Clinical Parameters In Drug Pharmacokinetics

Pharmacokinetics is the study of drug absorption, distribution, metabolism and elimination over time or, in other words, what the body does to a drug.

Absorption: drug absorption from the site of administration permits entry of the therapeutic agent (either directly or indirectly) into plasma.

Distribution: the drug may then reversibly leave the bloodstream and distribute into the interstitial and intra cellular fluids.

Metabolism: the drug may be biotransformed by metabolism by the liver, or other tissues.

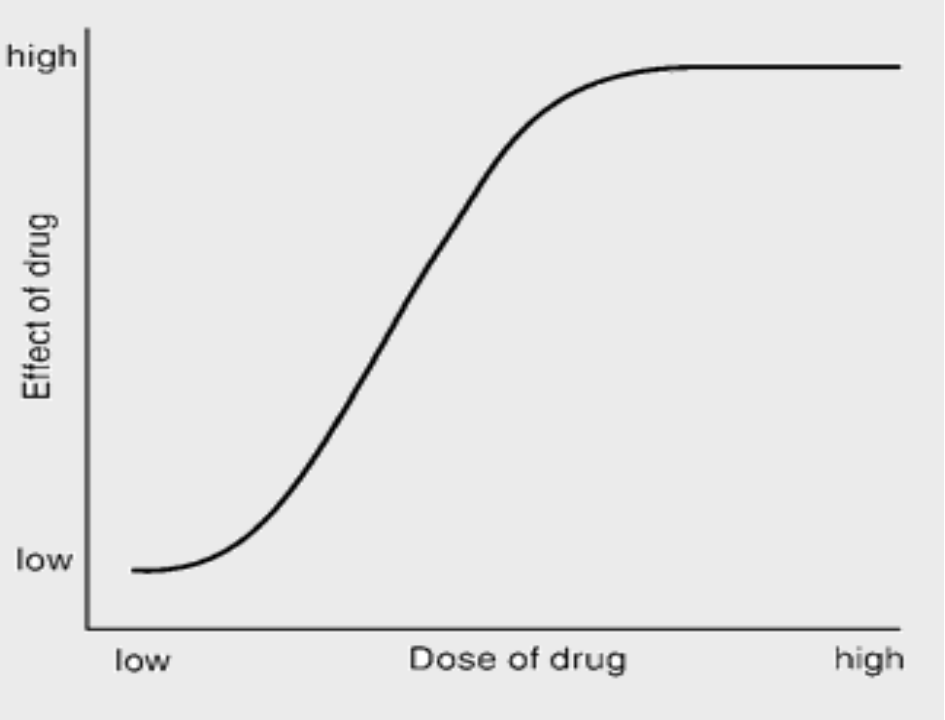
Elimination: the drug and its metabolites are eliminated from the body in urine, bile, or feces.

❖**Pharmacokinetic parameters allow the clinician to design and optimize treatment regimens, including decisions as to the route of administration for a specific drug, the amount and frequency of each dose, and the duration of treatment**.

Dose–response curve

A dose–response curve is a simple X–Y graph relating the concentration or amount of a drug, to the response of the receptor or the drug effect.

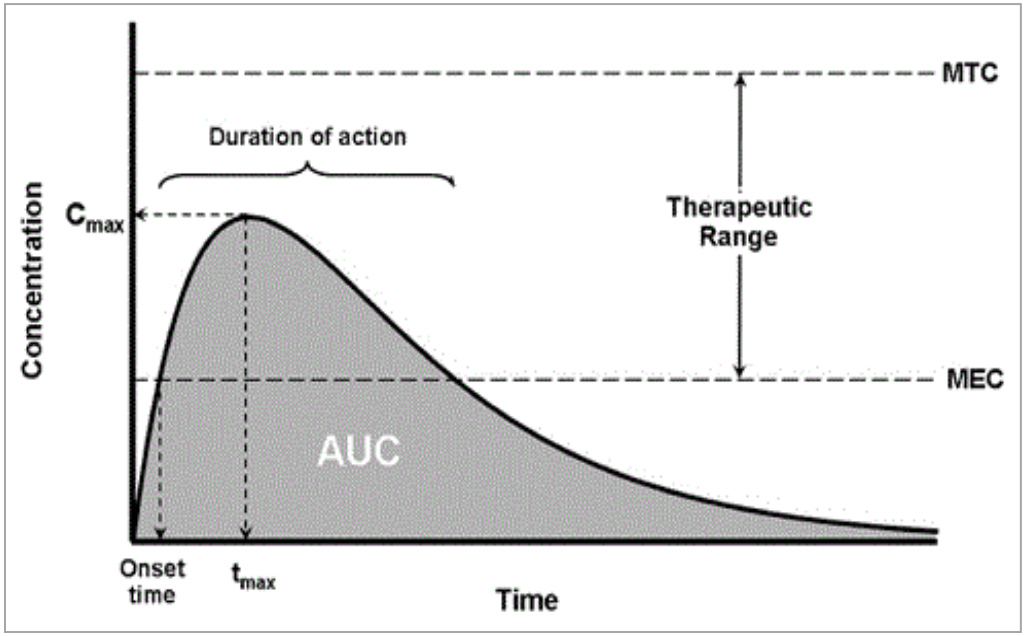
The measured dose is generally plotted on the X axis and the response is plotted on the Y axis.



☺ ☻ ***The most important pharmacokinetic parameters are:***

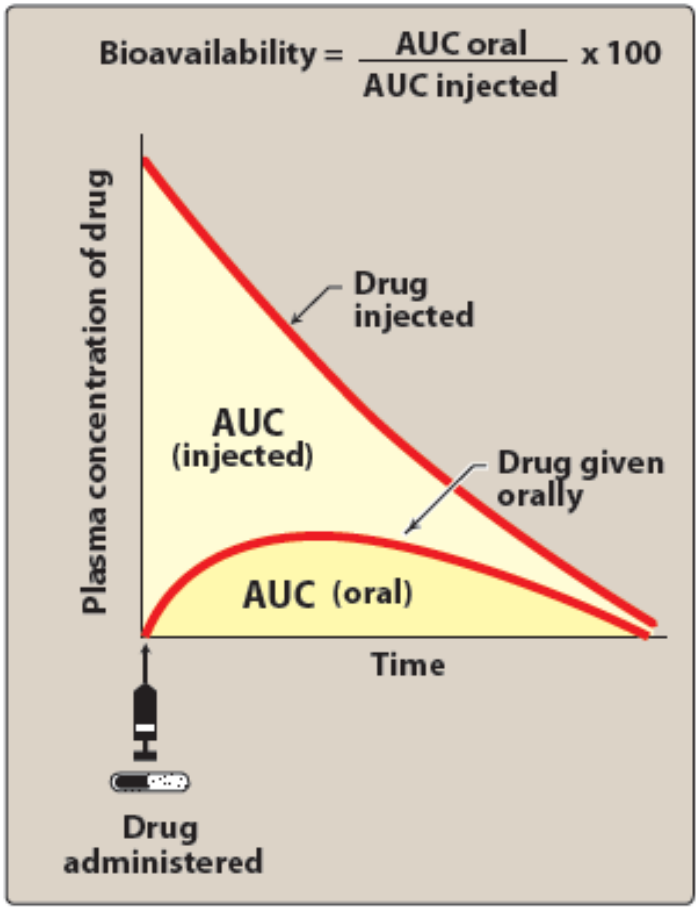
Area under the Drug Concentration Curve(AUC):

If a plot of the plasma drug concentration versus time is made, then the area under this curve (AUC) represents the total amount of drug absorbed. This parameter is very important in defining how well the drug is absorbed, and is required by the FDA in the drug approval process. The usual unit is mg/L.h.



Bioavailability(BA, F): is the fraction of administered drug that reaches unchanged to the systemic circulation.

Bioavailability = AUC(oral) / AUC(IV) X 100



Drug Concentration (C): is the amount of drug in a given volume of plasma. The usual unit is mg/L.

Volume of Distribution (Vd):

The volume of distribution is a kinetic parameter that is used to estimate the degree to which a drug permeates the different fluid compartments of the body. It is defined as the amount of drug in the body divided by the concentration of drug in the blood or plasma. The usual unit is L.

$$V_d = \text{Total amount of drug in the body (A)} / \text{Drug plasma conc. (C)}$$

Clearance: is the volume of plasma cleared of the drug per unit time. The usual units are ml/min or L/h.

The total body clearance = renal clearance + hepatic clearance + lung clearance etc…

Elimination rate constant (K_{el}): is the rate at which a drug is removed from the body. The usual unit is h^{-1}.

$$K_{el} = CL/Vd$$

- The great majority of drugs follow what is called **First-order kinetic**, in which the rate of elimination is directly proportional to the serum drug concentration.

- Some few drugs are eliminated at a fixed rate, regardless of drug concentration. This is referred to as **Zero-order kinetic**.

Elimination half-life ($t_{1/2}$): The time required for the concentration of the drug to reach half of its original value.

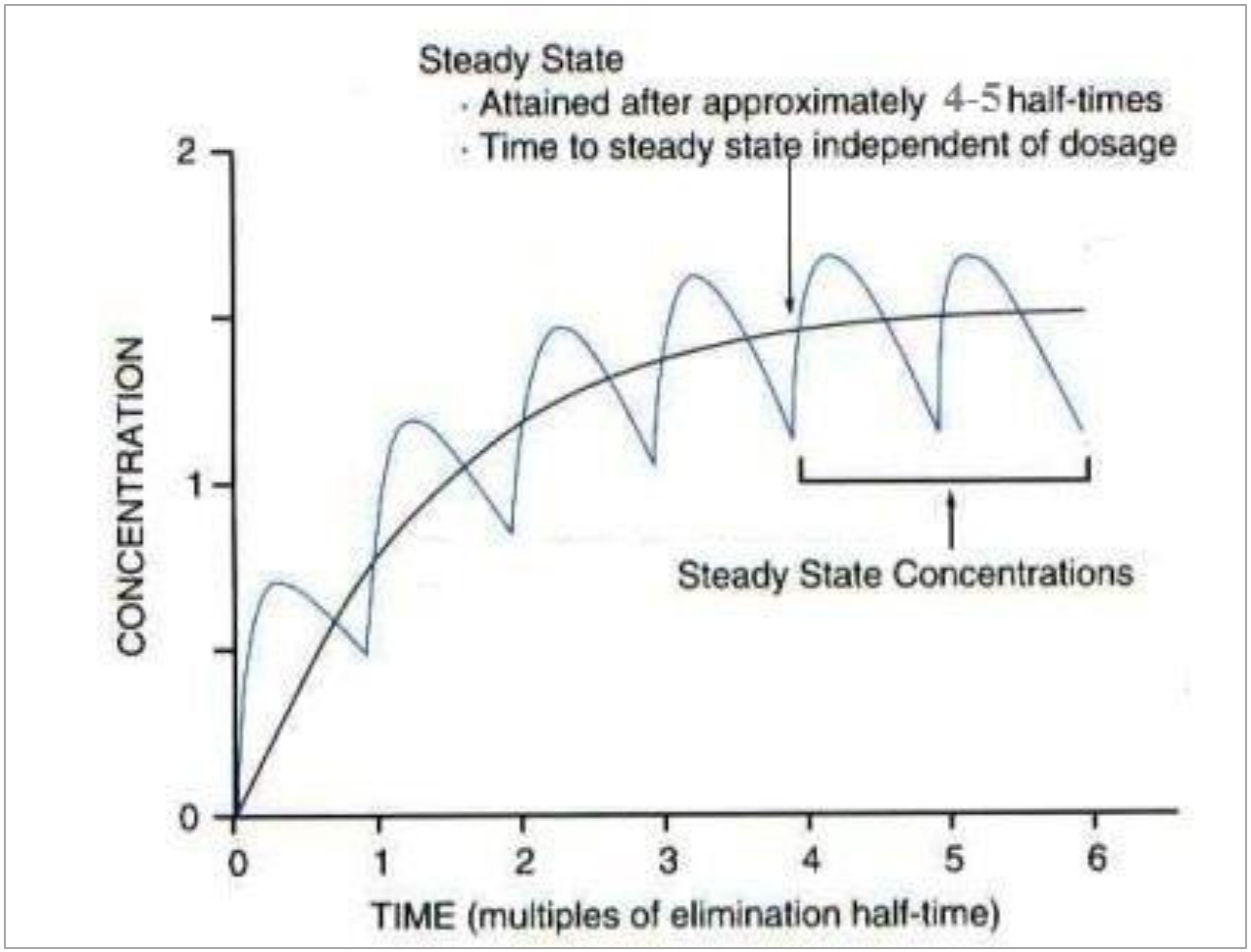
$$T_{1/2}=0.693/K_{el}$$

For drugs that follow first-order kinetic, t1/2 is independent of drug concentration. After starting a new drug, about 5 half lives are required to achieve a steady state concentration of a drug in plasma.

☻ What is Steady State (SS)?

- Rate in = Rate Out (dosing rate= eliminating rate)
- Reached in 4 – 5 half-lives.

☺ Also, 5 half lives are required to eliminate drug from the body.


Steady State
· Attained after approximately 4-5 half-times
· Time to steady state independent of dosage
CONCENTRATION
2
1
0
0
1
2
3
4
5
6
TIME (multiples of elimination half-time)
Steady State Concentrations

- **Ex. If a drug initial concentration was 100 mg/ml in plasma, after the first t1/2 it will be 50 mg/ml, after the second 25 mg/ml, the third 12.5, the forth 6.25, the fifth 3.125.**

- **If the t1/2 was 2 hours then we need (2*5) 10 hours to achieve steady state level and 10 hours to eliminate drug from the body.**

Questions and Answers

Q/ If a drug was given orally to a patient with an initial concentration of 120 mg/L, the bioavailability was 70%, what is the concentration of this drug in plasma after the second half life?

A/

The conc. that reaches the systemic circulation = 120 X 70/100 = 84 mg/ml.

After the first t1/2 = (84/2) = 42 mg/ml.

After the second t1/2 = (42/2) = 21 mg/ml.

Q/A patient take 50mg of a drug that has a half life of 12 hours. What percent of the dose remains in the body 36 hours after the drug is administered?

A/ You're starting with 50 mg.

12 hours later you will have 25 mg.

12 hours later (24 from the beginning) you will have 12.5 mg.

12 hours later (36 from the beginning) you will have 6.25 mg.

6.25 / 50 X 100 = 12.5% remaining.


many
Thanks!