**Clearance**

- Dose rate= clearance x steady-state concentration
  (mass/time) (volume/time) (mass/volume)
  [assuming complete bio-availability & 1st order kinetics]
- If plasma-protein binding saturates, the free-drug concentration increases, hence the clearance increases
- Clearance is the volume of biological fluid from which the drug would need to be completely removed to account for its clearance from the body. It does not represent the amount of drug being removed. Clearance is the rate of elimination normalized to the concentration of the drug in some biological fluid (blood/plasma).
- Clearance= Rate of elimination/ C
  (volume) (mass/time) (mass/volume)
- Clearance=Dose/AUC [ for a single dose of a drug with complete bio-availability and 1st order kinetics]
- Clearance from blood=Clearance from plasma/ drug's blood:plasma concentration ratio
- For drugs with hepatic clearance, limiting factor is the hepatic blood flow in case of high extraction ratio.
- For drugs with intrinsic clearance, enzyme induction/ inhibition does not have much effect on the clearance.

**Volume of distribution**

- Volume of distribution (V) represent the volume of biological fluid which contains the entire amount of drug in the body at the same concentration as it is present in the blood/ plasma.
- V= Amount of drug in body/C
  (vol) (mass) (mass/volume)
- V represents the extent to which the drug is present in extravascular tissues.
- For drugs with extensive tissue binding, V is much larger than the plasma volume, whereas for drugs with extensive plasma protein binding, V is equal to the plasma volume.

**Half-life**

- Half-life ($t_{½}$) =0.693 x $V_{ss}$/CL
- As clearance decreases, half-life would also increase.

**Bioavailability**

- Bio-availability (F) is the fraction of the drug which is absorbed and avoids 1st pass metabolism.
- F x Dosing Rate= Clearance x Steady-state concentration
- F varies between 0-1
- Loading dose rate= Target plasma concentration x $V_{ss}$/F
- Loading dose rate depends on V and F, but not on CL, whereas, the maintenance dose rate depends on CL , F and V.