Vascular Physiology 4

Fatima Ryalat, MD, PhD

Assistant Professor, Department of Physiology and Biochemistry
School of Medicine, University of Jordan

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Capillaries

Exchange of substances across the capillary wall

- Not all capillaries are perfused with blood at all times. Rather, there is selective perfusion of capillary beds, depending on the metabolic needs of the tissues.
- This selective perfusion is determined by the degree of dilation or constriction of the arterioles and precapillary sphincters (smooth muscle bands before the capillaries).
- The exchange of solutes and gases across the capillary wall occurs by simple diffusion.
- Some solutes can diffuse through the endothelial cells, and others must diffuse between the cells, depending on whether the solute or gas is lipid soluble.

Exchange of substances across the capillary wall

- Gases such as O_2 and CO_2 are highly lipid soluble.
- These gases readily cross the capillary wall by diffusing through the endothelial cells; diffusion is driven by the partial pressure gradient for the individual gas.

- the rate of diffusion depends on the driving force (the partial pressure difference for the gas) and the surface area available for diffusion. Thus, the greater the number of open capillaries, the greater the surface area for diffusion.

Exchange of substances across the capillary wall

- Water-soluble substances such as water itself, ions, glucose, and amino acids are not lipid soluble; thus they cannot cross the endothelial cell membranes.

- The diffusion of water-soluble substances is limited to the aqueous clefts between endothelial cells; hence, the surface area for their diffusion is much less than that for the lipid-soluble gases.

Factors enhancing diffusion across capillaries

- Diffusion across the capillaries is fast due to the short distance of travel between blood and cells.

- That’s because of the thin capillary wall and small capillary diameter, coupled with the proximity of every cell to a capillary.

Exchange across capillaries

- 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, in a process called transcytosis.

Velocity of blood flow

- The velocity of blood flow is the rate of displacement of blood per unit time.
- The velocity with which blood flows through the different segments of the vascular tree varies because velocity of flow is inversely proportional to the total cross-sectional area of all vessels at any given level.

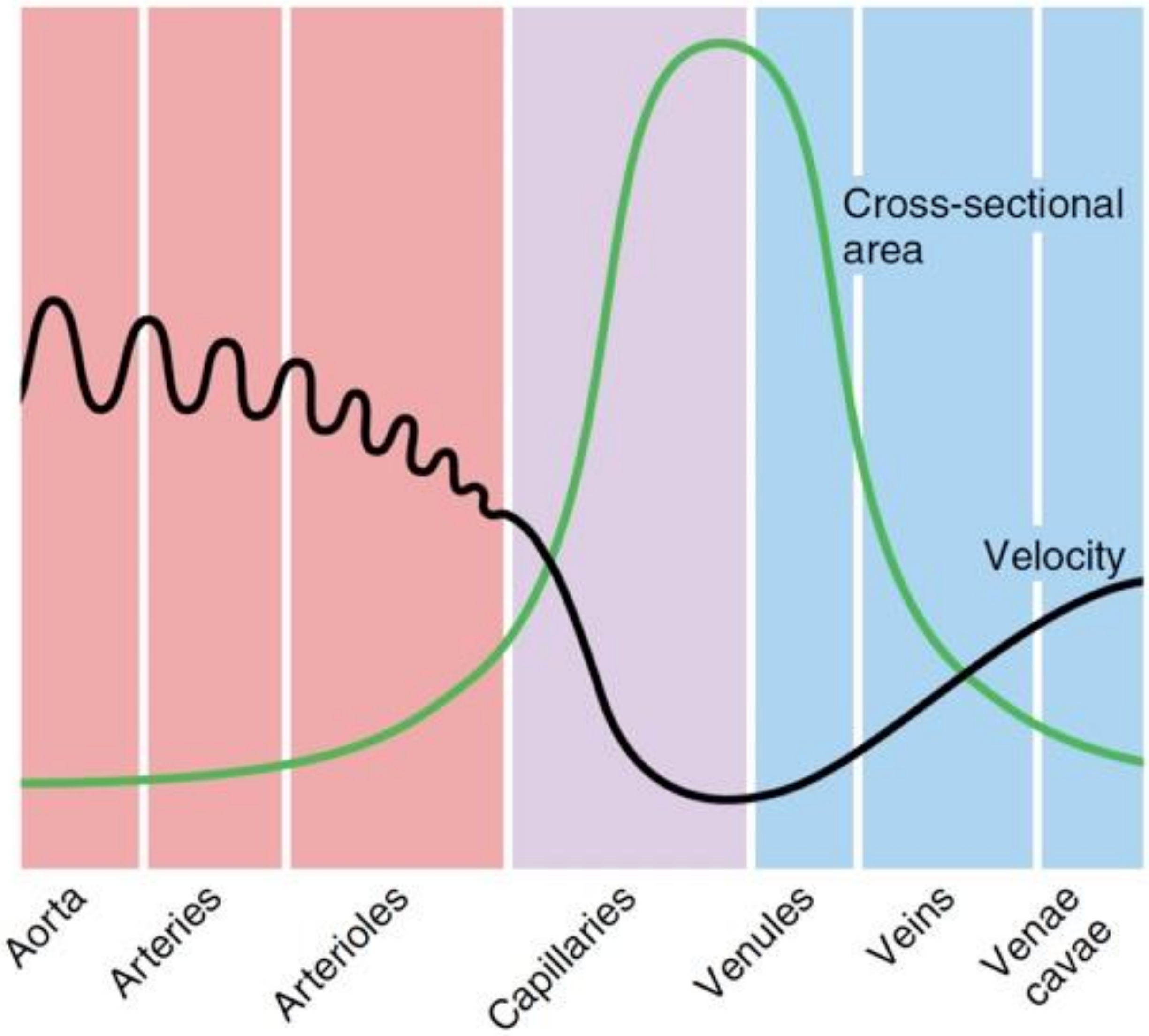
- $V = Q / A$

- Where:
- V = Velocity of blood flow (cm/s)
- Q = Flow (mL/s)
- A = Cross-sectional area (cm2)

Velocity of blood flow through capillaries

- Even though the cross-sectional area of each capillary is extremely small compared to that of the large aorta, the total cross-sectional area of all capillaries added together is about 750 times greater than the cross-sectional area of the aorta because there are so many capillaries. Accordingly, blood slows considerably as it passes through the capillaries.
- This slow velocity allows adequate time for exchange of nutrients and metabolic end products between blood and tissue cells.
- As capillaries rejoin to form veins, the total cross-sectional area is again reduced, and the velocity of blood flow increases as blood returns to the heart.

Velocity of blood flow is slowest in the capillaries because they have the largest total cross-sectional area.



Capillaries role in resistance

- Also, because of the capillaries' tremendous total cross-sectional area, the resistance offered by all capillaries is lower than that offered by all arterioles, even though each capillary has a smaller radius than each arteriole.
- Furthermore, capillary diameter can not be adjusted like in the arterioles.

Pressure in capillaries

- In the capillaries, pressure decreases further for two reasons:

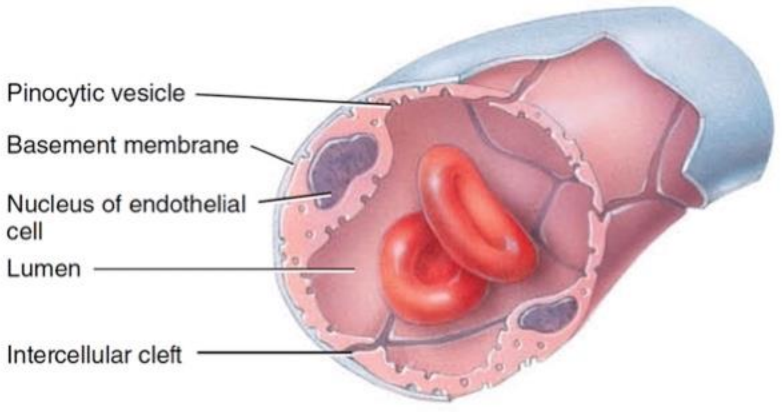
1. frictional resistance to flow.
2. filtration of fluid out of the capillaries.

- When blood reaches the venules and veins, pressure has decreased even further, because capacitance of the veins is high, the veins can hold large volumes of blood at low pressure.

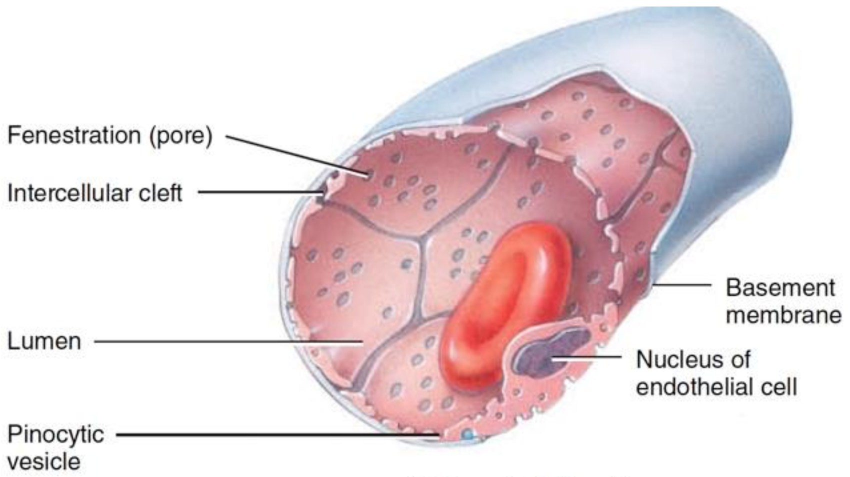
Capillary wall permeability

- Diffusion across capillary walls depends on the walls' permeability to the materials being exchanged.
- Most capillaries, endothelial cells are continuous, with only narrow clefts, or pores.
- The size of capillary pores varies from organ to organ depending on the organ needs.
- Endothelial cells can actively change to regulate capillary permeability in response to appropriate signals, Thus, the degree of leakiness does not necessarily remain constant for a given capillary bed.

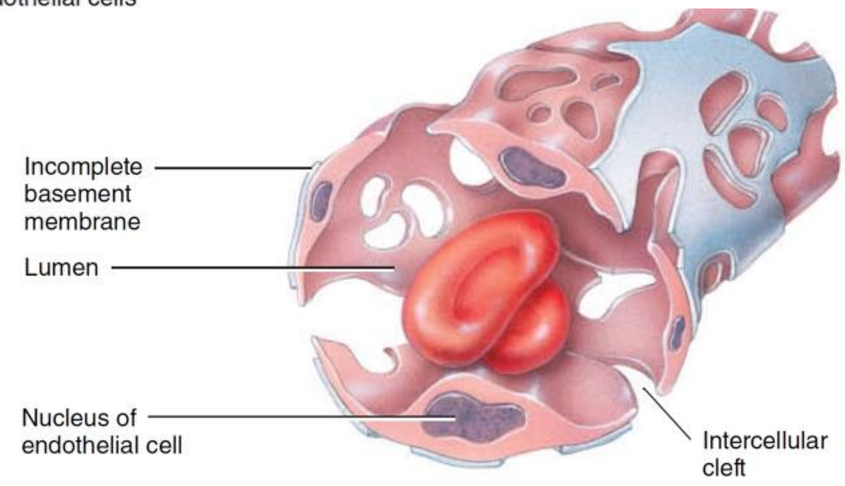
Capillary types



(a) Continuous capillary formed by endothelial cells



(b) Fenestrated capillary



(c) Sinusoid

Exchange across the capillaries

- 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.
- (2) bulk flow, a process that determines the distribution of the ECF volume between the vascular and the interstitial fluid compartments.

Exchange across the capillaries

- Exchanges between blood and tissue cells are not made directly.
- Interstitial fluid is the true internal environment in immediate contact with the cells.
- Cells exchange materials directly with interstitial fluid, with the type and extent of exchange being governed by the properties of cellular plasma membranes.

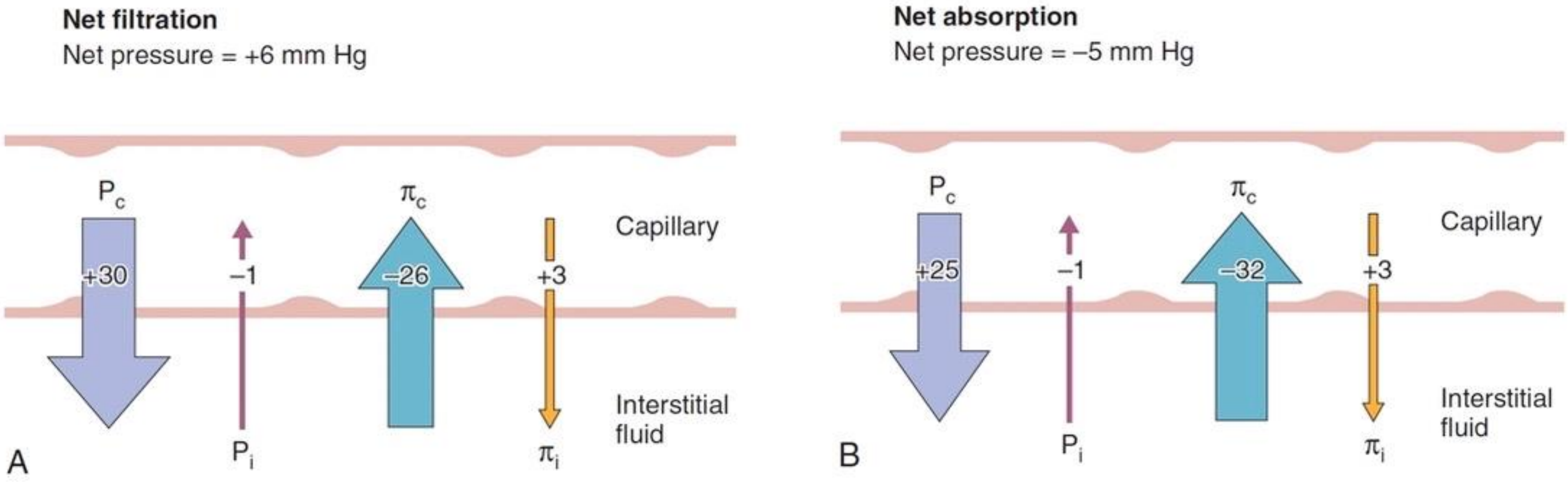
Bulk flow across capillaries

- Bulk flow occurs because of differences in hydrostatic and colloid osmotic pressures between plasma and interstitial fluid.
- Four forces influence fluid movement across the capillary wall

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

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)

Starling equation



Bulk flow

- Ultrafiltration and reabsorption, collectively known as bulk flow, are thus the result of a shift in the balance between the passive physical forces acting across the capillary wall.

- No active forces or local energy expenditures are involved in bulk exchange of fluid between plasma and surrounding interstitial fluid.

- Ultrafiltration occurs at the beginning of the capillary because capillary blood pressure exceeds plasma-colloid osmotic pressure, whereas by the end of the capillary, reabsorption takes place because blood pressure has fallen below osmotic pressure.

Significance of bulk flow

- 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 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.

Lymphatic system

- Even 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.
- Because of this pressure differential, on average more fluid is filtered out of the first half of the capillary than is reabsorbed in its last half.
- The extra fluid filtered out as a result of this filtration–reabsorption imbalance is picked up by the lymphatic system.
- This extensive network of one-way vessels provides an accessory route by which fluid can be returned from the interstitial fluid to the blood.

Lymphatic system

- 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. 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, and 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 lymphatics

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

Edema

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

TABLE 4.6 Causes and Examples of Edema Formation

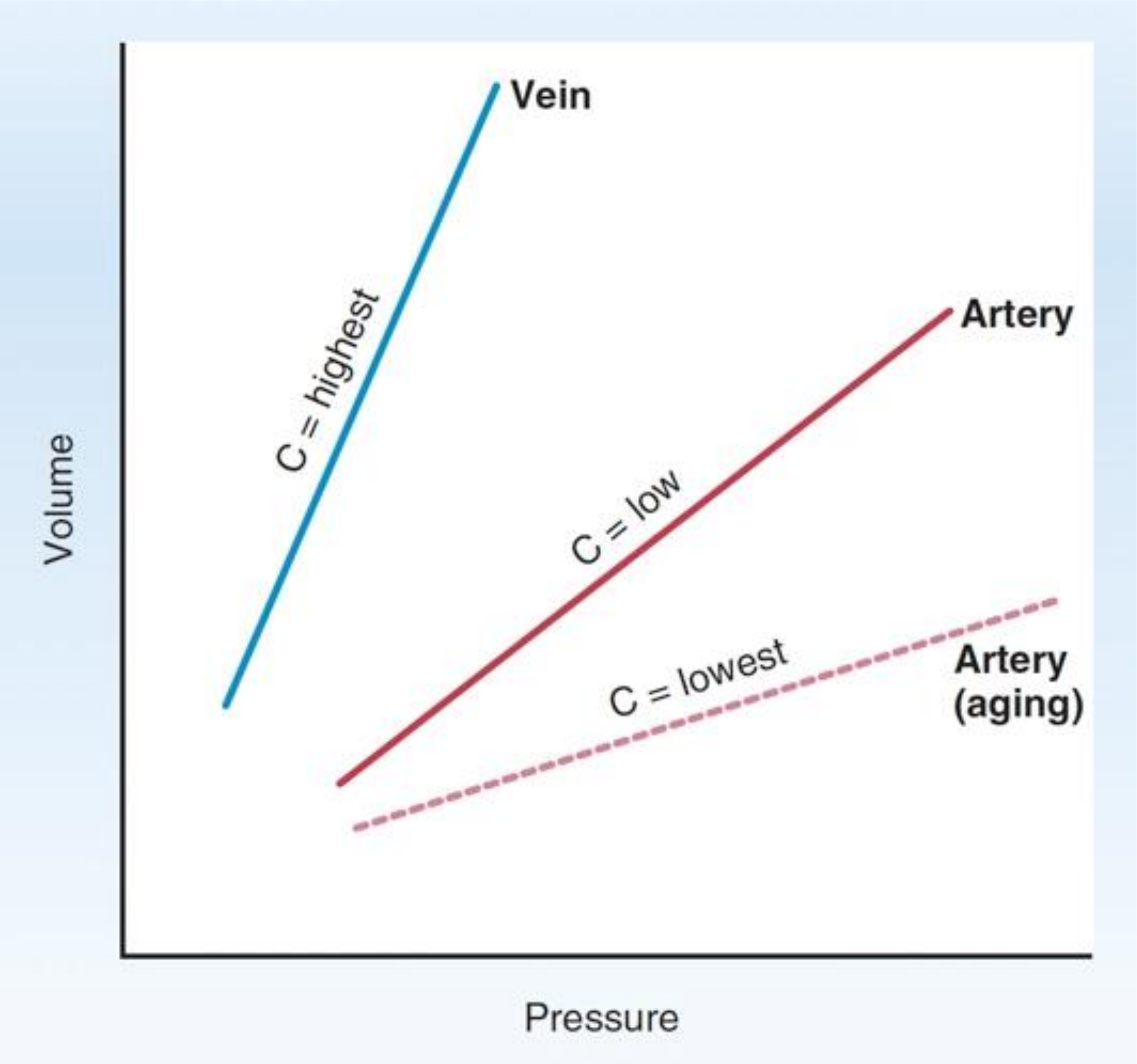
Cause	Examples
↑ P_c (capillary hydrostatic pressure)	Arteriolar dilation Venous constriction Increased venous pressure Heart failure Extracellular fluid volume expansion
↓ π_c (capillary oncotic pressure)	Decreased plasma protein concentration Severe liver failure (failure to synthesize protein) Protein 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

Veins

- Veins have a large radius, so they offer little resistance to flow.
- Furthermore, because the total cross-sectional area of the venous system gradually decreases as smaller veins converge into progressively fewer but larger vessels, blood flow speeds up as blood approaches the heart.
- In addition to serving as low-resistance passageways to return blood from the tissues to the heart, systemic veins also serve as a blood reservoir. Because of their storage capacity, veins are often called capacitance vessels.

Compliance in veins vs arteries

- Compliance of the veins is high; in other words, the veins hold large volumes of blood at low pressure.
- Compliance of the arteries is much lower than that of the veins; the arteries hold much less blood than the veins, and they do so at high pressure.
- The veins are most compliant and contain the unstressed volume (large volume under low pressure).
- The arteries are much less compliant and contain the stressed volume (low volume under high pressure).
- The total volume of blood in the cardiovascular system is the sum of the unstressed volume plus the stressed volume (plus whatever volume is contained in the heart).
- Changes in compliance of the veins cause redistribution of blood between the veins and the arteries (i.e., the blood shifts between the unstressed and stressed volumes).

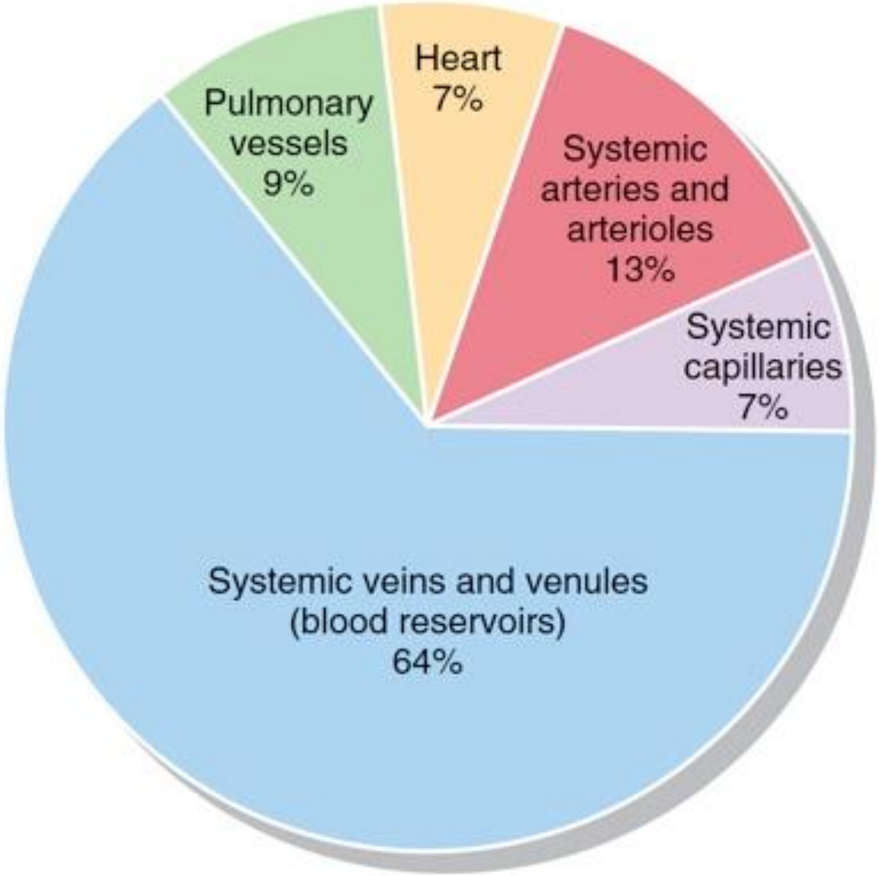


Vein
C = highest
Artery
C = low
C = lowest
Artery
(aging)
Volume
Pressure

Veins

- Because of their storage capacity, veins are often called capacitance vessels.
- They easily distend to accommodate additional volumes of blood with only a small increase in venous pressure.
- veins serve as a blood reservoir— that is, when demands for blood are low, the veins can store extra blood in reserve because of their passive distensibility.
- Under resting conditions, the veins contain more than 60% of the total blood volume

Blood volume distribution in the circulation at rest



Venous capacity

- Venous capacity (the volume of blood that the veins can accommodate) depends on the distensibility of the vein walls (how much they can stretch to hold blood) and the influence of any externally applied pressure squeezing inwardly on the veins.
- At a constant blood volume, as venous capacity increases, more blood remains in the veins instead of being returned to the heart.
- Such venous storage decreases the effective circulating blood volume, the volume of blood being returned to and pumped out of the heart.

Venous capacity

- Changes in venous capacity directly influence the magnitude of venous return, which in turn is one of the important determinants of effective circulating blood volume.
- The effective circulating blood volume is also influenced short term by passive shifts in bulk flow between plasma and interstitial fluid and long term by factors that control total ECF volume, such as salt and water balance.

Venous return

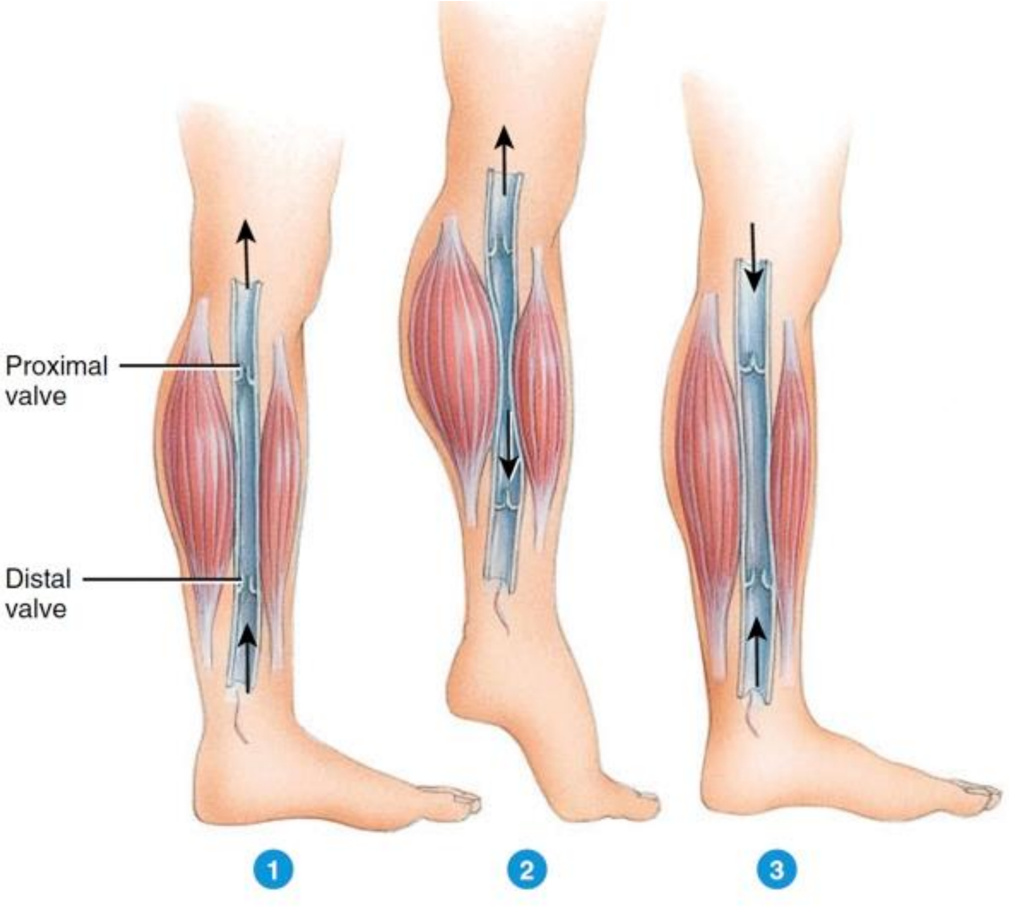
- venous return refers to the volume of blood per minute entering each atrium from the veins.
- In addition to the driving pressure imparted by cardiac contraction, five other factors enhance venous return: sympathetically induced venous vasoconstriction, skeletal muscle pump, venous valves, respiratory pump, and cardiac suction.
- Most of these secondary factors affect venous return by increasing the pressure gradient between the veins and the heart.

Sympathetic stimulation

- Sympathetic stimulation produces venous vasoconstriction, which modestly elevates venous pressure; this, in turn, increases the pressure gradient to drive more of the stored blood from the veins into the right atrium, thus enhancing venous return.

Skeletal muscle pump

- This external venous compression decreases venous capacity and increases venous pressure, in effect squeezing blood in the veins forward toward the heart
- The skeletal muscle pump also counters the effect of gravity on the venous system.



Venous valves

- These venous valves also play a role in counteracting the gravitational effects of upright posture by helping minimize the backflow of blood that tends to occur when a person stands up and by temporarily supporting portions of the column of blood when the skeletal muscles are relaxed.
- Varicose veins occur when the venous valves become incompetent and can no longer support the column of blood above them.

Respiratory pump

- As the venous system returns blood to the heart from the lower regions of the body, it travels through the chest cavity, where it is exposed to this sub-atmospheric pressure.
- This pressure difference pushes blood from the lower veins to the chest veins, promoting increased venous return.

Cardiac suction

- During ventricular contraction, the AV valves are drawn downward, enlarging the atrial cavities. As a result, atrial pressure transiently drops below 0 mm Hg, thus increasing the vein-to-atria pressure gradient so that venous return is enhanced.
- In addition, rapid expansion of the ventricular chambers during ventricular relaxation creates a transient negative pressure in the ventricles so that blood is “sucked in” from the atria and veins—that is, the negative ventricular pressure increases the vein-to-atria-to-ventricle pressure gradient, further enhancing venous return.

Special circulations

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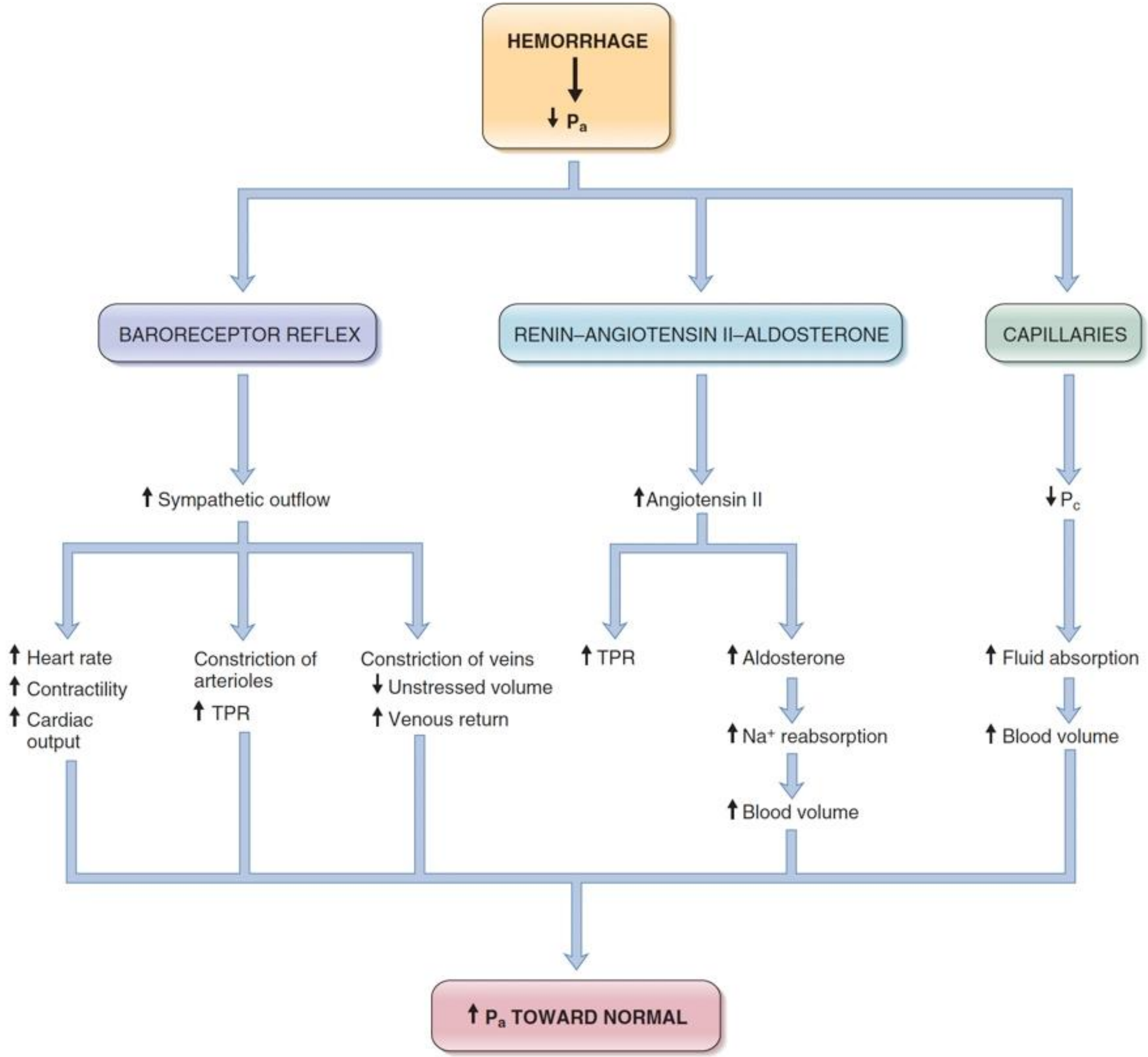
Circulation	Local Metabolic Control	Vasoactive Metabolites	Sympathetic Control	Mechanical Effects
Coronary	Most important mechanism	Hypoxia Adenosine	Least important mechanism	Mechanical compression during systole
Cerebral	Most important mechanism	CO_2 H^+	Least important mechanism	Increases in intracranial pressure decrease cerebral blood flow
Skeletal Muscle	Most important mechanism during exercise	Lactate CO_2 K^+ Adenosine	Most important mechanism at rest (α_1 receptors, vasoconstriction; β_2 receptors, vasodilation)	Muscular activity compresses blood vessels
Skin	Least important mechanism	—	Most important mechanism for temperature regulation (α_1 receptors, vasoconstriction)	—
Pulmonary	Most important mechanism	Hypoxia vasoconstricts	Least important mechanism	Lung inflation
Renal	Most important mechanism (myogenic; tubuloglomerular feedback)	—	Least important mechanism	—


HEMORRHAGE
↓ P_a
BARORECEPTOR REFLEX
RENIN–ANGIOTENSIN II–ALDOSTERONE
CAPILLARIES
↑ Sympathetic outflow
↑ Angiotensin II
↓ P_c
↑ Heart rate
↑ Contractility
↑ Cardiac output
Constriction of arterioles
↑ TPR
Constriction of veins
↓ Unstressed volume
↑ Venous return
↑ TPR
↑ Aldosterone
↑ Na^+ reabsorption
↑ Blood volume
↑ Fluid absorption
↑ Blood volume
↑ P_a TOWARD NORMAL

Thank you