

Pharmacokinetics:

Distribution of Drugs (Part-2)

VPT: Unit I; Lecture-14
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VOLUME OF DISTRIBUTION

Apparent Volume of Distribution (Vd):

- ✓ It is defined as the fluid volume that is required to contain the entire drug in the body at the same concentration measured in the plasma.
- ✓ It is calculated by dividing the dose that ultimately gets into the systemic circulation by the plasma concentration at time zero (C_0).

$$Vd = \frac{\text{Amount of drug in the body}}{C_0}$$

- ✓ Although Vd has no physiologic or physical basis, it can be useful to compare the distribution of a drug with the volumes of the water compartments in the body.

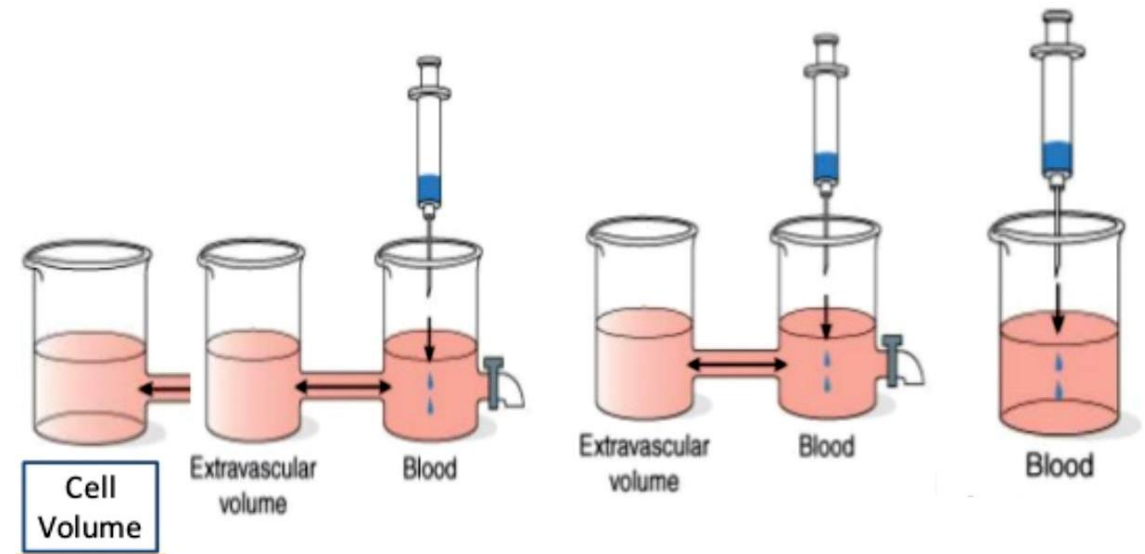
Volume of Distribution

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1. Distribution into the water compartments in the body:

- ✓ Once a drug enters the body, it has the potential to distribute into any one of the three functionally distinct compartments of body water or to become sequestered in a cellular site.

Water compartments in the body:

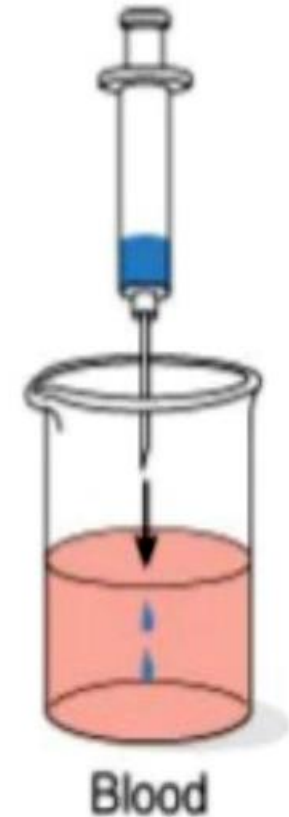


Volume of Distribution

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(i). Plasma compartment

- ✓ If a drug has a high molecular weight or is **extensively protein bound**, it is too large to pass through the slit junctions of the capillaries and, thus, is effectively trapped within the plasma (vascular) compartment.
- ✓ As a result, it has a **low V_d** that approximates the plasma volume, or about 4 L in a 70-kg individual. **Heparin** shows this type of distribution.

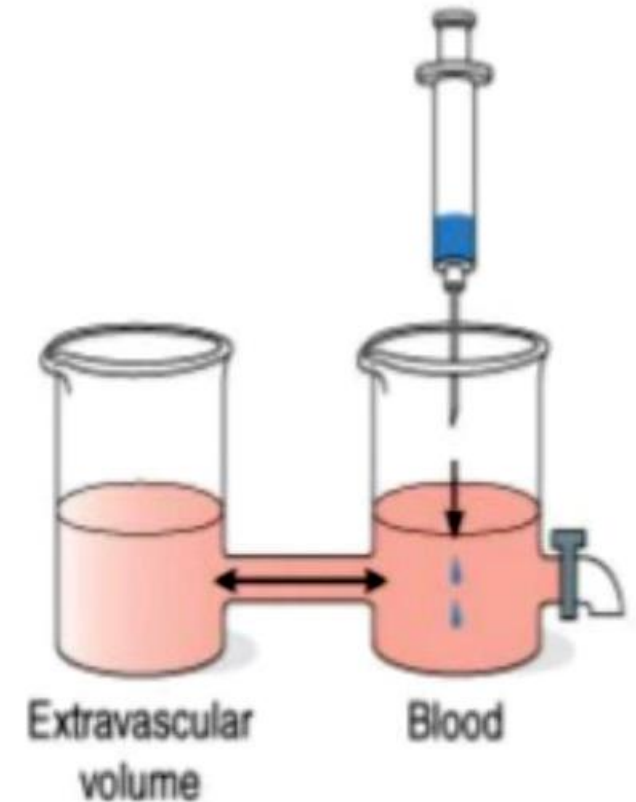


Volume of Distribution

contd...

(ii). Extracellular fluid

- ✓ A low molecular weight, hydrophilic drug will pass through the endothelial slit junctions of the capillaries into the interstitial fluid. However, hydrophilic drugs cannot move across the lipid membranes of cells to enter the intracellular fluid.
- ✓ V_d will constitute the extracellular fluid (about 20% of body weight or 14 L in a 70-kg individual).
- ✓ **Aminoglycoside antibiotics** show this type of distribution.

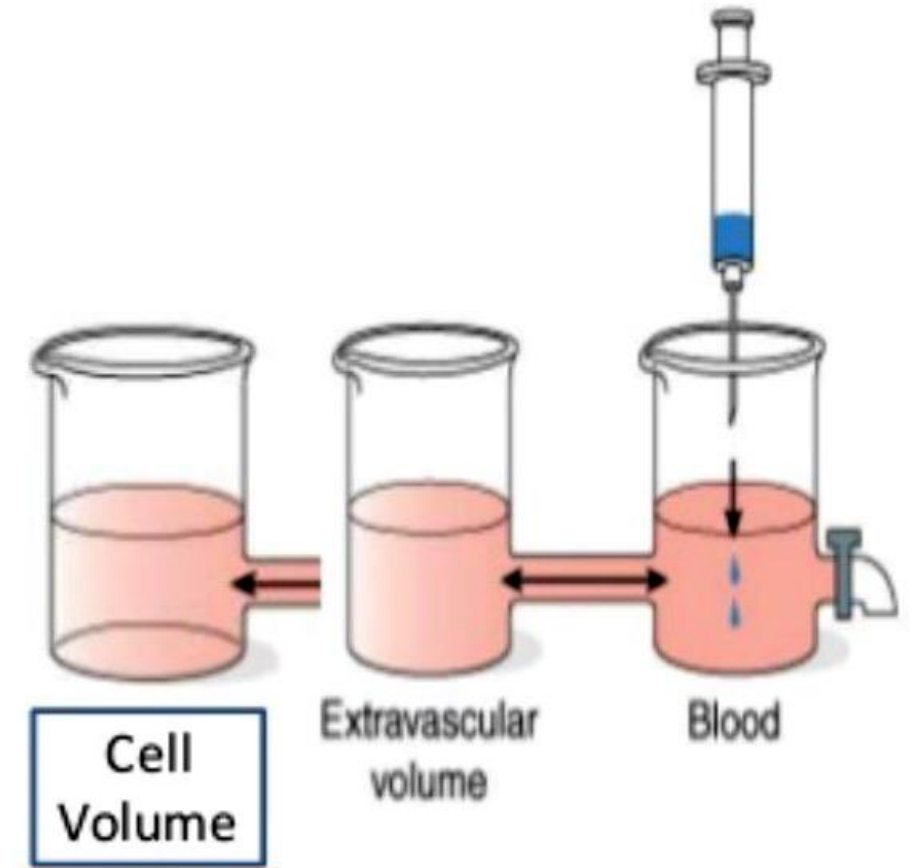


Volume of Distribution

contd...

(iii). Total Body Water

- ✓ If a drug has a **low molecular weight** and has **enough lipophilicity**, it can move into the interstitium through the slit junctions and pass through the cell membranes into the intracellular fluid.
- ✓ These drugs distribute into a volume of about **60% of body weight** or about 42 L in a 70-kg individual.
- ✓ **Ethanol** exhibits this apparent V_d .



REDISTRIBUTION

- ✓ Highly lipid soluble drugs given i.v. or by inhalation initially get distributed to organs with high blood flow, e.g. brain, heart, kidney etc.
- ✓ Later, less vascular but more bulky tissues (muscle, fat) take up the drug - plasma concentration falls and the drug is withdrawn from these sites. If the site of action of the drug was in more of the highly perfused organs, **redistribution results in termination of drug action.**
- ✓ Greater the lipid solubility of the drug, faster is its redistribution.
- ✓ Anaesthetic action of thiopentone is terminated in few minutes due to redistribution.

Thank You

