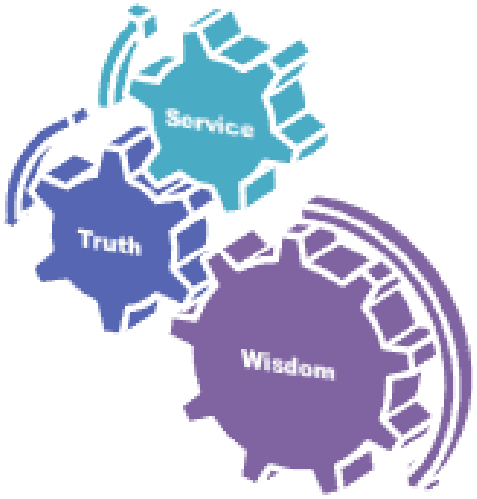
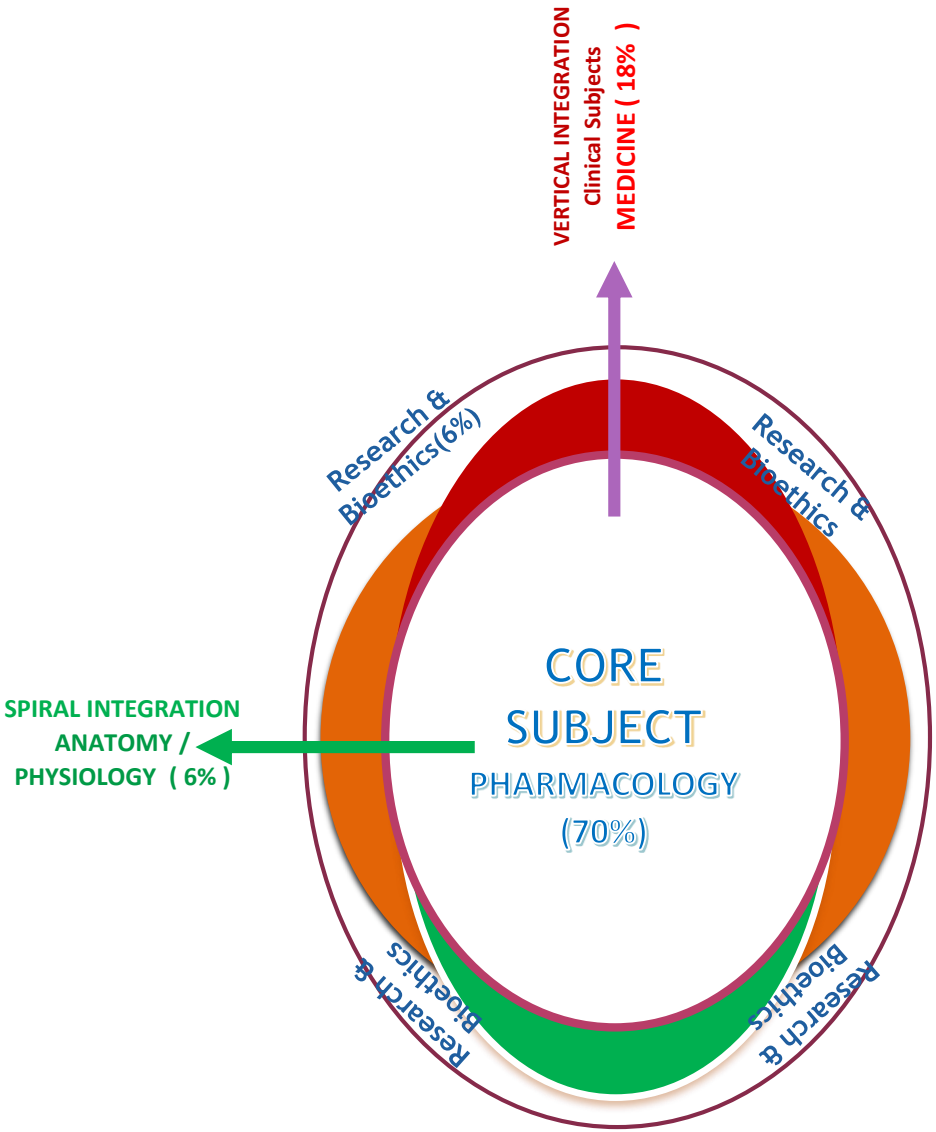

بسم الله الرحمن الرحيم

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



3rd Year Pharmacology LGIS(30 slides)	
Core Subject - 21 slides (70%)	
Spiral Integration (anatomy/physiology)-(3 slide) (10%)	
Vertical integration	• (Medicine) - 5 slides (15%)
Research & Bioethics 1 slide(5%)	

FOUNDATION MODULE (II)
LGIS
Plasma Half Life

SOURCE :

Bertram G.Katzung Basic & Clinical Pharmacology 15th Edition

Google for images & research article

PRE LECTURE ASSESSMENT

MCQ # 1

What effect does a drug's volume of distribution (Vd) have on its half-life?

a) Larger Vd usually results in a longer half-life

b) Larger Vd usually results in a shorter half-life

c) Vd does not affect half-life

d) Vd only affects the half-life in the liver

e) Vd determines the drug's therapeutic index

MCQ # 2

In which of the following scenarios will a drug likely have a prolonged half-life?

a) The drug undergoes rapid hepatic metabolism

b) The drug is highly protein-bound

c) The drug is excreted by the lungs

d) The drug is administered intravenously

e) The drug has a high renal clearance rate

MCQ # 3

How does aging affect the half-life of many drugs?

a) It decreases due to increased renal clearance
b) It remains unchanged
c) It decreases due to faster metabolism
d) It increases due to slower renal and hepatic function
e) It decreases due to less drug absorption

MCQ # 4

Which of the following factors can cause a prolonged half-life of a drug due to impaired drug clearance?

a) Hyperthyroidism

b) Increased renal blood flow

c) Decreased liver function

d) Decreased adipose tissue

e) Hyperventilation

MCQ # 5

Approximately how many half-lives does it take for medication concentration to reach a steady state?

a) Five to six

b) Two to three

c) Seven to ten

d) One to two

MCQ # 6

Which one of the following is not a characteristic of a zero-order drug decomposition reaction?

a) The rate of reaction is constant

b) The rate of reaction is independent of the concentration of any of the reactants

c) The half-life is directly proportional to the initial concentration of drug.

MCQ # 7

7. Drug A has a half-life of 2 hours. If the initial plasma level of the drug, given as a single dose, is 1200mg/L, what will its plasma level be after 8 hours?

MCQ # 8

Which of the following can increase the half-life of a drug that is primarily metabolized in the liver?

a) Induction of cytochrome P450 enzymes

b) Decreased body temperature

c) A drug that displaces the drug from plasma proteins

d) Enzyme inhibition

e) Increased renal clearance

MCQ # 9

A young patient is being given a drug. The clearance and volume of distribution of drug in this patient are 2.56L/h and 50L respectively. What will be the half life of that drug?

MCQ # 10

A 45-year-old male patient with hypertension is prescribed a daily dose of 20 mg of Lisinopril, which has a half-life of 12 hours. He has been taking the medication for 3 days. After how many days will the patient likely reach a steady-state concentration of Lisinopril?

a) 1 day
b) 3 days
c) 5 days
d) 7 days
e) 9 days

LEARNING OBJECTIVES

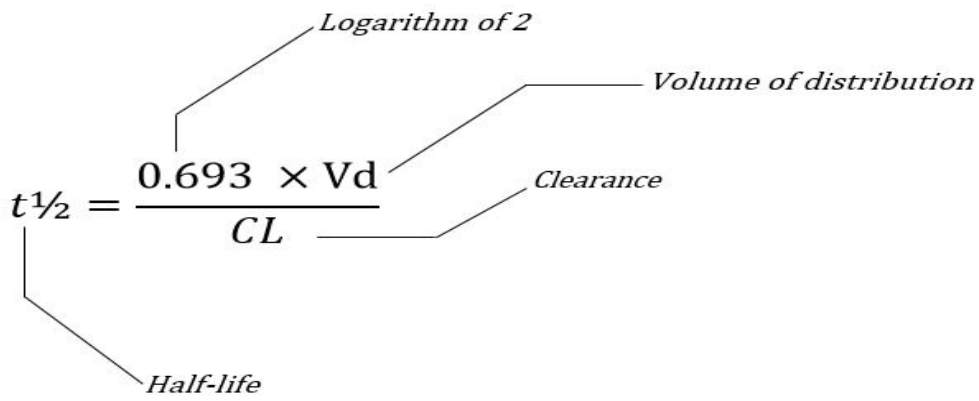
By the end of lecture you should be able to

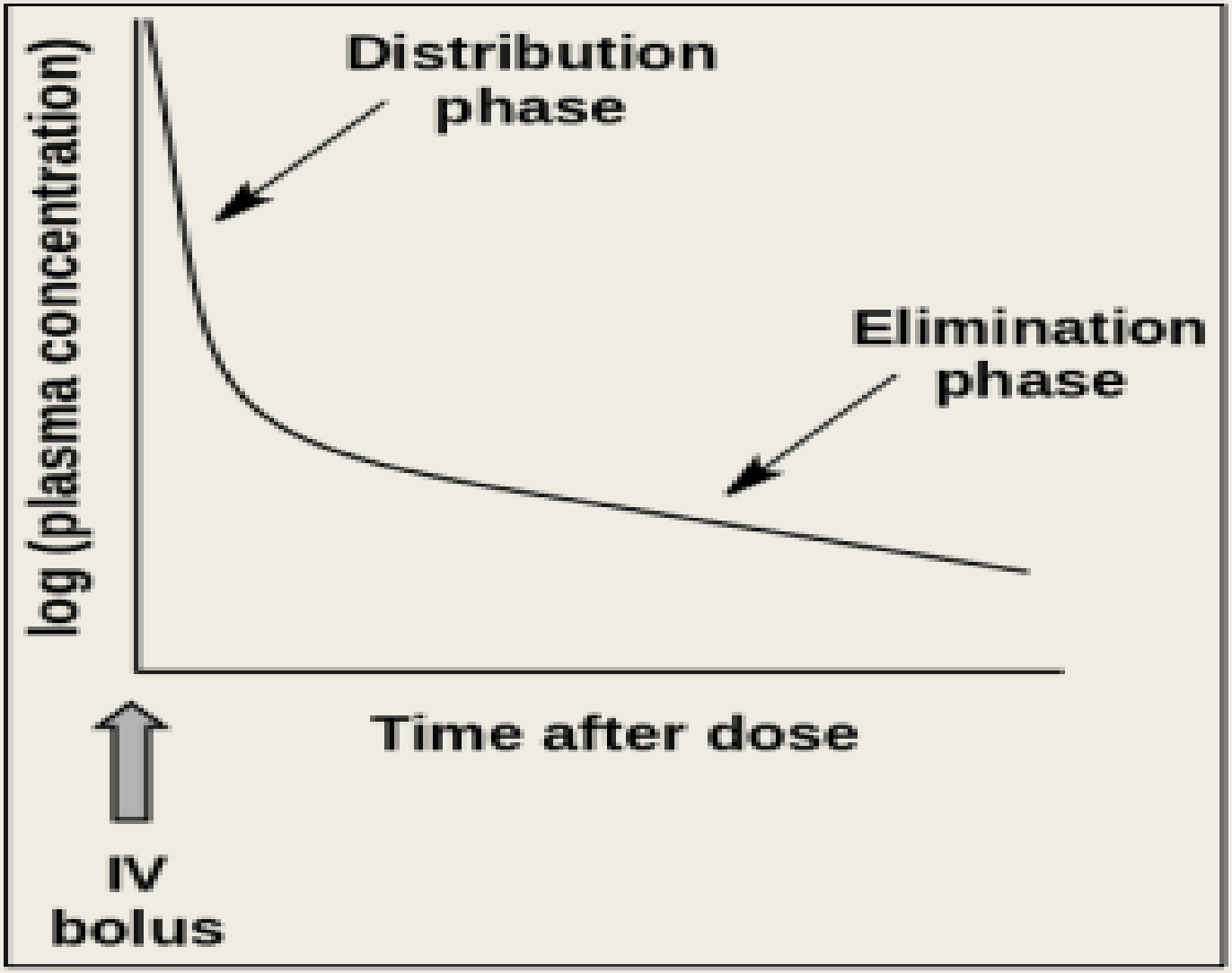
- Define and calculate plasma half life of drugs
- Explain steady state concentration of drugs
- Discuss factors affecting half life of drugs
- Clinical significance of plasma half life of drugs

Core subject

HALF LIFE OF A DRUG

- It is the Time required to reduce the amount of drug in the body by one-half(50%) of its initial concentration.
- Time in which plasma concentration of a drug decreases to half of its initial levels after peak has been achieve




Distribution phase
Elimination phase
log (plasma concentration)
Time after dose
IV bolus

Core subject

STEADY STATE CONCENTRATION

- The amount of drug administered is equal to amount of drug eliminated within one dosing interval resulting in a plateau or constant serum drug concentration

Core subject

FACTORS AFFECTING HALF LIFE

1. Volume of distribution (Vd)
2. Plasma protein binding
3. Clearance (Cl)
4. Kinetics pattern
5. Presence of other drug
6. Diseases
7. Active metabolites
8. Enterohepatic circulation
9. Physiological factors

Core subject

I. **Volume Of Distribution**

Large Vd → long $T_{1/2}$

II. **Plasma protein binding (PPB)**

Low PPB → short $T_{1/2}$

High PPB → long $T_{1/2}$

III. **Clearance**

increased clearance → short $T_{1/2}$

Core subject

IV. KINETICS PATTERN

ZERO ORDER

Constant amount of drug is eliminated (e.g ethanol)

Time (hrs)	Plasma conc. (mg)	Plasma conc. (mg)
0	100	200
1	90	190
2	80	180
3	70	170
4	60	160
5	50	150
10	-	100

Core subject

1st ORDER

Constant fraction of drug is eliminated (95% of drugs)

Time (hrs)	Plasma conc. (mg)	Plasma conc. (mg)
0	100	200
1	50	180
2	25	162
3	12.5	145.8
4	6.25	131.22
5	3.12	118.01
6	1.5	106.29

V. Presence of other drug

Enzyme Inducer

Enzyme Inhibitor

VI. Diseases

- renal failure
- Liver cirrhosis

VII. Active Metabolites

e.g aspirin , morphine

Viii. Enterohepatic Circulation

drugs excreted in bile …reabsorbed …. increased T1/2 e.g rifampicin

Core subject

IX. Physiological Factors

- Age
- Diet
- Gender
- Obesity
- Race/genetics
- Smoking

Vertical

WHY $T_{1/2}$ IS IMPORTANT??

It is determinant of

1. Time required to reach steady state concentration
2. Estimation of time of drug elimination
3. Duration of action after single dose
4. Dose interval

Vertical

1) Time required to reach steady state concentration

- rate of drug elimination = to rate of drug administration
- Is equal to 4 to 5 $T_{1/2}$

2) Estimation of time of drug elimination (esp. imp for toxic drugs)

97% eliminated after 4 to 5 $T_{1/2}$

↑ $T_{1/2}$ ⟶ slow elimination

↓ $T_{1/2}$ ⟶ fast elimination

Vertical

3) Duration of action

- long $T_{1/2}$ → long Duration of action
- short $T_{1/2}$ → short Duration of action

4) Dose interval

- long $T_{1/2}$ → long dosing interval
- short $T_{1/2}$ → short dosing interval

Further reading

BIOETHICS AND RESEARCH

- Physician should keep in mind pharmacokinetic parameters of the prescribing drugs so as to achieve maximal clinical benefits

- Gunaydin H, Altman MD, Ellis JM, Fuller P, Johnson SA, Lahue B, Lapointe B. Strategy for extending half-life in drug design and its significance. ACS Medicinal Chemistry Letters. 2018 Apr 2;9(6):528-33.

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