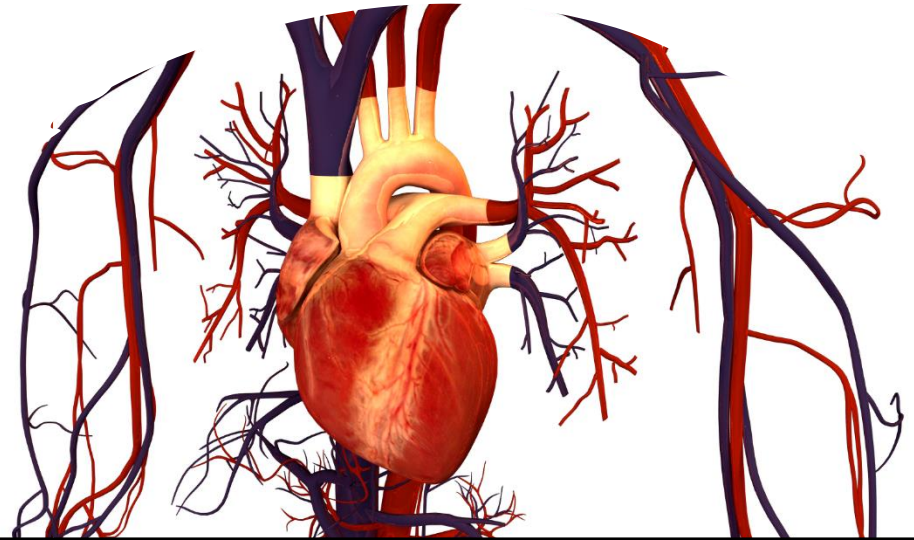
Capillary Circulation



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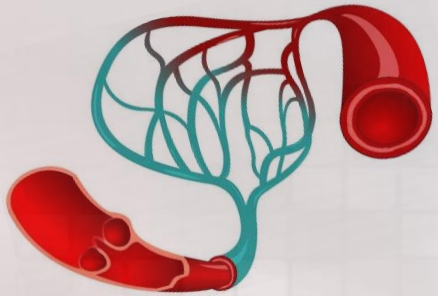


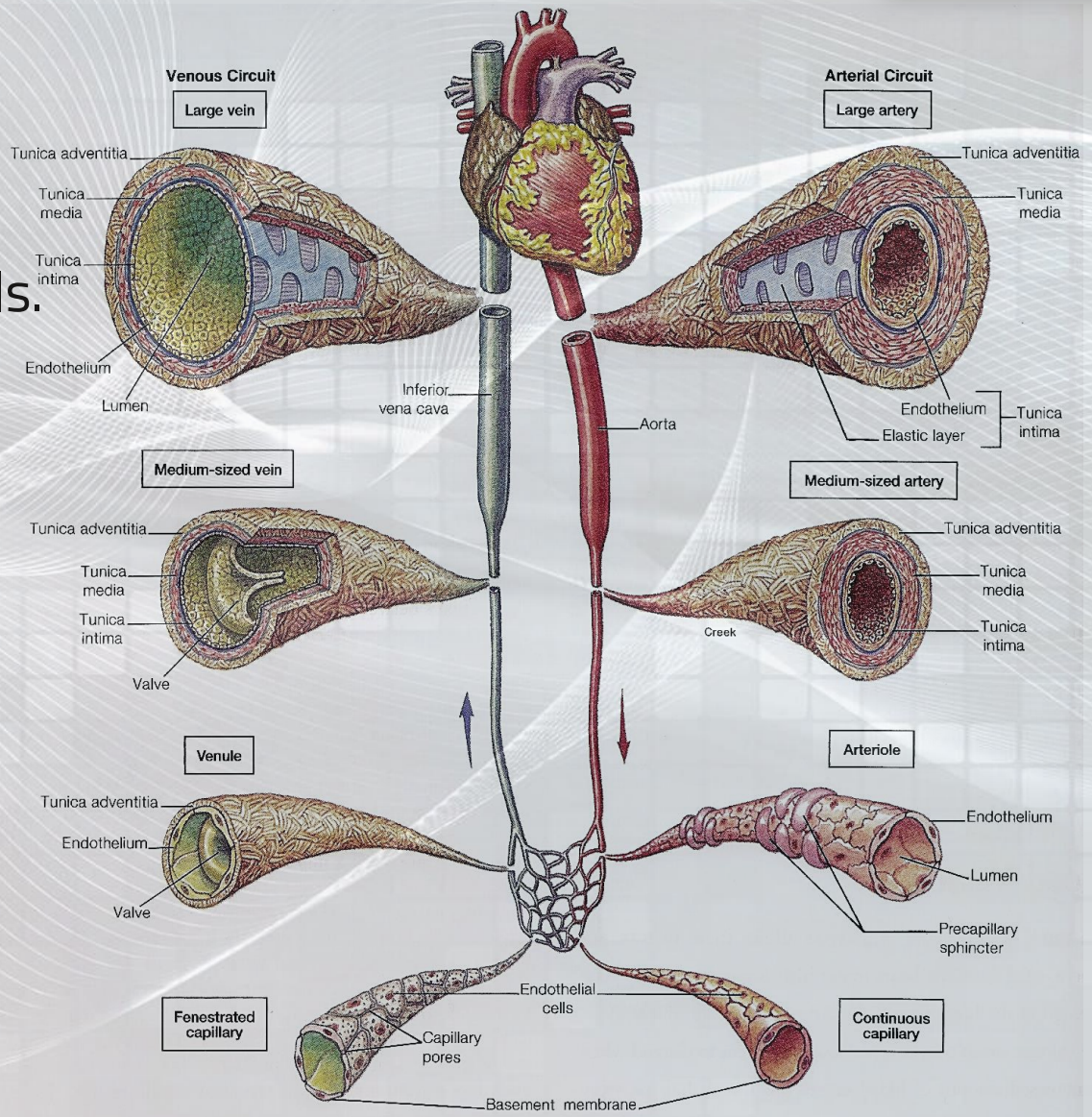
Capillary Circulation

Lecture Outcomes

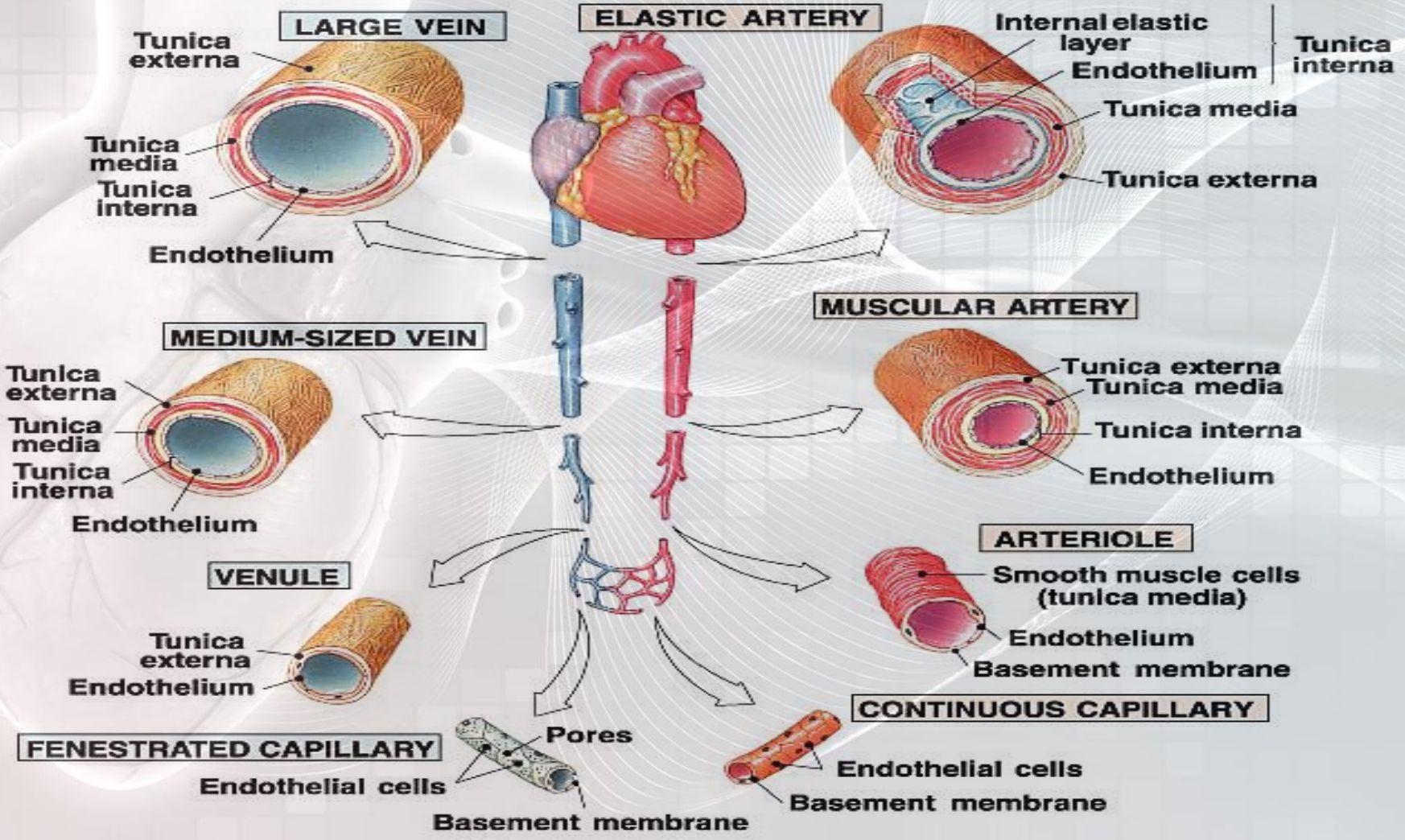
- To identify capillaries & their different types.
- To understand regulation of flow in capillary beds.
- To understand the formation of interstitial fluid & mechanism of edema formation.
- To understand the role of lymphatics.

The Vascular System

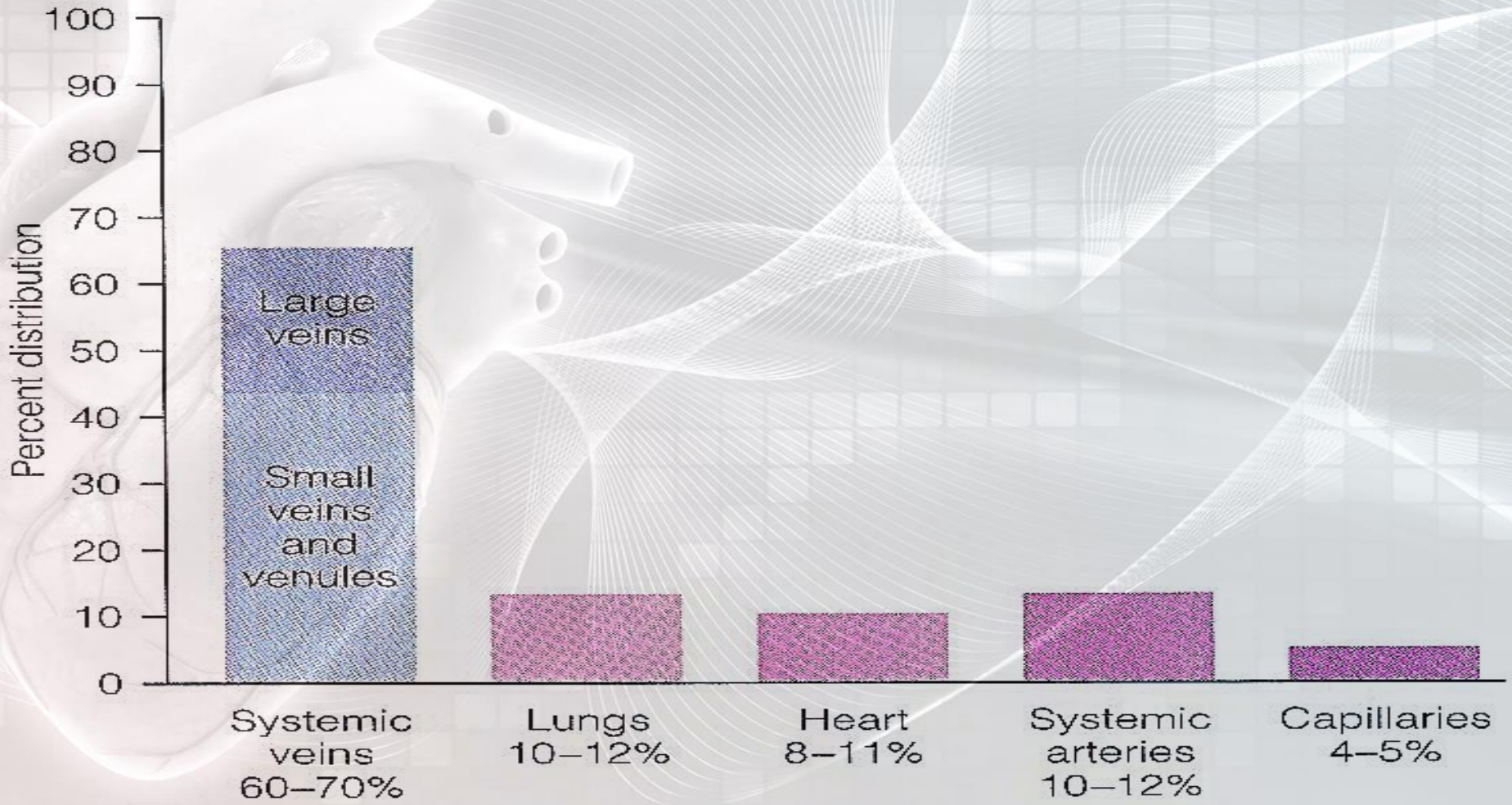
1. **Aorta:** Elastic recoil.
2. **Arteries:** Muscular, low resistance vessels.
3. **Arterioles:** High resistance vessels.
4. **Capillaries: Exchange vessels.**
5. **Venules.**
6. **Veins:** Capacitance vessels.



Comparison of structure of Blood Vessels Wall

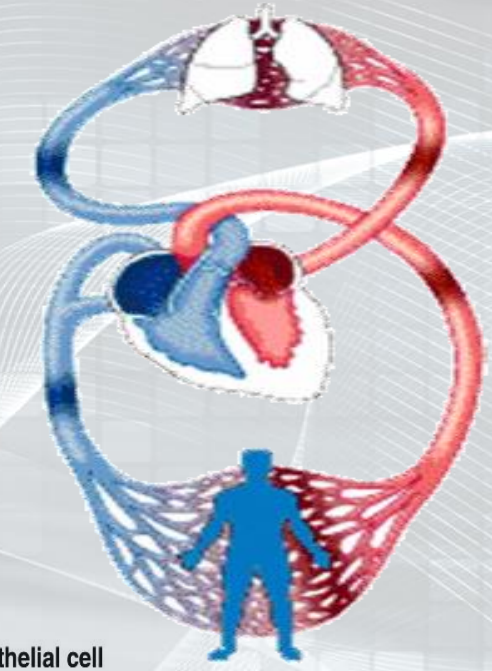


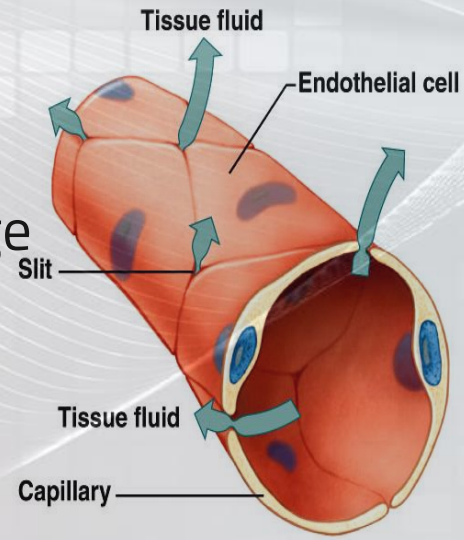
Distribution of Blood Within The Circulatory System: At Rest

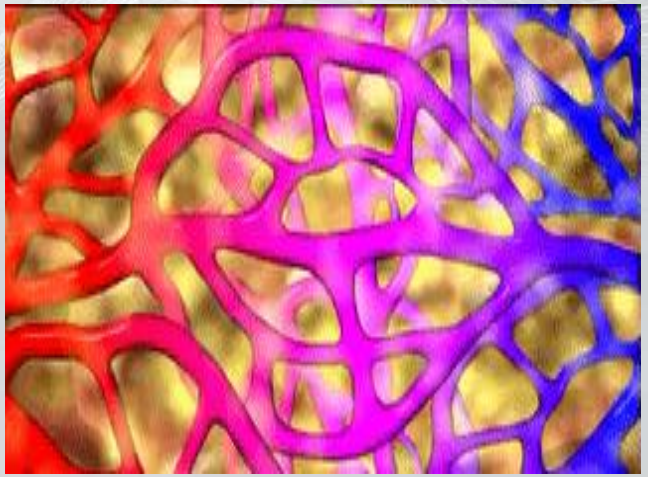


Capillaries (Microcirculatory Vessels)

- Capillaries are the smallest blood vessels in the vascular system.
- There are large in number (over 10 billion) in the body.
- Consists of **ONLY** of the Tunica Interna with a **SINGLE** Layer of endothelial cells.
- Provide direct access to the cells.
- Most permeable.
- Site of exchange with tissue: Permits exchange of nutrients & waste products.
- At rest, 4-5% of circulating blood is present in capillaries.





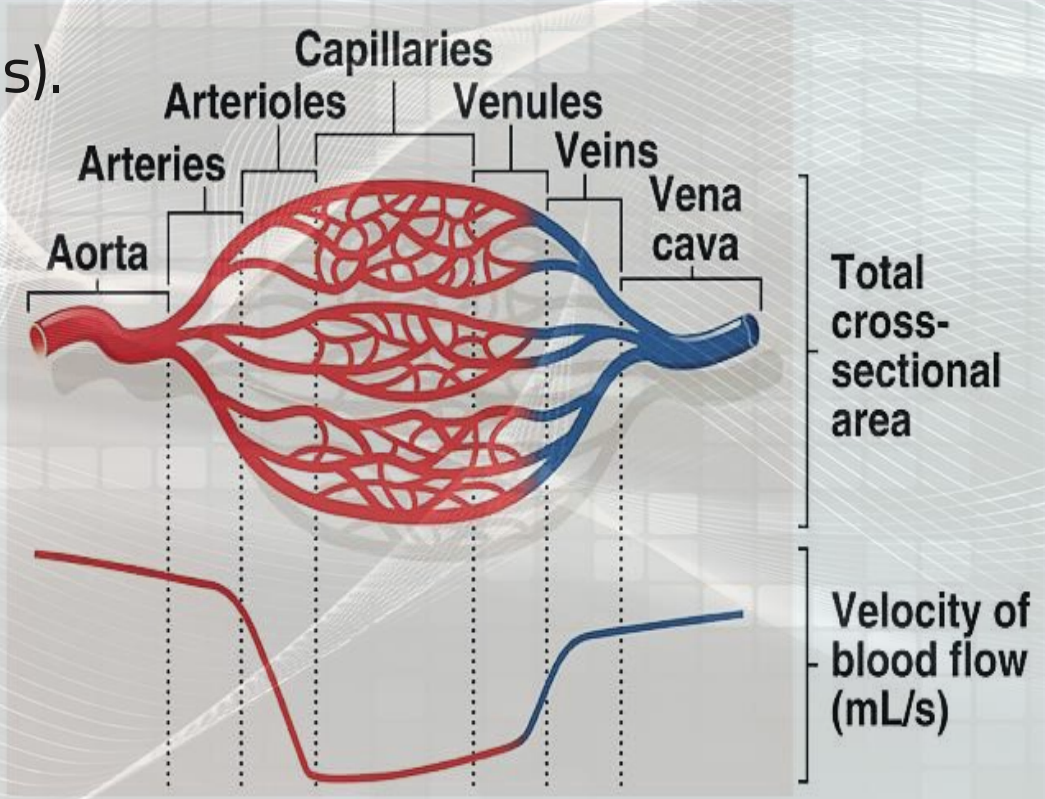


Capillaries Cross-Sectional Area

- Capillary is of 0.5-1mm in length.
- Capillary is very small in diameter (4-9 microns).
  - As the diameter of blood vessel decreases, the total cross-sectional area increases & the velocity of blood flow decreases.

V = Q/A

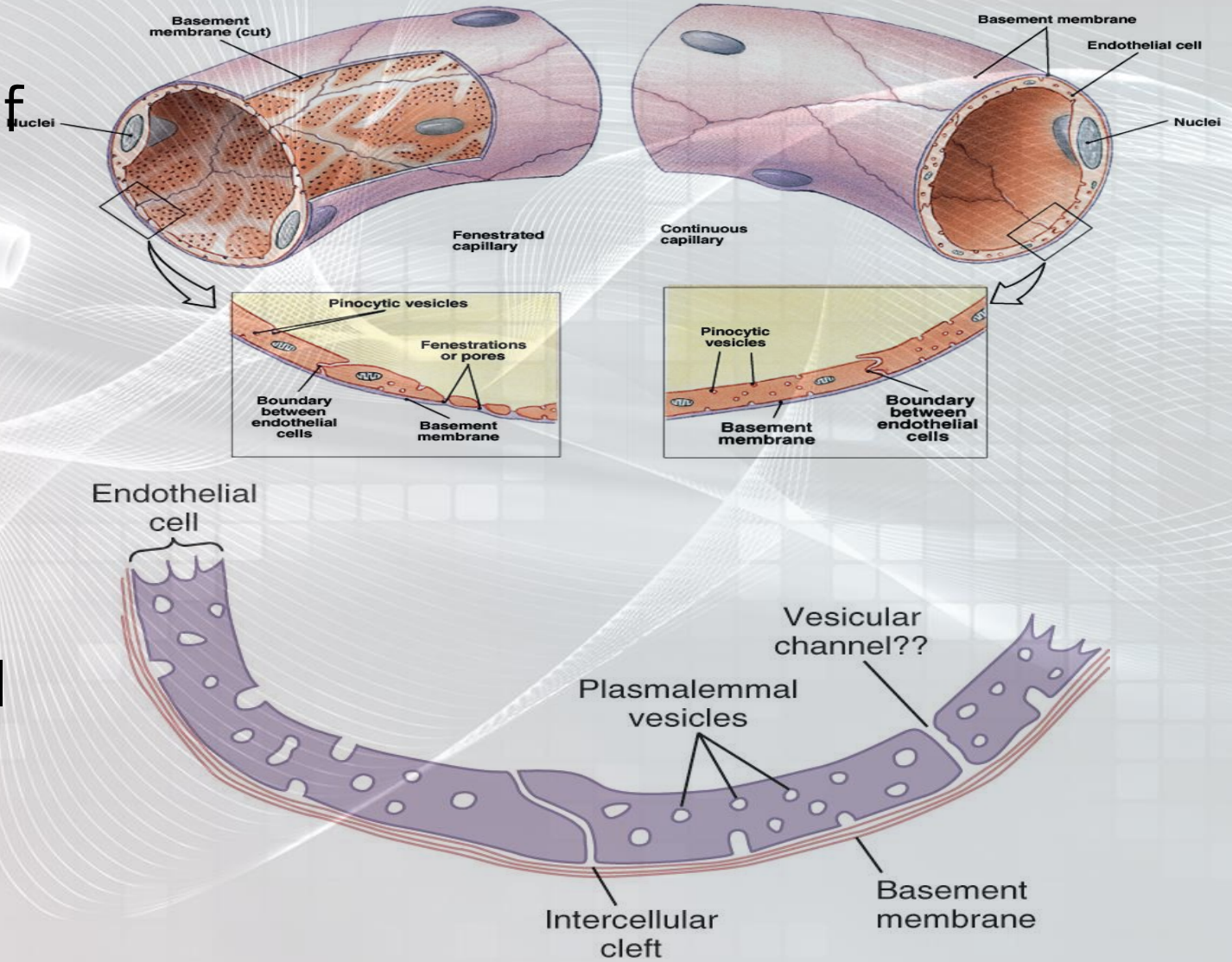
- The total capillary surface area ranges from 700-1000 m^2 of surface area (>3 tennis courts).



V= Velocity; Q= Flow; A= Cross sectional area.

Capillary Wall

- Capillary wall is composed of a single layer of simple squamous epithelia.
- Capillary wall is of 0.5 micrometers in thickness.
- It regulates transfer of fluid from blood to the interstitial fluid space & vice versa.



Types of Capillaries

- Capillaries are classified into (3) types according to their wall permeability.
- Wall permeability is affected by the size & diameter of the pores.

Continuous/ True

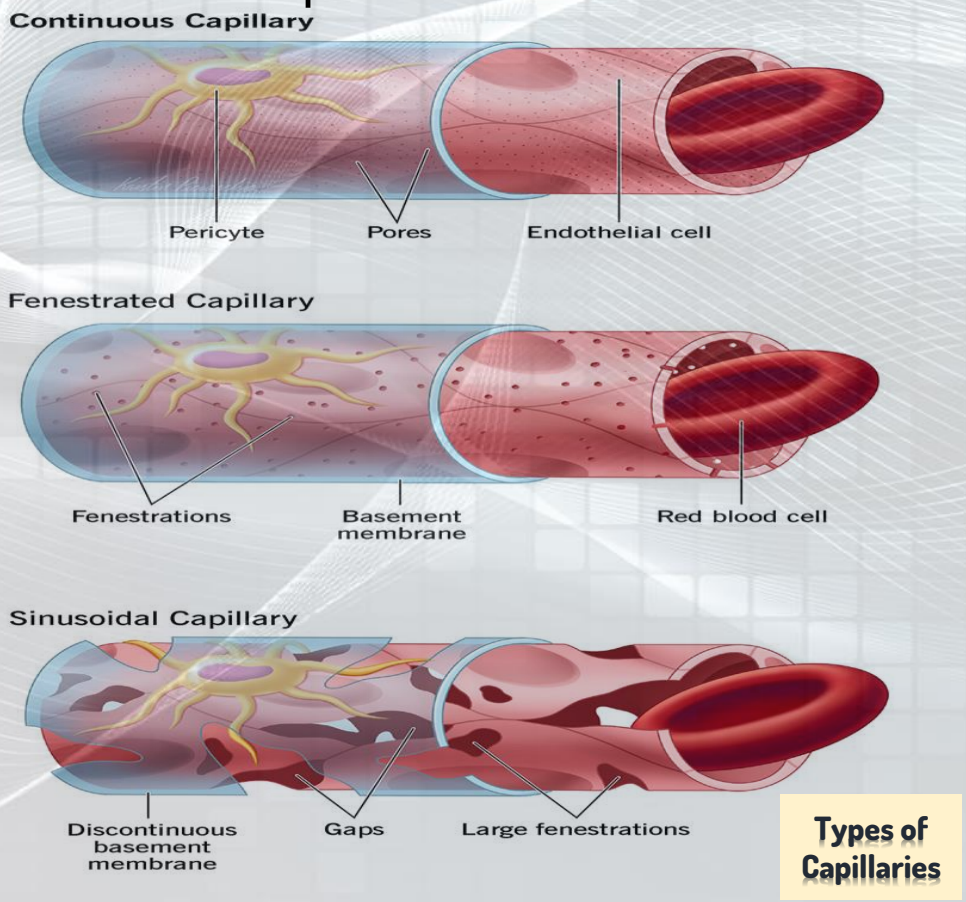
- Do not have fenestrae.
- Allow only very small molecules to pass.
- Found in brain, muscles, lungs & adipose tissue.

Fenestrated

- Have wider pores.
- Allow large substances to pass but not plasma proteins.
- Found in kidney glomeruli, small intestines & endocrine glands.

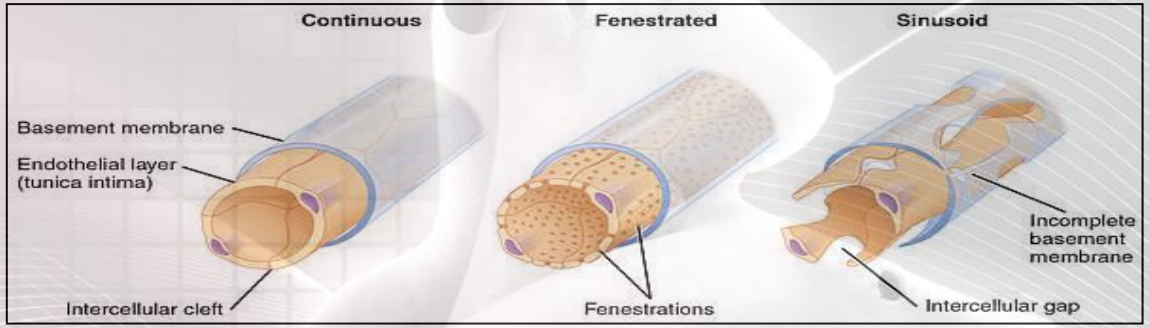
Sinusoidal

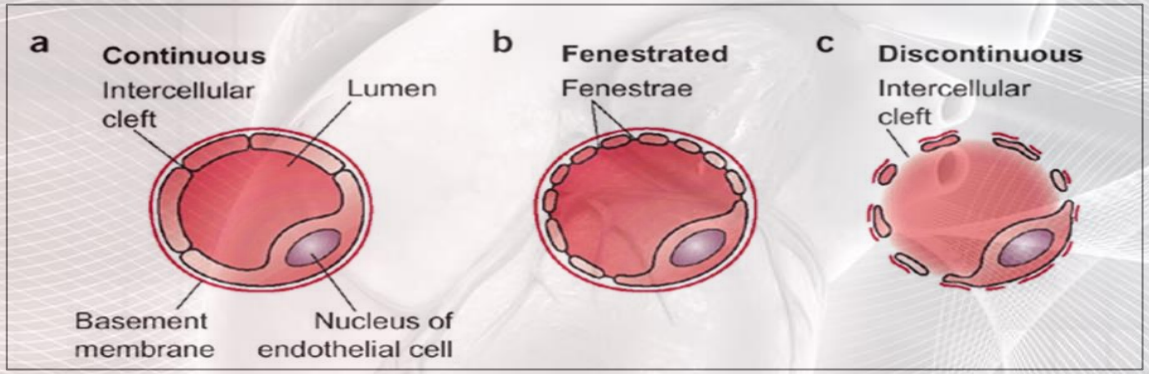
- Large diameter with large fenestrae (wider gaps between the cells).
- The endothelium is discontinuous.
- Found in liver, spleen, bone marrow, lymphoid tissue, & some endocrine glands.

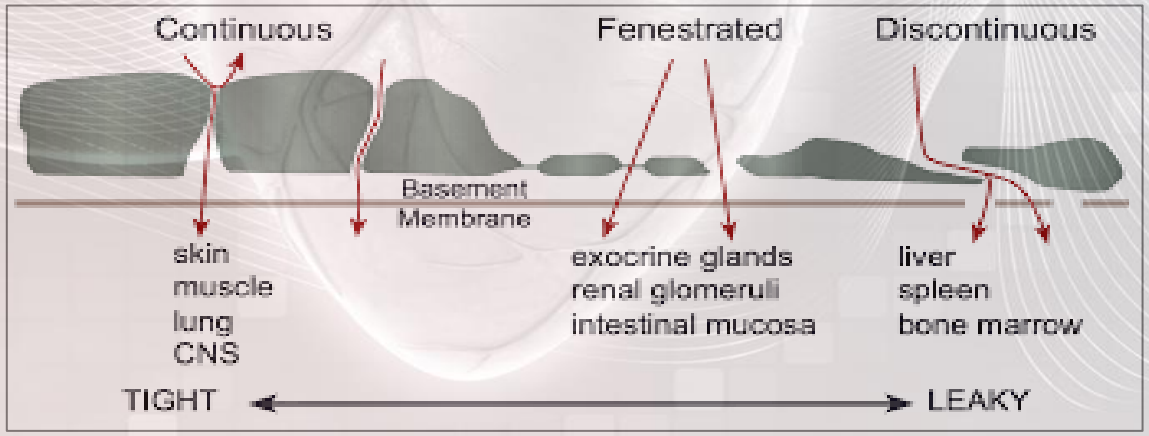


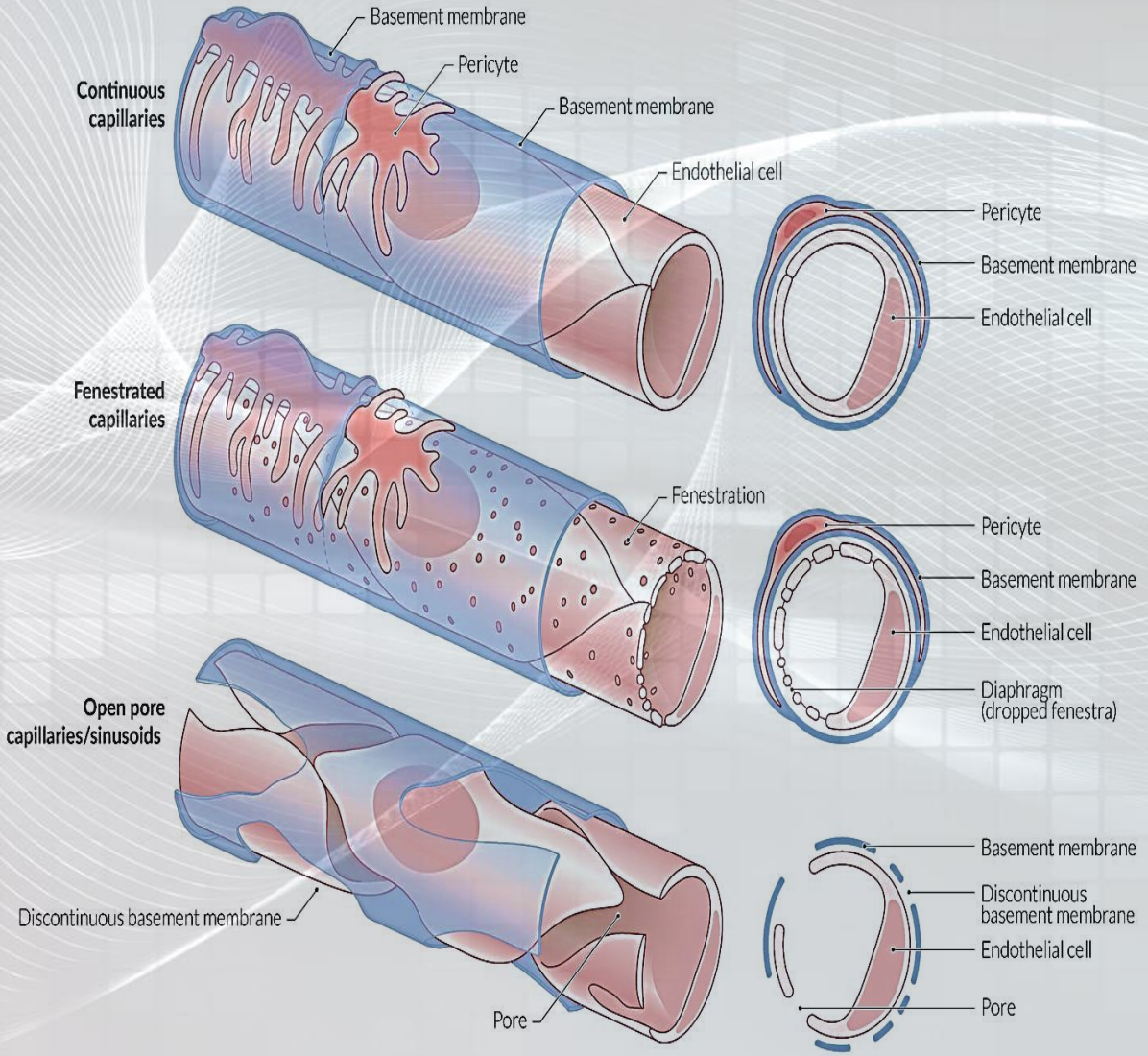
Types of Capillaries

Types of Capillaries









Organ Variability of Capillary Filtration

Brain & Muscle	Small
Subcutaneous Tissue	Moderate
Intestines	Large
Liver & Spleen	**Extremely large**

- **Why is there a difference?**
  Due to their **permeability**.
- **How does the permeability change?**
  By alteration of **pores/clefts size** between the cells.

How does the permeability change?

❑ Factors mediates pore size change:

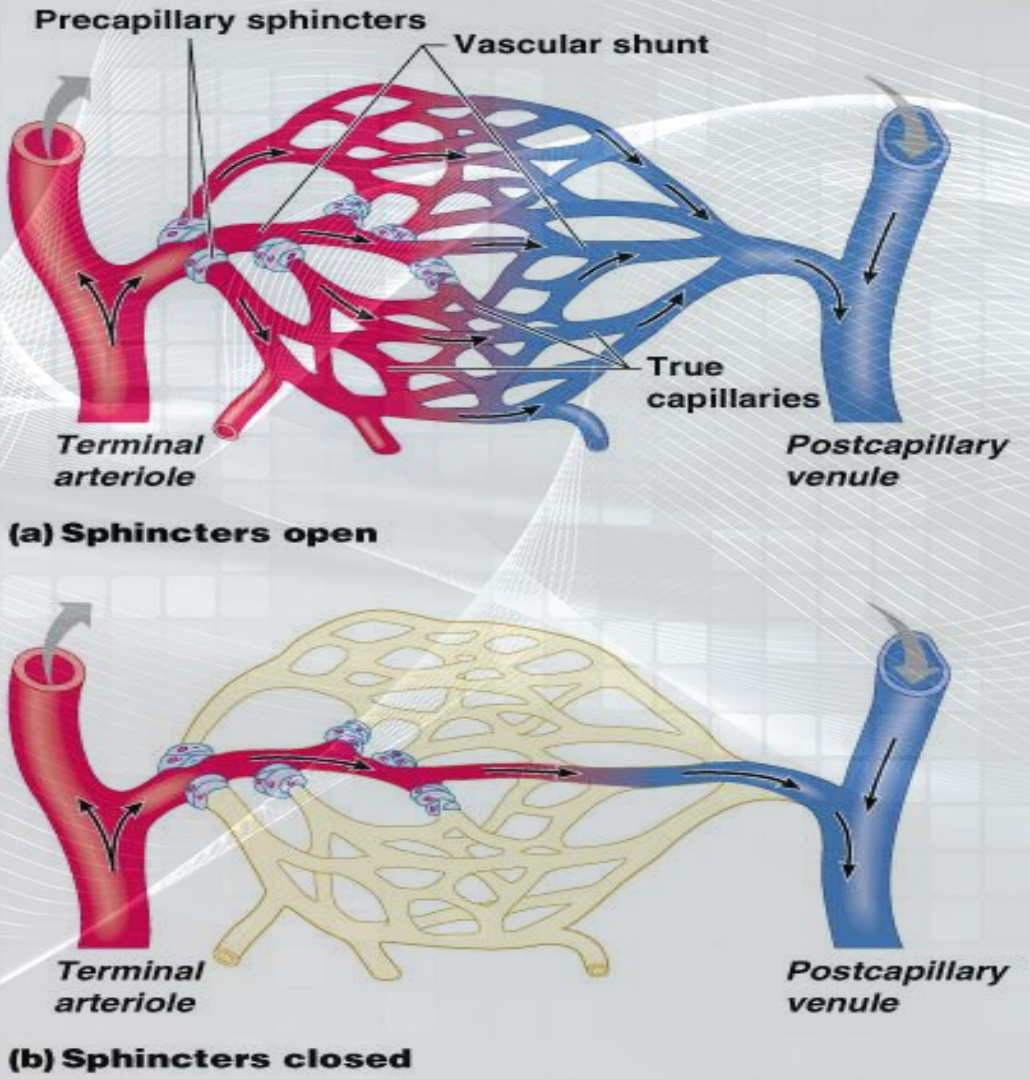
1. **Histamine:**
   - If little = will increase the flow (distends vessel).
   - If a lot = will decrease the arterial blood pressure (anaphylaxis).
2. **Cytokines:** Alters flow/pressure & permeability.
3. **Drugs:** Any drug influencing contraction or dilation of smooth muscle & endothelial permeability.
4. **Nerves:** Sympathetic.
5. **Inflammation:** Stretches the cells apart & increases the cleft size.
   - If too much, can compress the vessels as well.

Functions of Capillaries

- **Exchange vessels between blood & tissues:**
  - Provide direct access to the cells.
  - Most permeable.
  - Transport nutrients & Oxygen from blood to the tissues.
  - Remove CO_2 & cellular waste products from the tissues to the blood.
- **Capillary tone.**
- **Play a metabolic role:** Produce PgI2; Growth factors for blood cells: fibroblast GF, platelet GF; & in the lungs, angiotensin converting enzyme.
  - Inactivation of intercellular messengers.
  - Antithrombotic function.
- **Play a role in temperature regulation:**
  - Blood vessel dilatation (vasodilatation), Increase heat loss across epidermis.
  - Blood vessel constriction (vasoconstriction), Heat conservation across epidermis.

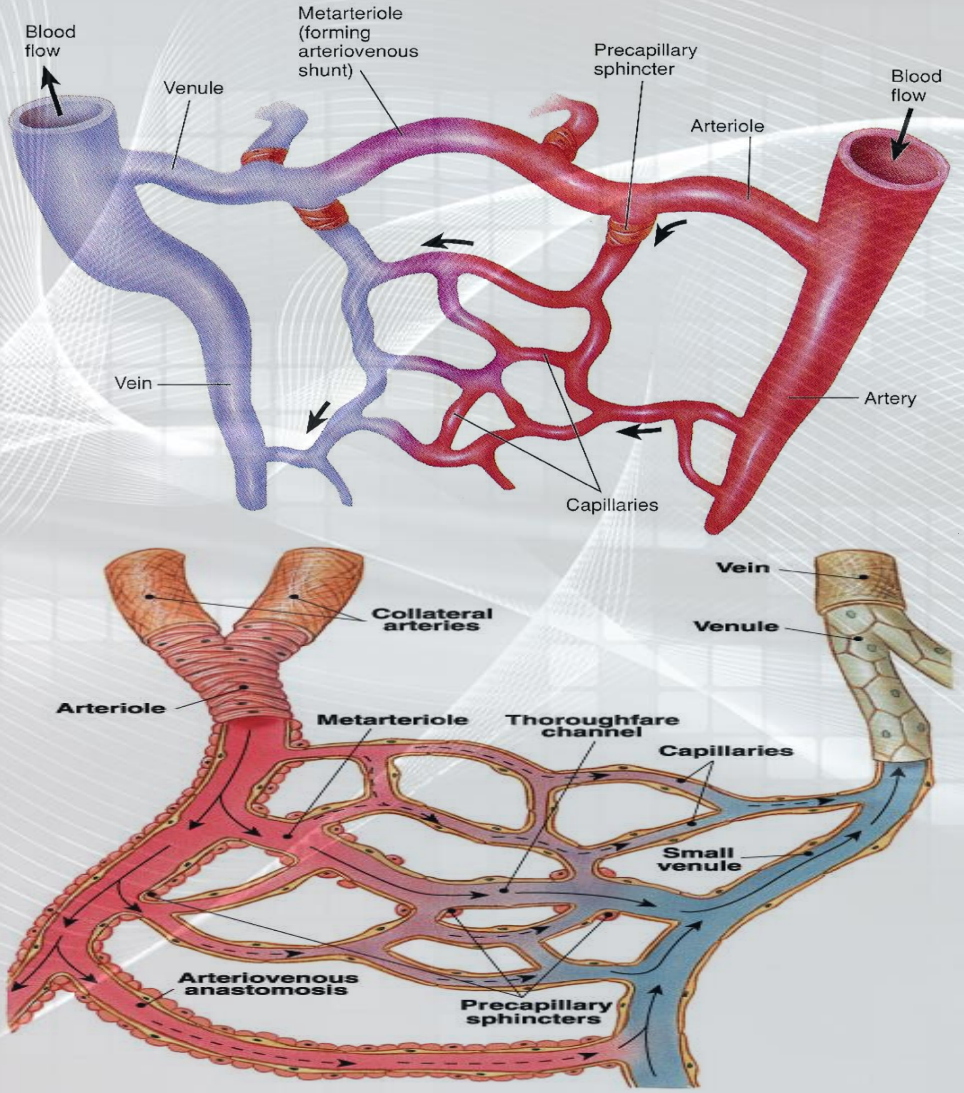
Structure of Capillary Beds (Network)

- **Capillaries are arranged in capillary beds.**
- **Arterioles** divides into a number of **Metarterioles**, which do not have a continuous smooth muscle coat.
- Blood flow through the Metarteriole to enters capillary bed via **Precapillary Sphincters**.
- **Venules** drain capillary network.



Capillary Beds (Network)

- **Capillary beds consist of two types of vessels:**
  - **Vascular shunt** – **Directly connects** an **Arteriole** to a **Venule**.
  - **True capillaries** – **Exchange vessels.**
    - Cross of O_2 & nutrients to cells
    - Cross of CO_2 & metabolic waste products into blood.

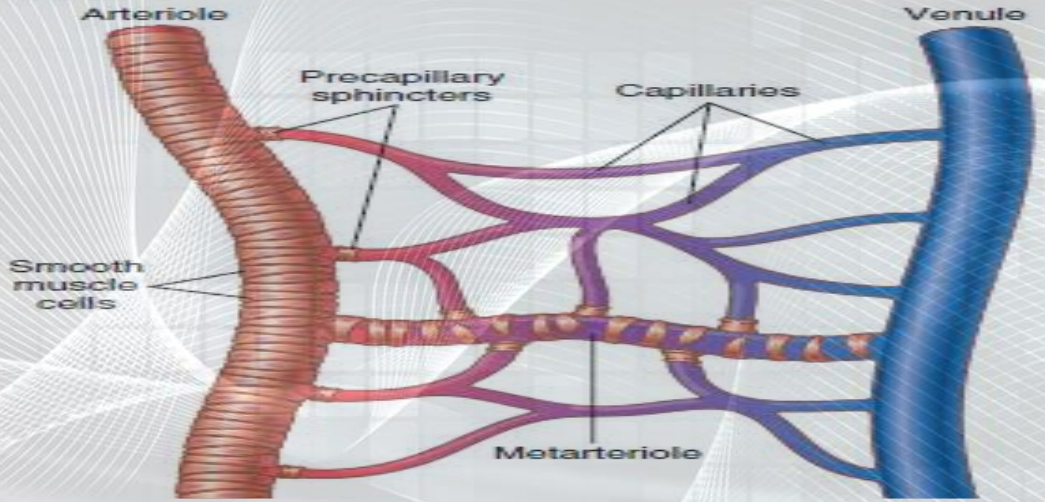


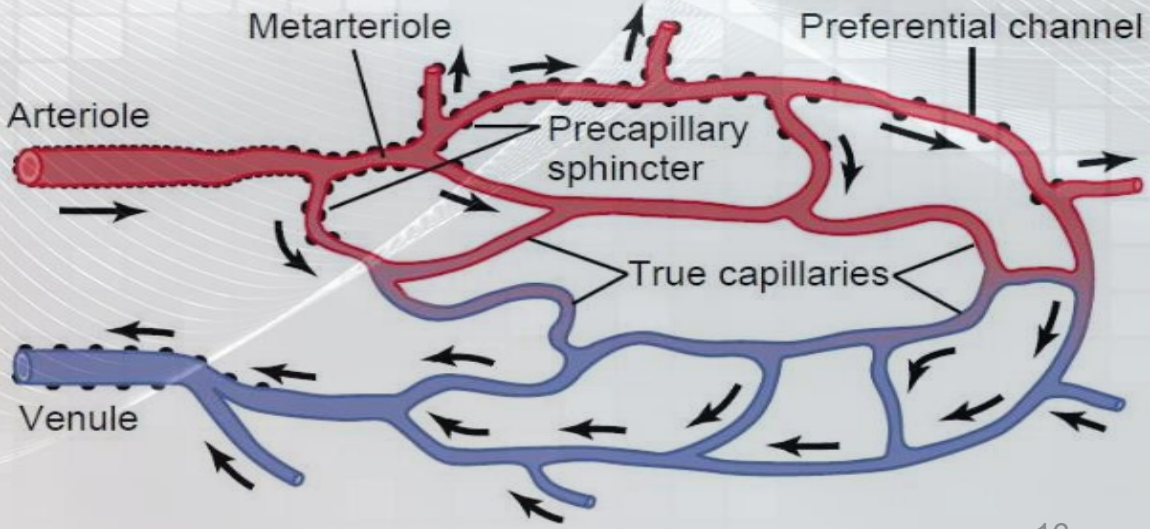
Blood Flow Through Capillary Beds (Network)

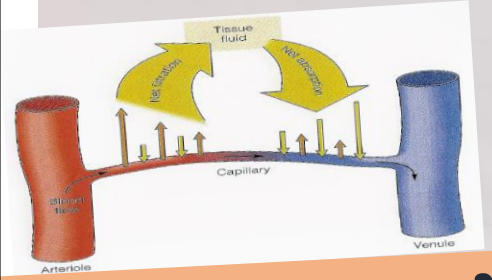
Blood flows from Arterioles through Metarterioles, then to Capillary bed network.

Venules drain network.

Arteriolar smooth muscle, Metarterioles, & Precapillary sphincters **regulates** the blood flow through the Capillary bed network.

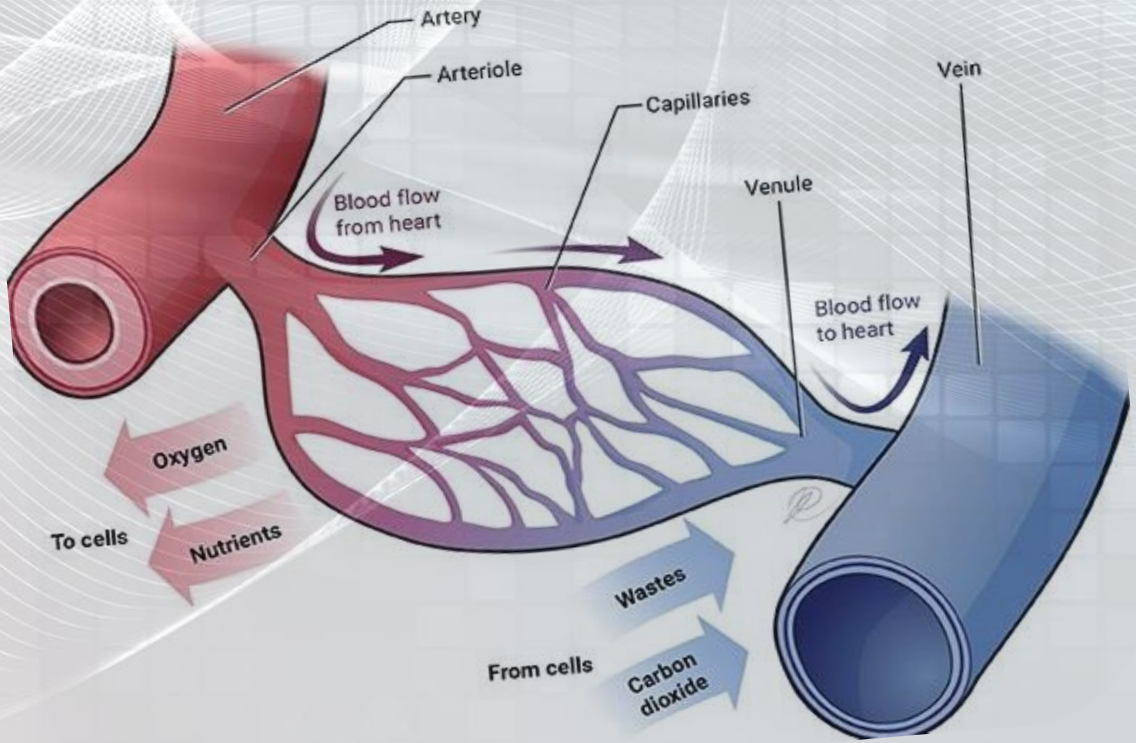






Mechanisms of Trans- Capillary Exchange

- **Simple diffusion:** of lipid soluble gases (O_2 & CO_2) according to concentration gradient.
- **Filtration:** Bulk flow for fluid transfer by Starling's forces according to pressure gradient.
- **Vesicular transport:** Transcytosis.
- **Mediated (membrane) Transport:** Occurs only in capillaries of the **brain** & involves secondary active transport, e.g., transport of glucose by co-transporters in cell membrane.



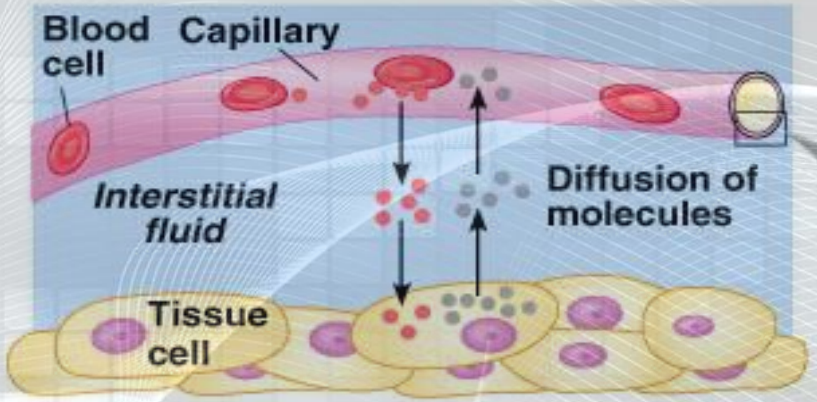
Trans-Capillary Fluid Transfer

- **Trans- capillary transfer occurs either by diffusion, or by filtration vesicular transport.**

- **Diffusion occurs through the,**
  - **Cells:** for lipid soluble molecules.
  - **Intercellular clefts between cells:** for non-lipid soluble molecules.

- **Filtration (Bulk Flow):**

  Fluid movement is affected & influenced by the concentration gradients, cleft size (permeability) & hydrostatic pressure (varies by organ & situation).



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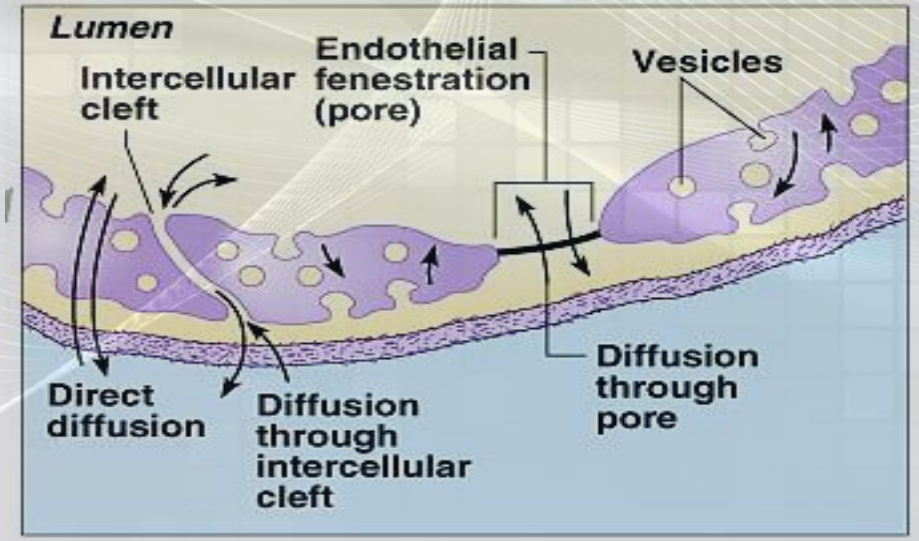


(b)

Formation of Interstitial Fluid (IF)

- The Interstitial Fluid (IF) formation is **regulated by** the **net filtration pressure** force at the two vascular ends (arteriolar & venular) of the capillary bed.
- **Net filtration pressure** is **affected by** the **net balance** between the two forces (hydrostatic & oncotic pressures) found in the capillaries & in the interstitial fluid.
- **Movement of fluid** from **Capillaries** is **affected by** the:
  - Blood pressure,
  - Capillary permeability, &
  - Osmosis.
- **Excessive fluid** gained by tissues is removed by the **Lymphatic system**.

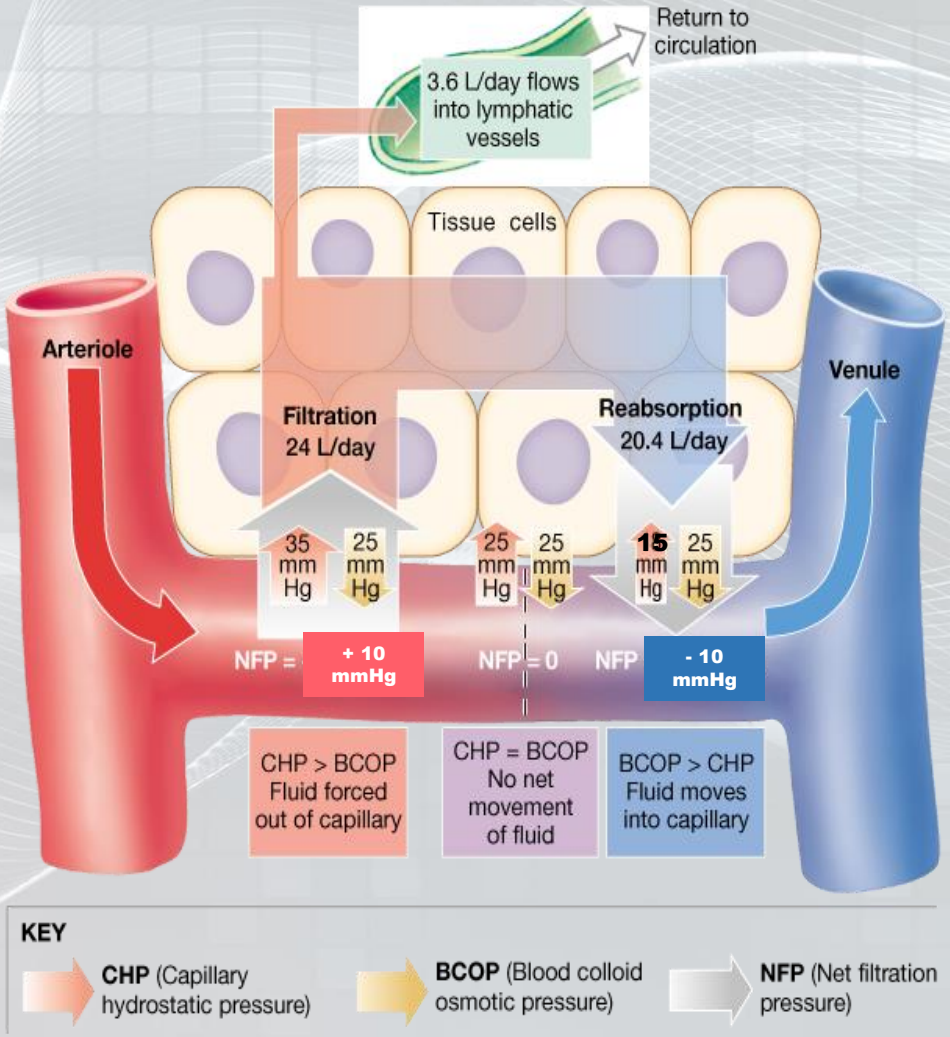
Interstitial Hydrostatic & Oncotic Pressures

- **Interstitial Hydrostatic Pressure (Outward Force):**
  - **Interstitial hydrostatic pressure (P_{IF}) is almost 0 mmHg.**
  - **The interstitial fluid pressure** which is caused by pumping of lymphatic system is **negative 3 mmHg** in most tissues.
  - Encapsulated organs have positive interstitial pressures (+5 to +10 mmHg).
  - **P_{IF} varies from one organ to another:**
    - Subcutaneous tissues: -2 mmHg.
    - Liver, Kidney: +1mmHg.
    - Brain: As high as +6mmHg.
- **Oncotic (osmotic) Pressure (Inward Force):**
  - **Colloid osmotic pressure** is caused by presence of large proteins.
  - **There is almost no colloid osmotic pressure** in the interstitial space.

Capillaries Hydrostatic & Oncotic Pressures

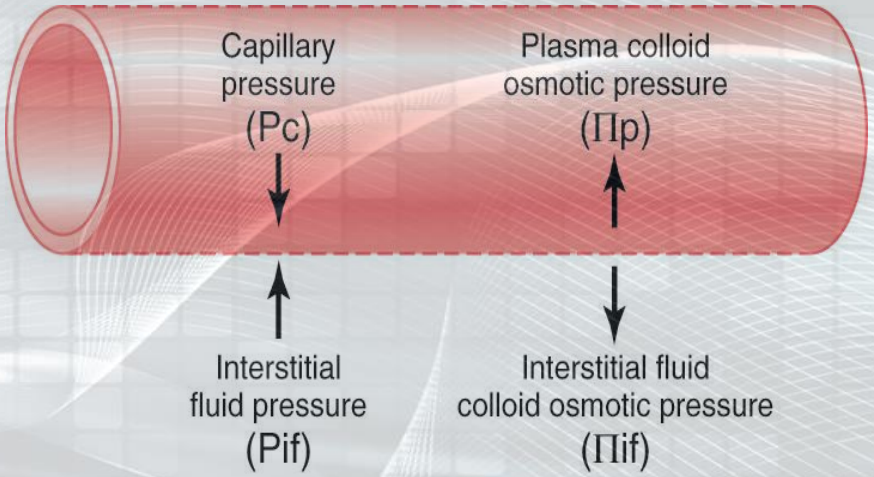
- **Hydrostatic Pressure (Outward Force):**
  - **Normal Capillary hydrostatic pressure** ranges from 30-**35 mmHg** at the **arterial end**, **& from 10**-15 **mmHg** at the **venous end**.
- **Oncotic (osmotic) Pressure (Inward Force):**
  - **Colloid osmotic pressure** is caused by presence of large proteins.

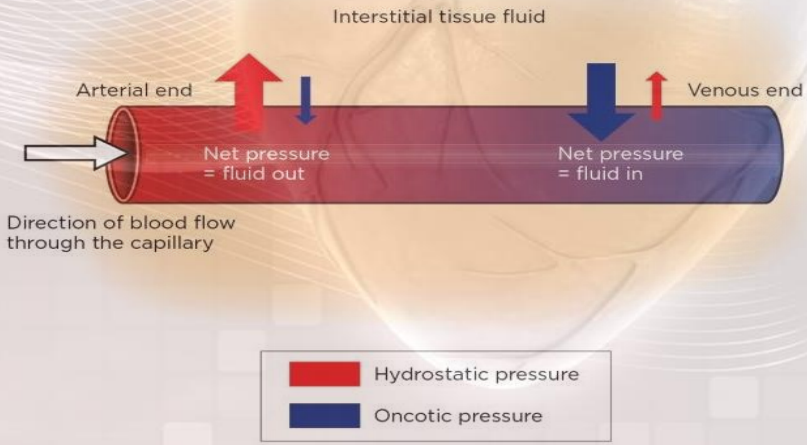
    High content of proteins in plasma accounts for its higher osmotic pressure compared to that of the Interstitial fluid (IF).
  - **Plasma osmotic pressure:** Is high (**25**-28 mmHg) & will attract fluid & dissolved substances from tissue spaces into the circulation.

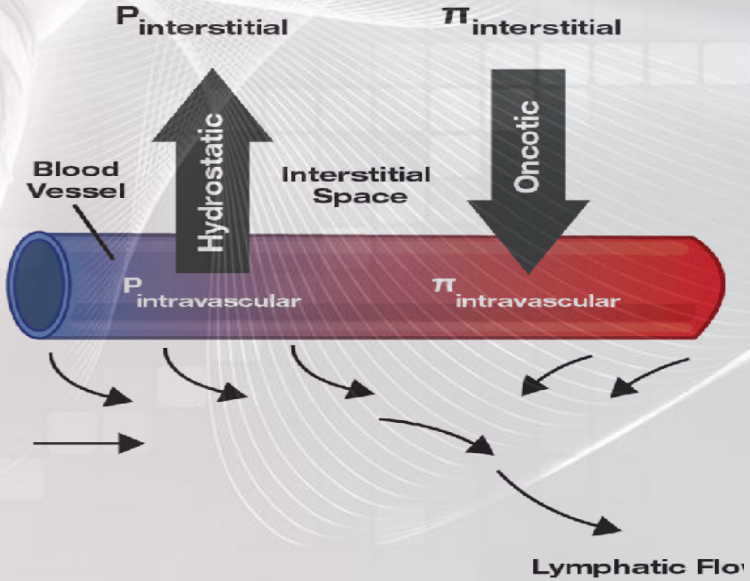


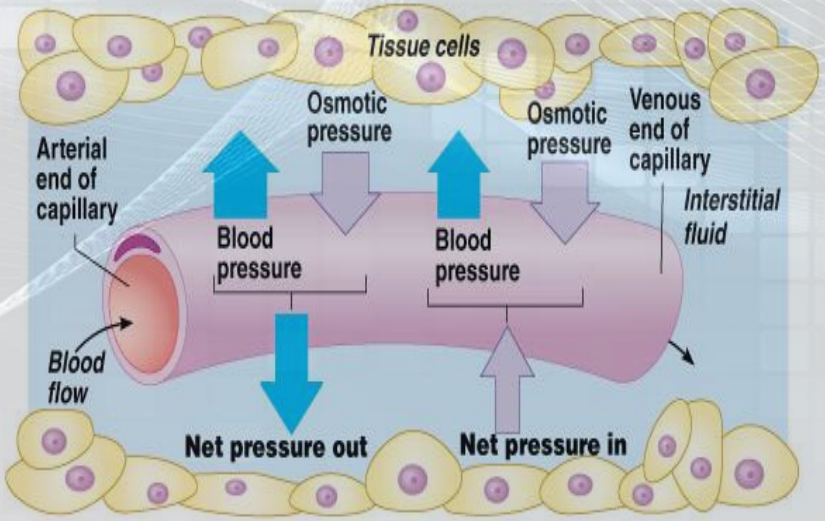
How Does Fluid Filtrate at The Capillary Bed?

- Fluid transfer depends on the relative **balance** & **equilibrium between the hydrostatic & osmotic pressures** found in capillary plasma & interstitial space.
- Any loss of plasma colloids will result in an increase loss of fluid from the vasculature to the interstitial space.









How Do We Calculate The Net Movement at The Capillary Bed?

- **Filtration rate of fluid at the Capillary:**

  Equals to the **Net Filtration Pressure** (***NFP***) multiplied by the **Filtration Coefficient** (***Kf***).

Filtration Rate = K_f X NFP

- **Filtration Coefficient** (***Kf***) is a product of surface area times the hydraulic conductivity of membrane (membrane permeability).
- **If NFP = positive, then fluid is lost from capillary.**
- **If NFP = negative, then fluid is gained by capillary.**

Starling's Equation for Capillary Filtration:

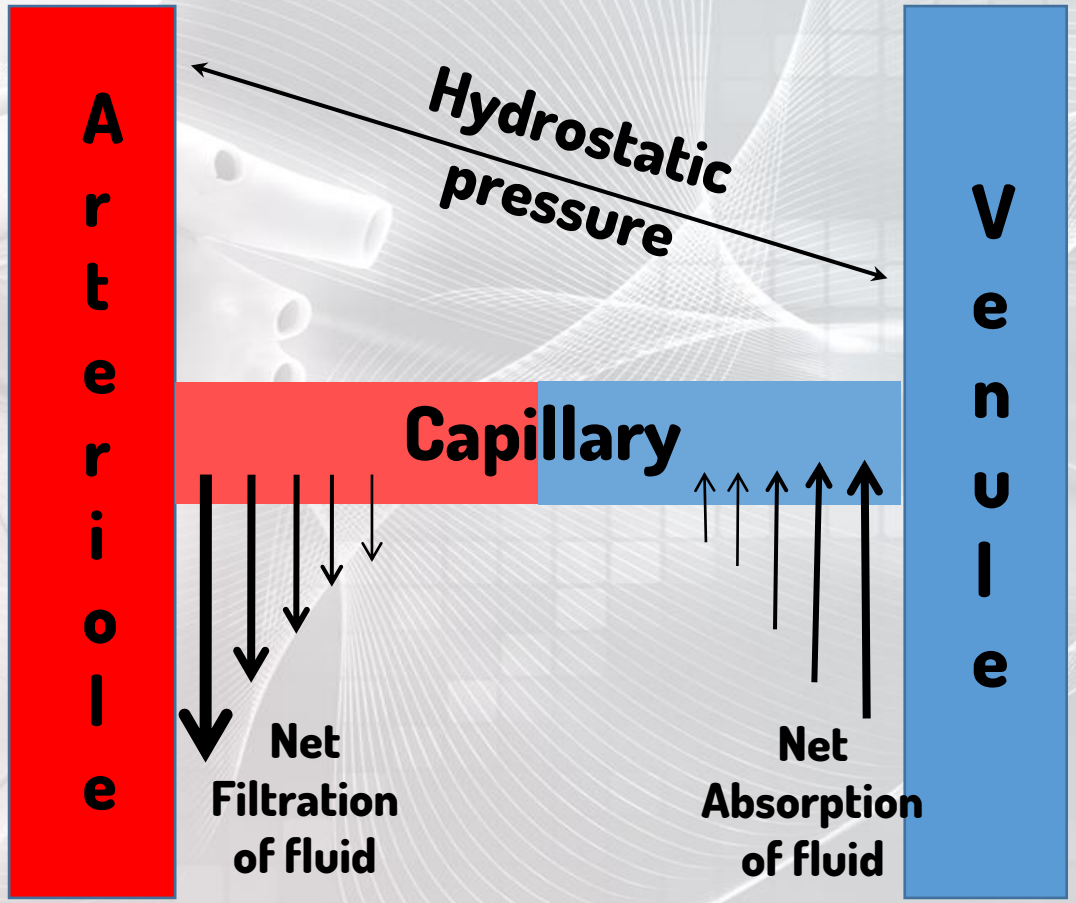
Flux = Kf [(Pc – Pif) – σ (πp – πif)]

- **Kf =** Capillary filtration coefficient (surface area & permeability)
- **Pc =** Capillary hydrostatic pressure
- **Pif =** Interstitial hydrostatic pressure
- **σ =** Capillary reflection coefficient (0 to 1) 1 = impermeable to proteins
- **πc =** Capillary colloid osmotic pressure
- **πif =** Interstitial colloid osmotic pressure

Starling's Forces & Filtration at Capillary Beds

Fluid Balance: Net Filtration & Absorption of Fluid Across The Capillary Membrane

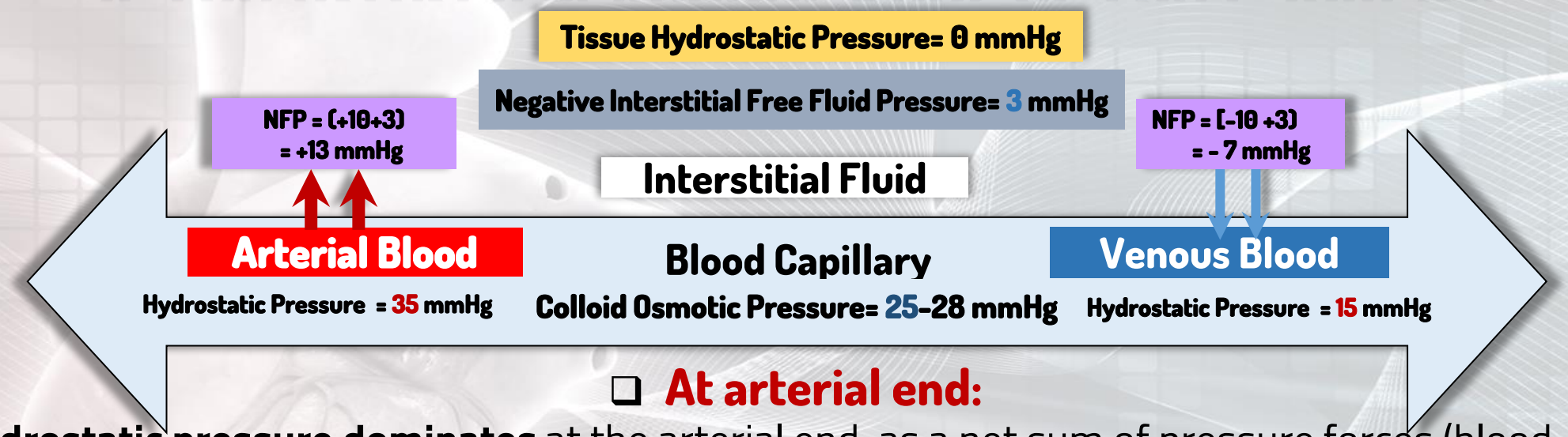
At Arterial End of Capillary	
Outward Forces:	**Value**
• Capillary blood pressure	(P_c = 30-35 mmHg)
• Negative Interstitial free fluid pressure	(P_{IF} = - 3 mmHg)
TOTAL Outward Force	38 mmHg
Inward Forces	**Value**
• Plasma colloidal osmotic pressure	(μ_C = 25-28 mmHg)
TOTAL Inward Force	25 mmHg
NET OUTWARD FORCE	38 – 25 = + 13 mmHg



At Venous End of Capillary	
Outward Forces:	**Value**
• Capillary blood pressure	(P_c = 10-15 mmHg)
• Negative Interstitial free fluid pressure	(P_{IF} = - 3 mmHg)
TOTAL Outward Force	18 mmHg
Inward Forces	**Value**
• Plasma colloidal osmotic pressure	(μ_C = 25-28 mmHg)
TOTAL Inward Force	25 mmHg
NET INWARD FORCE	18 – 25 = -7 mmHg

Net filtration & absorption of fluid across the capillary membrane

Normal Forces at The Arterial & Venous Ends of The Capillary



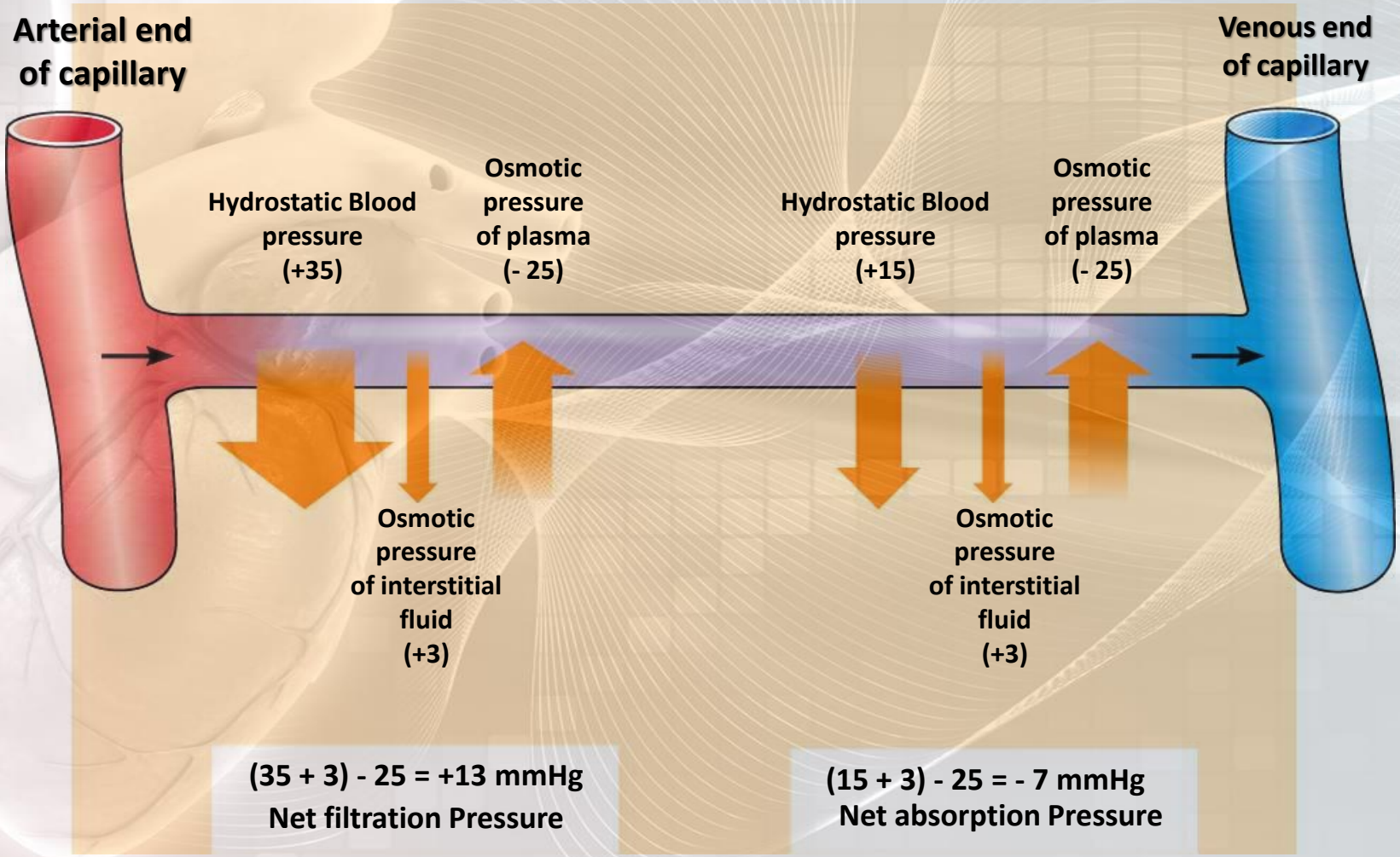
❑ At arterial end:

- **Hydrostatic pressure dominates** at the arterial end, as a net sum of pressure forces (blood hydrostatic pressure + Interstitial fluid (IF) osmotic pressure) flow fluid out of the circulation.
- **Water moves out** of the capillary with a net filtration pressure (**NFP**) of **+13 mmHg**.
- 13 mmHg NFP causes an average of 1/200 of plasma in flowing blood to filter **out** of arterial end of the capillary **into the intestinal space**.

❑ At venous end:

- **Oncotic pressure dominates** at the venous end, as a net sum of pressure forces (blood osmotic pressure + Interstitial fluid (IF) hydrostatic pressure) flow fluid into the bloodstream.
- **Water moves into** the capillary with a **NFP** of **-7 mmHg**.

Normal Forces at The Arterial & Venous Ends of The Capillary



Summary of Factors Affecting Capillary Filtration

1. Blood pressure
2. Permeability
3. Organ Structure (Encapsulated or not?)
4. Osmotic pressure

Q: Under normal circumstances, Which of the following has the greatest influence on capillary fluid exchange ?

1. Blood pressure
2. Permeability
3. Osmotic pressure
4. Lymphatic pressure

Q: Which of the following is altered by the body to increase capillary filtration?

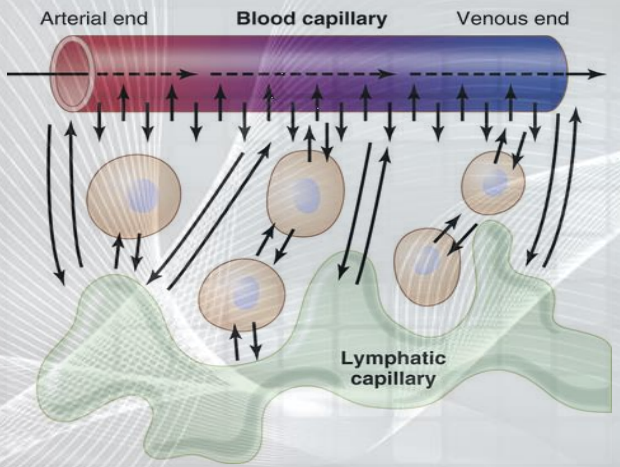
1. Blood pressure
2. Permeability
3. Osmotic pressure
4. Lymphatic pressure

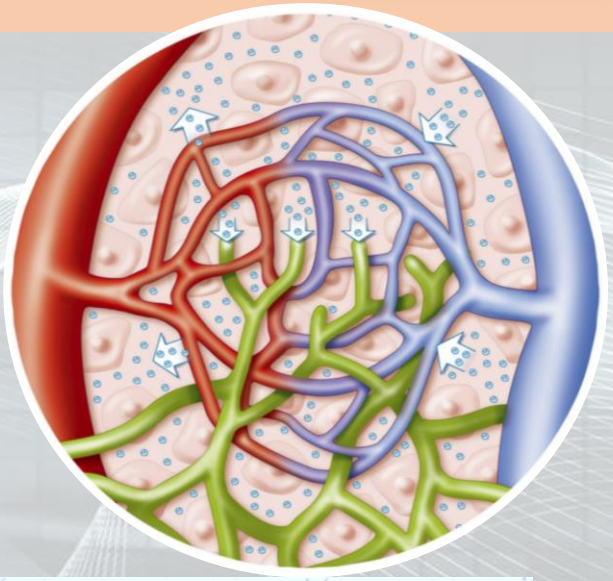
Clinical Significance of Capillary Filtration

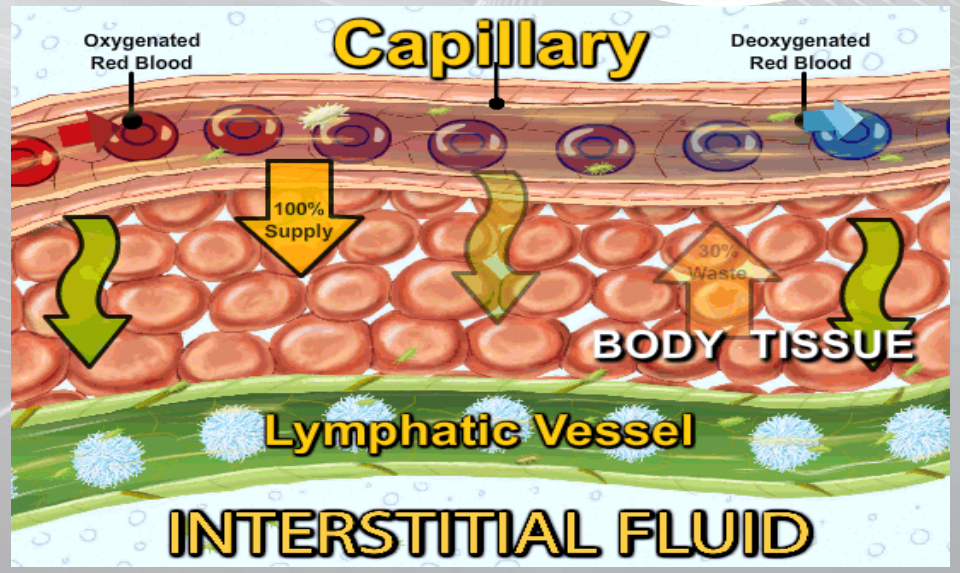
- **In case of blood loss:** Vasoconstriction of arterioles → will decrease the capillary hydrostatic pressure. The osmotic pressure of plasma proteins favours absorption of interstitial fluid →↑ **Blood volume**.
- **In case of congestive heart failure:** Venous pressure rises → will build-up of blood in capillaries →↑ capillary hydrostatic pressure →↑ filtration → **edema**.
- **In case of hypo-proteinemia** (Starvation, liver disease): ↓ plasma protein colloid osmotic pressure → loss of fluid from capillaries → **edema**.
- **In case of inflammation:** The gaps between the endothelial cells increase because of the inflammatory mediators →↑ movement of proteins into the interstitial space → **edema**.

Lymphatic System

- Lymphatic vessels present between capillaries.
- Begin as blind ended tubes.
- Parallel to the venous system.
- Collect the excess interstitial fluid & return it to blood vessels in the subclavian vein.
- Approximately **120 ml/day** is returned to the blood vessels.
- Muscle activity pumps fluid in lymph vessels.

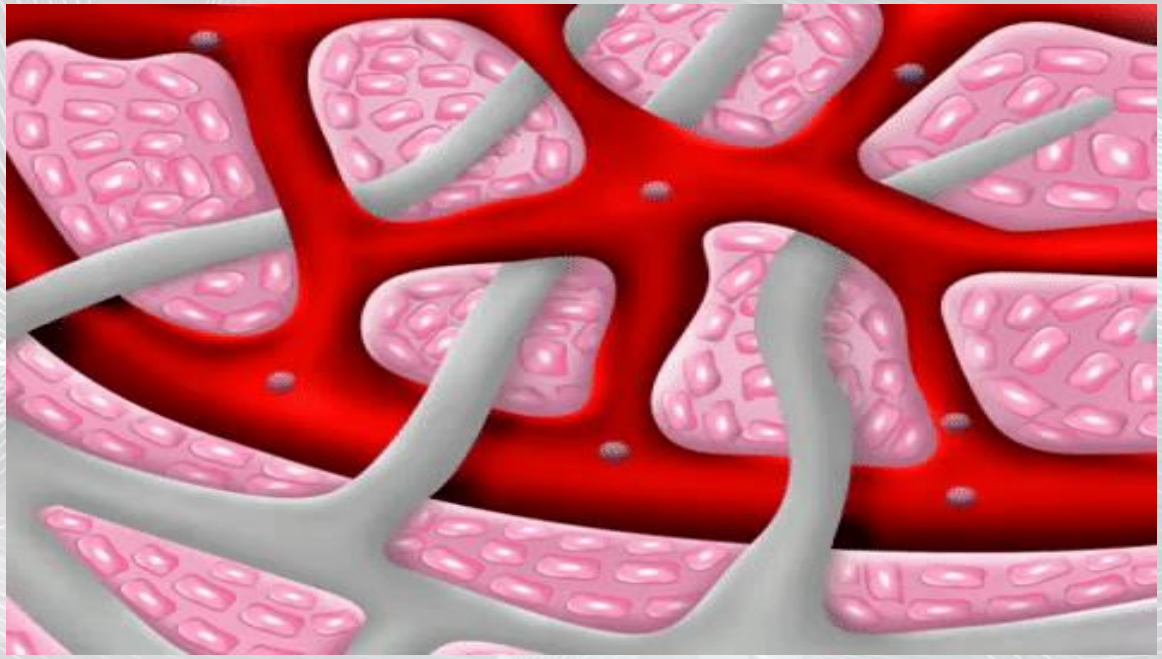


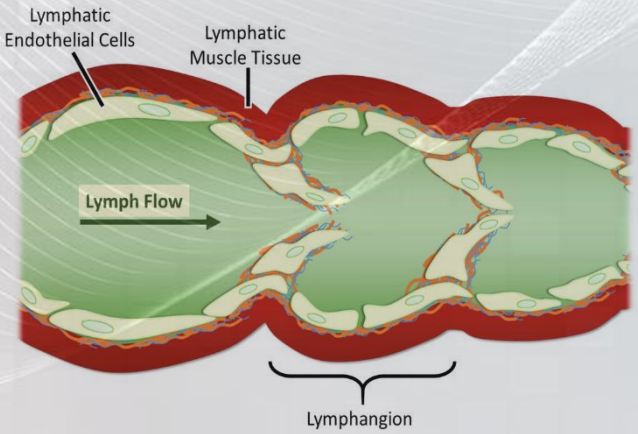


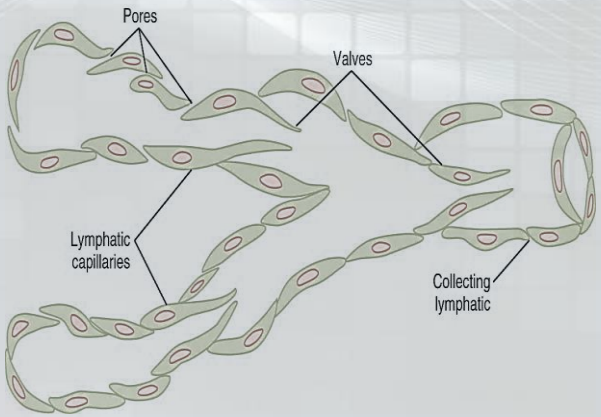


Lymphatic-Capillaries System

- Interstitial fluid enter the lymphatic capillaries through loose junctions between endothelial cells.
- Lymph flow back to the thoracic duct with the help of contraction of both the lymphatic vessel wall's smooth muscle & the surrounding skeletal muscle.
- **Failure of lymphatic drainage can lead to edema.**

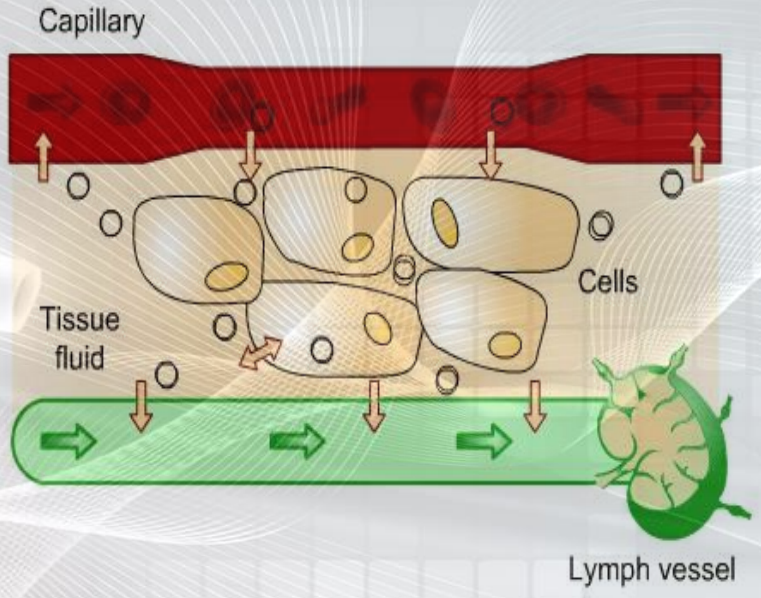


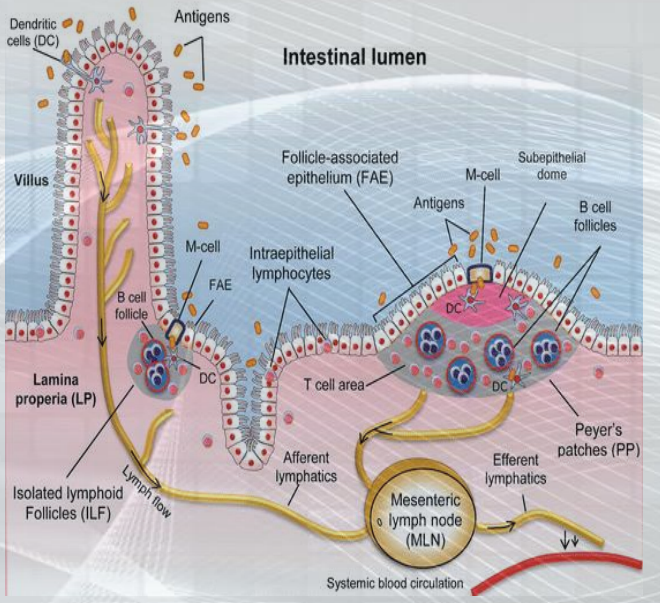


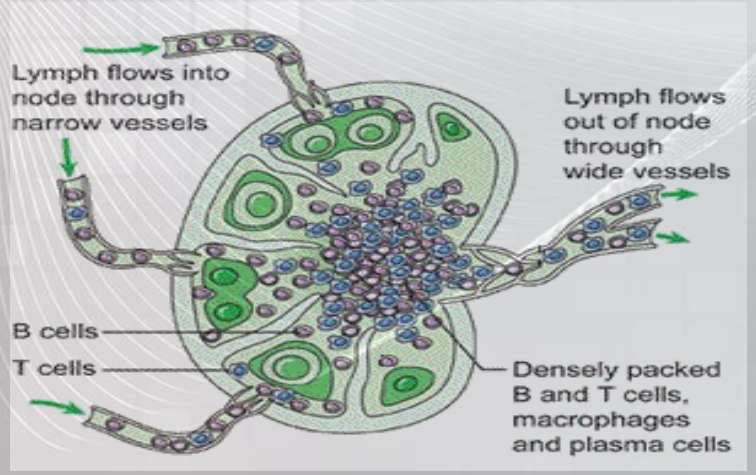


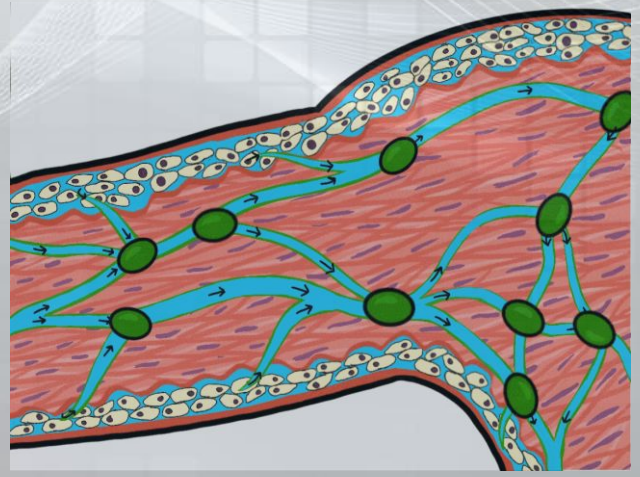
Function of Lymphatic System

- **3 basic functions:**
  1. Drain excess interstitial (tissue) fluid back to the blood, in order to maintain original blood volume.
  2. Transports absorbed fat from small intestine to the blood.
  3. Helps provide immunological defenses against pathogens.









Edema

- **The term used to describe unusual accumulation of interstitial fluid.**
- Loss of fluid from the vascular space into the extravascular or interstitial space will result in:
  - Low blood volume which will result in low blood pressure.
  - Loss of fluid from capillaries into the tissue which will result in edema.

Causes:

1. **Alteration in Starling's forces balance due to**:
   - A **decrease or loss in Plasma protein** (colloids) concentration, will lead to a decrease in plasma osmolarity, allowing fluid to escape from circulation to the interstitial space. Or
   - An **increase in Capillary hydrostatic pressure**.
2. **Failure of Lymphatic drainage**.
3. An **increase in capillary permeability** or in **pores size** secondary to:
   - **Histamine** release,
   - **Bradykinin** or certain **drugs** administration.
   - **Inflammation** & release of **cytokines**.
4. Involvement of **some types of hormones**.

Hormones Involved In Edema

- **Activation** of **Renin-Angiotensin-Aldosterone System** which will result in secondary Hyperaldosteronism, leading to sodium (Na+) & water retention.

- **Activation** of **Anti-diuretic hormone (ADH)/Vasopressin**, leading to water retention.


Thank You