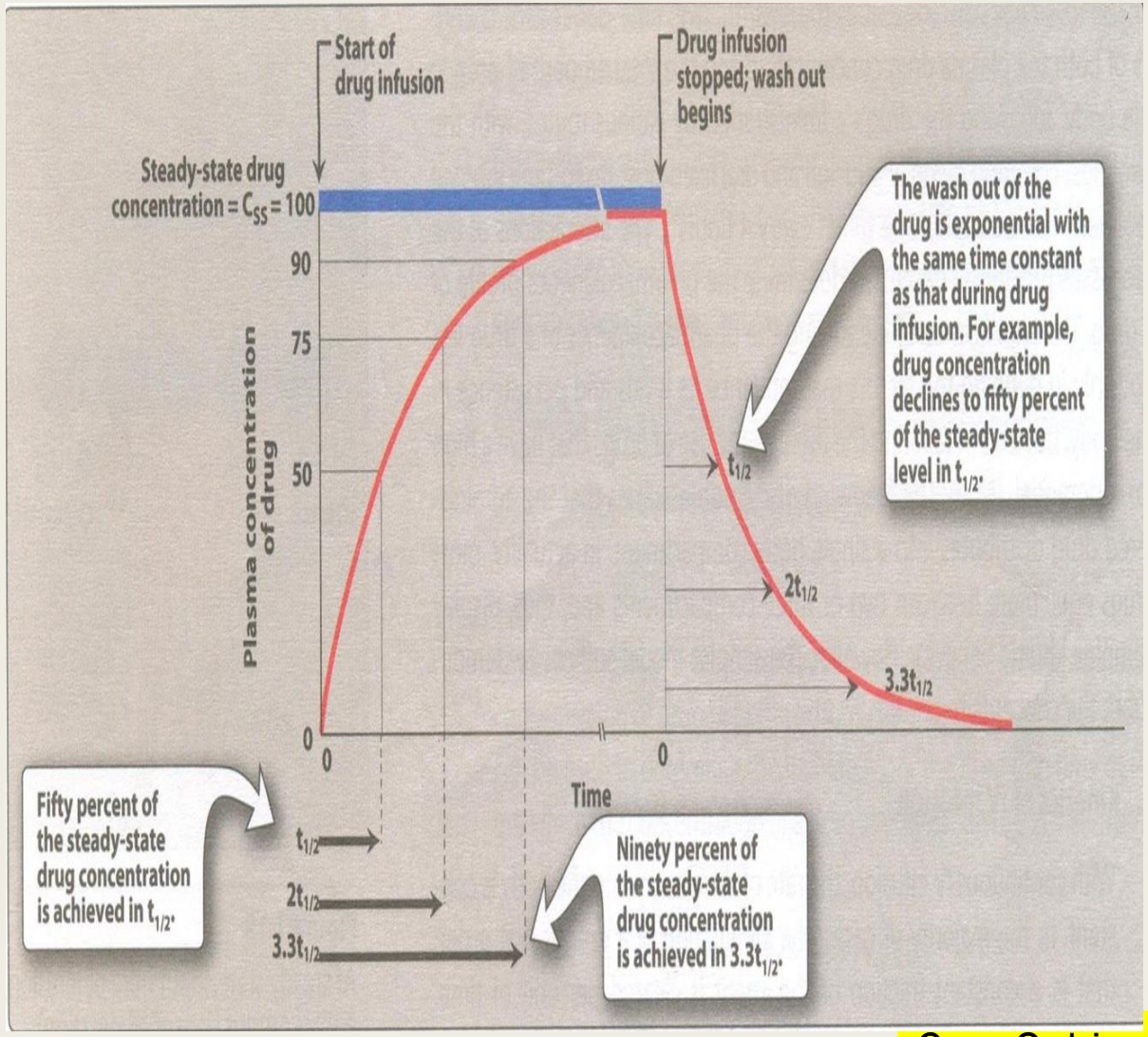
Core Subject

Half life: Css

Time to reach steady state concentration (C_{SS})

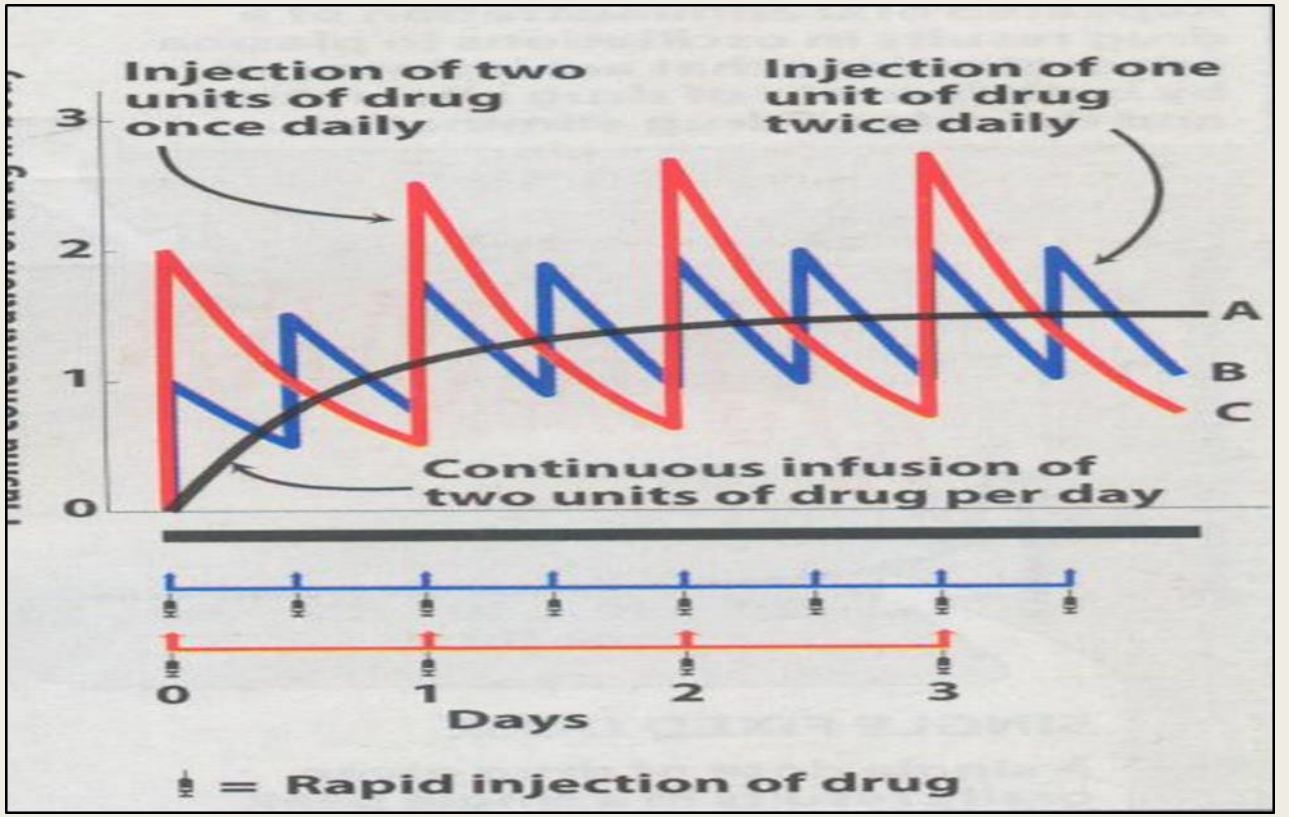
Time to reach C_{SS} = 4- 5x $t_{½}$

$$C_{SS} \alpha \frac{\text{Infusion rate}}{\text{Clearance}}$$

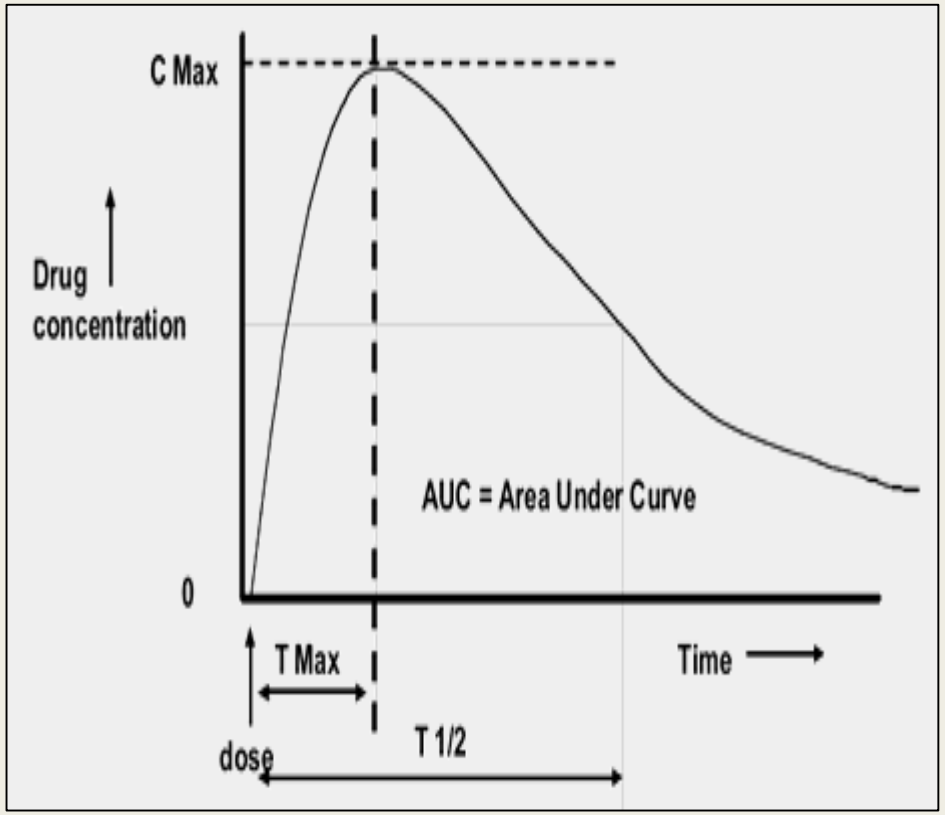


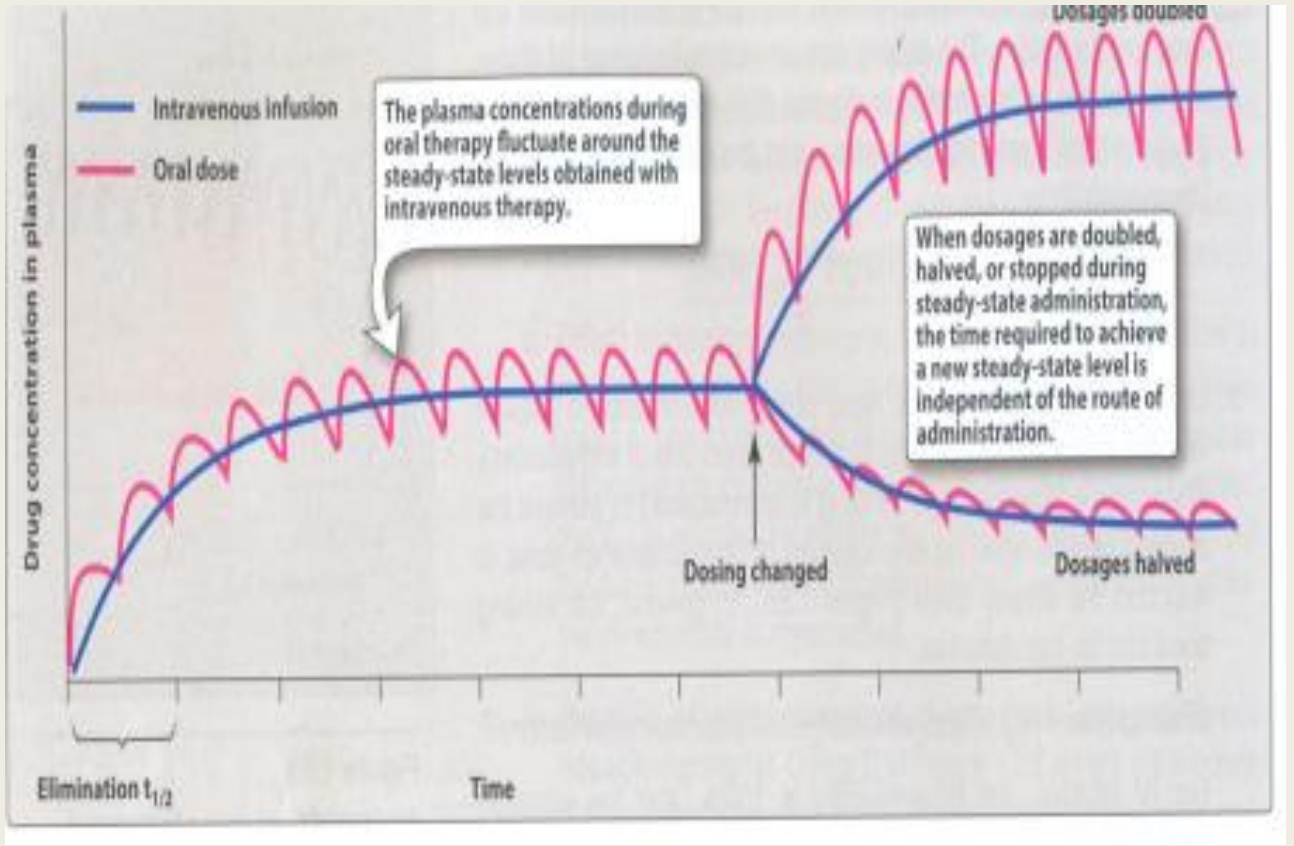
Core Subject

Half Life : Css



Core Subject





Core Subject

Half Life: Factors Affecting

- Factors affecting half-life
  - Plasma protein binding
  - Pharmacokinetic pattern of drug elimination
  - Hepatic & Renal status
  - Active metabolites
    - Diazepam/Enalapril
  - Entero hepatic circulation
    - OCPs/Digoxin
  - Volume of distribution
    - Chloroquine
  - Presence of other drugs
  - Diseases
  - Physiological factors

Age
Enzyme inducers/Inhibitors
Flow Dependent Kinetics

Core Subject

Half Life: Factors Affecting

- Pharmacokinetic pattern of drug elimination
  - First order kinetics
    - Fixed fraction of drug is eliminated in unit time
    - Elimination α Concentration
  - Zero order kinetics
    - Fixed amount of drug is eliminated
    - Saturation kinetics
    - Phenytoin/Salicylates/Alcohol
    - Relation with Half life

Core Subject

EOLA

During an investigational study, the pharmacokinetics of a newly synthesized drug is studied in volunteers. Assuming the drug is eliminated by first-order elimination kinetics, half-life will be longer in individuals who have :

a) Decreased volume of distribution and decreased clearance
b) Decreased volume of distribution and increased clearance
c) Increased volume of distribution and decreased clearance
d) Increased volume of distribution and increased clearance
e) Unaffected volume of distribution and increased clearance

End of lecture assessment

Half Life: Clinical Significance

- Clinical significance of half life
  - Rate of elimination
  - Duration of action
    - Active metabolite
    - Mechanism of action
  - Interval of dose
    - Half life
    - Duration of action
  - Time of steady state concentration
    - Therapeutic drug Monitoring
  - Time for complete elimination

Vertical Integrations

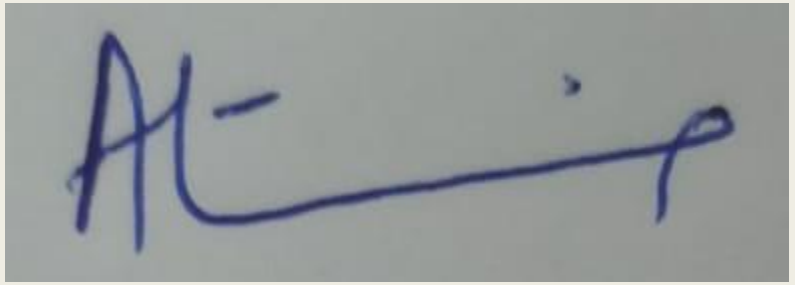
Research, Bioethics, Artificial Intelligence

- Martin JH, Hill C, Walsh A, Efron D, Taylor K, Kennedy M, Galettis R, Lightfoot P, Hanson J, Irving H, Agar M. Clinical trials with cannabis medicines—guidance for ethics committees, governance officers and researchers to streamline ethics applications and ensuring patient safety: considerations from the Australian experience. Trials. 2020 Dec;21(1):1-7.

Spiral Integrations

Digital Library

- Zaman, R., Islam, R.A., Ibnat, N., Othman, I., Zaini, A., Lee, C.Y. and Chowdhury, E.H., 2019. Current strategies in extending half-lives of therapeutic proteins. Journal of Controlled Release, 301, pp.176-189.
- Forte-Soto, P., Albayaty, M., Brooks, D., Arends, R.H., Tillinghast, J., Aksyuk, A.A., Bouquet, J., Chen, C., Gebre, A., Kubiak, R.J. and Pilla Reddy, V., 2023. Safety, Tolerability and Pharmacokinetics of Half-Life Extended SARS-CoV-2 Neutralizing Monoclonal Antibodies AZD7442 (Tixagevimab/Cilgavimab) in Healthy Adults. The Journal of Infectious Diseases, p.jiad014.



Further reading