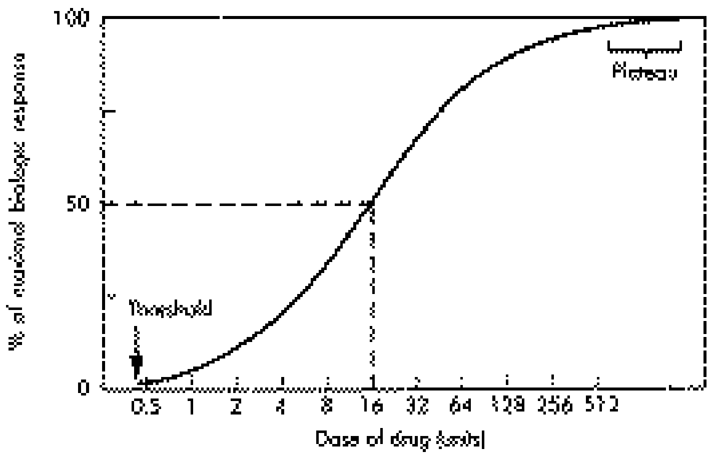
GRAPHIC ILLUSTRATIONS: PHARMACODYNAMICS & PHARMACOKINETICS

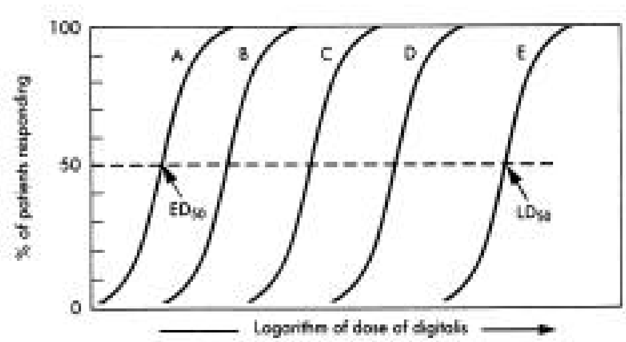
I. Dose-Response Curves

- demonstrates that a certain dose is required to achieve a response
- the degree of pharmacological response (measured in percentage of maximum biological effect) is plotted on linear scale on the vertical axis; whereas, the dose of the drug is measured is plotted on log scale on the horizontal axis
- the plateau is the part of the curve where increasing drug dose does not increase pharmacological (therapeutic) response



graph 1: log dose-response curve

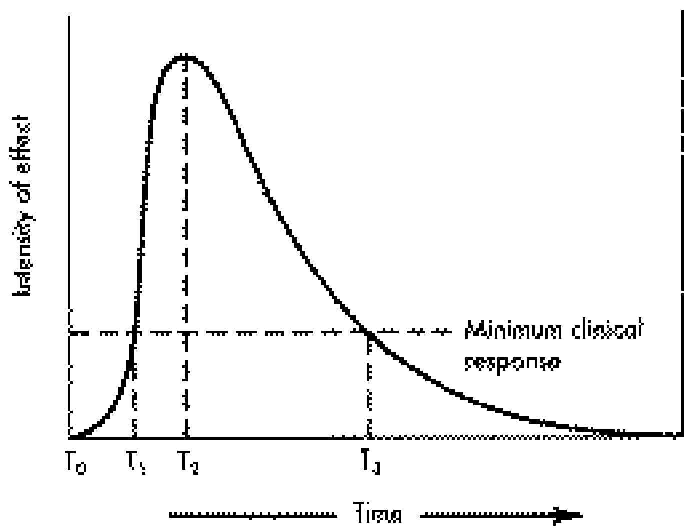
- example: log dose-response curves for effects of digoxin (drug used in CHF)
  - curve A: increased force of contraction of heart (therapeutic effect)
  - curve B: nausea
  - curve C: visual disturbances
  - curve D: cardiac arrhythmias
  - curve E: ventricular fibrillation → death



graph 2: log dose-response curves for effects of digoxin

II. Time Course of Drug Action

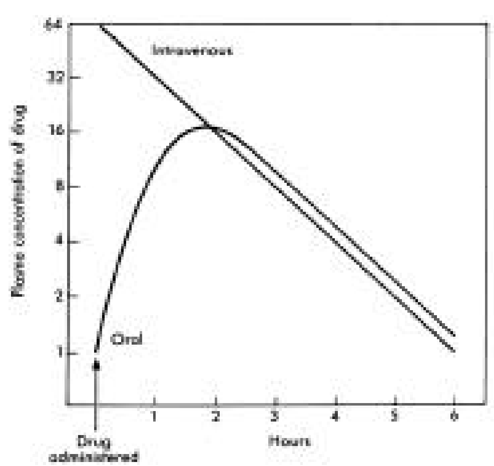
- onset of action: the time, after a drug is administered, to achieve a drug serum concentration required to produce a detectable response ($t_0 \rightarrow t_1$)
- time to peak: the time required for a drug to achieve its highest therapeutic serum concentration ($t_0 \rightarrow t_2$)
- duration of action (DOA): the amount of time a drug is present in adequate serum concentration necessary to produce a therapeutic effect ($t_1 \rightarrow t_3$)
    - DOA depends on the rate of drug absorption and elimination
- half-life ($t_{1/2}$): the amount of time required for elimination processes to reduce the drug serum concentration by one-half



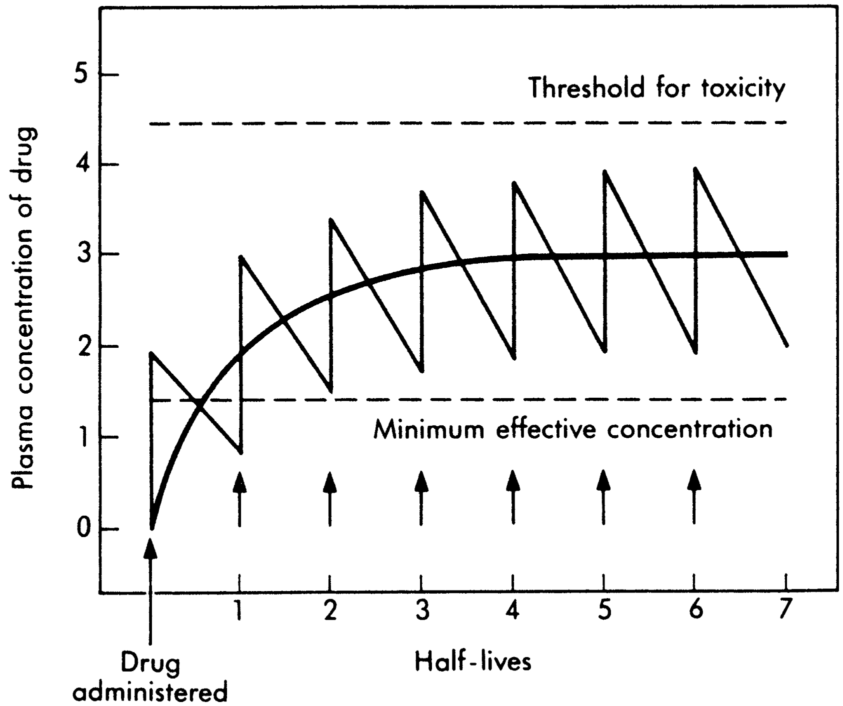
graph 3: time course of drug action

III. Oral vs Intravenous Graph

graph 4: PO vs IV Curves



IV. Continuous vs Intermittent Drug Administration



V. Estimated Creatinine Clearance (for drug dosing considerations)

A. Calculation of Ideal Body Weight (IBW)

1. Female

$$IBW = (2.3 \times \text{inches above } 5') + 45.5 \text{ kg}$$

2. Male

$$IBW = (2.3 \times \text{inches above } 5') + 50 \text{ kg}$$

B. Creatinine Clearance (CrCl) Formula

$$CrCl\ (ml/min) = \frac{(140 - Age) \times IBW}{sCr \times 72}$$

(sCr = serum creatinine level)

$$CrCl_{female} = CrCl \times 0.85$$

C. Adjusted Body Weight (ABW)

$$ABW = IBW + 0.4\ (\text{Actual Body Wt} - IBW)$$

CREATININE CLEARANCE SAMPLE PROBLEM

NOTE: The CrCl formula will be provided to students during the exam. The emphasis will be on application and making the right assessment.

Jane Smith (JS) is a 69-year old female who was admitted to University Hospital complaining of UTI symptoms. Dr. Urobact, Jane's physician, would like you to recommend an appropriate dose of Keflex (cephalexin), based on Jane's kidney function.

Jane's HT / WT = 5' 4" / 152 LBS.
A blood chemistry panel reported the following values:

Na = 145
K = 3.8
Cl = 101
Glucose = 98
CO_2 = 24
BUN = 27
Cr = 1.5

QUESTIONS
1. Calculate Jane's IBW (ideal body wt)
2. Calculate her CrCl (creatinine clearance).
3. Recommend the appropriate dose of Keflex for Jane.

KEFLEX (Cephalexin) Package Insert
According to the package insert of Keflex (cephalexin), 500 mg every 6 hours is recommended for a CrCl > 50 ml/min. But, if the patient's kidney function reflects a range of 10 to 50 ml/min, the dose of cephalexin should be reduced to 500 mg every 8 to 12 hours. For CrCl < 10 ml/min, the recommendation is 250 to 500 mg every 12 to 24 hours.

ANSWERS:

1. Jane's IBW = 54.7 kg

2. Jane's CrCl = (140-69)(54.7) / (1.5)(72) = 35.96 ml/min

> **NOTE: Since females have 15% less kidney function than males, you must subtract 15% from Jane's CrCl result.**
>
> **(0.85)(35.96) = 30.5 ml/min**

3. Since Jane's CrCl (30.5 ml/min) falls within the 10 to 50 ml/min range of the dosage guideline of Keflex, the recommended dose is: 500 mg every 8 to 12 hours.