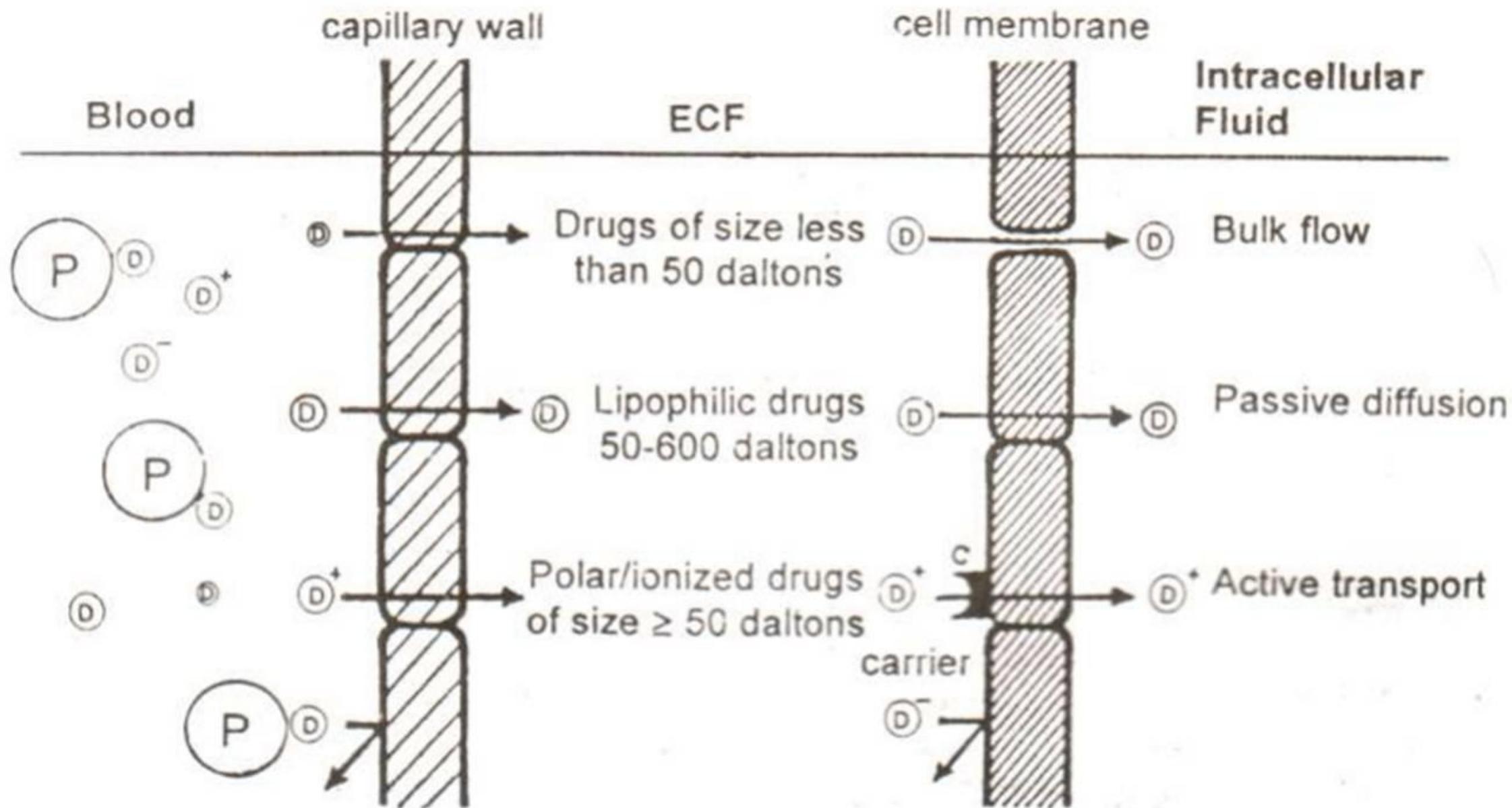


DRUG DISTRIBUTION



- Drug distribution: refers to the reversible transfer of a drug between **the blood** and the **extra vascular fluids and tissues** of the body (for example, fat, muscle, and brain tissue).



Significance :-

Pharmacological action of drug depends upon its concentration at the site of action

Thus distribution plays important role in

- Onset of Action**
- Intensity of Action**
- Duration of Action**

Factors Affecting Drug Distribution

- Distribution of drugs throughout the body fluid is not equal.

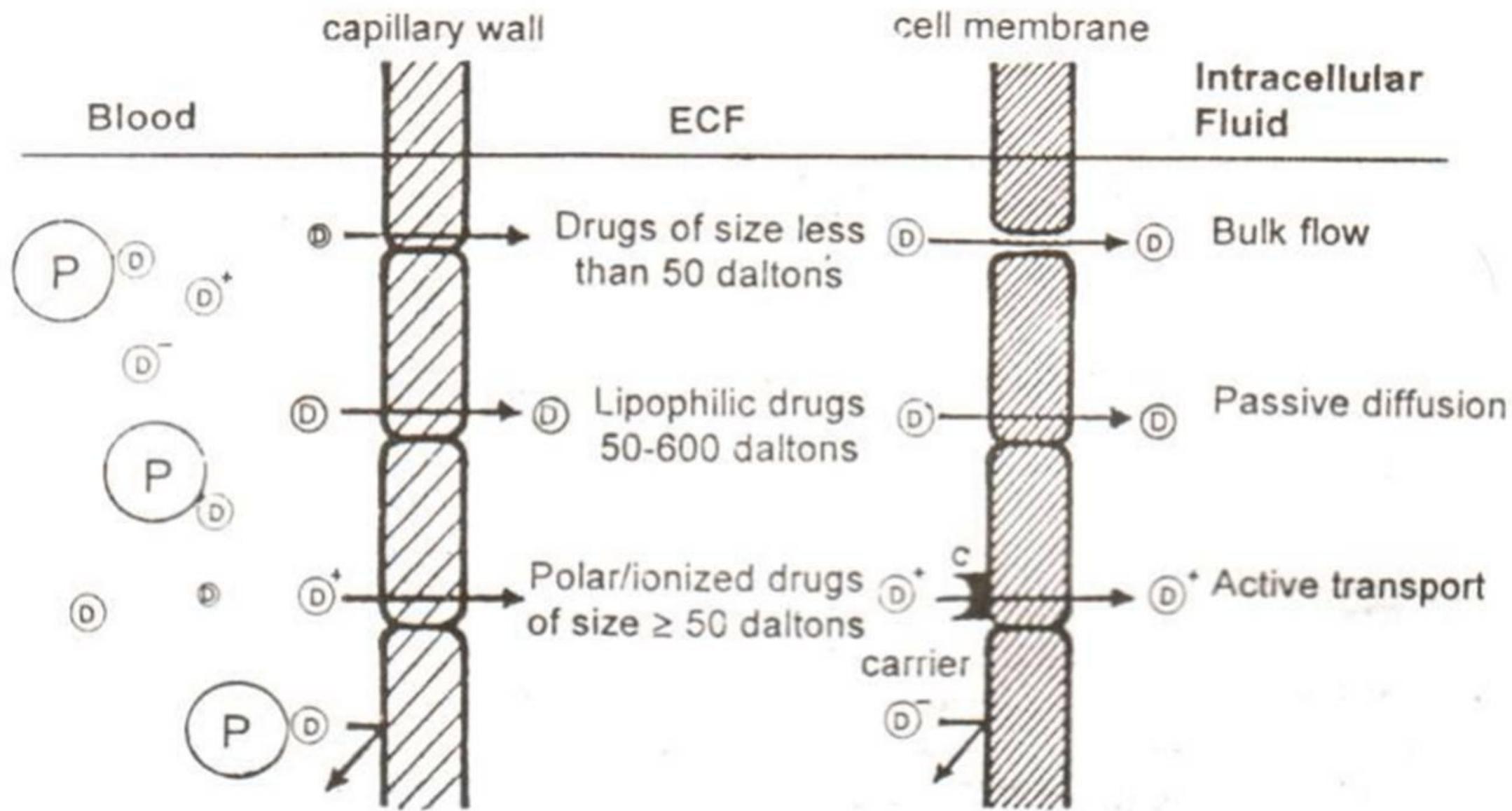
The reasons for unequal distribution are:

- § Drug factors
- § pH of the media
- § Regional blood flow
- § Drug binding...protein / tissue
- § Membranes **and Others**

Drug factors

- Lipid solubility of the drugs
- Molecular weight of the drugs
- pKa of drug

pH of the media



Blood flow/Perfusion rate

Organ perfused	Blood flow (mL/min)	Organ mass (kg)	Normalized blood flow (mL/min/kg)
Liver	1700	2.5	680
Kidney	1000	0.3	3333
CNS	800	1.3	615
Myocardium	250	0.3	833
Fat	250	10	25
Other (muscle...)	1400	55.6	25
total	5400	70	

Greater the blood flow, faster the distribution

Drug binding

Binding

- Plasma protein binding of the drugs
- Tissue binding property of the drugs

BINDING OF DRUGS TO PLASMA PROTEINS

- The binding of drug to plasma protein is **reversible**
 - The **extent** or **order** of binding of drugs to various plasma proteins is:

Albumin > α_1 -Acid Glycoprotein > Lipoproteins > Globulins

Acidic drugs	Basic drugs	acidic, basic, neutral drug	steroidal drugs and fat soluble vitamin, ferrous ion
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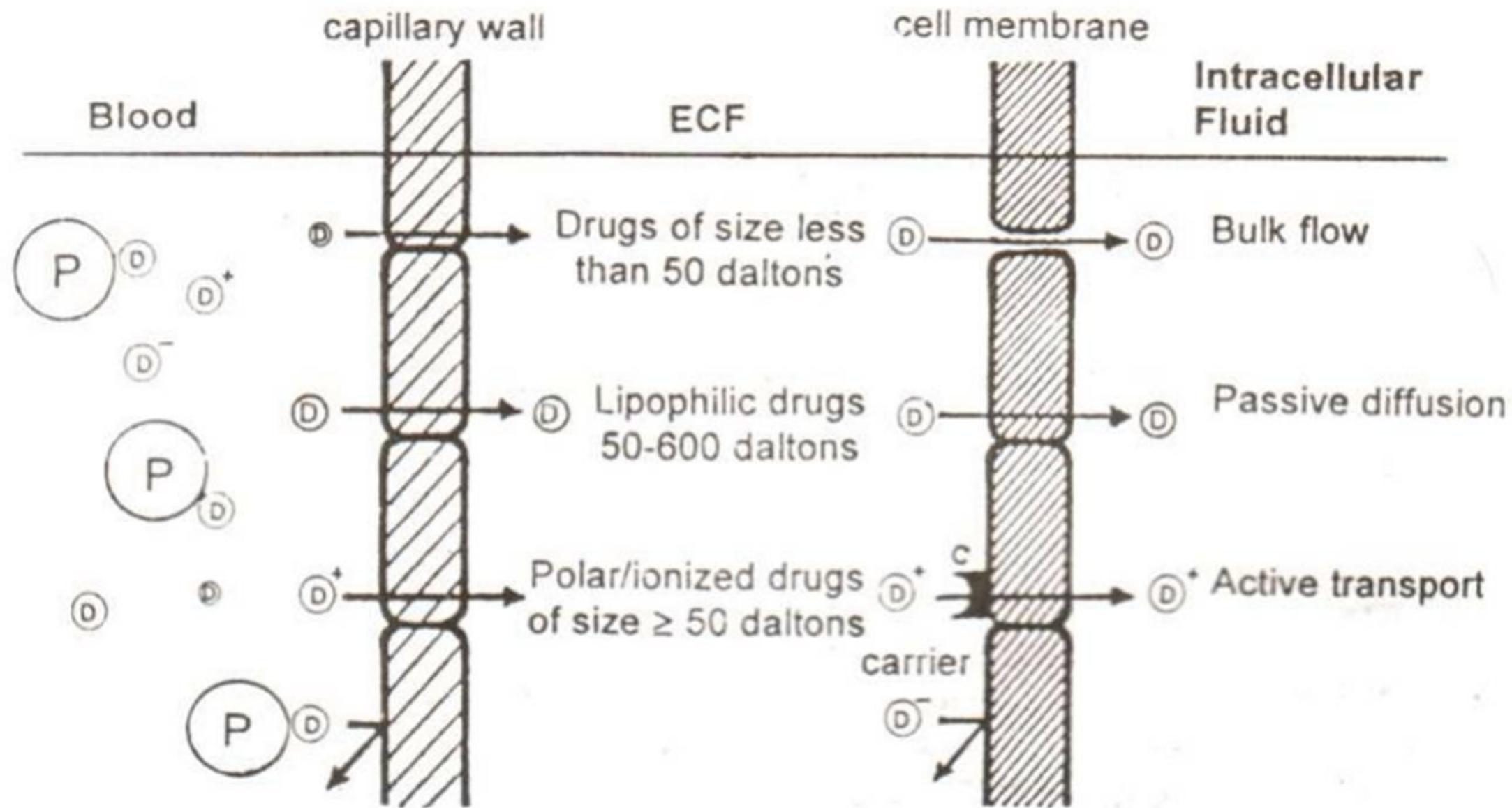
Binding of drug to extra vascular tissue proteins

- Tissue–drug binding result in localization of drug at specific site in body and serve as **reservoir**
- As binding **increases** it also **increase** bio–logical half life.
- **Irreversible** binding leads to drug **toxicity**.
(carbamazepin–autoinduction)
- **liver > kidney > lungs > muscle > skin > eye > bone > Hair, nail**

Binding with blood cells

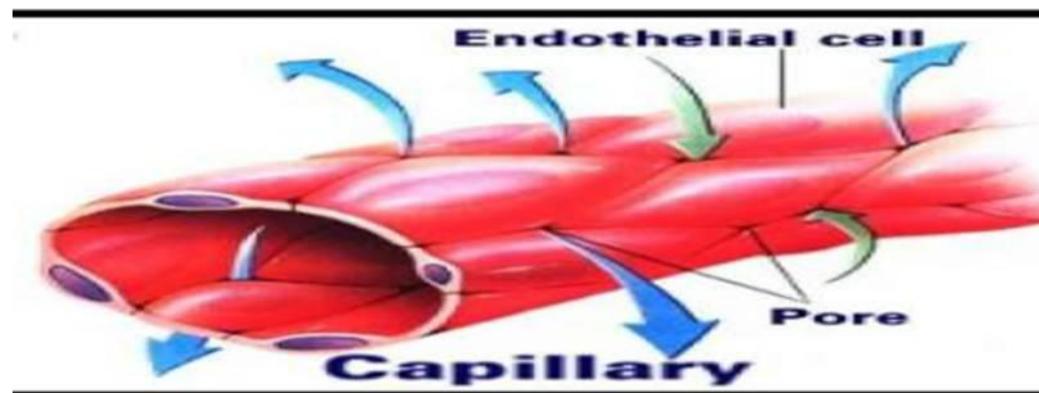
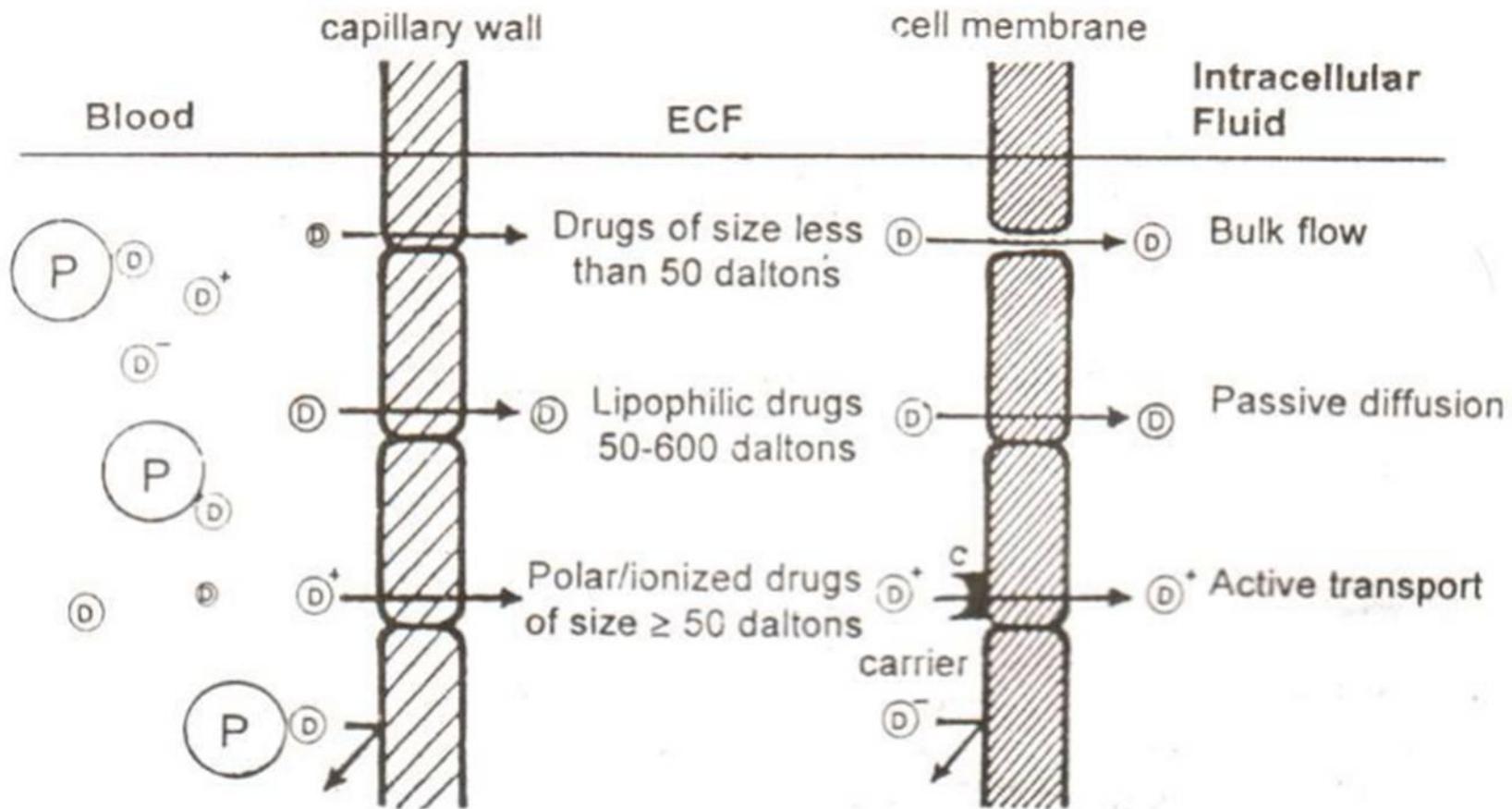
- The drugs mostly bind with the RBC.
- Hb: drugs like phenytoin, phenobarbitol.
- Carbonic anhydrase: acetazolamide.
- Cell membrane of RBC: imipramine.

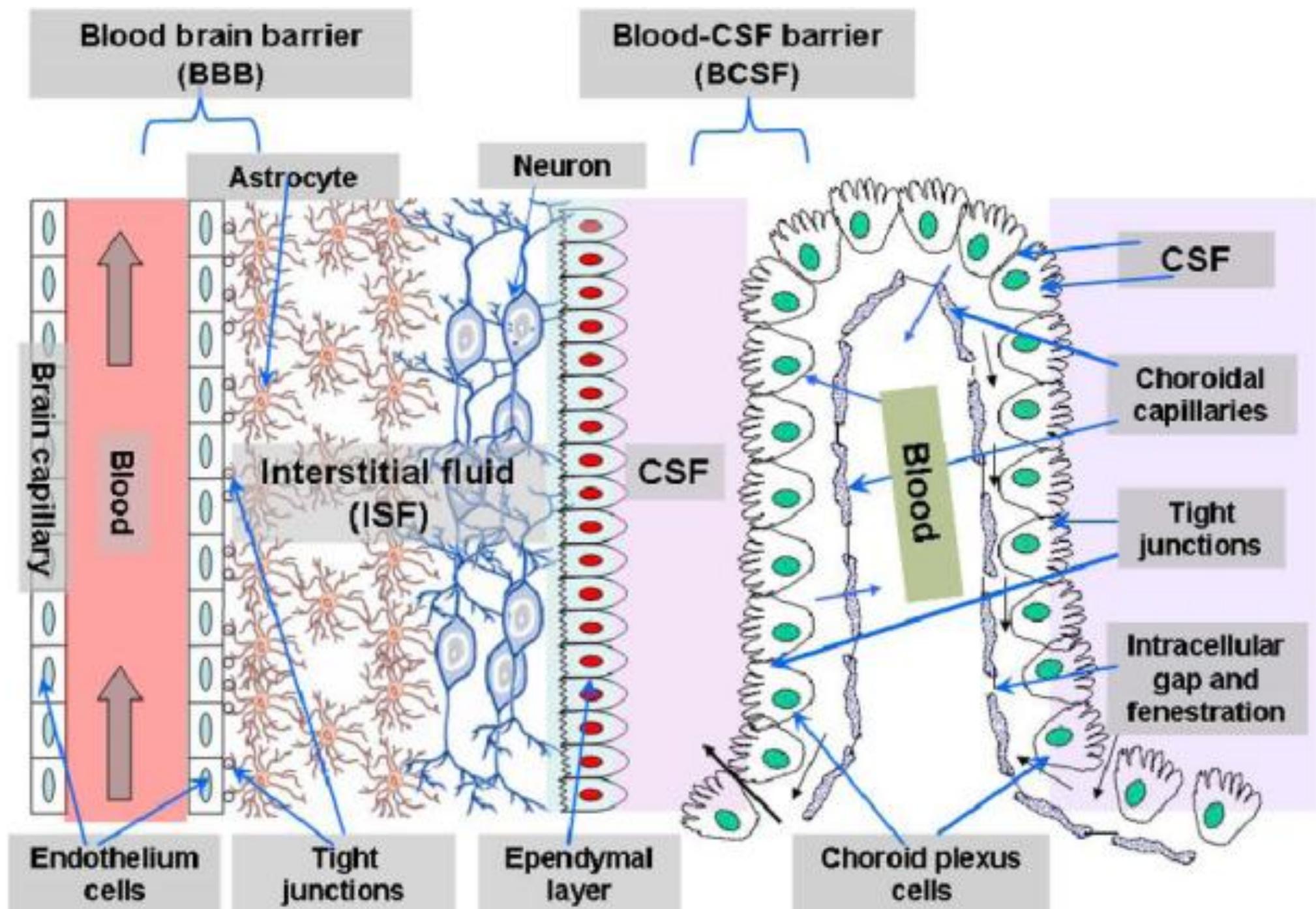
Ex- liver : paracetamol
Lung : Imipramine
Kidney : Heavy metals like lead,mercury.
Skin : Chloroquine
Eye : retinal pigment contain melanin
Hair : Osnicles
Bones : Tetracycline, phenytoin
Fat : DDT, thiopental

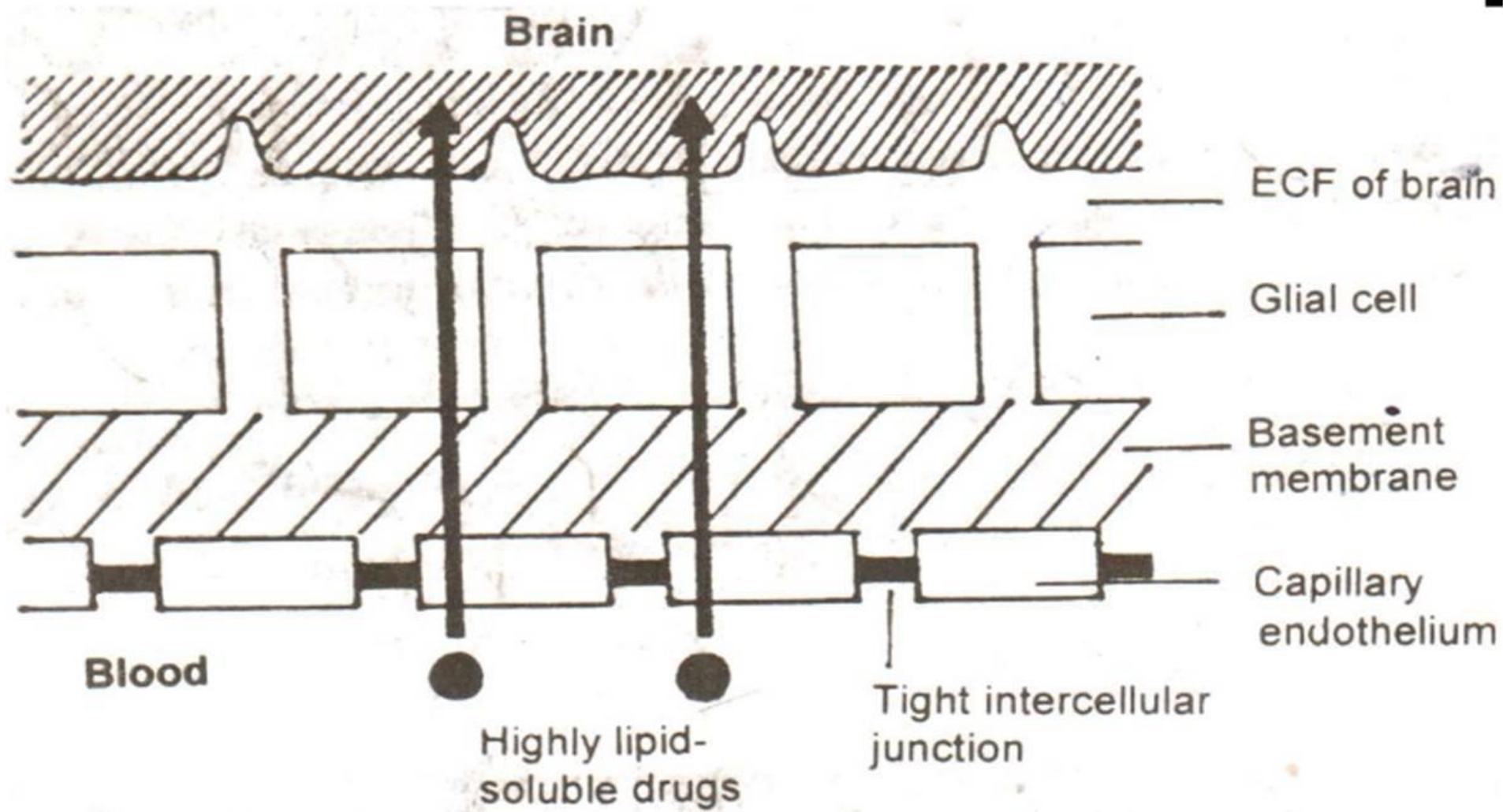


Physiological barriers to Diffusion of Drugs

- **Simple Capillary Endothelial Barrier**
- **Simple Cell Membrane Barrier**
- **Blood Brain Barrier**
- **Blood – CSF Barrier**
- **Blood Placental Barrier**
- **Blood Testis Barrier**







Blood-Brain Barrier

Other factors such as

Age

Pregnancy

Obesity

Disease states

[https://en.wikipedia.org/wiki/Distribution_\(pharmacology\)](https://en.wikipedia.org/wiki/Distribution_(pharmacology))

<https://www.pharmatutor.org/pharmacology/general-pharmacology/distribution-factors.html>

<https://www.msmanuals.com/professional/clinical-pharmacology/pharmacokinetics/drug-distribution-to-tissues>