PHARMACOLOGY & THERAPEUTICS
PHARMACOKINETICS

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Volume of distribution (V_d):

V_d = amount of drug/concentration of drug in plasma

$$V_d = \frac{dose}{C_p}$$

AUC: the area under the plasma or blood-concentration:time curve.

Bioavailability: $F = \frac{AUC\ (oral)}{AUC\ (IV)}$

MEC: usually a minimum effective concentration (i.e., MTC minimum therapeutic concentration) of drug in the blood or plasma is needed for a therapeutic effect.

Clearance:

A. The rate of elimination of a drug by all routes relative to the concentration of the drug in a biological fluid (usually blood or plasma).

$$CL = \text{rate of elimination} / \text{concentration}_{plasma}$$

B. $CL = KV_d$
K = elimination rate constant

Elimination kinetics:

A. 1st order kinetics:

1. Half-life:

$t2 = 0.693V_d / CL$

$CL = KV_d$ so $t2 = \frac{0.693}{K}$

B. 0 order kinetics:

A constant amount of the drug is eliminated in a given period of time.
A half-life cannot be described.

Extraction ratio:

1. $ER = (C_i - C_o / C_i)$

ER= extraction ratio
C_i = concentration of drug in the blood entering an organ
C_o = concentration of drug in the blood exiting an organ

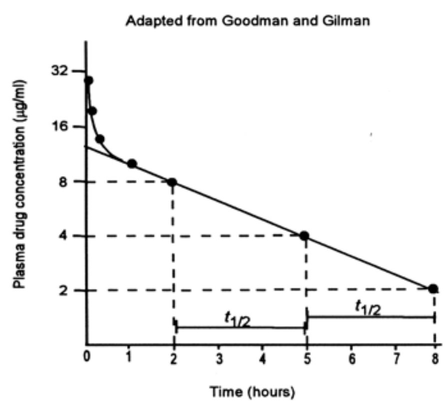
2. $CL_{organ} = Q \times ER$
Q = blood flow

DOSAGE REGIMEN DESIGN

Single dose:
. Estimates can be made from the graph

a. Half-life estimated from the slope

b. Volume of distribution from extrapolation of second phase of curve back to y-intercept.



Multiple Doses:
A. Maintenance dose
1. For IV dose: dosing rate = $CL_p \times C_p$

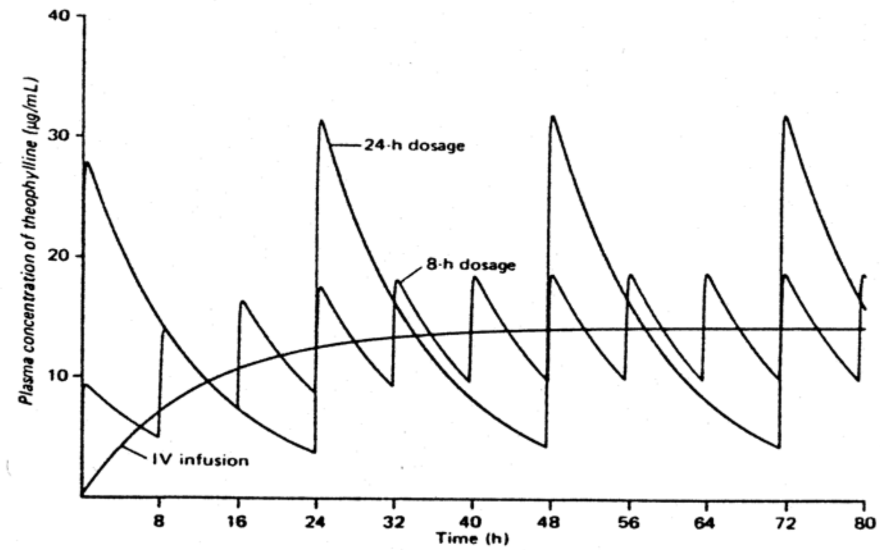
2. For multiple intermittent doses:

a. (F x Dose) / dosing interval = $CL_p \times C_p$

b. Peak and trough drug concentrations.

Peak: $C_{p,\,max} = (F \times dose / V_d)) /$ fraction loss in a dosing interval

Trough: $C_{p,\,min} = C_{p,\,max} \times$ fraction remaining after dosing interval



From: Katzung

Concentration kinetics:

$$\log C = \log C_0 \frac{-k}{2.3}(t)$$

$$\frac{-k}{2.3} = \frac{\log C_1 - \log C}{t_1 - t_2}$$

Plateau levels of a drug (given such that administration rate equals rate of elimination) are reach after four and one-half-lives (i.e., 4.5 x t2)

B. Loading dose

$$LD = V_d \times C_p$$

Renal disease: $$D_r = (D)\frac{CL_{sr}}{CL_s}$$

$$T_r = (T)\frac{CL_s}{CL_{sr}}$$

$$\text{creatinine clearance (L/h)} = \frac{160 - \text{age (years)}}{22 \times \text{serum creatinine (mg/dL)}} \times \frac{\text{weight (kg)}}{70}$$

The predicted clearance in women is 90% of the value calculated above.