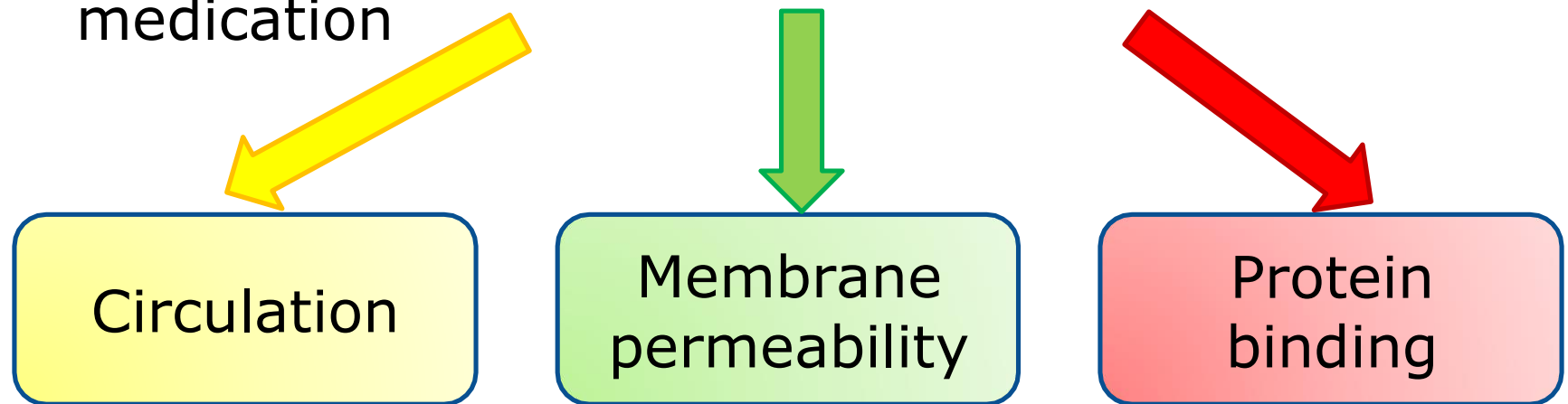


Distribution

- After a medication is absorbed, it is distributed within the body to tissues and organs and ultimately to its specific site of action
- Rate and extent of distribution depend on the physical and chemical properties of medications and the physiology of the person taking the medication



- **Apparent volume of distribution (aVd) :-** is the hypothetical volume of body fluid into which a drug is uniformly distributed at a concentration equal to that in plasma, assuming the body to be a single compartment.

$$aV_d = \frac{\text{Total amount of drug in the body}}{\text{Concentration of the drug in plasma}}$$

Factors affecting drug distribution / Vd

Physicochemical properties of the drug: Lipid soluble and unionized form of drugs readily cross the cell membrane and are widely distributed

e.g.. lignocaine, propranolol, tricyclic antidepressants etc.

Drugs like heparin (strongest acid in the body) is confined only to intravascular compartment as it exists in ionized form.

Plasma protein binding:

- Acidic drugs bind to albumin, Basic drugs bind to α_1 acid glycoprotein etc

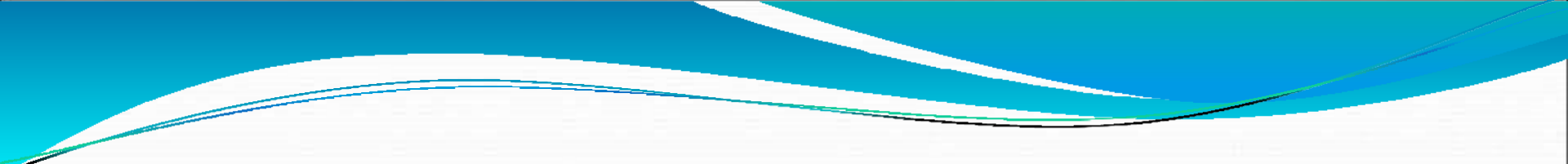
Clinical importance of Plasma protein binding:

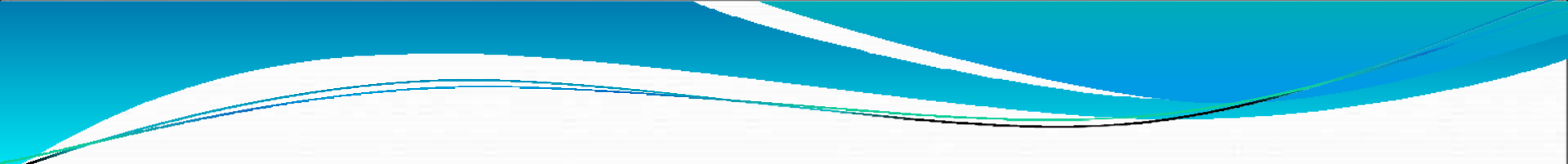
- Free form \rightleftharpoons Bound form

Free form – Pharmacologically active

Bound form - Pharmacologically inactive,
acts as a “temporary store” of the drug

- Plasma protein binding favours drug absorption.
- Drugs which are highly bound to plasma proteins have a low volume of distribution.
- Plasma protein binding delays the metabolism of drugs.
- Bound form is not available for filtration at the glomeruli, hence delays its excretion.

- 
- Highly protein bound drugs have a longer duration of action.
 - In cases of poisoning, highly plasma protein bound drugs are difficult to be removed by Hemodialysis.

- 
- Plasma protein binding can cause displacement interactions
 - More than one drug can bind to the same site on albumin. The drug with higher affinity will displace the one having lower affinity and may result in a sudden increase in the free concentration of the drug

- **Disease states:**

Eg: In CHF, the V_d of some drugs can increase **due to increase in ECF volume** or it could **decrease due to reduced perfusion of tissues**.

- **Fat: lean body mass ratio:** If the ratio is high, fat acts as a **reservoir for certain drugs**

Redistribution

- Highly lipid soluble thiopentone → IV administration immediately gets distributed to areas of high blood flow - brain → general anaesthesia.
- In few minutes, it **re crosses the BBB gets distributed to less perfuse tissues** such as muscle, adipose tissue → termination of action Thiopentone
- Has a very short duration of action (5-10 min) and is used for induction of general anaesthesia.

