Volume of distribution \((V_d)\):

\[ V_d = \frac{\text{amount of drug/concentration of drug in plasma}}{\text{dose}} \]

\[ V_d = \frac{\text{dose}}{C_p} \]

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

Bioavailability: \[ F = \frac{\text{AUC (oral)}}{\text{AUC (IV)}} \]

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).

\[ CL = \frac{\text{rate of elimination}}{\text{concentration}_{\text{plasma}}} \]

B. \[ CL = KV_d \]

\( K = \text{elimination rate constant} \)

Elimination kinetics:

A. 1st order kinetics:

1. Half-life:

\[ t_2 = \frac{0.693V_d}{CL} \]

\[ CL = KV_d \]

so \[ t_2 = \frac{0.693}{K} \]

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. \[ ER = \left( \frac{C_i - C_o}{C_i} \right) \]

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. \[ CL_{\text{organ}} = Q \times ER \]
\( Q \) = 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. \( \frac{(F \times \text{Dose})}{\text{dosing interval}} = CL_p \times C_p \)
   b. Peak and trough drug concentrations.

  Peak: \( C_{p, \text{max}} = \frac{(F \times \text{dose} / V_d)}{\text{fraction loss in a dosing interval}} \)
  Trough: \( C_{p, \text{min}} = C_{p, \text{max}} \times \text{fraction remaining after dosing interval} \)
Concentration kinetics:

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

\[ -k = \frac{\log C_1 - \log C}{2.3} \frac{t_1 - t_2}{t} \]

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:

\[ D_t = (D) \frac{CL_{sr}}{CL_s} \]

\[ T_t = (T) \frac{CL_{sr}}{CL_{sr}} \]

Creatinine clearance = \[\frac{160 - \text{age (years)}}{22 \times \text{serum creatinine (mg/dL)}} \times \text{weight (kg)} \]

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