Cardiovascular Physiology

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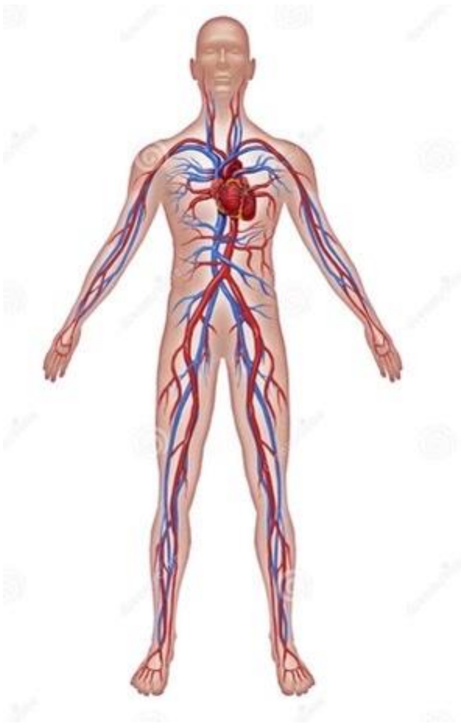

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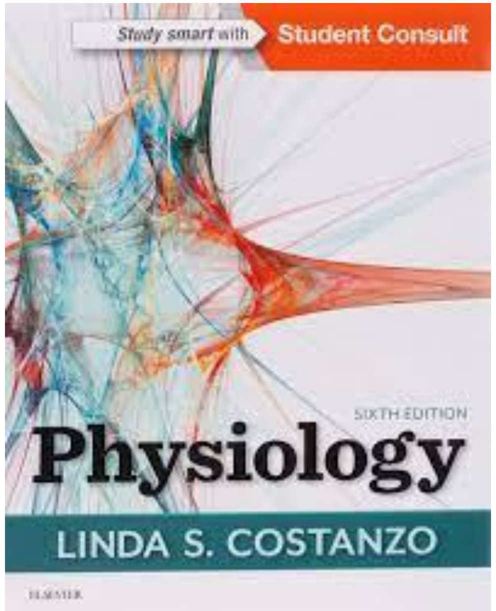
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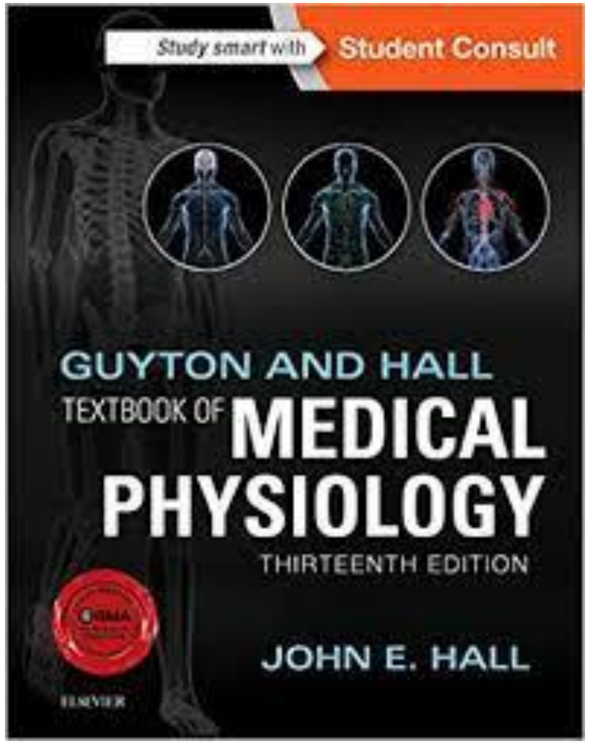
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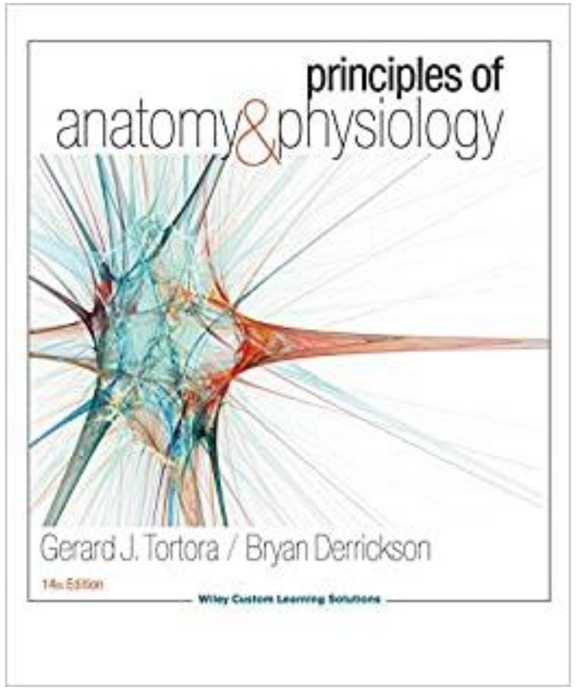
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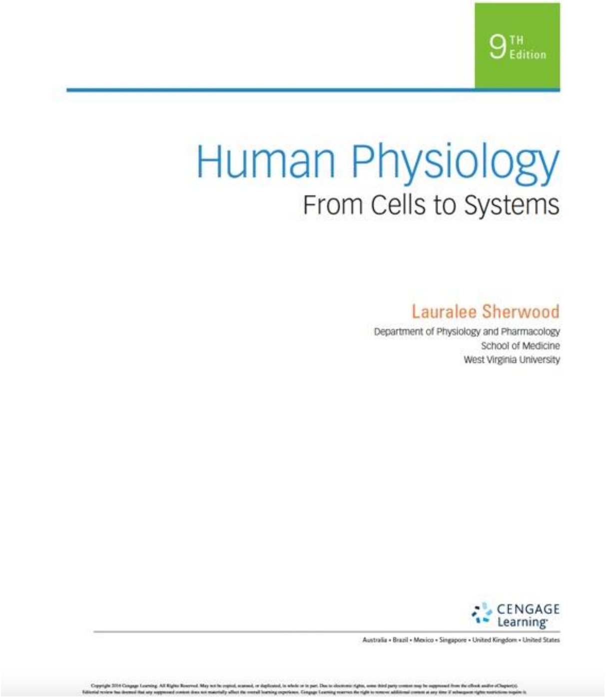
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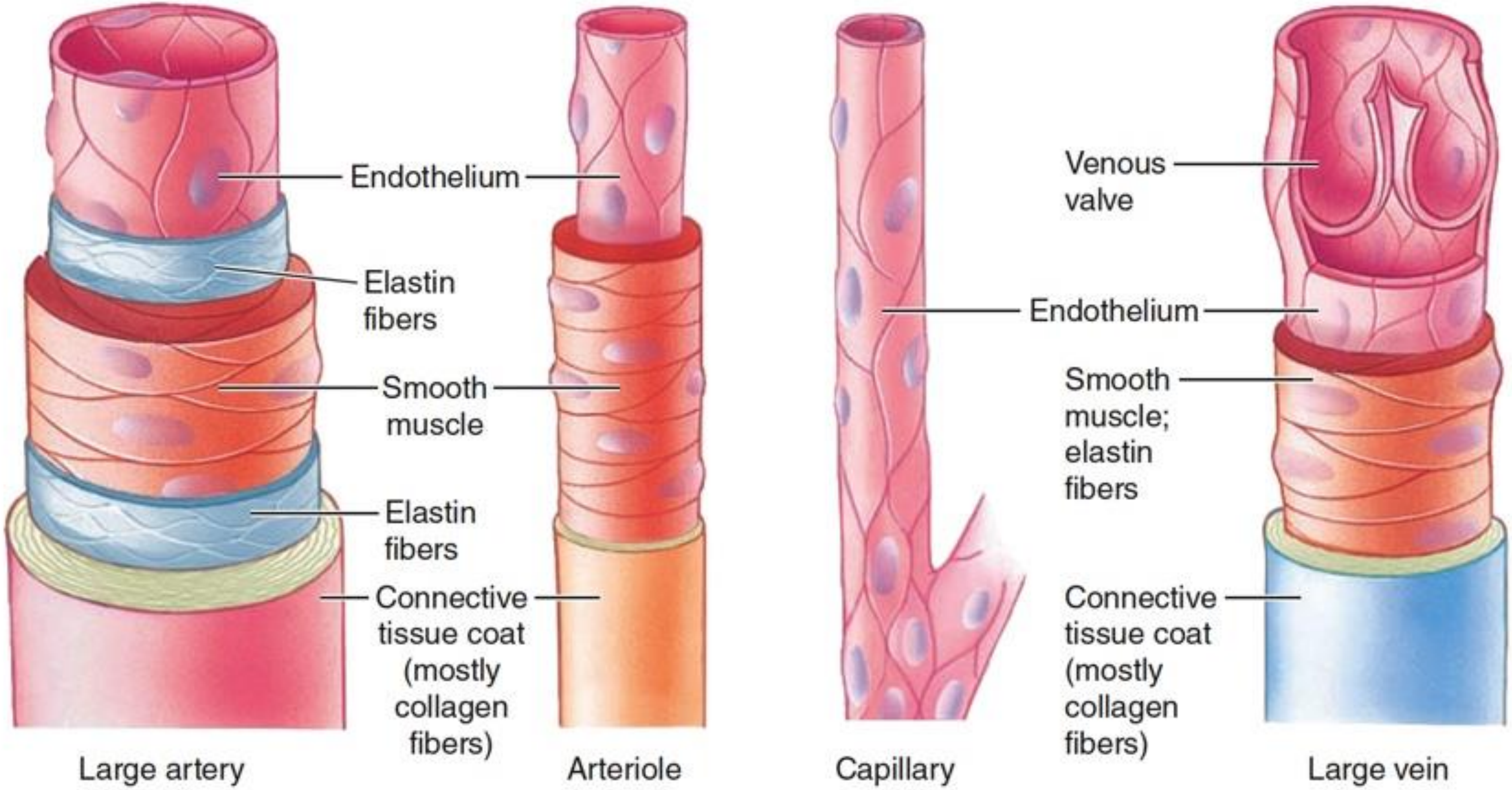
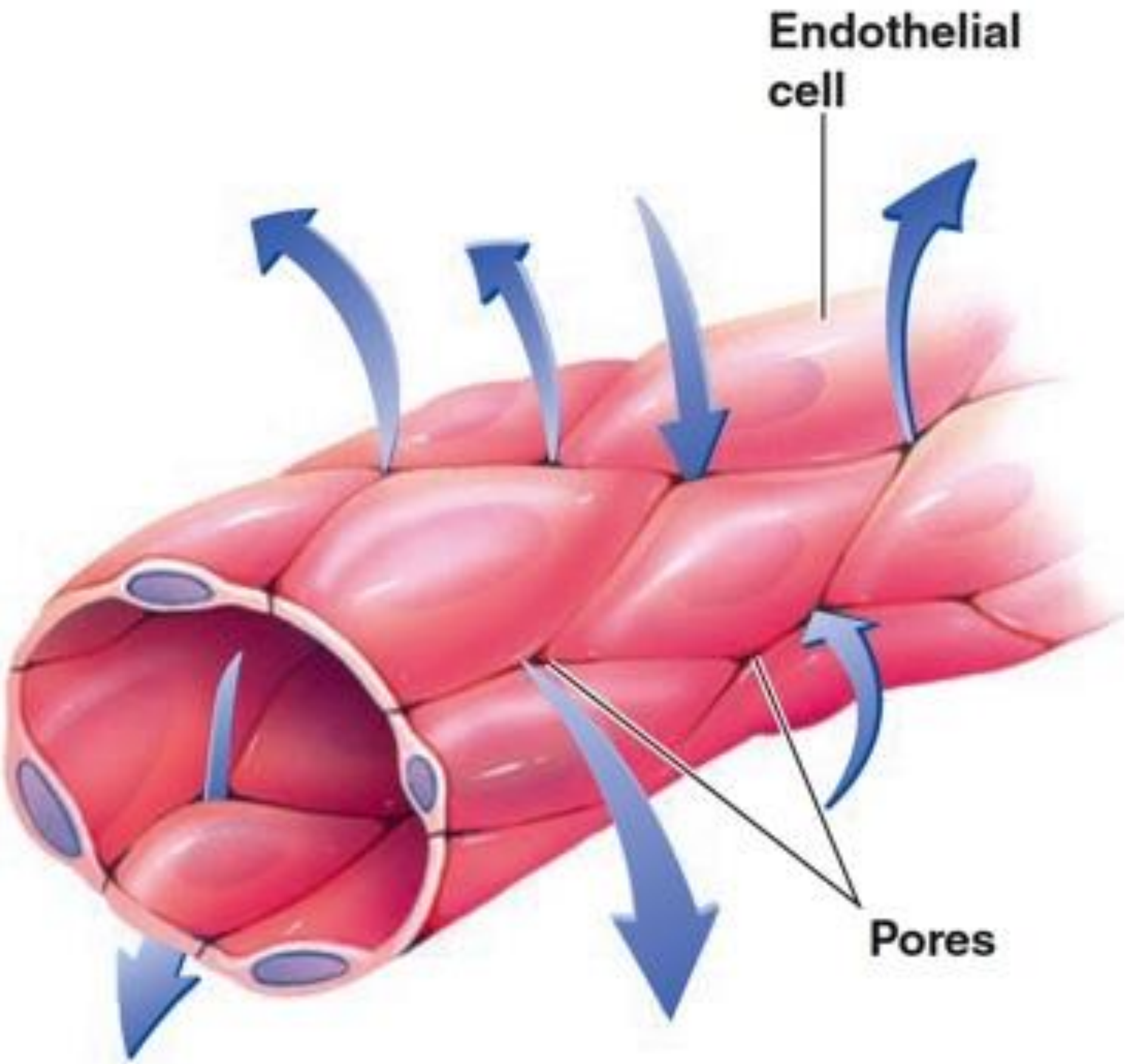
Capillaries and Lymphatics

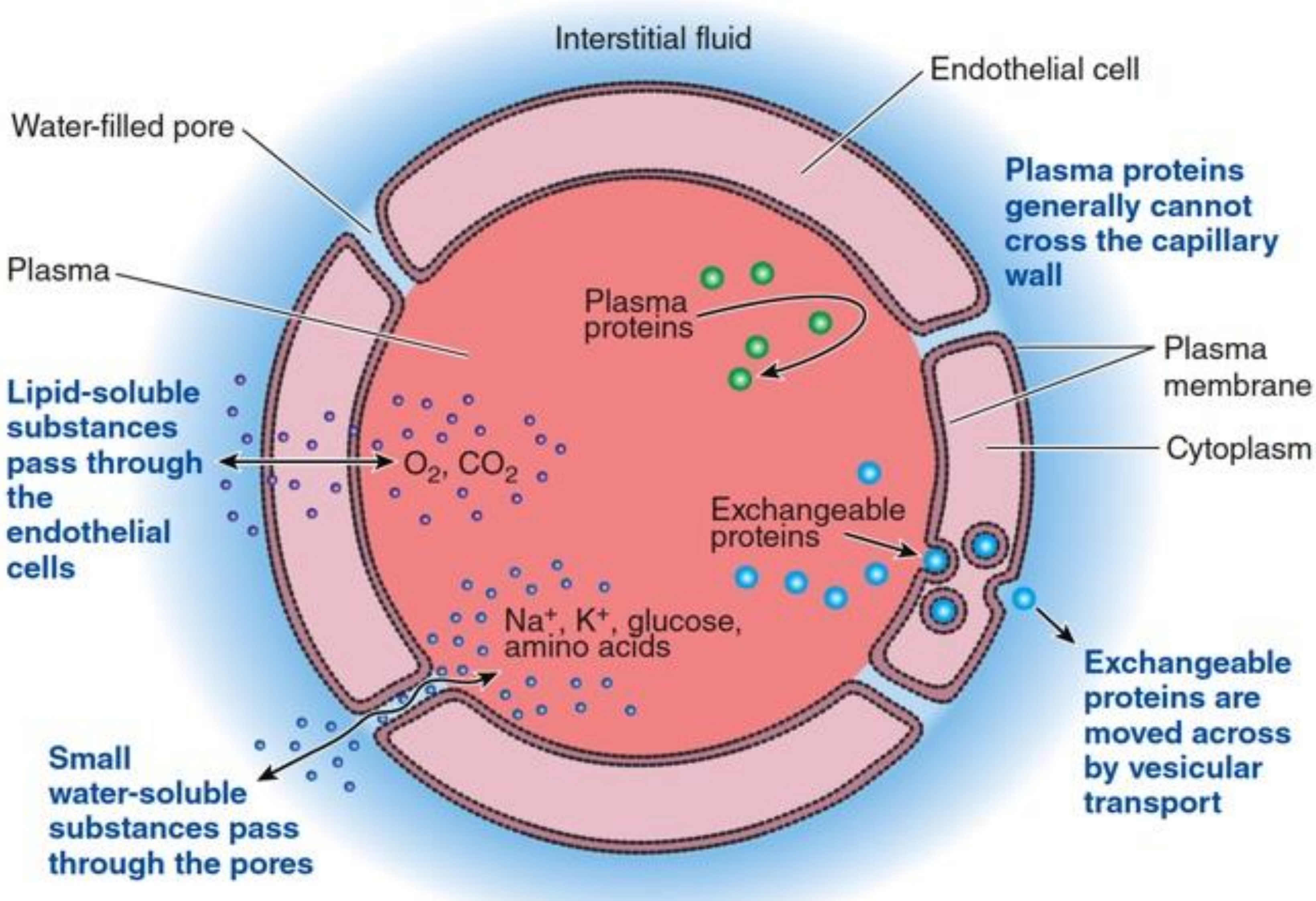


Endothelium
Elastin fibers
Smooth muscle
Elastin fibers
Connective tissue coat (mostly collagen fibers)
Large artery
Arteriole
Capillary
Venous valve
Endothelium
Smooth muscle; elastin fibers
Connective tissue coat (mostly collagen fibers)
Large vein


Endothelial cell
Pores

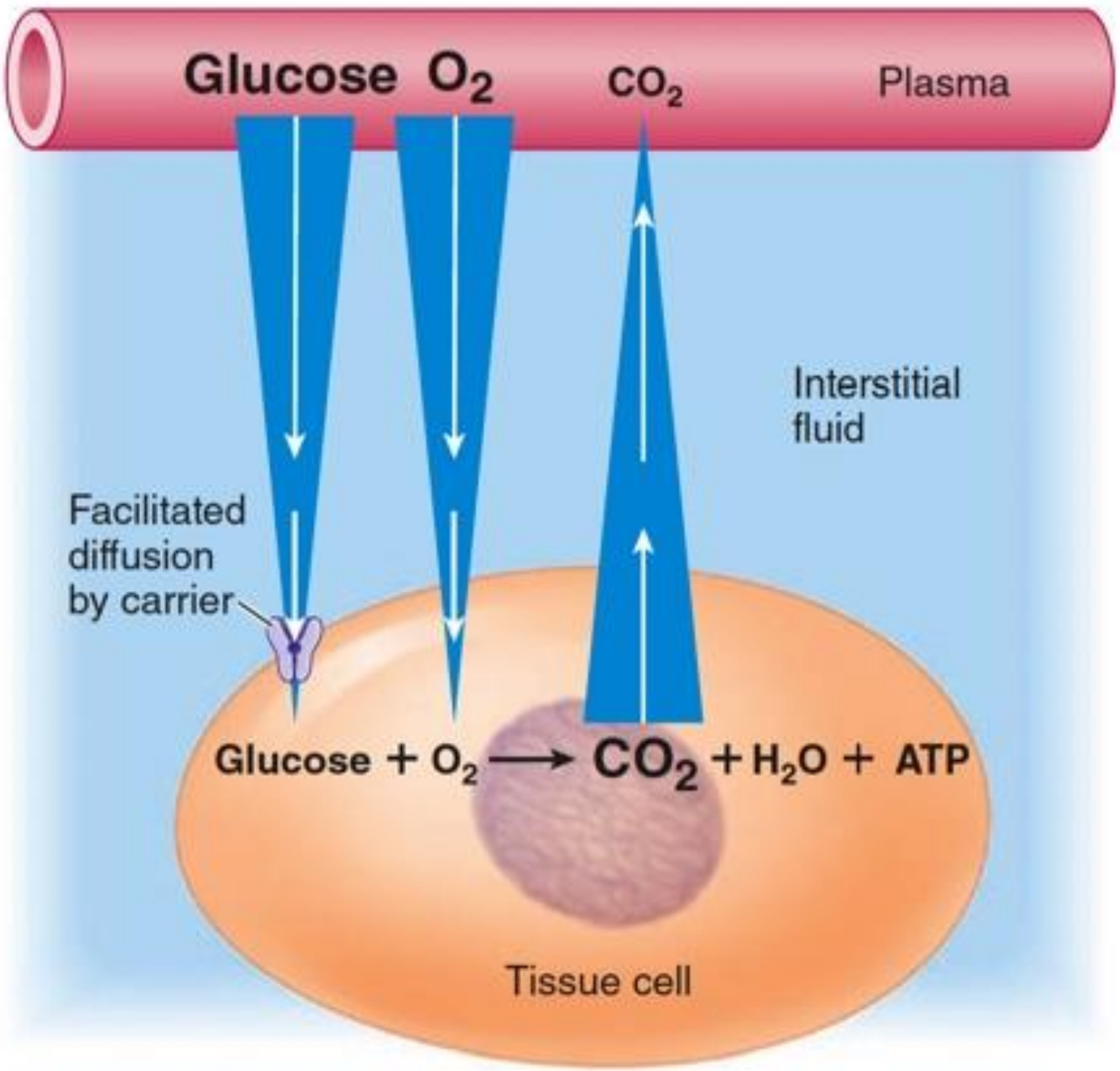
Capillaries

- Capillaries are the main sites for exchange of materials between blood and tissues.
- Materials are exchanged across capillary walls mainly by diffusion.
- Capillaries are ideally suited to enhance diffusion by:
- 1. Minimizing diffusion distances (thin capillary wall and small capillary diameter, coupled with the proximity of every cell to a capillary)
- 2. Maximizing surface area
- 3. Maximizing time available for exchange


Interstitial fluid
Endothelial cell
Water-filled pore
Plasma
Plasma proteins generally cannot cross the capillary wall
Plasma proteins
Plasma membrane
Cytoplasm
Lipid-soluble substances pass through the endothelial cells
O_2, CO_2
Exchangeable proteins
Na^+, K^+, glucose, amino acids
Exchangeable proteins are moved across by vesicular transport
Small water-soluble substances pass through the pores

Diffusion of different substances

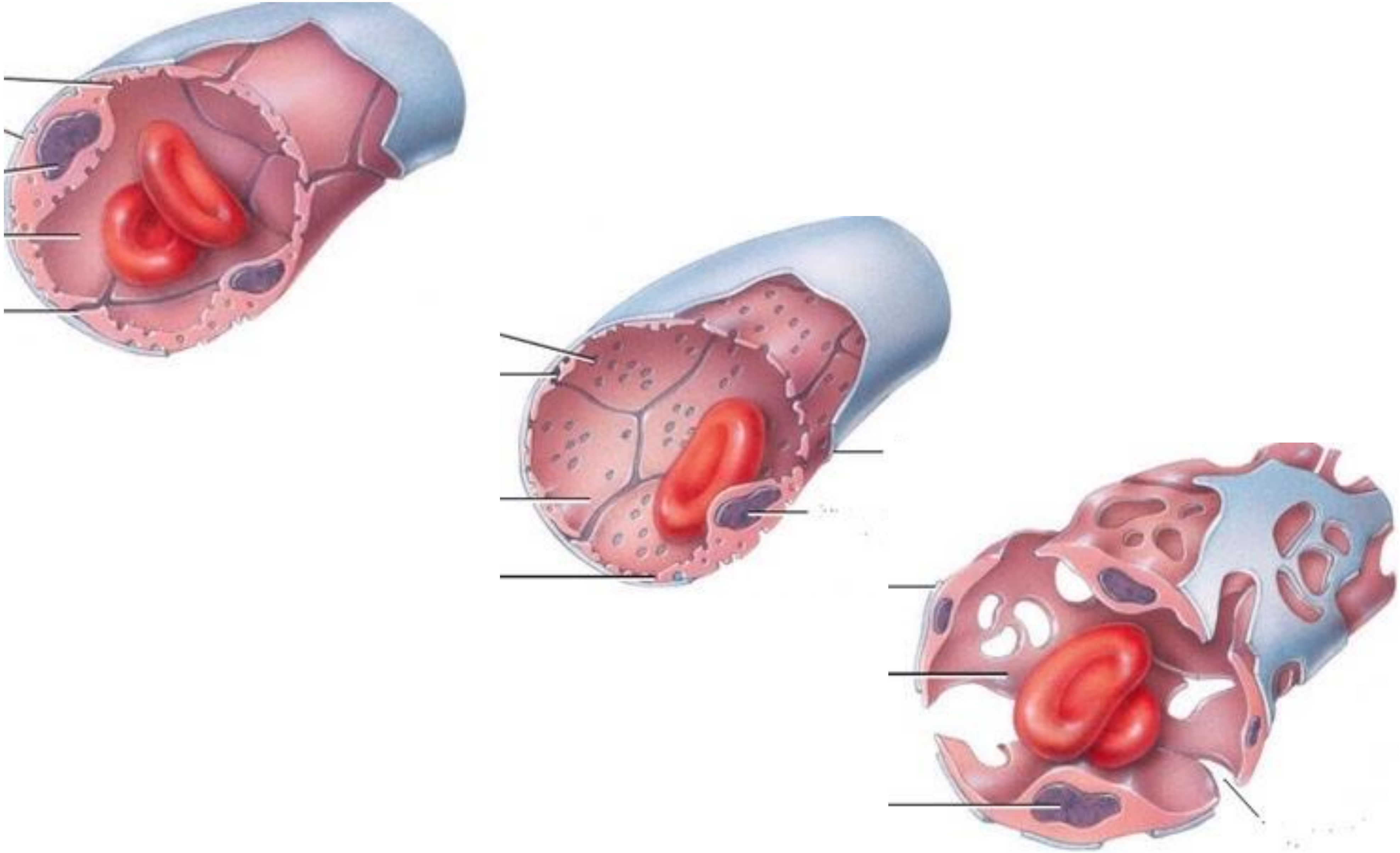
- In most capillaries, small, water-soluble substances such as ions, glucose, and amino acids can readily pass through the water-filled pores.
- But large, water-soluble materials such as plasma proteins are kept from passing through.
- Lipid-soluble substances, such as O2 and CO2, can readily pass through the endothelial cells themselves by dissolving in the lipid bilayer barrier of the plasma membrane surrounding the cells.



Glucose O_2
CO_2
Plasma
Interstitial fluid
Facilitated diffusion by carrier
Glucose + O_2 → CO_2 + H_2O + ATP
Tissue cell

Transcytosis

- Vesicular transport also plays a limited role in passage of materials across the capillary wall.
- Large molecules that are not lipid-soluble, such as protein hormones that must be exchanged between blood and surrounding tissues, are transported from one side of the capillary wall to the other in endocytic–exocytic vesicles, a process called transcytosis.



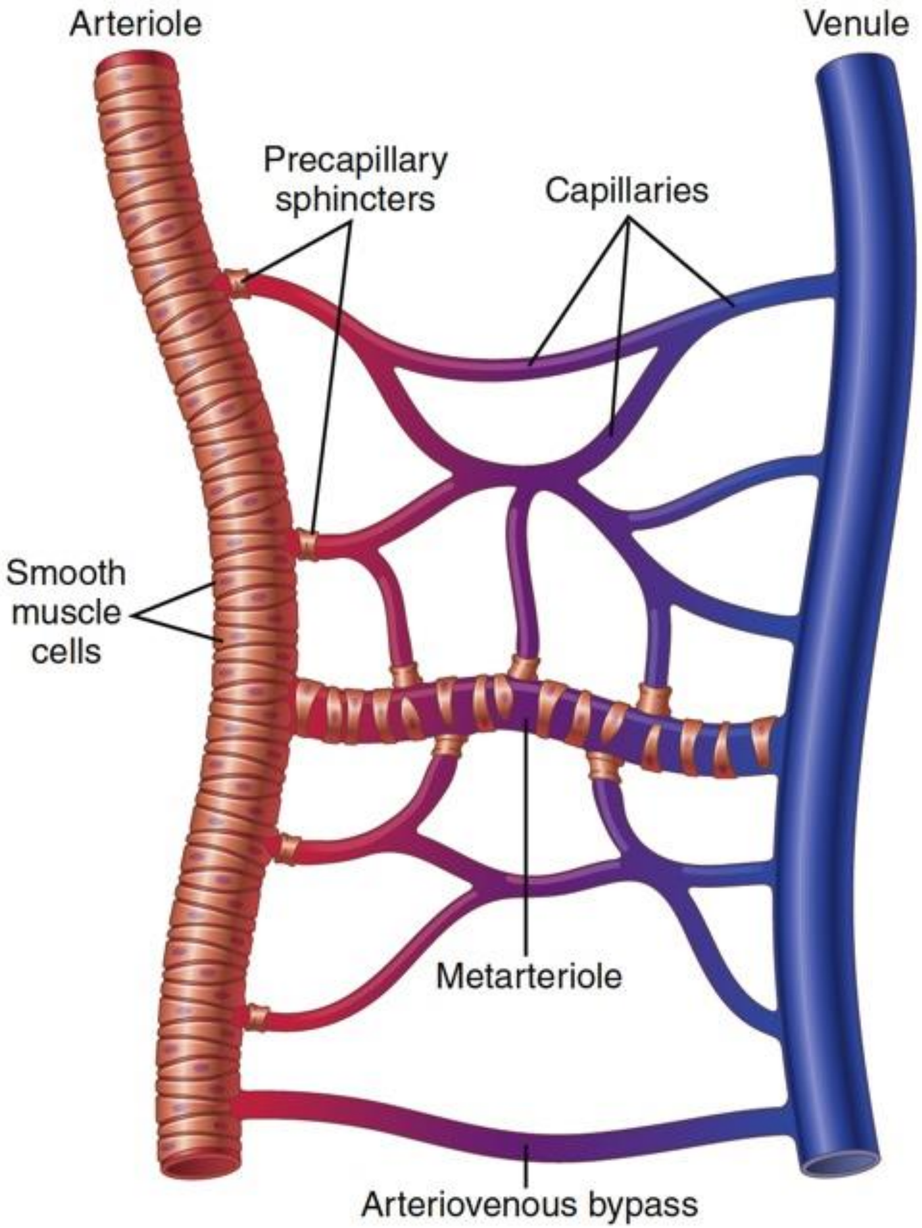
fenestrations

- Diffusion across capillary walls also depends on the walls' permeability to the materials being exchanged. The size of capillary pores varies from organ to organ.

- In addition to having the narrow pores between endothelial cells, the leakier capillaries of the kidneys and intestines have larger holes known as fenestrations.
- They are important in the rapid movement of fluid across the capillaries in these organs during the formation of urine and during the absorption of a digested meal, respectively.

Sinusoids

- Endothelial cells of liver cells are discontinuous.
- Liver sinusoids have fenestrations and such large intercellular pores that even proteins pass through readily.
- This is adaptive because the liver’s functions include synthesis of plasma proteins and the metabolism of protein-bound substances such as cholesterol. These proteins must all pass through the liver’s capillary (sinusoid) walls.

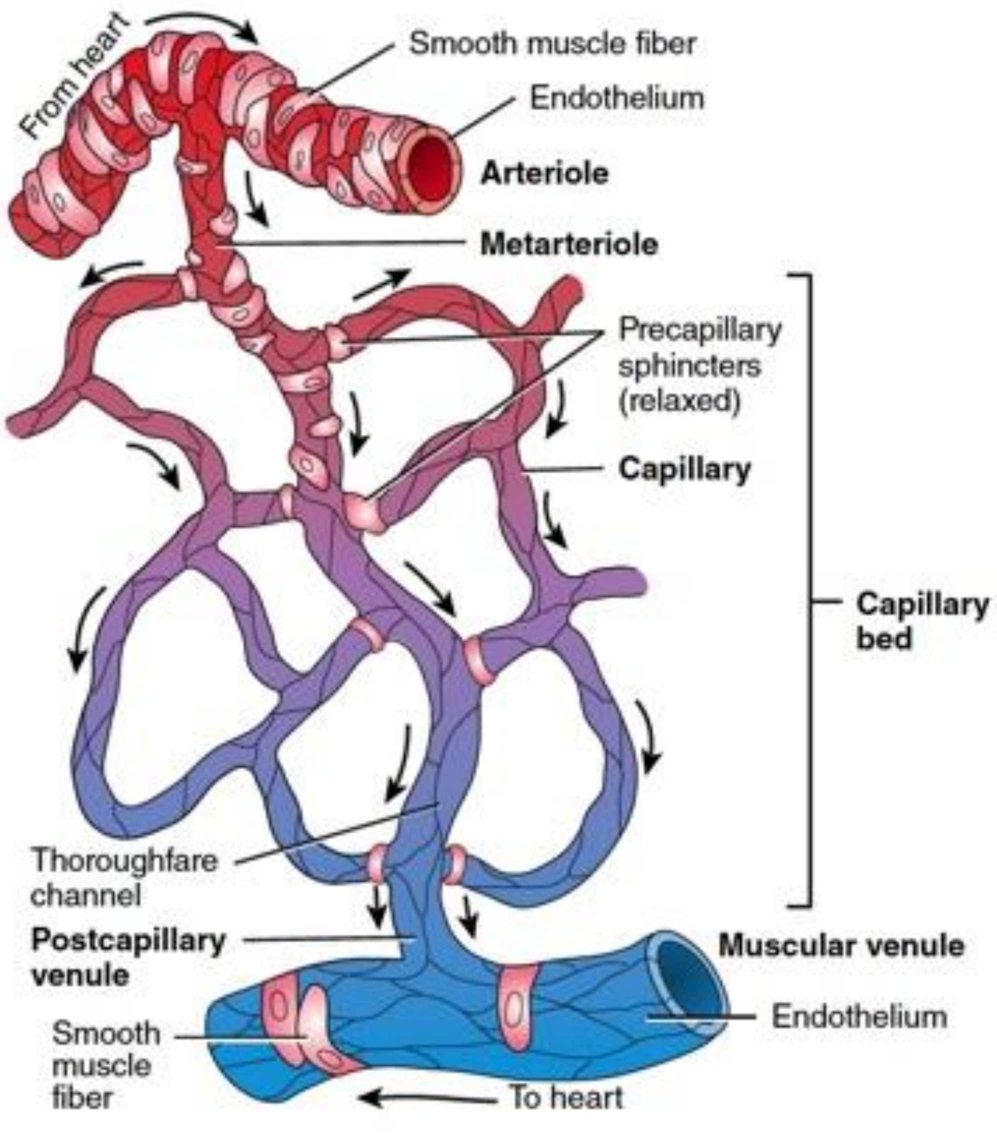

Arteriole
Venule
Precapillary sphincters
Capillaries
Smooth muscle cells
Metarteriole
Arteriovenous bypass

Vasomotion

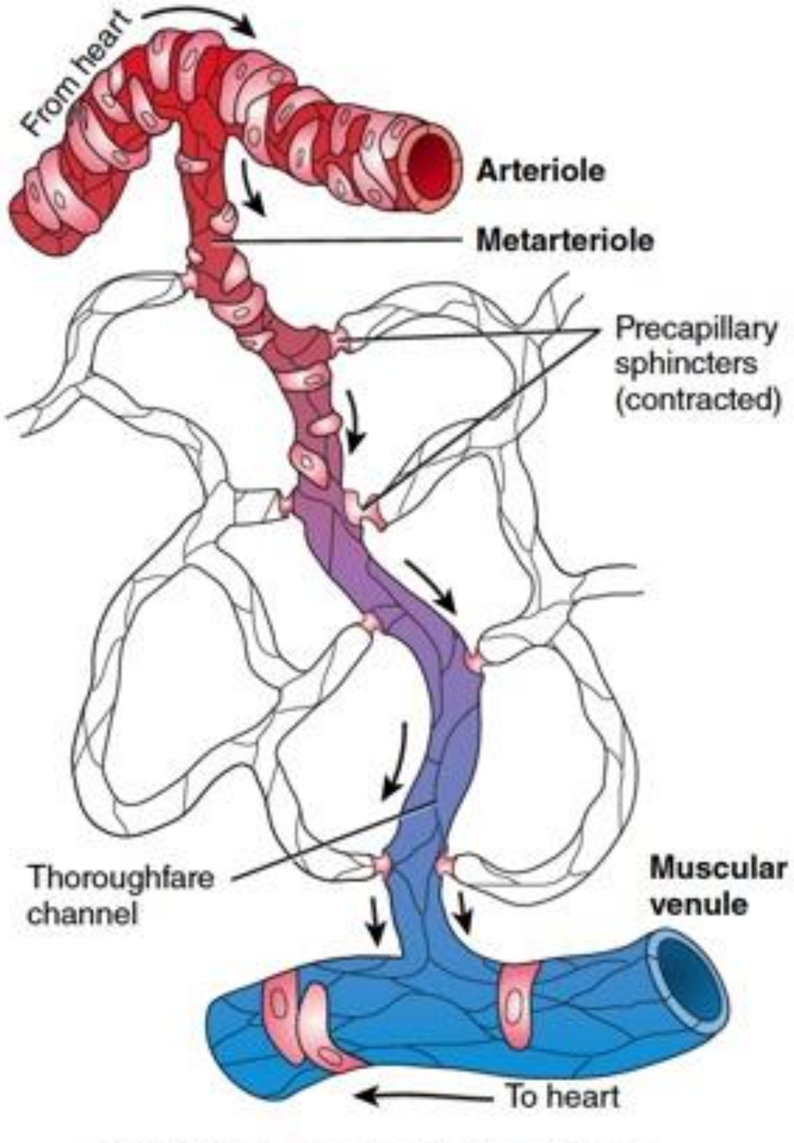
- Blood usually does not flow continuously through the capillaries. Instead, it flows intermittently, turning on and off every few seconds or minutes. The cause of this intermittency is the phenomenon called vasomotion, which means intermittent contraction of the metarterioles and precapillary sphincters.
- The most important factor affecting the degree of opening and closing of the metarterioles and precapillary sphincters that has been found thus far is the concentration of oxygen in the tissues.

Metarterioles

- Many capillaries are not open under resting conditions.
- The branching and reconverging arrangement within capillary beds varies somewhat, depending on the tissue.
- Capillaries typically branch either directly from an arteriole or from a metarteriole, which runs between an arteriole and a venule.
- Likewise, capillaries may rejoin at either a venule or a metarteriole.



(a) Sphincters relaxed: blood flowing through capillaries



(b) Sphincters contracted: blood flowing through thoroughfare channel

Precapillary sphincters

- Precapillary sphincters are not innervated, but they have a high degree of myogenic tone and are sensitive to local metabolic changes.
- They act as stopcocks to control blood flow through the particular capillary that each one guards.
- Capillaries themselves have no smooth muscle, so they cannot actively participate in regulating their own blood flow.
- When tissue metabolic activity increases, the local metabolic changes bring about relaxation of precapillary sphincters in the vicinity, thereby increasing the number of open capillaries.
- When tissue activity decreases, the local precapillary sphincters contract.
- As a result, blood bypasses the capillary bed and flows only through the metarterioles.

Exchange between blood and tissues

- Exchanges across the capillary wall between the plasma and the interstitial fluid are largely passive. The only transport across this barrier that requires energy is the limited vesicular transport.
- Because capillary walls are highly permeable, exchange is so thorough that the interstitial fluid takes on essentially the same composition as incoming arterial blood, with the exception of the large plasma proteins that usually do not escape from the blood. Therefore, when we speak of exchanges between blood and tissue cells, we tacitly include interstitial fluid as a passive intermediary.
- Exchanges between blood and surrounding tissues across capillary walls are accomplished in two ways: (1) passive diffusion down concentration gradients, the primary mechanism for exchanging individual solutes, and (2) bulk flow.

Bulk flow

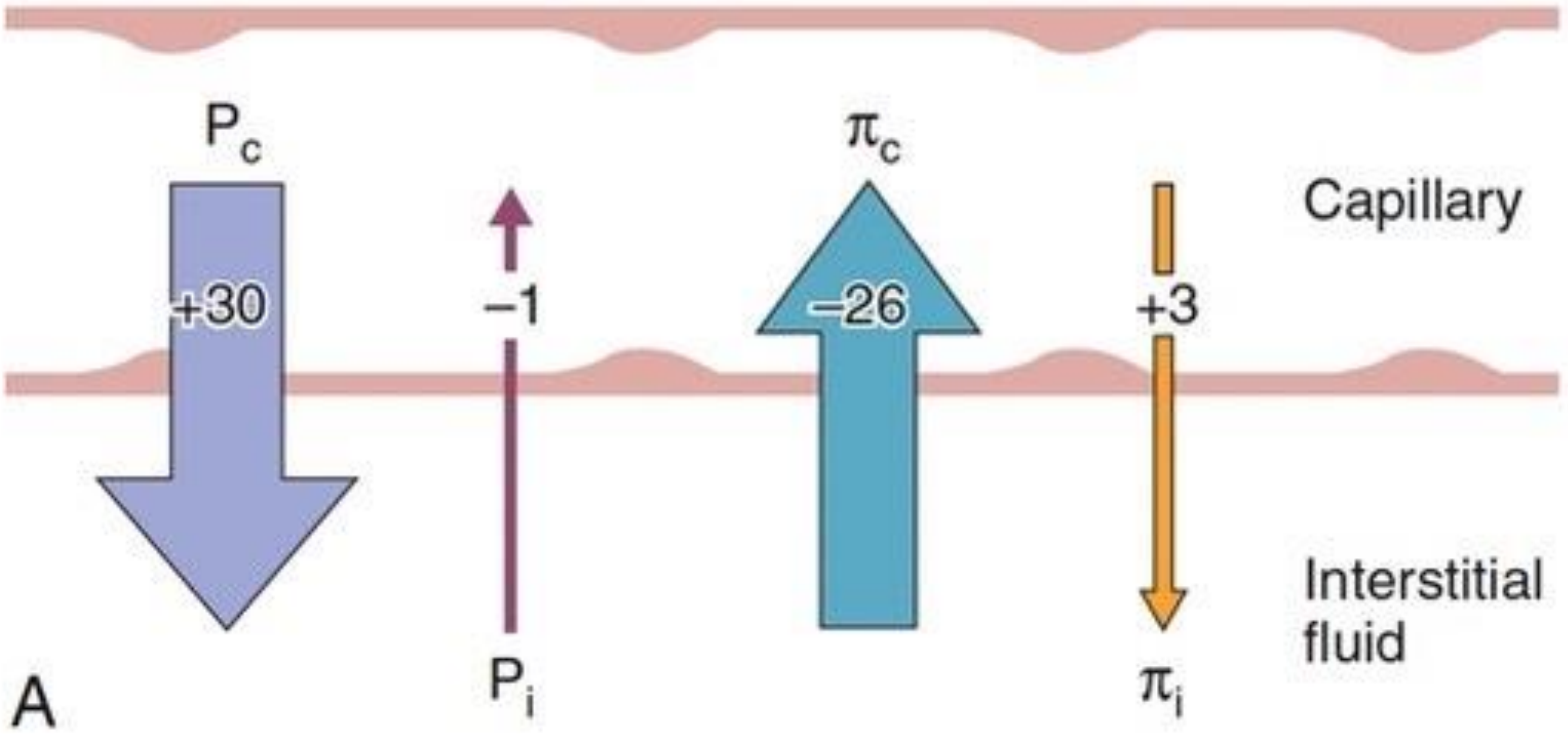
- The second means by which exchange is accomplished across capillary walls is bulk flow.
- A volume of protein-free plasma actually filters out of the capillary, mixes with the surrounding interstitial fluid, and then is reabsorbed.
- This process is called bulk flow because the various constituents of the fluid (water and all solutes) are moving in bulk, or as a unit, in contrast to the discrete diffusion of individual solutes down concentration gradients.

Bulk flow

- Bulk flow does not play an important role in exchange of individual solutes between blood and tissues because the quantity of solutes moved across the capillary wall by bulk flow is extremely small compared to the larger transfer of solutes by diffusion.
- The composition of the fluid filtered out of the capillary is essentially the same as the composition of the fluid that is reabsorbed.
- Thus, ultrafiltration and reabsorption are not important in exchange of nutrients and wastes.
- Bulk flow is extremely important, however, in regulating the distribution of ECF between plasma and interstitial fluid.
- Maintenance of proper arterial blood pressure depends in part on an appropriate volume of circulating blood.

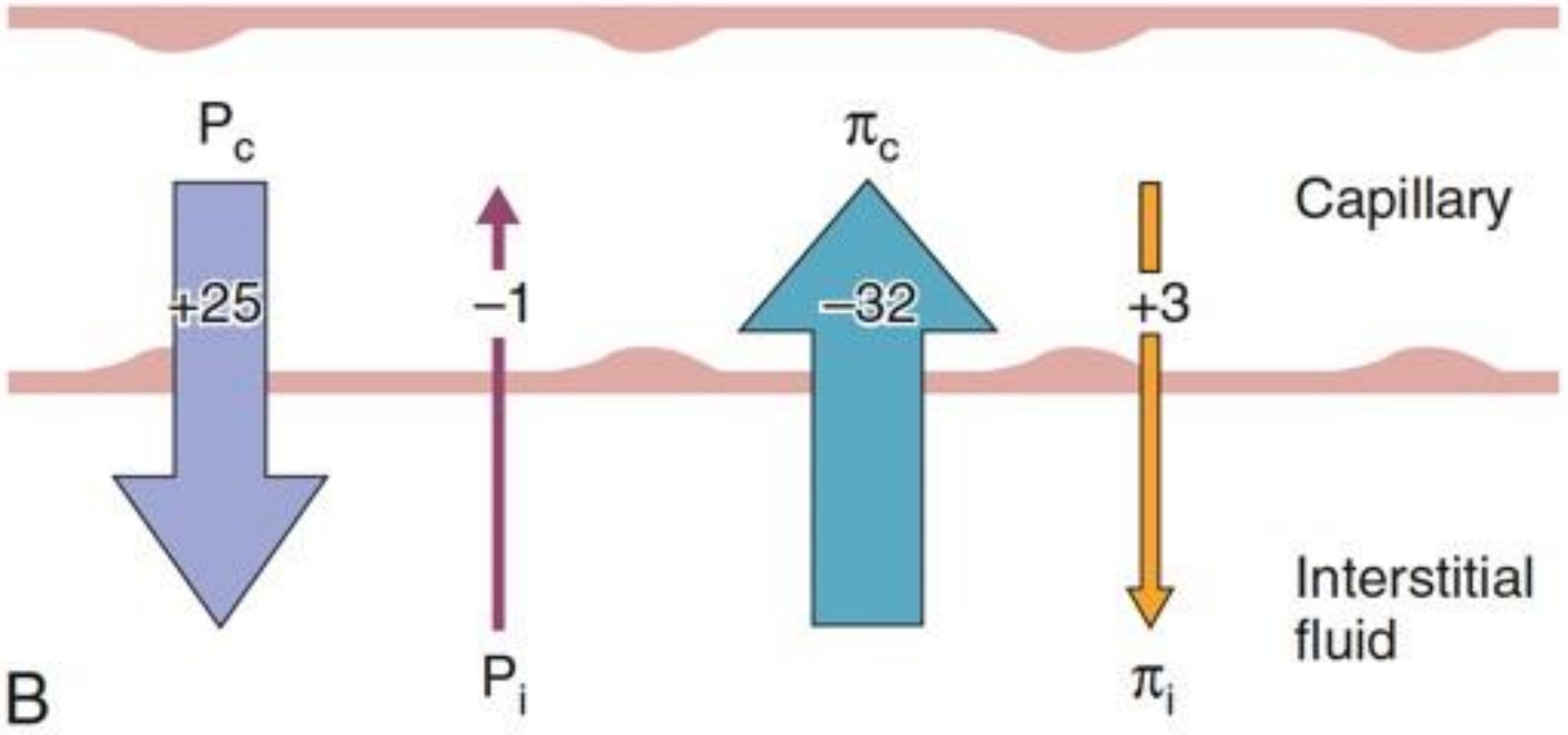
Net filtration

Net pressure = +6 mm Hg



Net absorption

Net pressure = –5 mm Hg



$$J_v = K_f[(P_c - P_i) - (\pi_c - \pi_i)]$$

where

J_v = Fluid movement (mL/min)

K_f = Hydraulic conductance (mL/min per mm Hg)

P_c = Capillary hydrostatic pressure (mm Hg)

P_i = Interstitial hydrostatic pressure (mm Hg)

π_c = Capillary oncotic pressure (mm Hg)

π_i = Interstitial oncotic pressure (mm Hg)

Capillary hydrostatic pressure

- Four forces influence fluid movement across the capillary wall:
- 1. Capillary blood pressure is the fluid or hydrostatic pressure exerted on the inside of the capillary walls by blood.
- This pressure tends to force fluid out of the capillaries into the interstitial fluid.
- By the level of the capillaries, blood pressure has dropped substantially because of frictional losses in pressure in the high-resistance arterioles upstream.
- On average, the hydrostatic pressure is 37 mm Hg at the arteriolar end of a tissue capillary.
- It declines even further, to 17 mm Hg, at the capillary’s venular end because of further frictional loss coupled with the exit of fluid through ultrafiltration along the capillary’s length

Plasma colloid osmotic pressure

- Plasma-colloid osmotic pressure, also known as oncotic pressure, is a force caused by colloidal dispersion of plasma proteins; it encourages fluid movement into the capillaries.
- Because plasma proteins remain in the plasma rather than entering the interstitial fluid, a protein concentration difference exists between plasma and interstitial fluid.
- Accordingly, a water concentration difference also exists between these two regions. Plasma has a higher protein concentration and a lower water concentration than interstitial fluid does. This difference exerts an osmotic effect that tends to move water from the area of higher water concentration in interstitial fluid to the area of lower water concentration in plasma.
- The other plasma constituents do not exert an osmotic effect because they readily pass through the capillary wall, so their concentrations are equal in plasma and interstitial fluid. This pressure averages 25 mm Hg.

Interstitial fluid hydrostatic pressure

- Interstitial fluid hydrostatic pressure is the fluid pressure exerted on the outside of the capillary wall by interstitial fluid.

- This pressure tends to force fluid into the capillaries.

Interstitial fluid colloid osmotic pressure

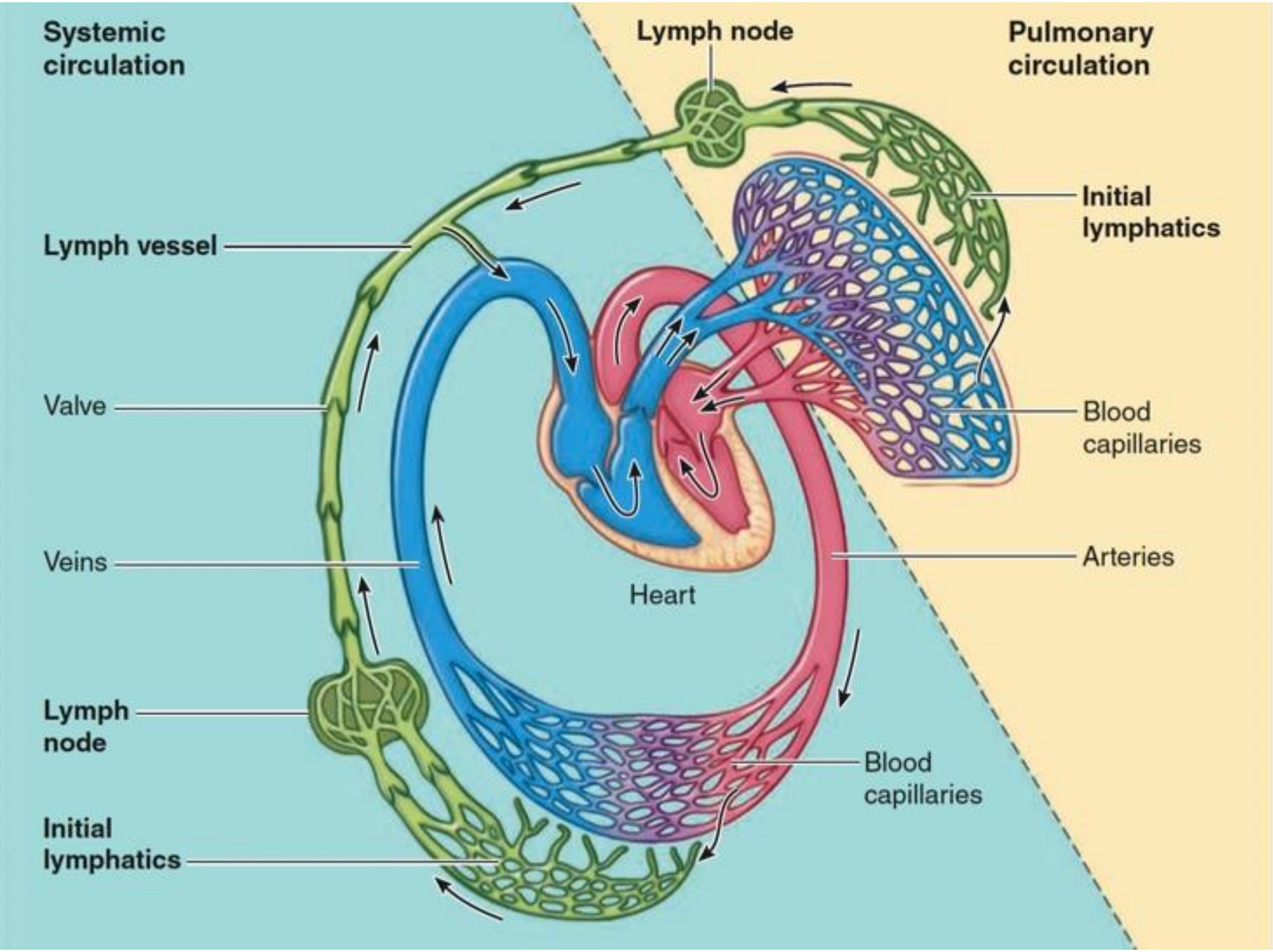
- Interstitial fluid–colloid osmotic pressure is another force that does not normally contribute significantly to bulk flow.
- The small fraction of plasma proteins that leak across the capillary walls into the interstitial spaces are normally returned to the blood by the lymphatic system.
- Therefore, the protein concentration in the interstitial fluid is extremely low, and the interstitial fluid–colloid osmotic pressure is essentially zero.

Net exchange pressure

- A positive net exchange pressure (when outward pressure exceeds inward pressure) represents an ultrafiltration pressure.
- A negative net exchange pressure (when inward pressure exceeds outward pressure) represents a reabsorption pressure.
- At the arteriolar end of the capillary, Ultrafiltration takes place at the beginning of the capillary as this outward pressure gradient forces a protein-free filtrate through the capillary pores.
- By the time the venular end of the capillary is reached, capillary blood pressure has dropped but the other pressures have remained essentially constant. At this point, Reabsorption of fluid takes place as this inward pressure gradient forces fluid back into the capillary at its venular end.

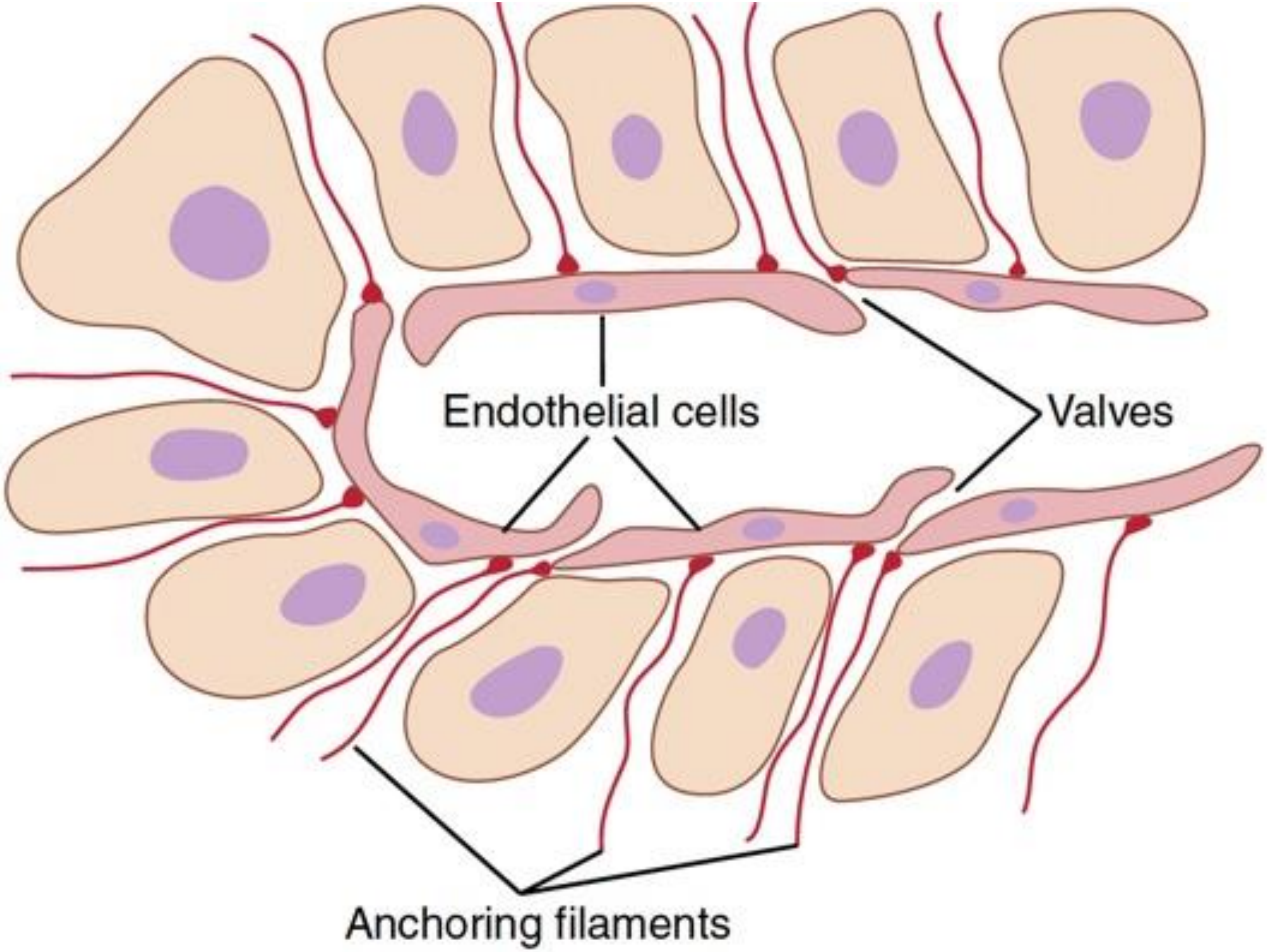
Net filtration pressure

- the NFP is slightly positive under normal conditions, resulting in a net filtration of fluid across the capillaries into the interstitial space in most organs.
- The rate of fluid filtration in a tissue is also determined by the number and size of the pores in each capillary, as well as the number of capillaries in which blood is flowing.
- These factors are usually expressed together as the capillary filtration coefficient (Kf).
- The Kf is therefore a measure of the capacity of the capillary membranes to filter water for a given NFP.


Systemic circulation
Lymph node
Pulmonary circulation
Initial lymphatics
Lymph vessel
Valve
Blood capillaries
Veins
Arteries
Heart
Lymph node
Blood capillaries
Initial lymphatics

The lymphatic system

- under normal circumstances, slightly more fluid is filtered out of the capillaries into the interstitial fluid than is reabsorbed from the interstitial fluid back into the plasma.
- The extra fluid filtered out as a result of this filtration–reabsorption imbalance is picked up by the lymphatic system.


Endothelial cells
Valves
Anchoring filaments

The lymphatic system

- Small, blind-ended terminal lymph vessels known as initial lymphatics permeate almost every tissue of the body.
- The endothelial cells forming the walls of initial lymphatics slightly overlap, with their overlapping edges being free instead of attached to the surrounding cells.
- This arrangement creates one-way, valvelike openings in the vessel wall.
- Fluid pressure on the outside of the vessel pushes the innermost edge of a pair of overlapping edges inward, creating a gap between the edges (that is, opening the valve).
- This opening permits interstitial fluid to enter.

The lymphatic system

- Once interstitial fluid enters a lymphatic vessel, it is called lymph.
- Fluid pressure on the inside forces the overlapping edges together, closing the valves so that lymph does not escape.
- These lymphatic valvelike openings are larger than the pores in blood capillaries.
- Consequently, large particles in the interstitial fluid, such as escaped plasma proteins and bacteria, can gain access to initial lymphatics but are excluded from blood capillaries.

The lymphatic flow

- Initial lymphatics converge to form larger lymph vessels, eventually empty into the venous system before it enters the right atrium.
- There is no “lymphatic heart” to provide driving pressure, but lymph is directed from the tissues toward the venous system in the thoracic cavity by two mechanisms.
- Lymph vessels beyond the initial lymphatics are surrounded by smooth muscle, which contracts rhythmically as a result of myogenic activity. When this muscle is stretched because the vessel is distended with lymph, the muscle inherently contracts more forcefully, pushing the lymph through the vessel.

The lymphatic flow

- This intrinsic “lymph pump” is the major force for propelling lymph.
- Stimulation of lymphatic smooth muscle by the sympathetic nervous system further increases the pumping activity of the lymph vessels.
- Because lymph vessels lie between skeletal muscles, contraction of these muscles squeezes the lymph out of the vessels.
- One-way valves spaced at intervals within the lymph vessels direct the flow of lymph toward its venous outlet in the chest.

Functions of the lymphatic system

- Return of excess filtered fluid.
- Defense against disease.
- Transport of absorbed fat.
- Return of filtered protein.

TABLE 4.6 Causes and Examples of Edema Formation

Cause	Examples
↑ P_c (capillary hydrostatic pressure)	Arteriolar dilation Venous constriction Increased venous pressure Heart failure Extracellular fluid volume expansion
↓ π_c (capillary oncotic pressure)	Decreased plasma protein concentration Severe liver failure (failure to synthesize protein) Protein malnutrition Nephrotic syndrome (loss of protein in urine)
↑ K_f (hydraulic conductance)	Burn Inflammation (release of histamine; cytokines)
Impaired lymphatic drainage	Standing (lack of skeletal muscle compression of lymphatics) Removal or irradiation of lymph nodes Parasitic infection of lymph nodes

Edema

- Excessive interstitial fluid can accumulate when one of the physical forces acting across the capillary walls becomes abnormal for some reason.
- Swelling of the tissues because of excess interstitial fluid is known as edema.
- Whatever the cause of edema, an important consequence is reduced exchange of materials between blood and cells.

Causes of Edema

- A reduced concentration of plasma proteins decreases plasma oncotic pressure.
- Such a drop in the major inward pressure lets excess fluid filter out, whereas less-than-normal amounts of fluid are reabsorbed; hence, extra fluid remains in the interstitial spaces.
- Edema can be caused by a decreased concentration of plasma proteins in several ways:
- excessive loss of plasma proteins in urine, from kidney disease.
- reduced synthesis of plasma proteins, from liver disease.
- a diet deficient in protein.

Causes of Edema

- Increased permeability of the capillary walls allows more plasma proteins than usual to pass from the plasma into the surrounding interstitial fluid:
- The resultant fall in capillary oncotic pressure decreases the effective inward pressure, whereas the resultant rise in interstitial oncotic pressure caused by excess protein in the interstitial fluid increases the effective outward force.
- This imbalance contributes in part to the localized edema associated with injuries (for example, blisters) and allergic responses (for example, hives).

Causes of Edema

- Increased venous pressure, as when blood dams up in the veins, is accompanied by increased capillary hydrostatic pressure.
- Because the capillaries drain into the veins, damming of blood in the veins leads to a “backlog” of blood in the capillaries because less blood moves out of the capillaries into the overloaded veins than enters from the arterioles.
- The resultant elevation in outward hydrostatic pressure across the capillary walls is largely responsible for the edema seen with congestive heart failure.
- Regional edema can also occur because of localized restriction of venous return.
- An example is the swelling often occurring in the legs and feet during pregnancy. The enlarged uterus compresses the major veins that drain the lower extremities as these vessels enter the abdominal cavity.
- The resultant damming of blood in these veins raises blood pressure in the capillaries of the legs and feet, which promotes regional edema of the lower extremities.

Causes of Edema

- Blockage of lymph vessels produces edema because the excess filtered fluid is retained in the interstitial fluid rather than returned to the blood through the lymphatics. Protein accumulation in the interstitial fluid compounds the problem through its osmotic effect.

- Local lymph blockage can occur, for example, in the arms of women whose major lymphatic drainage channels from the arm have been blocked as a result of lymph node removal during surgery for breast cancer.

- More widespread lymph blockage occurs with filariasis, a mosquito borne parasitic disease found predominantly in tropical coastal regions. In this condition, small, threadlike filaria worms infect the lymph vessels, where their presence prevents proper lymph drainage. The affected body parts, particularly the scrotum and extremities, become grossly edematous. The condition is often called elephantiasis because of the elephantlike appearance of the swollen extremities.

Thank you