

Histology of Cardiovascular system

By :

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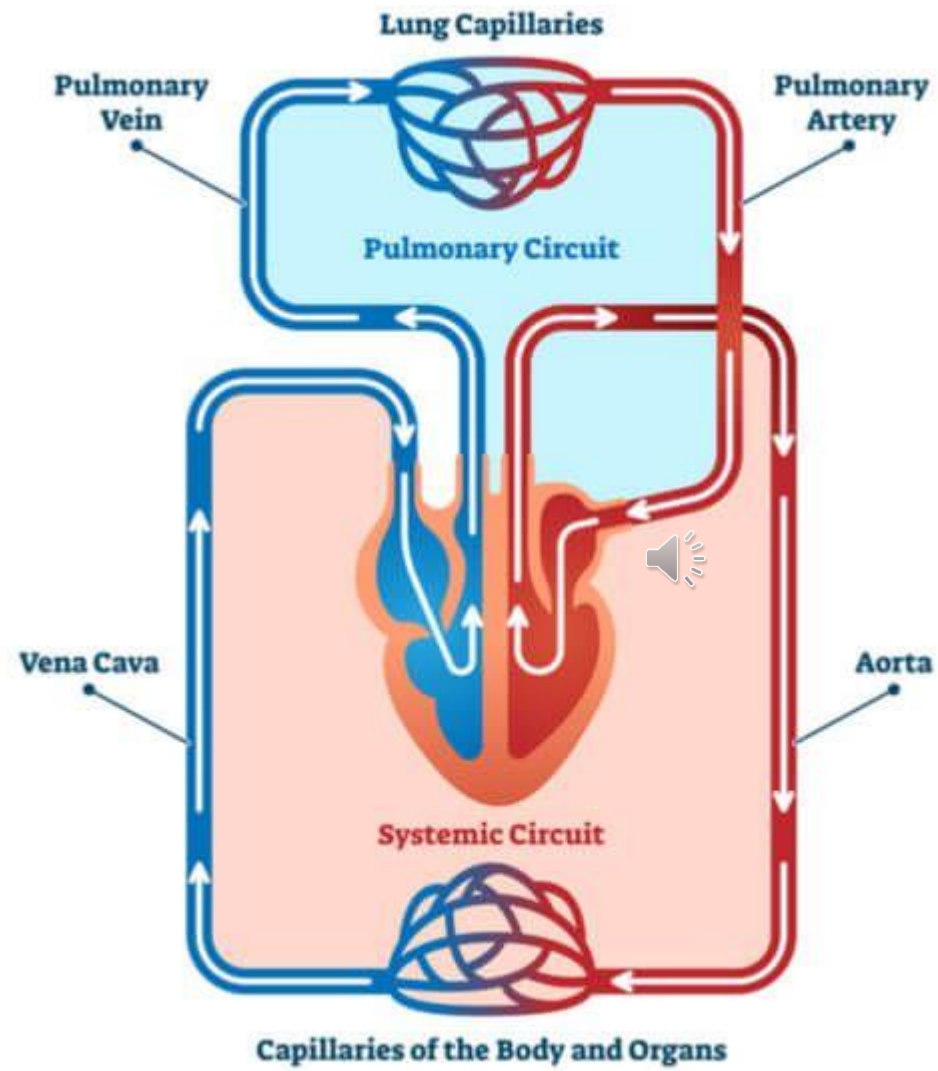


CARDIOVASCULAR SYSTEM

The **cardiovascular system** is composed of the **heart**, a muscular organ that pumps the blood into two separated circuits:

- 1- the **pulmonary circuit**, which carries blood to and from the lung
- 2- the **systemic circuit**, which distributes blood to and from all of the organs and tissues of the rest of the body.

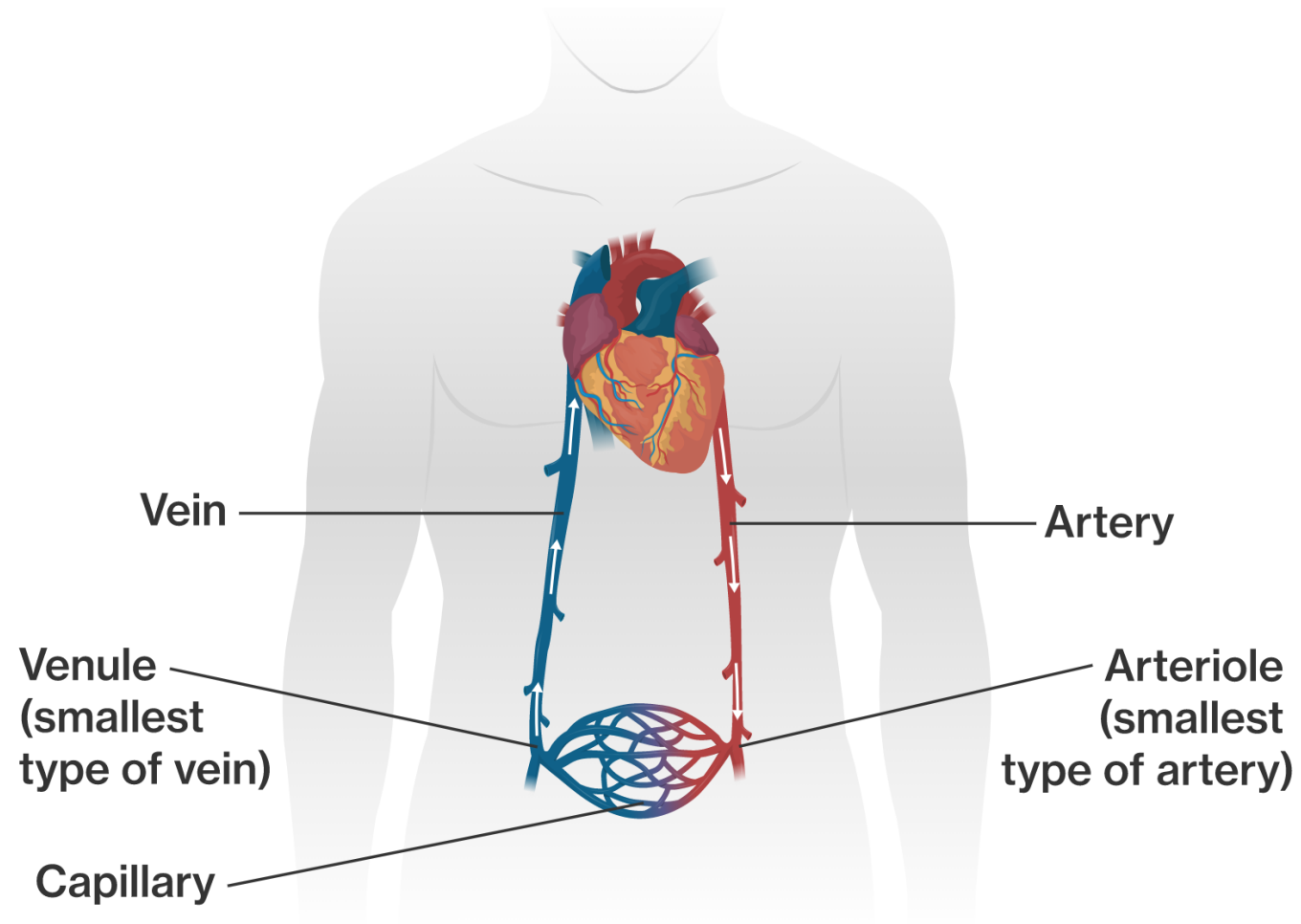




The components of these circuits are

- **Arteries.** A series of vessels that transport blood away from the heart by branching into vessels of smaller and smaller diameters, eventually to capillaries to supply all regions of the body with blood.
- **Capillaries.** Thin-walled vessels with the smallest diameter, forming capillary beds, where gases, nutrients, metabolic wastes, hormones, and signaling substances are interchanged or passed between the blood and the tissues of the body to sustain normal metabolic activities.
- **Veins.** Vessels that drain capillary beds and form larger and larger vessels returning blood to the heart.





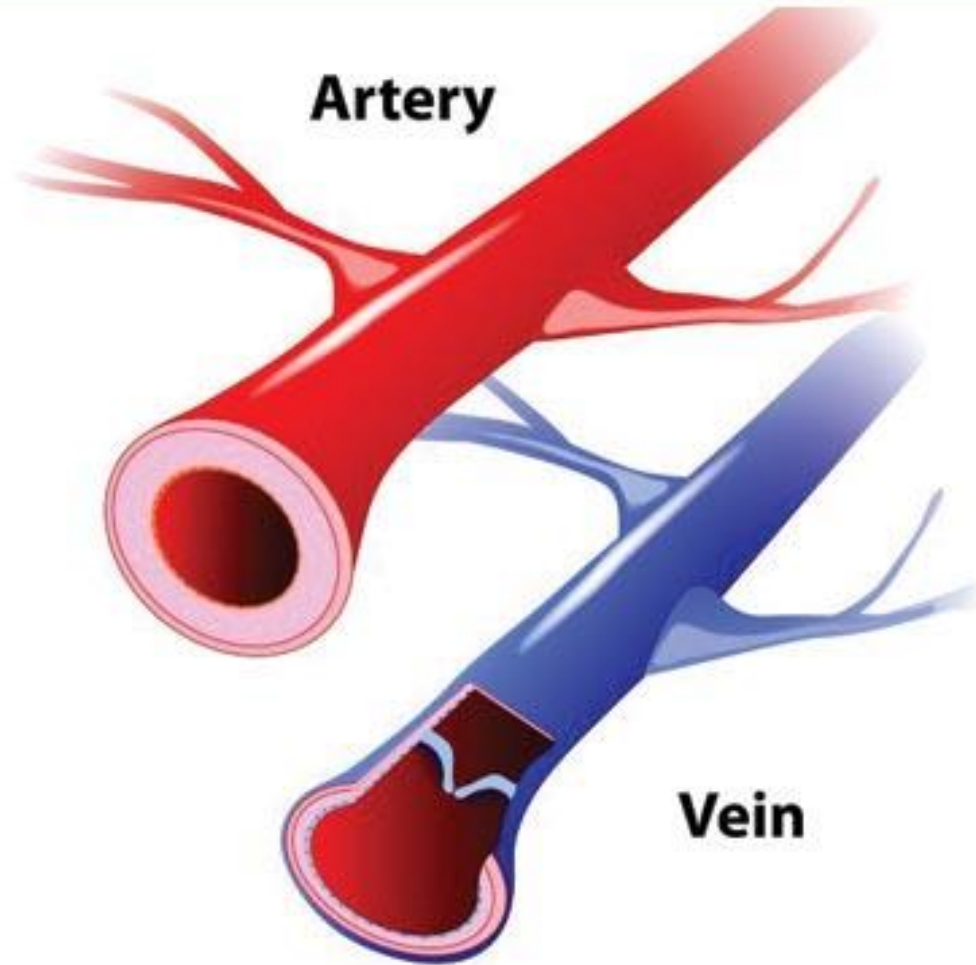
General Structure of Blood Vessels

Generally, arteries have thicker walls and are smaller in diameter than are the corresponding veins. Moreover, in histological sections, arteries are round whereas veins are flattened

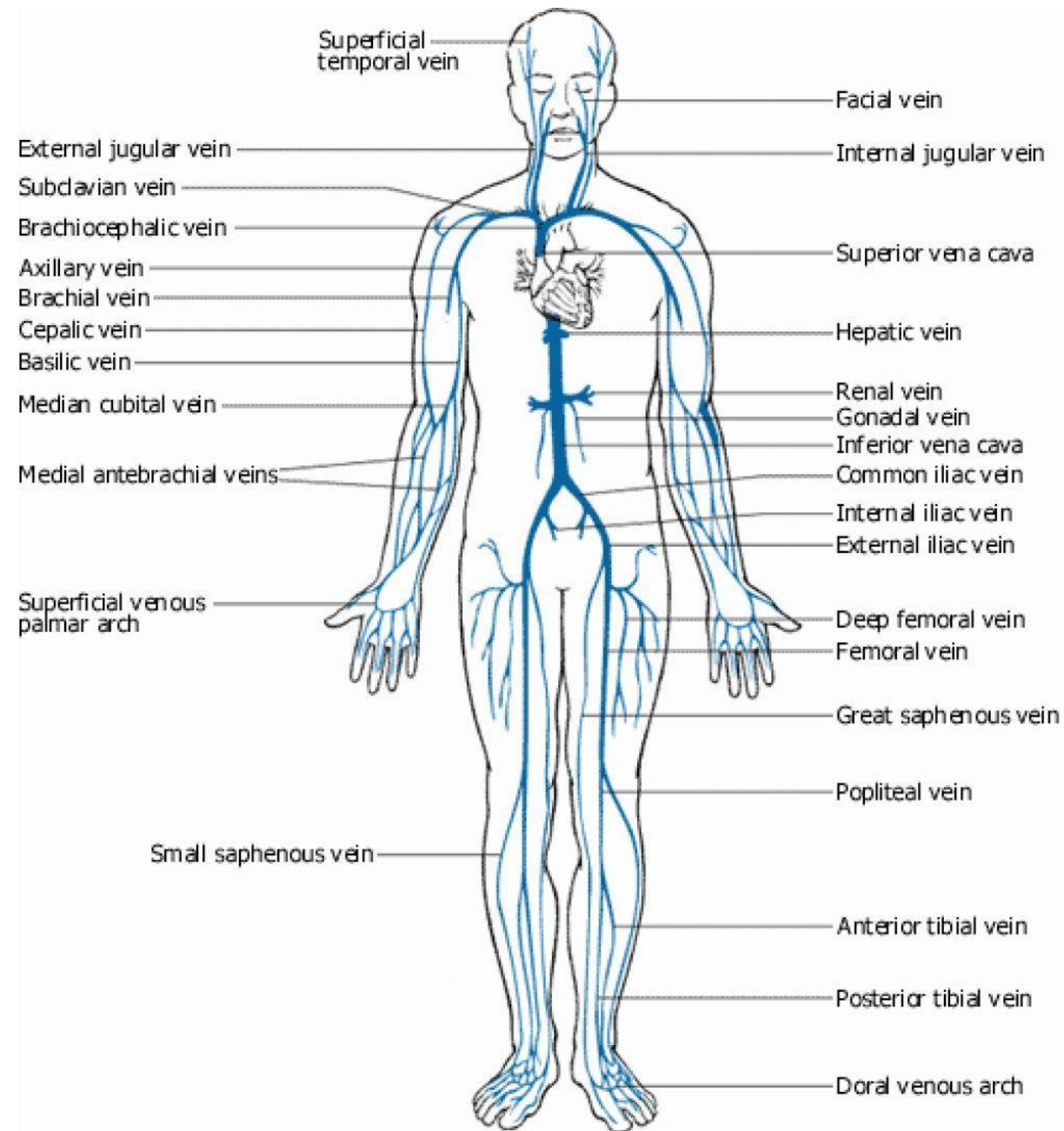
Arterial diameters continue to decrease at each branching, whereas vein diameters increase at each convergence, thus altering the respective layers of the walls of the vessels.

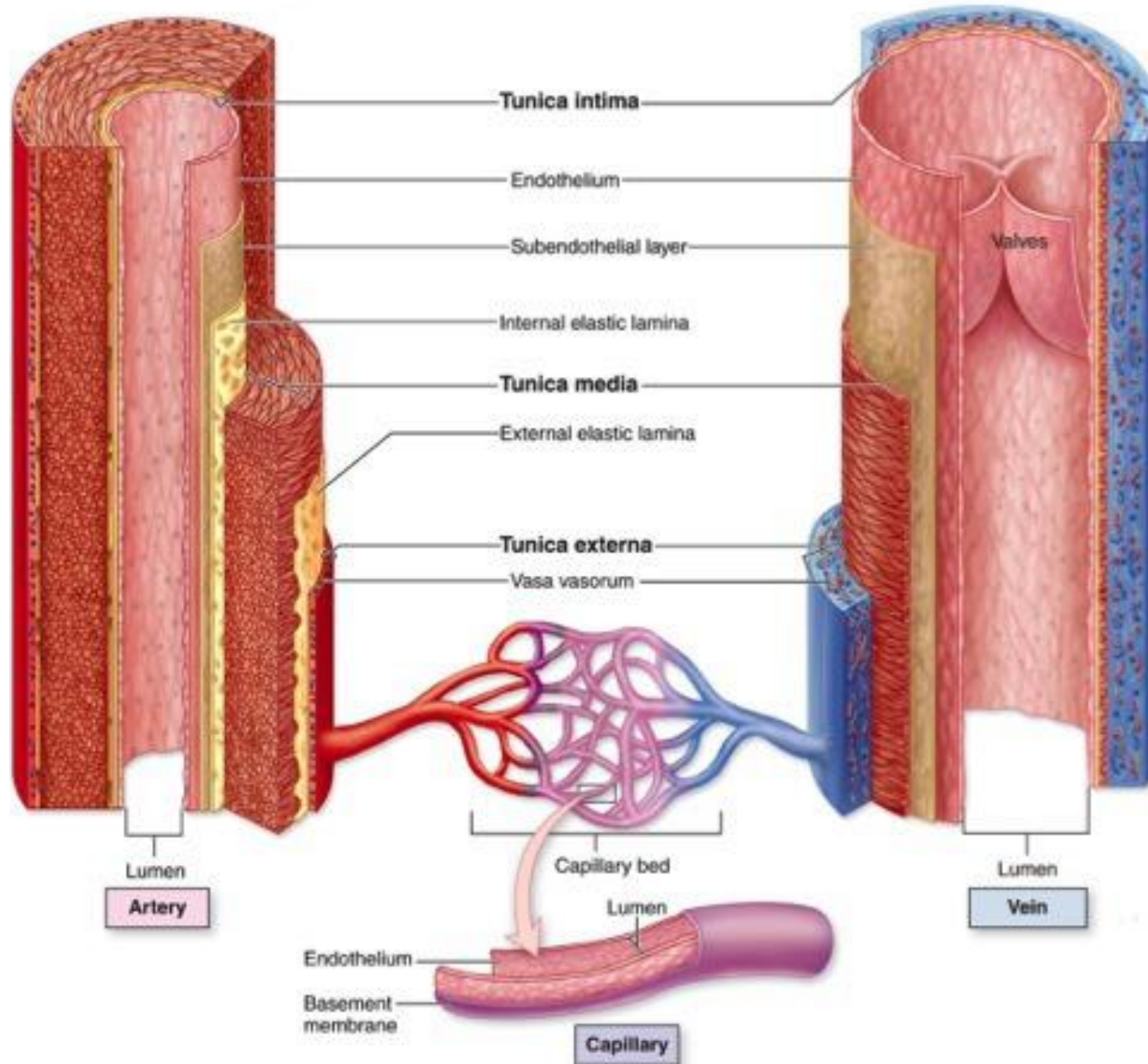


Arteries vs Vein



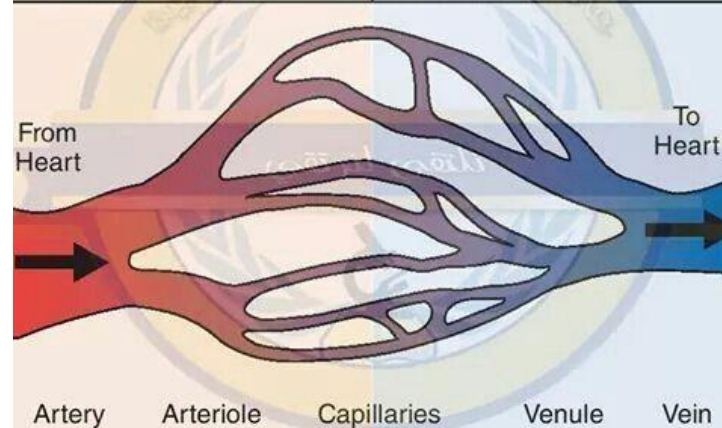






ARTERIES VERSUS VEINS

Arteries	Veins
1. Carry blood from the heart, carry oxygenated blood (except pulmonary artery)	1. Carry blood to the heart, carry deoxygenated blood (except pulmonary vein)
2. Normally bright red in color	2. Normally dark red in color
3. Elastic walls that expand with surge of blood	3. Thin walls/less elastic
4. No valves	4. Valves
5. Can feel a pulse	5. No pulse



Vessel Tunics

Walls of blood vessels are composed of three layers: the tunica intima, the tunica media, and the tunica adventitia.

1- The innermost layer, the **tunica intima**, is composed of a single layer of **flattened, squamous endothelial** cells, which form a tube lining the lumen of the vessel, and the underlying subendothelial connective tissue.

2- The intermediate layer, the **tunica media**, is composed mostly of **smooth muscle cells** oriented concentrically around the lumen.

3- The outermost layer, the **tunica adventitia**, is composed mainly **of fibroelastic connective tissue** whose fibers are arranged longitudinally.



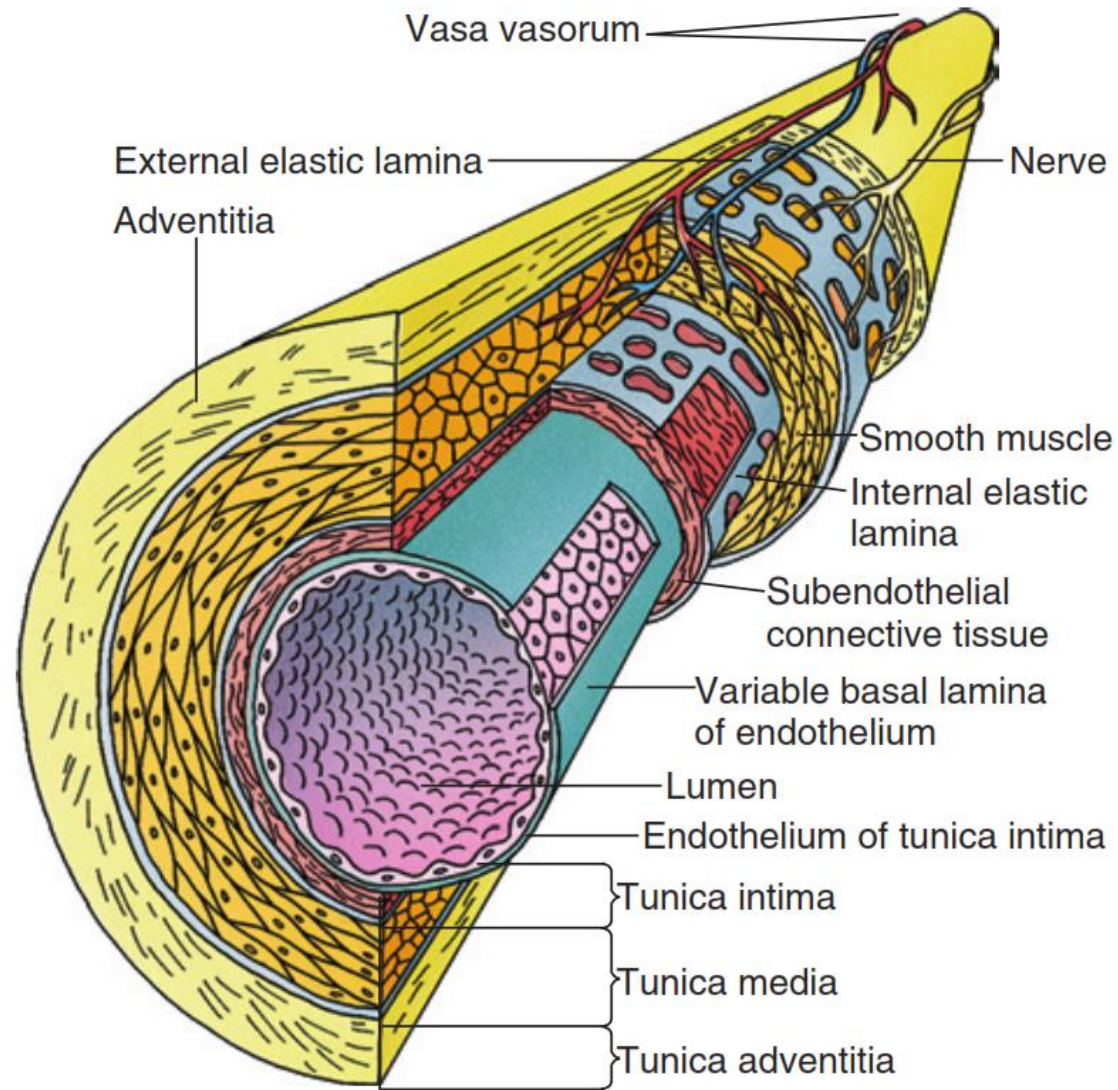


Figure 11-1 Diagram of a typical artery.



The tunica intima houses in its outermost layer the **internal elastic lamina, a thin band of elastic fibers** that is well developed in medium-sized arteries.

The outermost layer of the tunica media houses another **band of elastic fibers, the external elastic lamina,** although it is not distinguishable in all arteries.



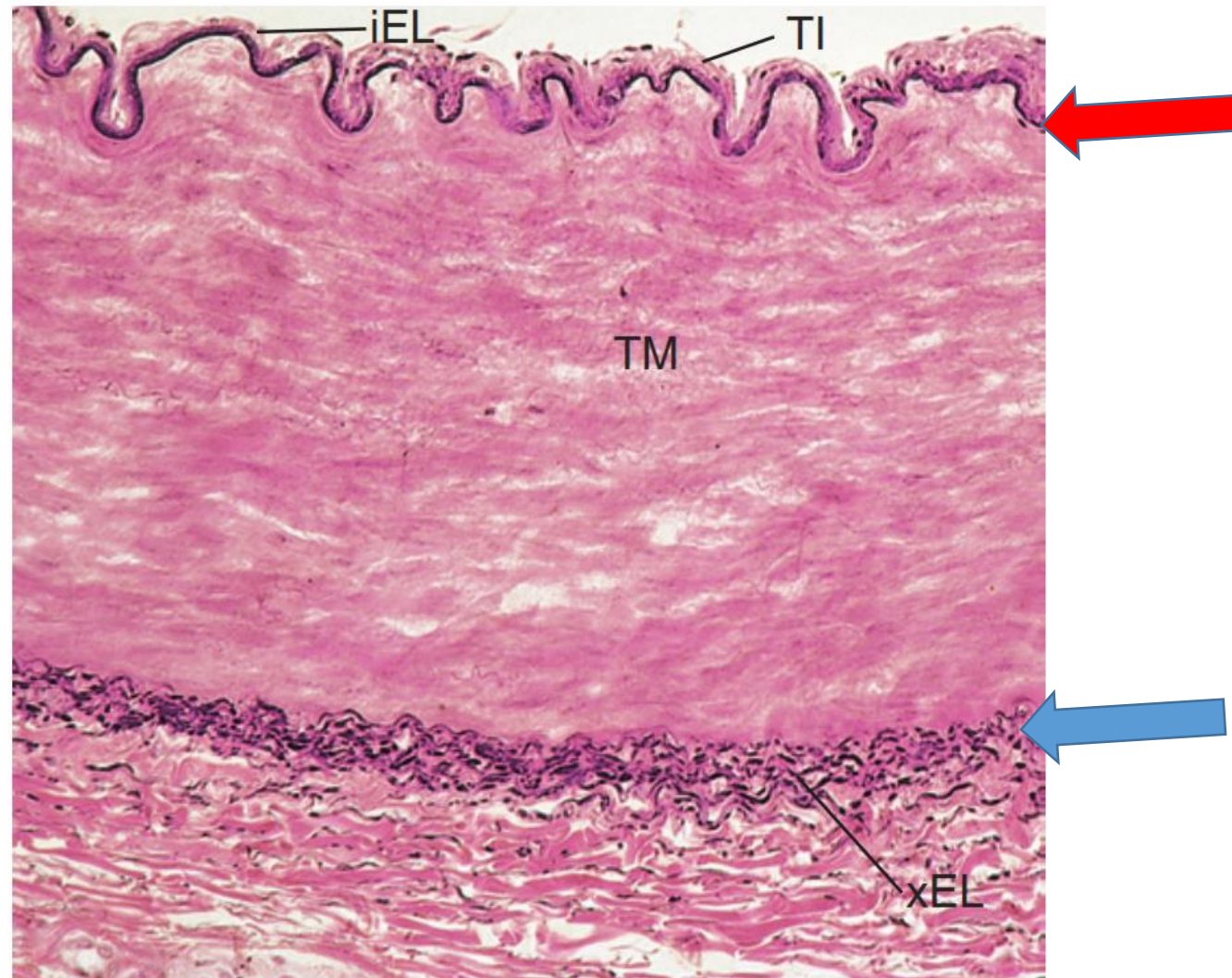
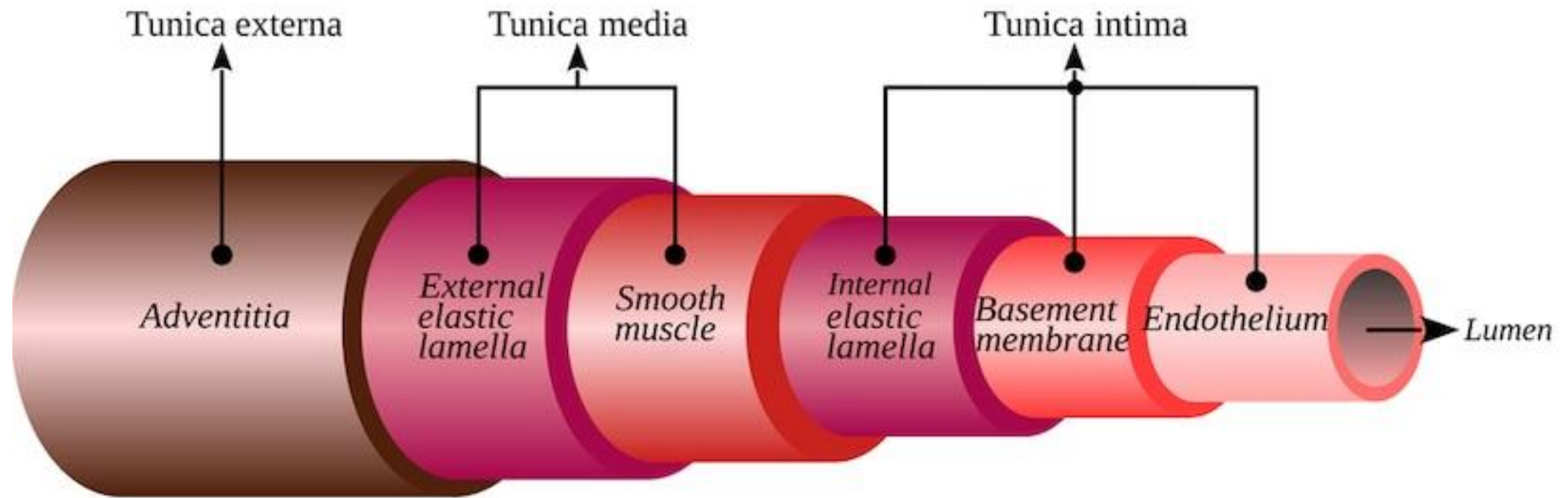


Figure 11-3 Light micrograph of a muscular artery ($\times 132$). Note the tunica adventitia, the internal (iEL) and external (xEL) elastic laminae within the thick tunica media (TM). TI, Tunica intima.





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Tunica Intima

*The tunica intima is composed of a simple squamous epithelium, known as the **endothelium**, and the **subendothelial connective tissue**, including the internal elastic lamina.*

The endothelial cells (simple squamous epithelium) lining the lumen of the blood vessel rest on a basal Lamina (basement membrane)



Endothelial cells functions:

- Secrete types II, IV, and V collagens, laminin, endothelin, nitric oxide, von Willebrand factor (vWF), tissue factor, and P-selectin
- Possess membrane-bound enzymes, such as **angiotensin-converting enzyme (ACE), which cleave angiotensin I to generate angiotensin II**
- Possess enzymes that inactivate bradykinin, serotonin, prostaglandins, thrombin, and norepinephrine
- Bind lipoprotein lipase, the enzyme that degrades lipoprotein triglycerides into glycerol and fatty acids



A subendothelial layer lies immediately beneath the endothelial cells. It is composed of loose connective tissue.

Beneath the subendothelial connective tissue layer is an internal elastic lamina that is especially well developed in muscular arteries. Separating the tunica intima from the tunica media, the internal elastic lamina is composed of **elastin, which is a fenestrated sheet that permits the **diffusion of substances** into the deeper regions of the arterial wall to **nourish the cells there.****



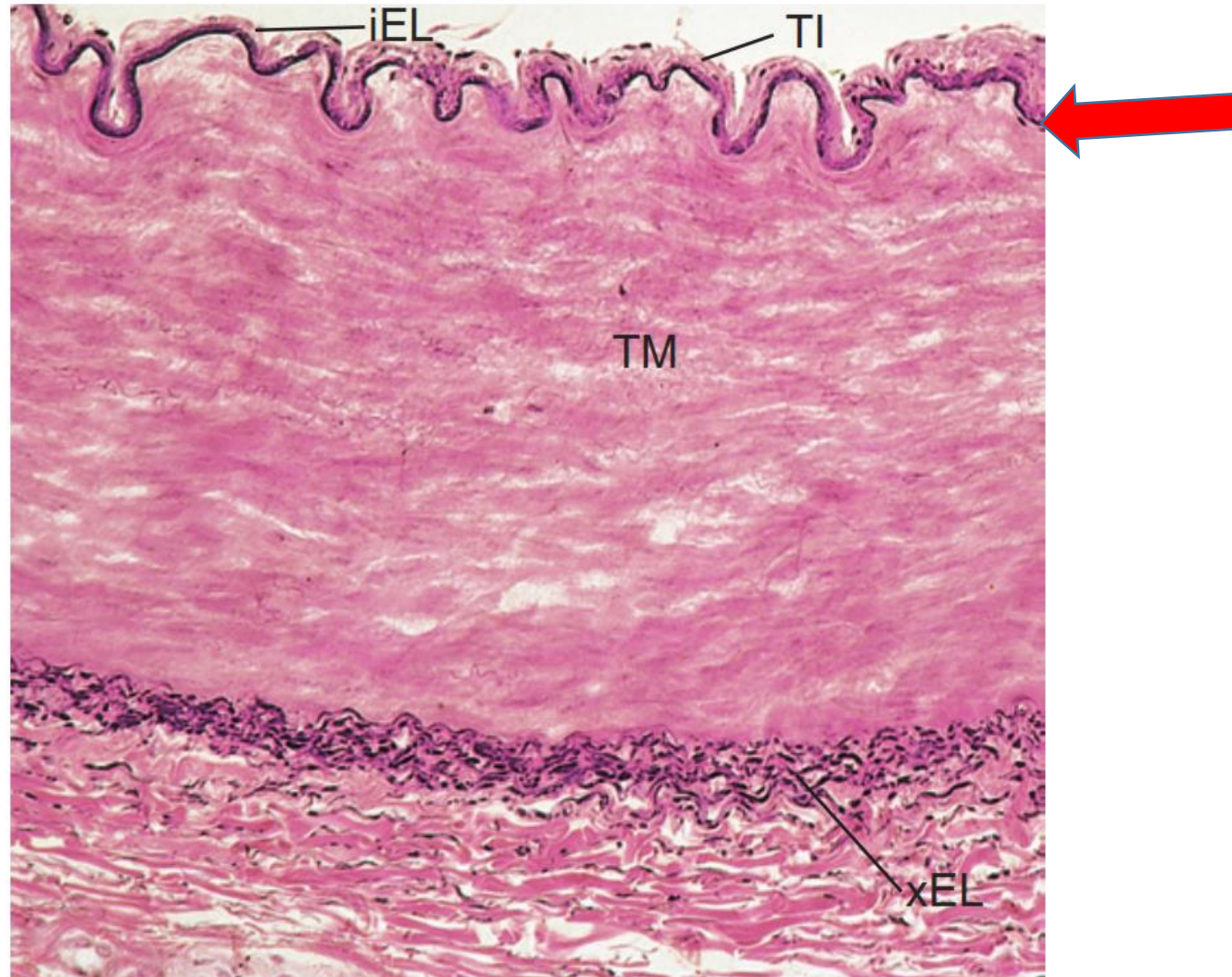


Figure 11-3 Light micrograph of a muscular artery ($\times 132$). Note the tunica adventitia, the internal (iEL) and external (xEL) elastic laminae within the thick tunica media (TM). TI, Tunica intima.



Tunica Media

*The tunica media, usually the **thickest layer** of the vessel wall, is composed of **helically** disposed layers of **smooth muscle** and the **external elastic lamina**, when present.*

Interspersed within the layers of smooth muscle cells are some **elastic fibers, type III collagen, and proteoglycans**.

Larger muscular arteries have an **external elastic lamina**, which is more delicate than the **internal elastic lamina** and separates the tunica media from the overlying tunica adventitia.

Capillaries and postcapillary venules do not have a tunica media; in these small vessels, **pericytes** replace the **tunica media**



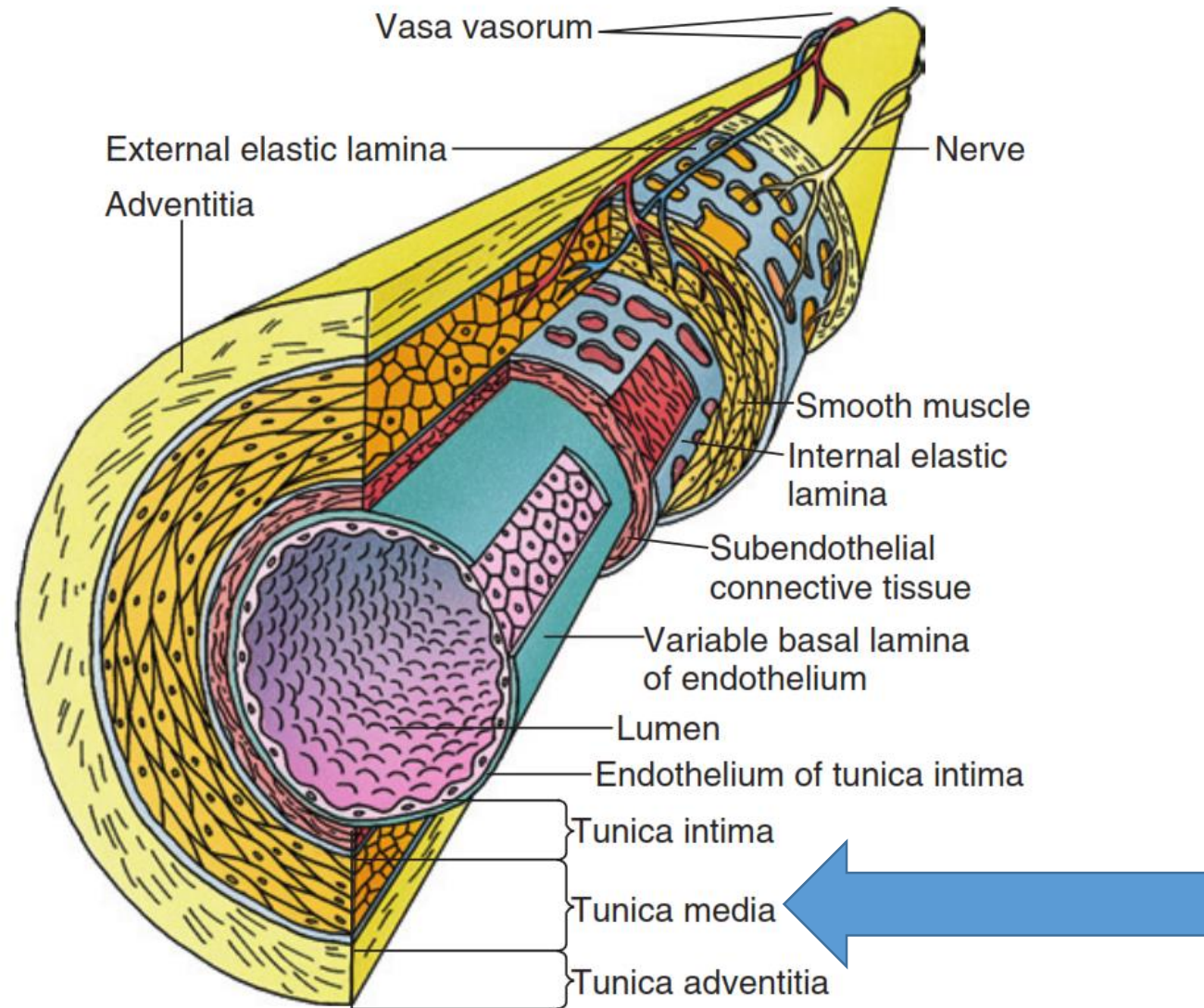


Figure 11-1 Diagram of a typical artery.



Tunica Adventitia

The tunica adventitia, the outermost layer of the vessel wall, blends into the surrounding connective tissue.

it **composed of a dense, irregular, collagenous connective tissue** consisting mostly of fibroblasts, types I and III collagen fibers, and longitudinally oriented elastic fibers.

This layer becomes continuous with (blend into) the connective tissue elements surrounding the vessel.



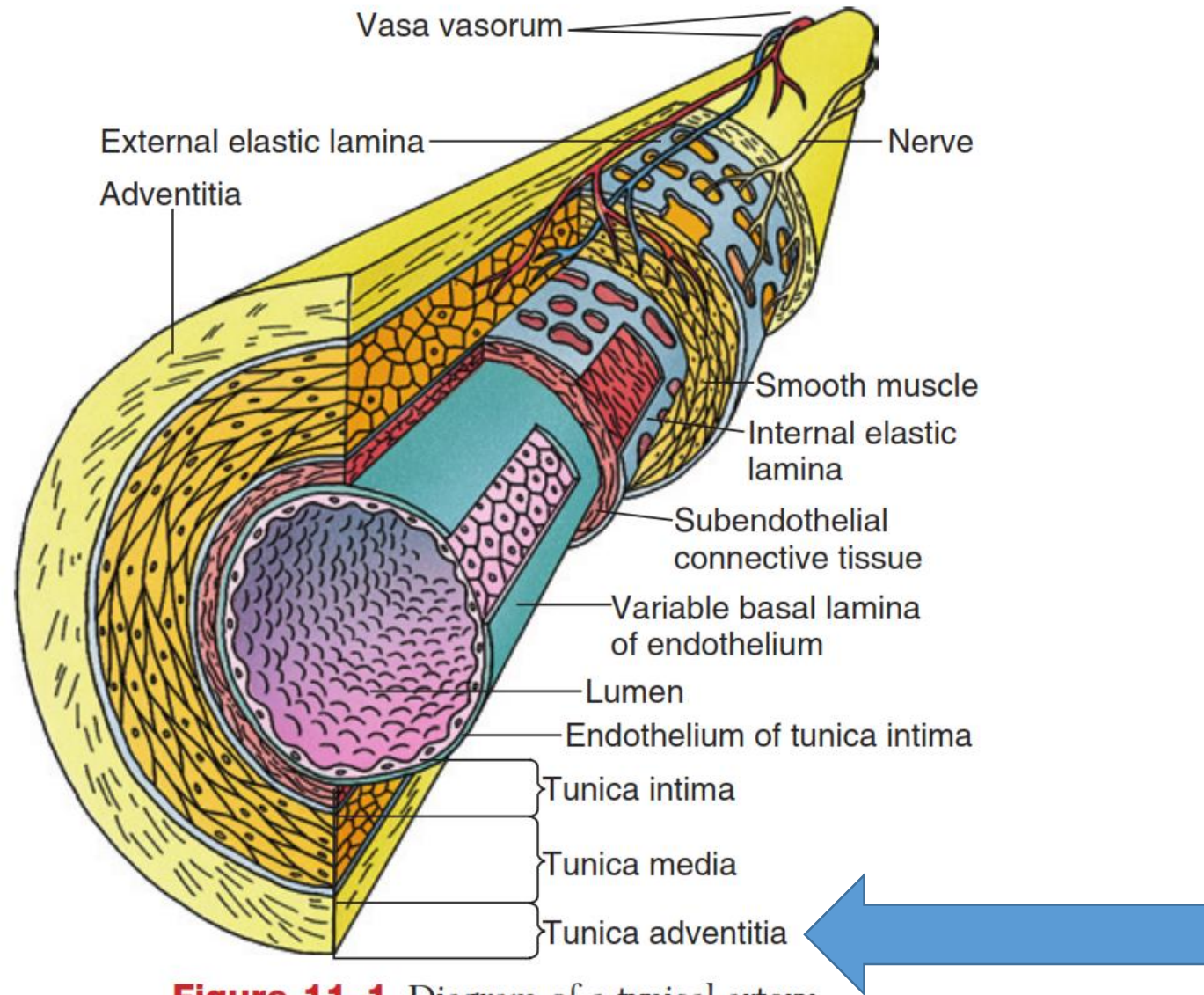


Figure 11-1 Diagram of a typical artery.



Vasa Vasorum

Vasa vasorum (vessels of the vessel) furnish the muscular walls of blood vessels with a blood supply.

The thickness and muscularity of **larger vessels** prevent the cells composing the tunics from being nourished by diffusion from the lumen of the vessel.

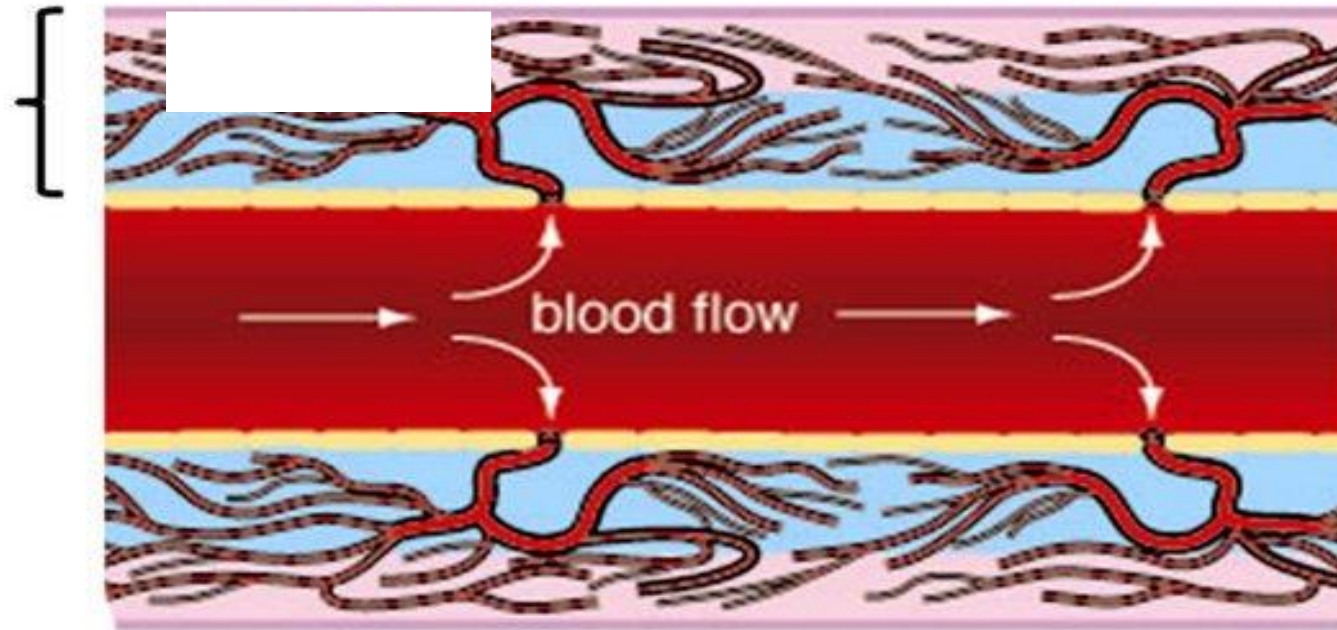
The deeper cells of the tunica media and tunica adventitia are nourished by the **vasa vasorum (vessels of the vessel)**, **small** arteries that **enter the vessel walls and branch profusely** to serve the cells located primarily in the tunica media and tunica adventitia.

Compared with arteries, **veins** have more cells that cannot be supplied with oxygen and nutrients by diffusion because venous blood contains less oxygen and nutrients than arterial blood. For this reason, the vasa vasorum are more prevalent in the walls of veins than arteries.



No-touch saphenous vein

Intact vasa
vasorum:
Blood/O₂



Adventitia

Media

Endothelium

Lumen



Nerve Supply to Vessels

*Sympathetic nerves supply vasomotor innervation to the smooth muscles of the **tunica media**.*

These unmyelinated, postganglionic sympathetic nerves are responsible for **vasoconstriction of the vessel walls**.

Because the nerves seldom enter the tunica media of the vessel, they do **not synapse directly** on the smooth muscle cells. Instead, they **release the neurotransmitter norepinephrine**, which diffuses into the media and acts on smooth muscle cells nearby. These impulses are propagated throughout all of the smooth muscle cells via their gap junctions.

Arteries are more heavily endowed with vasomotor nerves than the veins are

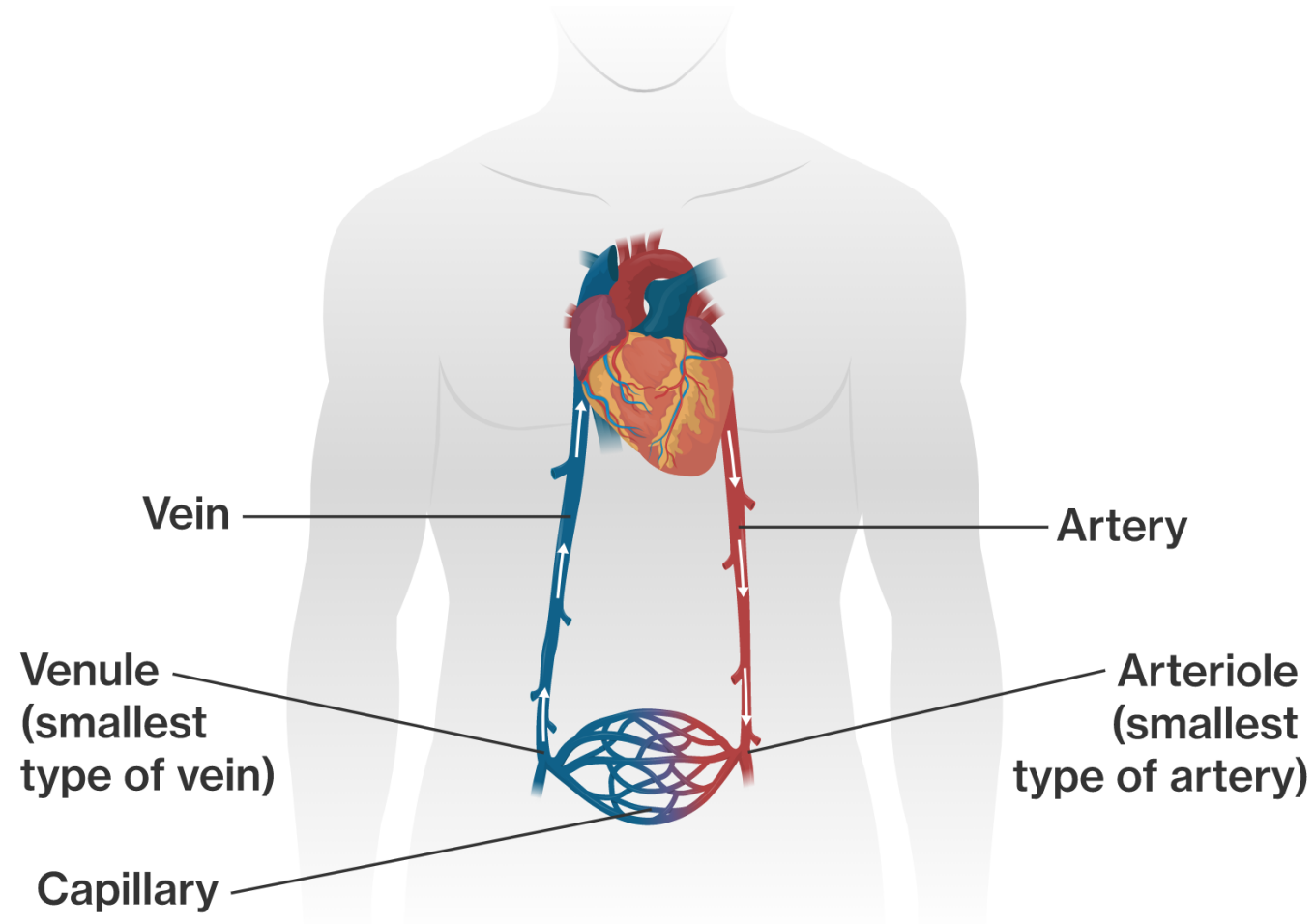
Veins also receive vasomotor nerve endings in the tunica **adventitia**.

The arteries supplying skeletal muscles also receive cholinergic (parasympathetic) nerves to bring about **vasodilation**.



Arteries

Arteries are blood vessels that carry blood away from the heart.



Classification of Arteries

Based on their relative size, morphological characteristics, or both : From largest to smallest, they are as follows:

- Elastic (conducting) arteries
- Muscular (distributing) arteries
- Arterioles

Because the vessels decrease in diameter in a continuous fashion, there are **gradual changes** in morphological characteristics in going from one type to another. Therefore, some vessels having characteristics **of two categories** cannot be assigned to a specific category with certainty.



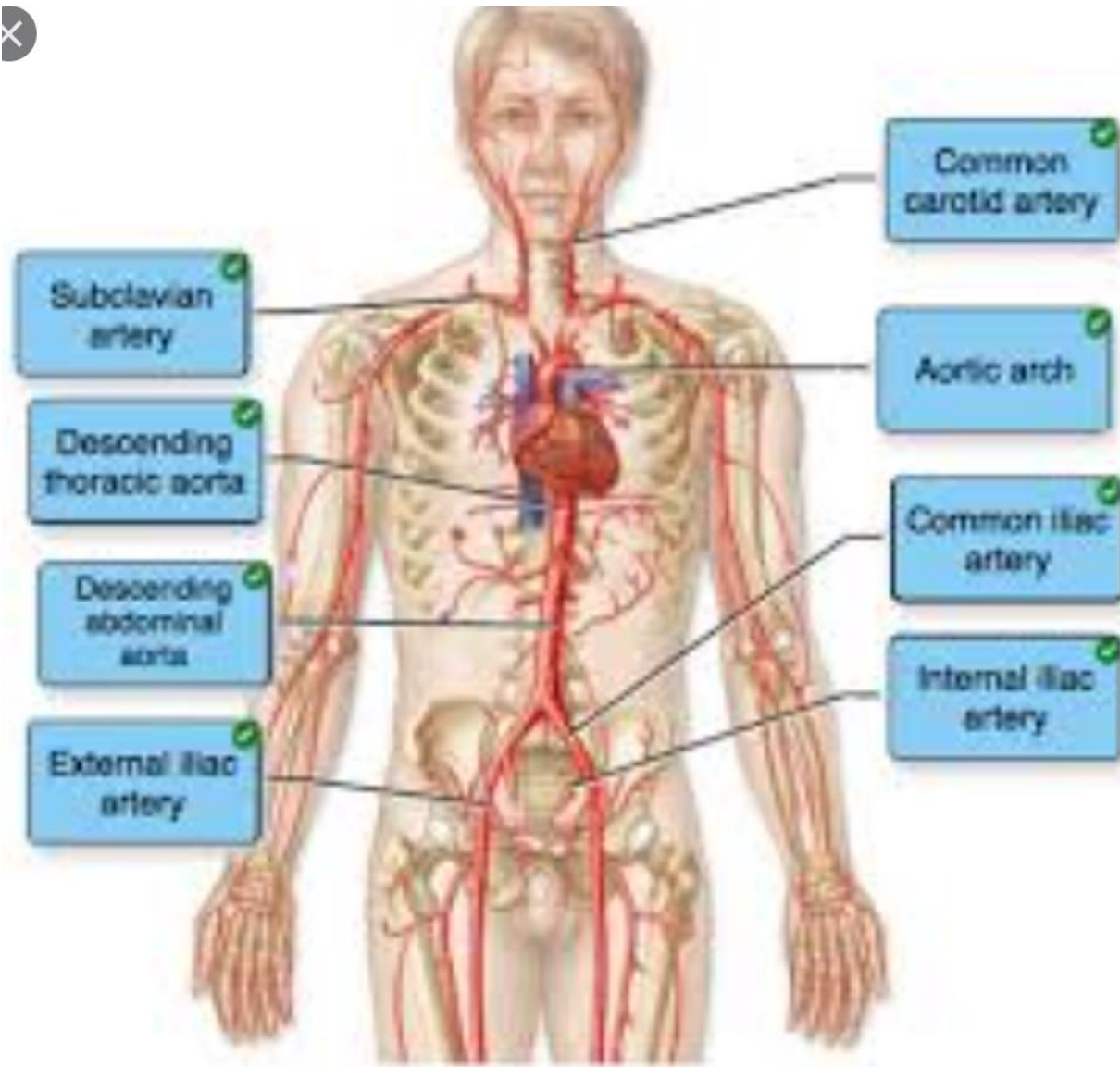
Elastic Arteries

*Concentric layers of elastic membranes, known as fenestrated membranes, occupy much of the **tunica media**.*

The walls of these vessels may be yellow in the fresh state because of the abundance of elastin.

The aorta and the branches originating from the aortic arch (the common carotid artery and the subclavian artery), the common iliac arteries, and the pulmonary trunk are **elastic (conducting) arteries**.





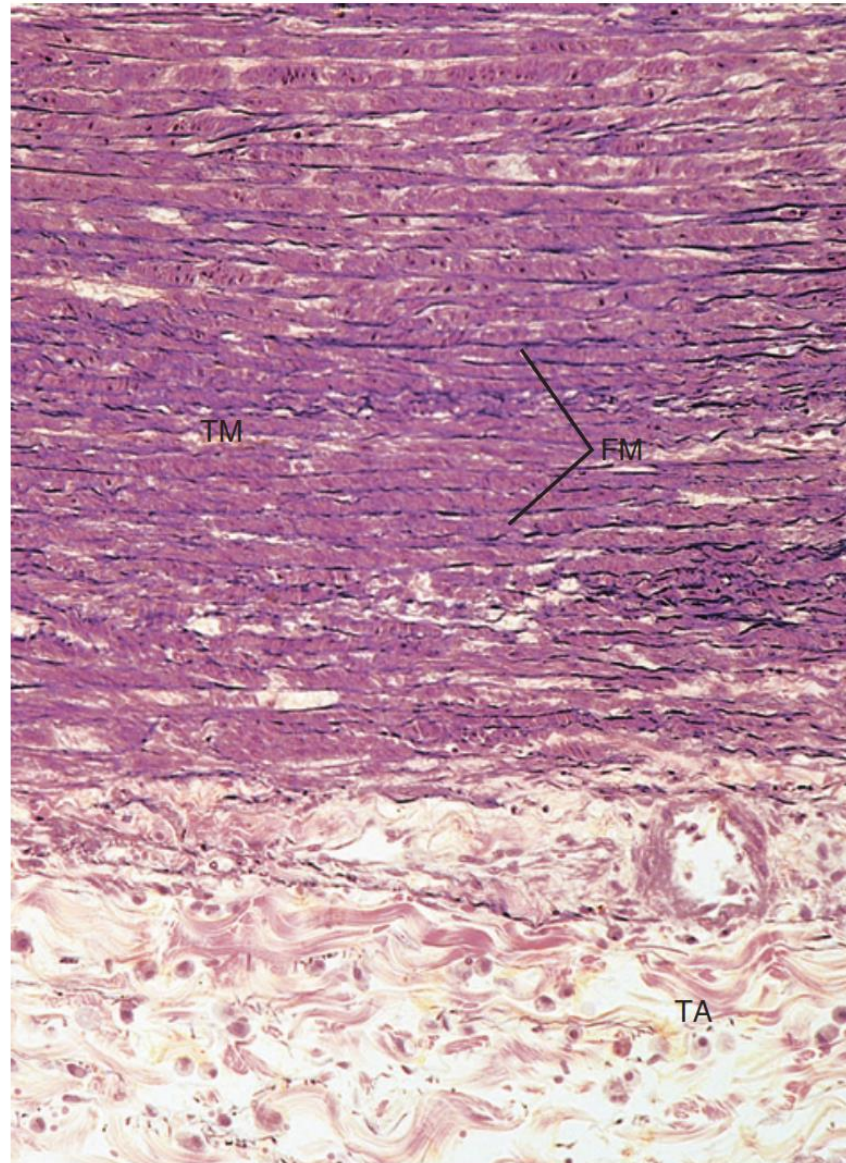


Figure 11-2 Light micrograph of an elastic artery ($\times 132$). Observe the fenestrated membranes (FM), the tunica media (TM), and the tunica adventitia (TA). The tunica intima is not shown.



Weibel-Palade bodies (in all arteries except meta artrioles)

membrane-bound inclusions, 0.1 μm in diameter and 3 μm long, that have a dense matrix housing tubular elements containing the glycoprotein **vWF (von Willebrand factor)** as well as **tissue factor and P-selectin**.

The vWF facilitates the **coagulation** of platelets during clot formation.

Tissue factor enhances the process of coagulation, and P-selectin induces leukocytes to leave the bloodstream, to enter the connective tissue spaces, and to function in the **immune process**.

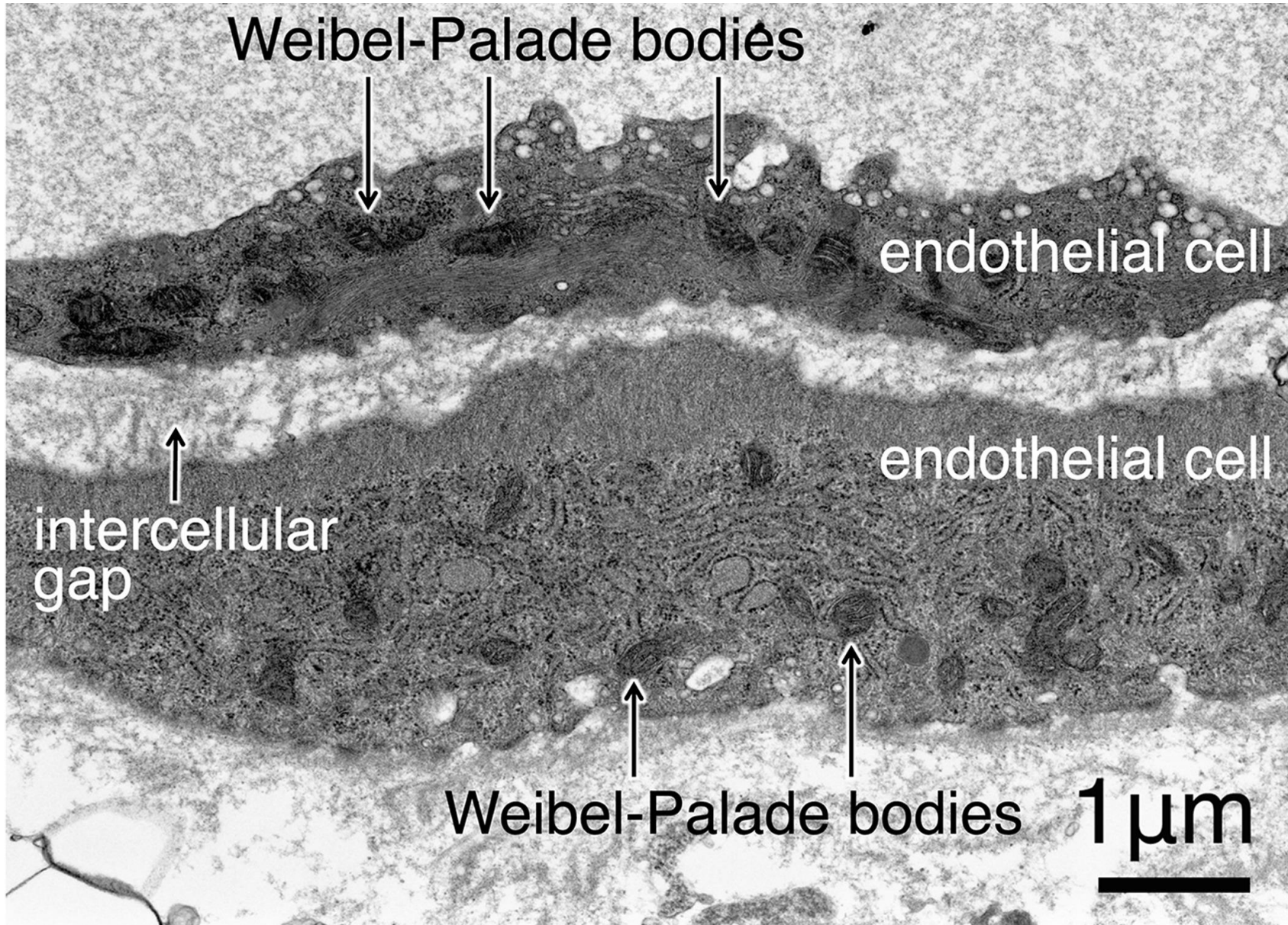
CLINICAL CORRELATIONS

Patients with **von Willebrand disease, an inherited** disorder that results in impaired adhesion of platelets, have prolonged coagulation times and excessive bleeding
At an injury site.



TABLE 11–1 Characteristics of Various Types of Arteries

Artery	Tunica Intima	Tunica Media	Tunica Adventitia
Elastic artery (<i>conducting</i>) (e.g., aorta)	Endothelium with Weibel-Palade bodies, basal lamina, subendothelial layer, incomplete internal elastic lamina	40–70 fenestrated elastic membranes, smooth muscle cells interspersed between elastic membranes, thin external elastic lamina, vasa vasorum in outer half	Thin layer of fibroelastic connective tissue, vasa vasorum, lymphatic vessels, nerve fibers
Muscular artery (<i>distributing</i>) (e.g., femoral artery)	Endothelium with Weibel-Palade bodies, basal lamina, subendothelial layer, thick internal elastic lamina	Up to 40 layers of smooth muscle cells, thick external elastic lamina	Thin layer of fibroelastic connective tissue; vasa vasorum not very prominent; lymphatic vessels, nerve fibers
Arteriole	Endothelium with Weibel-Palade bodies; basal lamina, subendothelial layer not very prominent; some elastic fibers instead of a defined internal elastic lamina	One or two layers of smooth muscle cells	Loose connective tissue, nerve fibers
Metarteriole	Endothelium, basal lamina	Smooth muscle cells form precapillary sphincter	Sparse, loose connective tissue



Muscular (distributing) arteries

include most vessels arising from the aorta, **except for the major trunks originating from the arch of the aorta and the terminal bifurcation of the abdominal aorta**, which are identified as elastic arteries.

Indeed, most of the named arteries, even those with a diameter of only slightly greater than 0.1 mm, are classified as muscular arteries (e.g., brachial, ulnar, renal).

The identifying characteristic of muscular arteries is a relatively **thick tunica media** composed mostly of layers of smooth muscle cells.

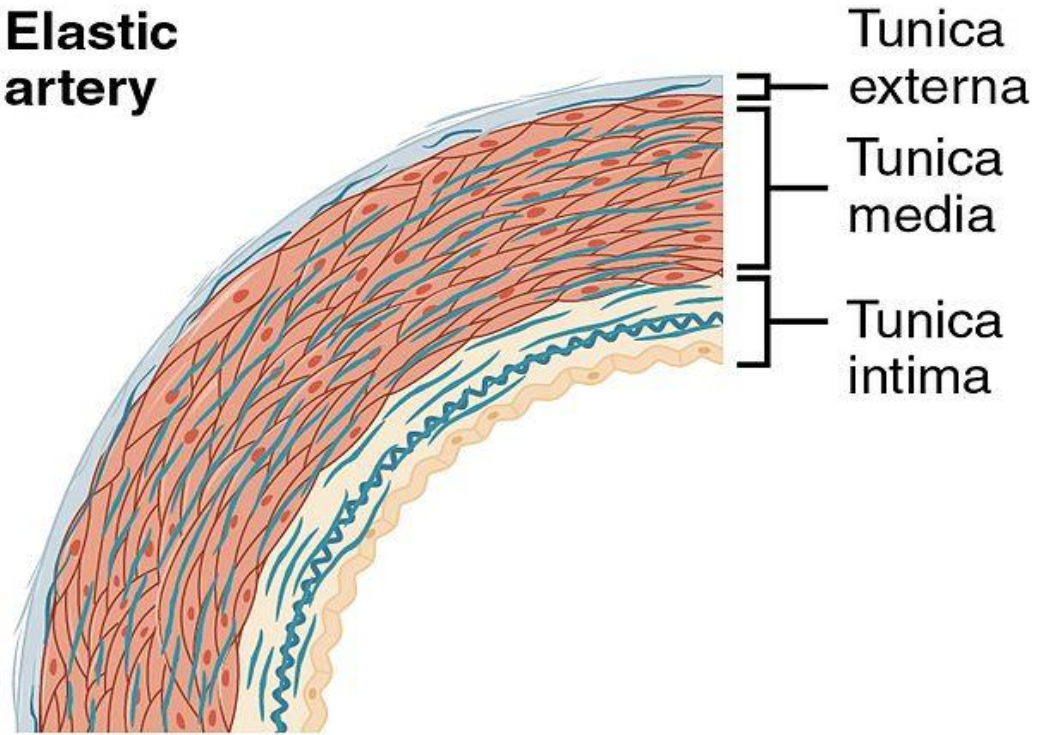


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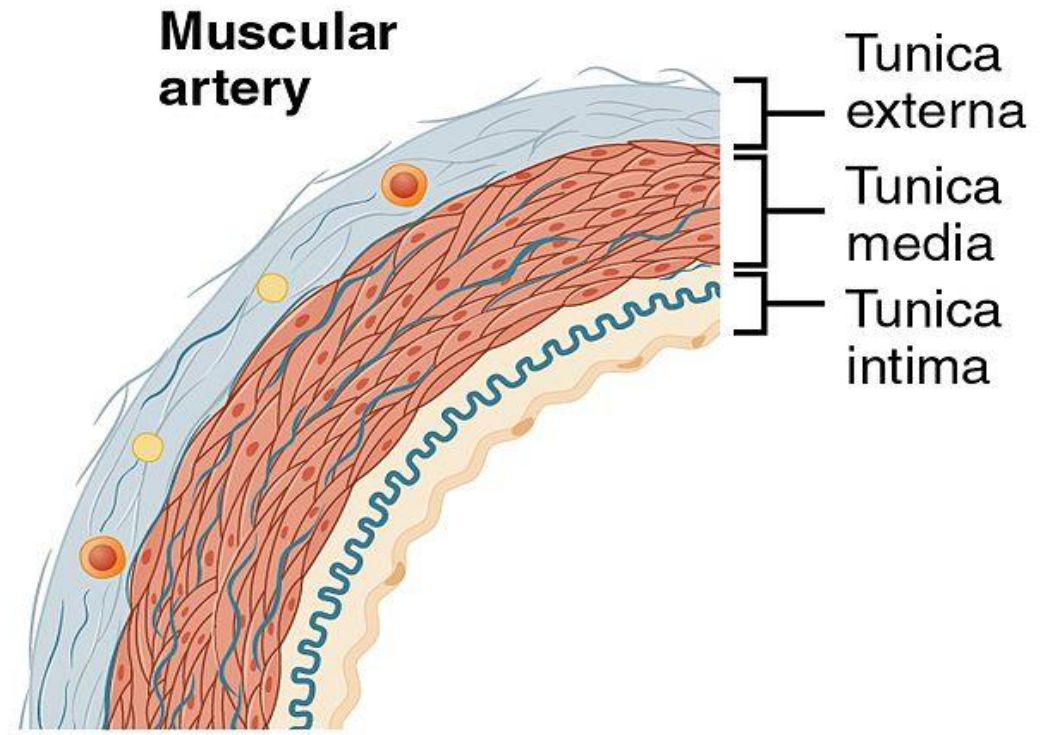
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Elastic artery



Muscular artery



Arterioles

Arteries with a diameter of **less than 0.1 mm** are considered to be arterioles.

Arterioles are the terminal arterial vessels that regulate blood flow into capillary beds.

The endothelium of the **tunica intima is supported by** a thin subendothelial connective tissue layer consisting of type III collagen and a few elastic fibers.

A thin, fenestrated **internal elastic lamina is present in larger arterioles but absent in small and terminal arterioles**.

In small arterioles, the **tunica media is composed of a single smooth** muscle cell layer that completely encircles the endothelial cells. In larger arterioles, the tunica media consists of two to three layers of smooth muscle cells.

Arterioles do **not have an external elastic lamina**.

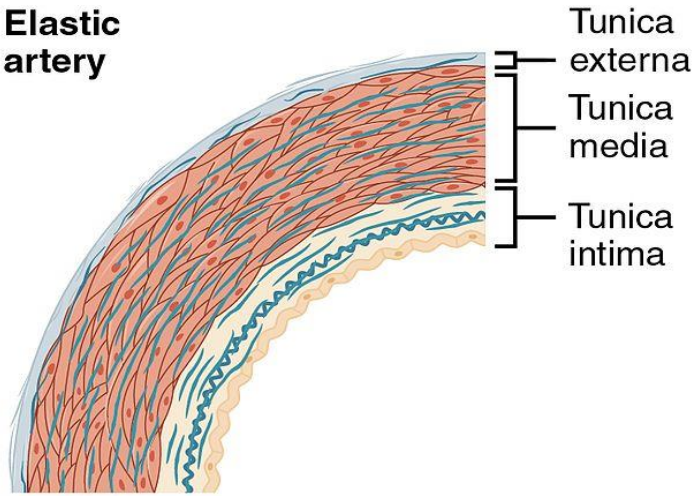
The **tunica adventitia** of arterioles is **scant** and is represented by fibroelastic connective tissue housing a few fibroblasts.



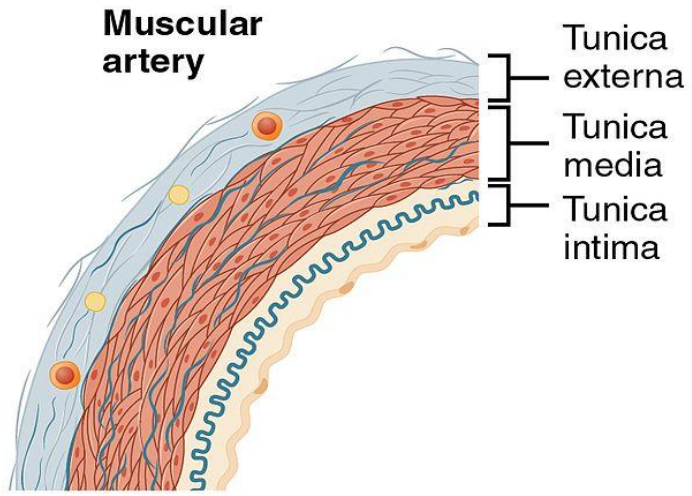
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Elastic artery



Muscular artery



Arteriole

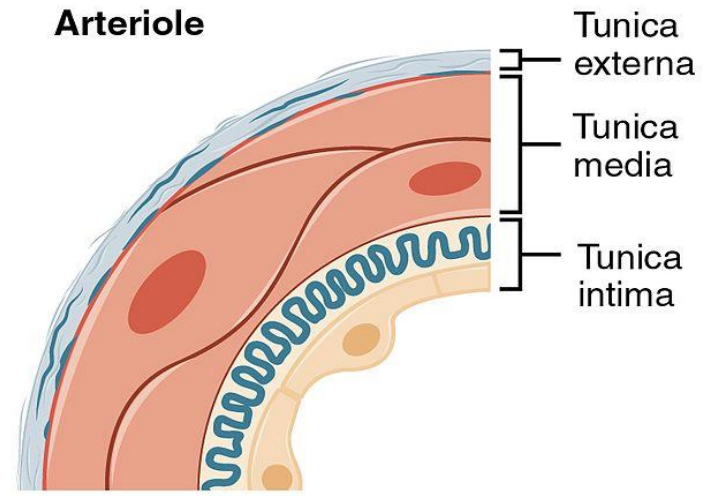
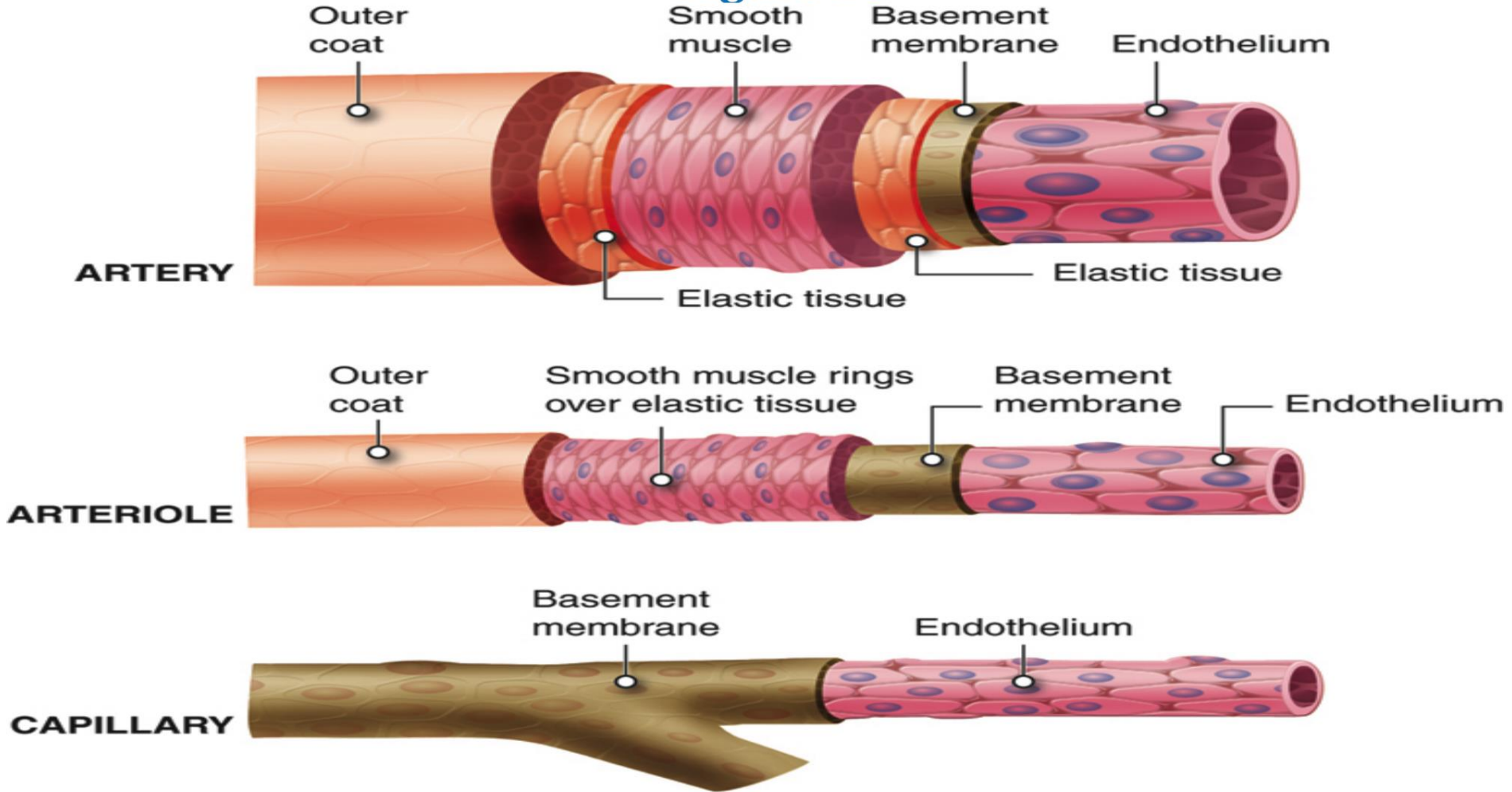


Figure 26



Arteries that supply blood to capillary beds are called **metarterioles**.

*They are approximately 8 μm in diameter and differ structurally from arterioles in that their **smooth muscle layer is not continuous**; rather, the individual muscle cells (**precapillary sphincters**) are spaced apart, and each encircles the endothelium of capillary arising from the metarteriole.*

Function of precapillary sphincters: controlling blood flow into the capillary bed)



Figure 27
Capillary network

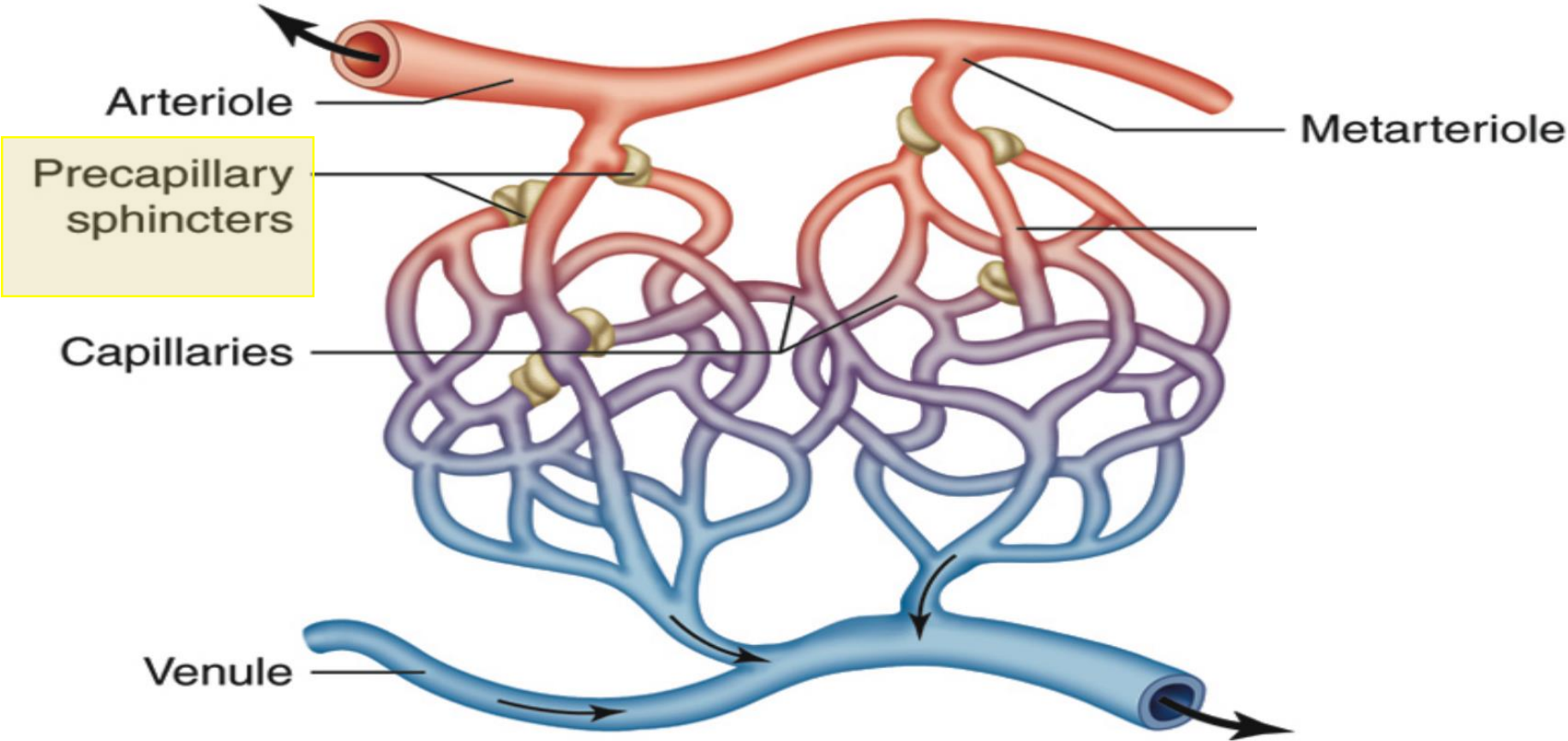


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Regulation of Arterial Blood Pressure

Arterial blood pressure is regulated by the vasomotor center in the brain.

The heart, which serves as the cardiovascular pump, rests between each stroke, thus developing a pressurized burst of blood that first enters into the elastic arteries, then

moves into the muscular arteries and arterioles, and finally into capillaries, which serve the tissues.

The **vasomotor center** in the brain responds to the continual monitoring of blood pressure by controlling **vasomotor tone, the constant state of contraction of the vessel walls**, which is modulated via vasoconstriction and vasodilation.

Vasoconstriction is accomplished via vasomotor nerves of the sympathetic nervous system, whereas vasodilation is a function of the parasympathetic system.



The structure of **elastic arteries** permits distention of their walls during **systole (heart contraction)**, followed by recoil of their walls during **diastole (heart relaxation)**, which assists in delivering a more constant blood pressure and flow of blood.

Muscular arteries branching from the elastic arteries distribute blood to the body and are subject to constant changes in diameter resulting from vasoconstriction and vasodilation. To assist in accommodating for these events, the tunica adventitia **blends loosely** into the surrounding connective tissue, thus **preventing restraint** on the vessel during contractions and expansions for changes in blood pressure.



Artery location also dictates the thickness of the various tunics. For example, the thickness of the tunica media in the arteries of the leg is greater than that found in the arteries of the upper extremity. This is in response to the continued pressure on the blood column in the vessel resulting from gravitational forces.

Moreover, the coronary arteries, serving the heart, are **high pressure arteries** and, as such, have a thick tunica media.

Conversely, arteries in the pulmonary circulation are under low pressure; thus, the tunica media in these vessels are thinner.



CLINICAL CORRELATIONS

Normal and Pathological Vascular Changes

The largest arteries continue to grow until about age 25 years, although there is progressive thickening of their **walls** and an increase in the number of **elastic laminae**.

In the muscular arteries, from middle age on, deposits of **collagen and proteoglycans increase in the walls, thus reducing their flexibility**.

The **coronary** vessels are the first to display the effects of aging, with the **intima** displaying the greatest age-related changes. These natural changes are not unlike the regressive changes observed in arteriosclerosis.



Arteriosclerosis

(hardening of the arteries), displaying a **hyaline** or concentric thickening that is often associated with hypertension and diabetes.

Small arteries and arterioles, especially those of the kidneys, are prone to the most common type of arteriosclerosis

Atherosclerosis

The largest of the arteries including the coronary arteries, the carotid arteries, and the major arteries of the brain among others, are susceptible to **atherosclerosis**, a disease that is the forerunner to heart attack and stroke.

Atherosclerosis is distinguished by infiltrations of soft, **noncellular lipid material into the tunica intima** (fibrous plaques); these infiltrations Can reduce the luminal diameter appreciably.



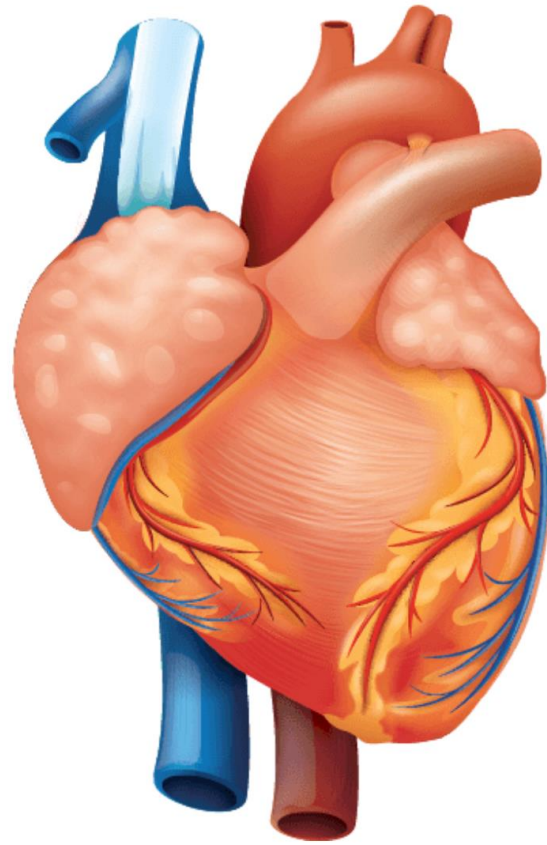
The smooth muscle cell layer in the tunica media of a healthy person undergoes renewal, but when the endothelium is **injured**, platelets that accumulate at the lesion site release **platelet-derived growth factor (PDGF)**, stimulating **proliferation of smooth muscle cells**.

As a consequence, these cells begin to get **packed with cholesterol rich lipids**, which stimulate the muscle cells to manufacture **additional collagen and proteoglycans**, resulting in a cycle whereby the tunica **intima becomes thickened**.

This further damages the endothelium leading to **necrosis**, which attracts more platelets, and, finally, clotting, forming a **thrombus that may occlude** the vessel at that site or, if released into the general circulation, it may occlude a more vulnerable vessel (e.g., a coronary vessel or a cerebral vessel).

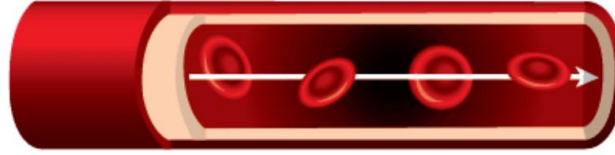
A correlation between blood cholesterol levels and heart disease has been demonstrated,



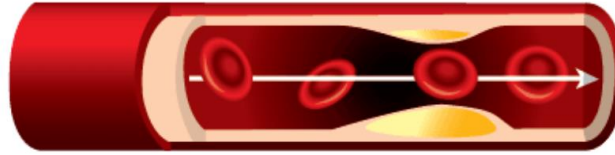


Atherosclerosis

Healthy artery



The plaque formation



Thrombosis



It has been noted that **C-reactive protein (CRP)**, synthesized by the liver, can be used as a marker for inflammation, which appears to be a far more accurate indicator of the risk for cardiovascular disease.

Statins, which have been used extensively for reducing cholesterol levels in the blood, thereby reducing the risk of heart disease, have also been shown to reduce the levels of CRP.

This fact is important because there are data supporting That the response to inflammation is as critical to heart disease as are high levels of cholesterol. Thus, there appears to be a commonality between inflammation and cardiovascular disease.



Capillaries

Capillaries arise from the terminal ends of arterioles and also from metarterioles .

By branching and anastomosing, capillaries form capillary beds (**capillary networks**) **between the arterioles and the venules.**



General Structure of Capillaries

*Capillaries, composed of a **single layer** of endothelial cells, are the smallest blood vessels.*

Capillaries are the smallest of the vascular channels, on the average approximately 50 μ m in length with a diameter of 8 to 10 μ m.

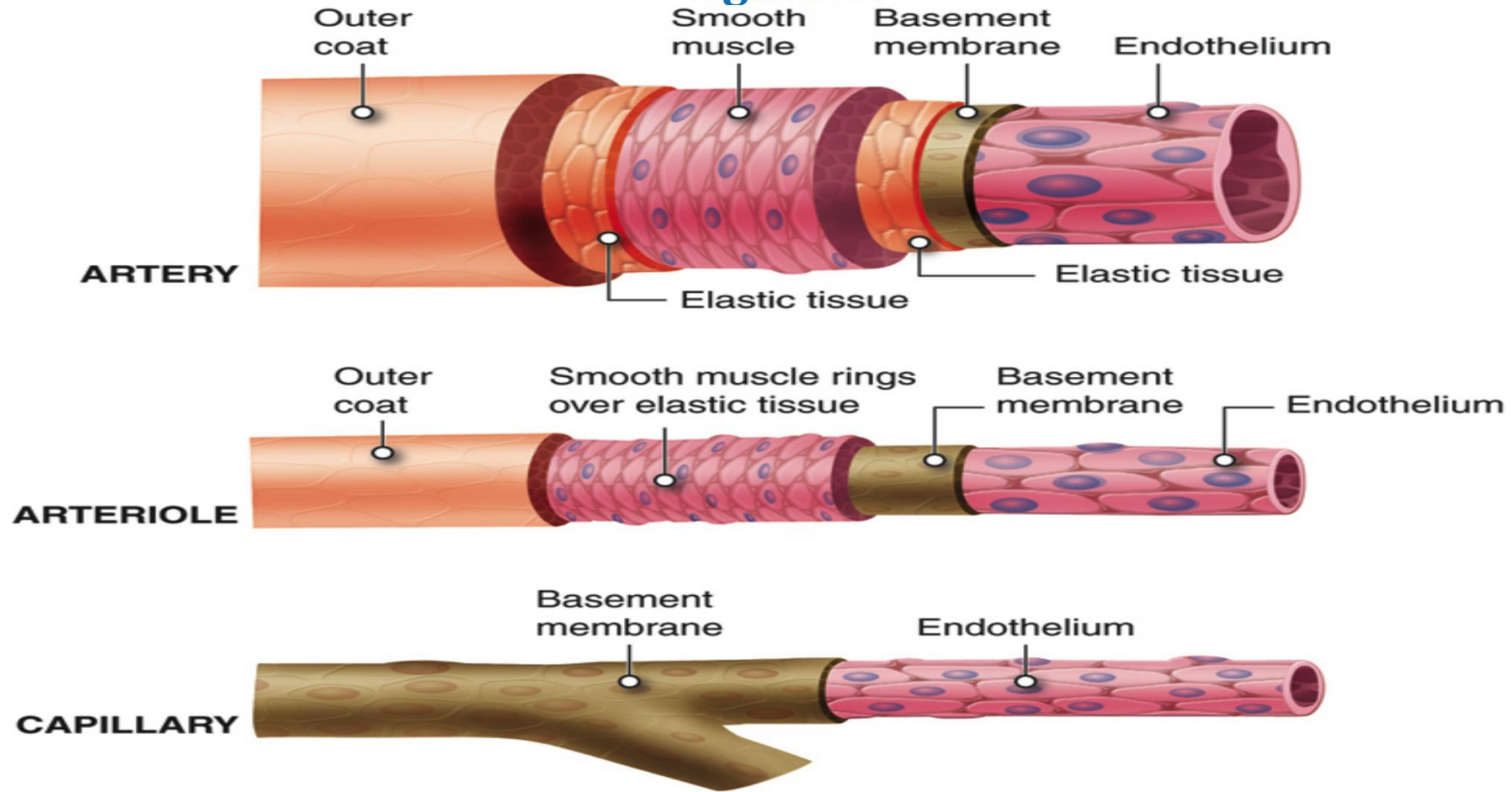
These slender, small vessels are formed by a single layer of squamous endothelial cells

These endothelial cells are **flattened, with the attenuated ends tapering** to a thickness to 0.2 μ m or less, although an **elliptical nucleus bulges out into the lumen** of the capillary.

The cytoplasm contains a Golgi complex, a few mitochondria, some rough endoplasmic reticulum (RER), and free ribosomes .



Figure 26

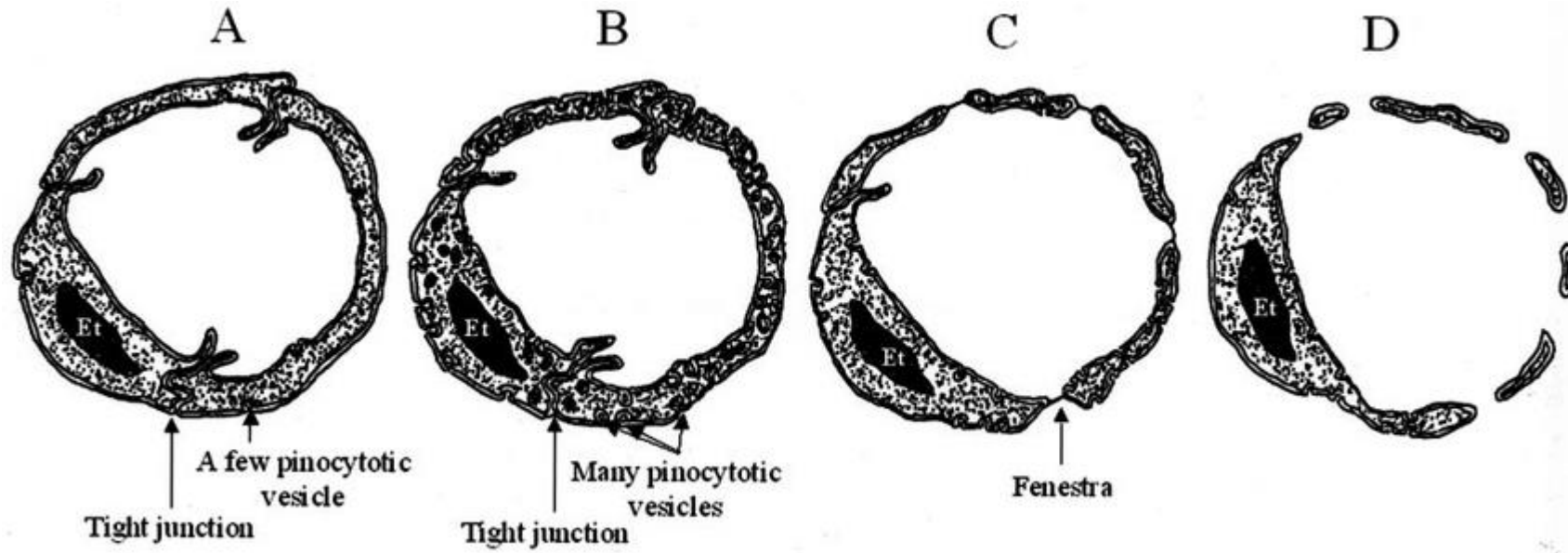


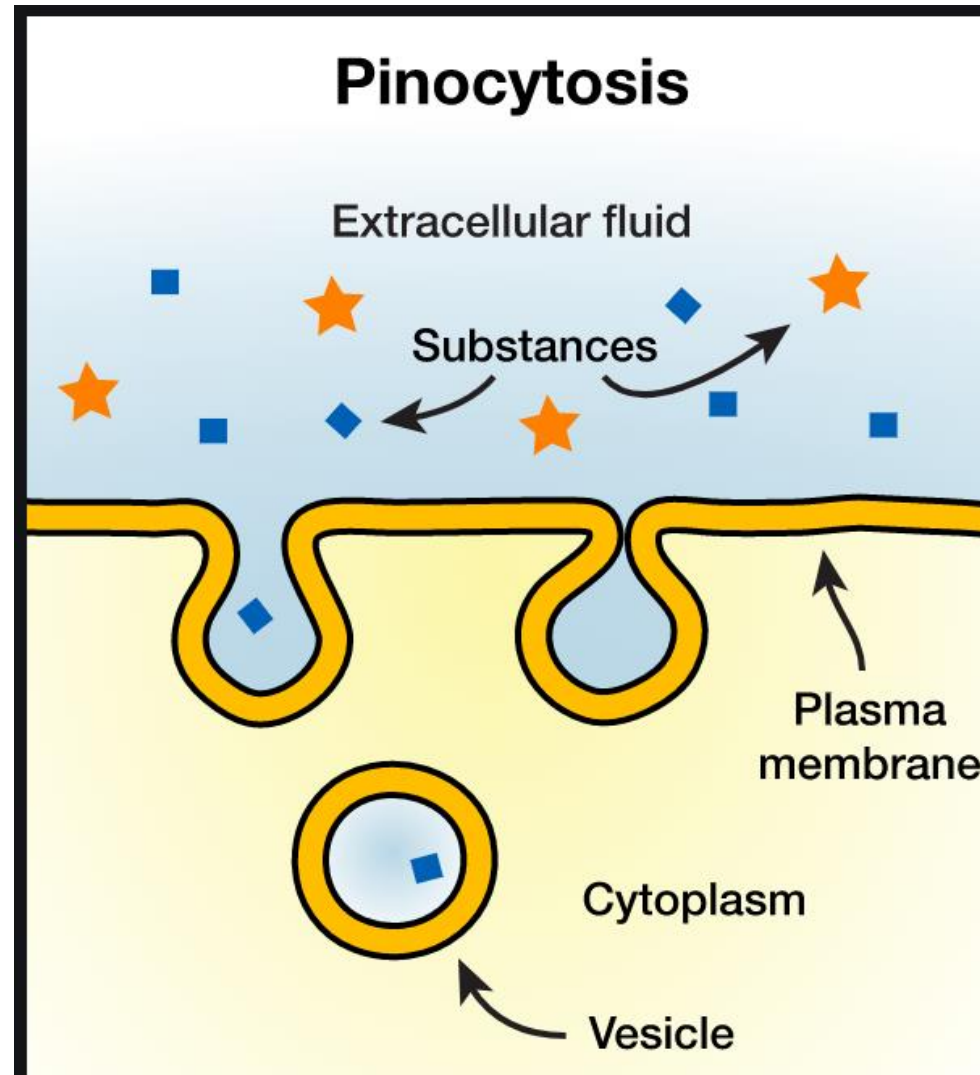
Intermediate filaments located about the perinuclear zone, are composed of **desmin and/or vimentin**. **These filaments** provide structural support to the endothelial Cells

The large number of **pinocytotic vesicles** associated with the endothelial cell plasmalemma is an identifying characteristic of capillaries.

These vesicles may be in singular array, two single vesicles may be fused together, or several vesicles may be fused, forming a transient channel.







(**Pinocytic** process, where the small particles are brought into the cell, forming an infolding or **invagination** which in turn are suspended in the small vesicles. This process is also known as *Cell Drinking*)



The endothelial cells of capillaries are rolled into a **tube**, giving the lumen a diameter that ranges from 8 to 10 μ m but remains **constant throughout the entire** length of a capillary. This diameter is sufficient to permit individual cells of the blood to pass without being hindered.

Not all of the capillary beds are open at any one time; however, **increased demand initiates the opening of more beds**, thus increasing blood flow to meet physiological needs.

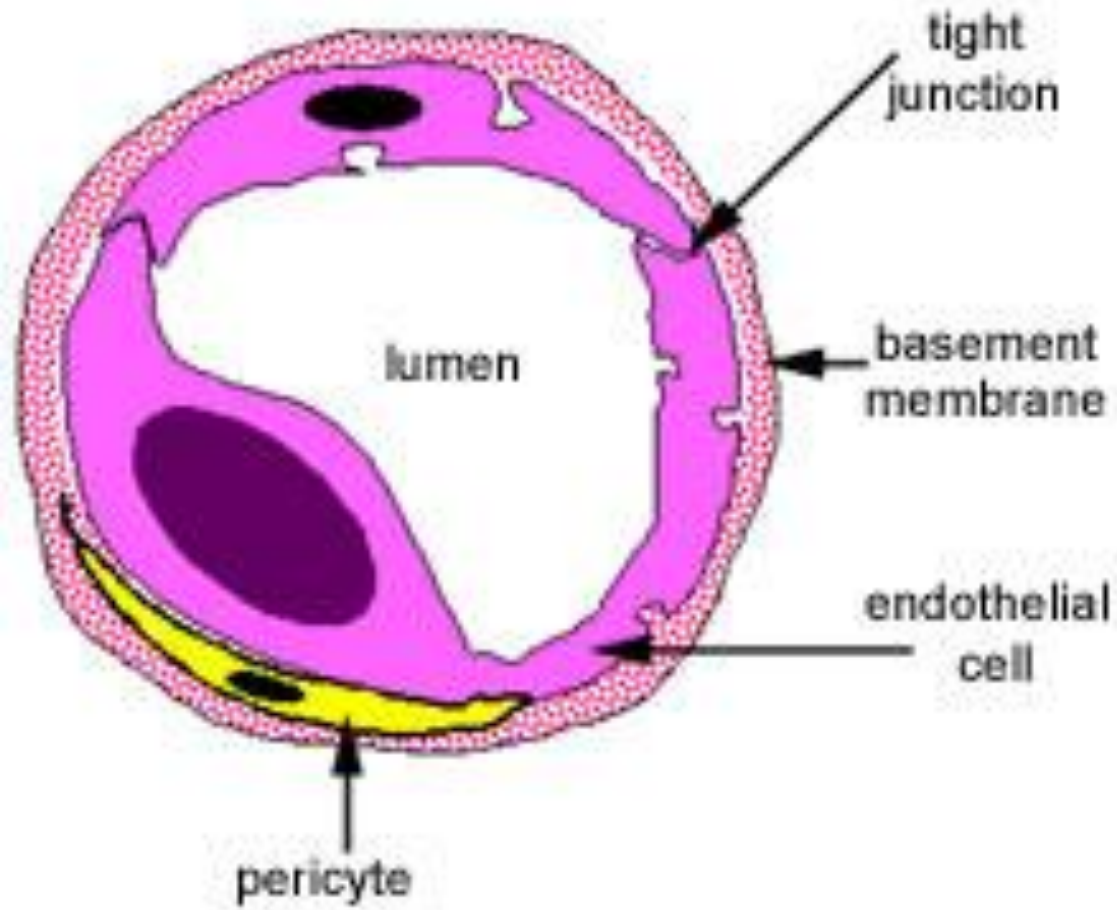
The external surfaces of the endothelial cells are surrounded by **a basal lamina** secreted by the endothelial cells



When viewed in the cross section, it is evident that the circumference of small capillaries is formed by a single endothelial cell, whereas portions of two or three endothelial cells contribute to forming the circumference of larger capillaries

Endothelial cells are joined together by **fasciae occludentes, or tight junctions,**





Pericytes, located along the outside of the capillaries and small venules, appear to be surrounding them, and share the basal laminae of the endothelial cells

These cells have long primary **processe**s, which are located along the long axis of the capillary and from which secondary processes arise to **wrap around** the capillary, forming a few **gap junctions** with the endothelial cells.

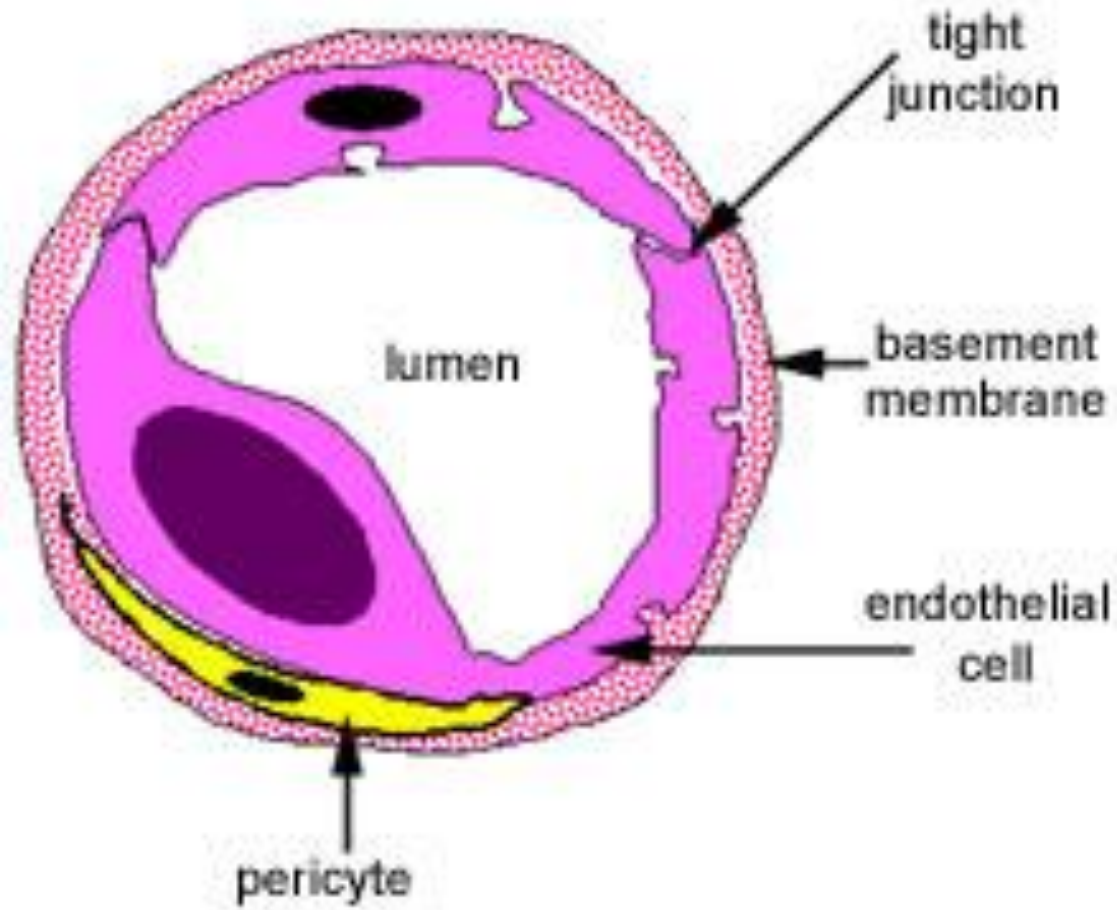
Pericytes possess a small Golgi complex, mitochondria, RER, microtubules, and filaments extending into the processes.

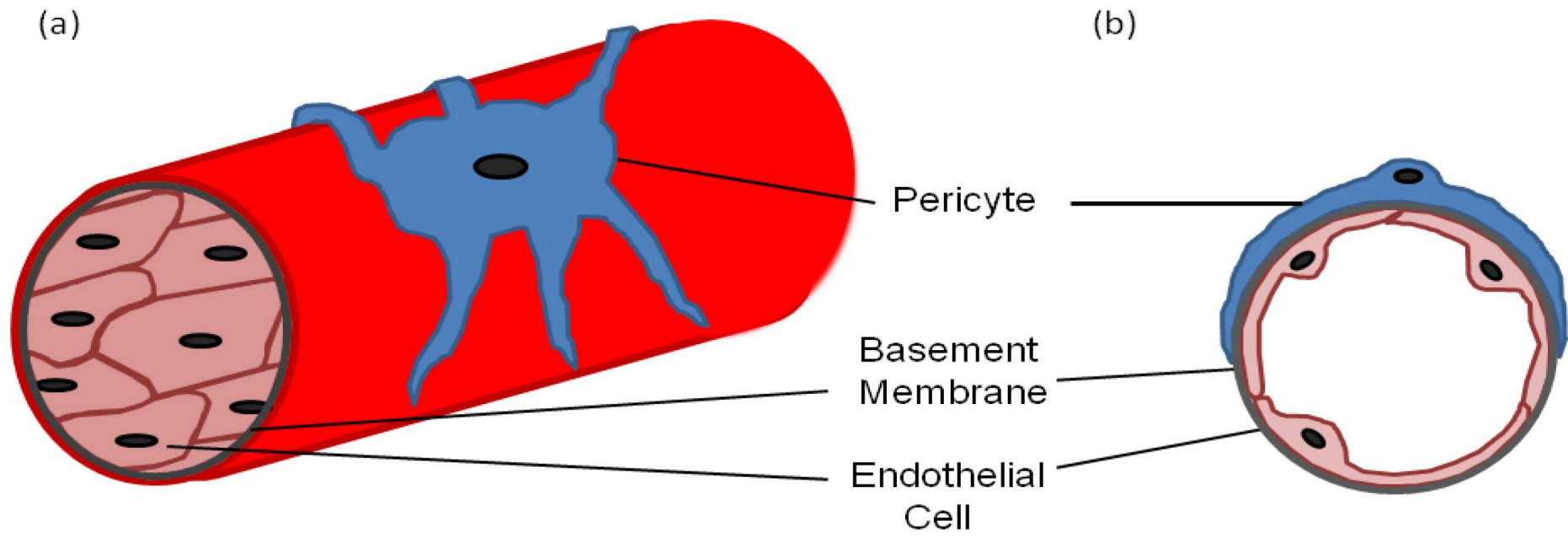
Function :

These cells also contain tropomyosin, isomyosin, and protein kinase, which are all related **to the contractile process that regulates blood flow through the capillaries**.

Furthermore, after injury, pericytes may undergo **differentiation to become smooth muscle cells and endothelial cells** in the walls of arterioles and venules.







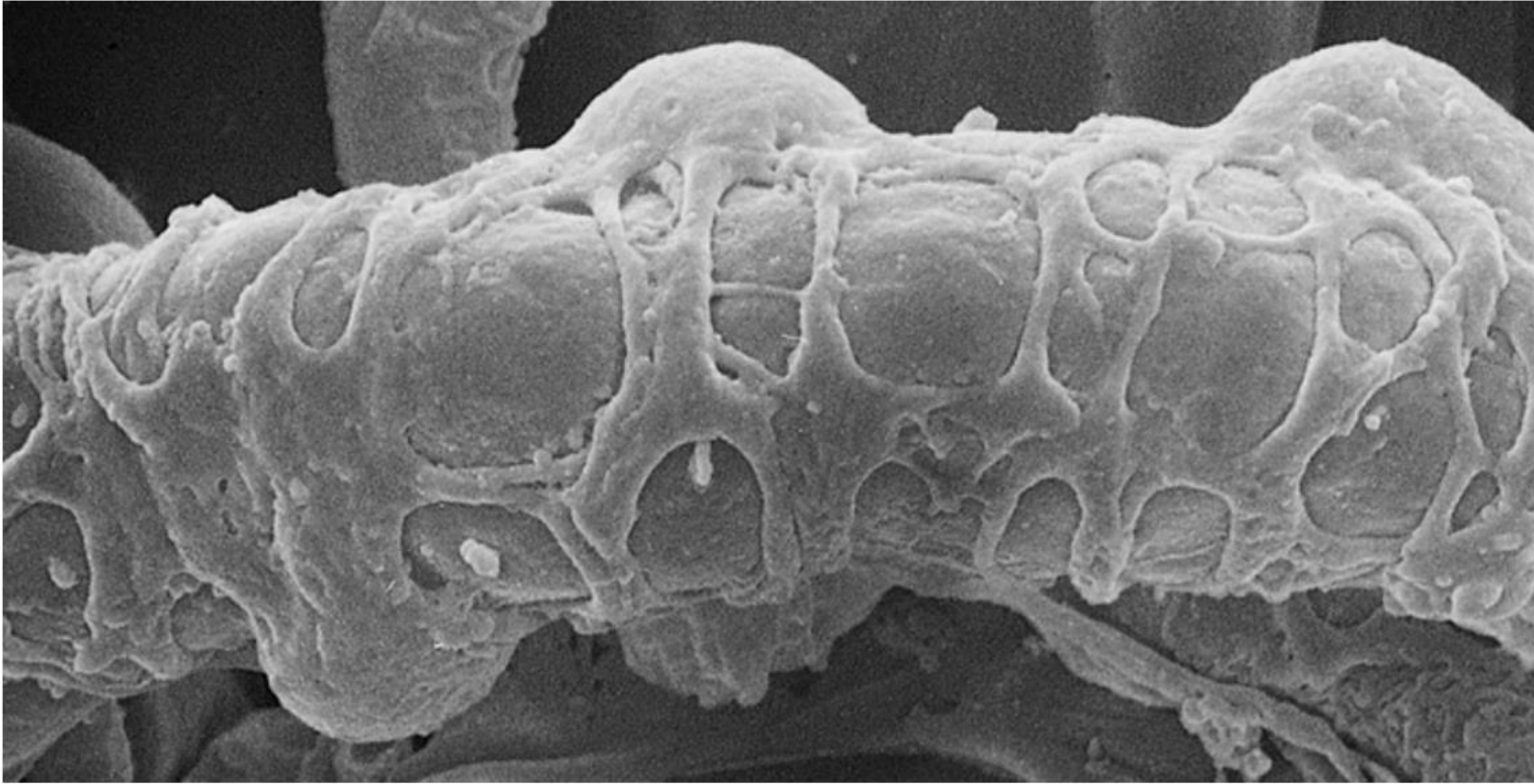


Figure 11-10 Scanning electron micrograph of a capillary displaying pericytes on its surface ($\times 5000$). (From Fujiwara T, Uehara Y. The cytoarchitecture of the wall and innervation pattern of the microvessels in the rat mammary gland: a scanning electron microscopic observation. *Am J Anat.* 1984;170:39-54. Reprinted with permission from Wiley-Liss, Inc., a subsidiary of John Wiley & Sons, Inc.)



Classification of Capillaries

Continuous Capillaries (Somatic Capillaries)

*Continuous capillaries (somatic capillaries) have **no pores or fenestrae** in their walls.*

*they are present in **muscle, nervous, and connective tissues** as well as in the **lungs and exocrine glands**.*

The intercellular junctions between their endothelial cells are **fasciae occludentes, which prevent passage** of many molecules. Substances such as amino acids, glucose, nucleosides, and purines move across the capillary wall via **carrier-mediated transport as evidenced by the numerous pinocytotic vesicles associated with these types of capillaries.**

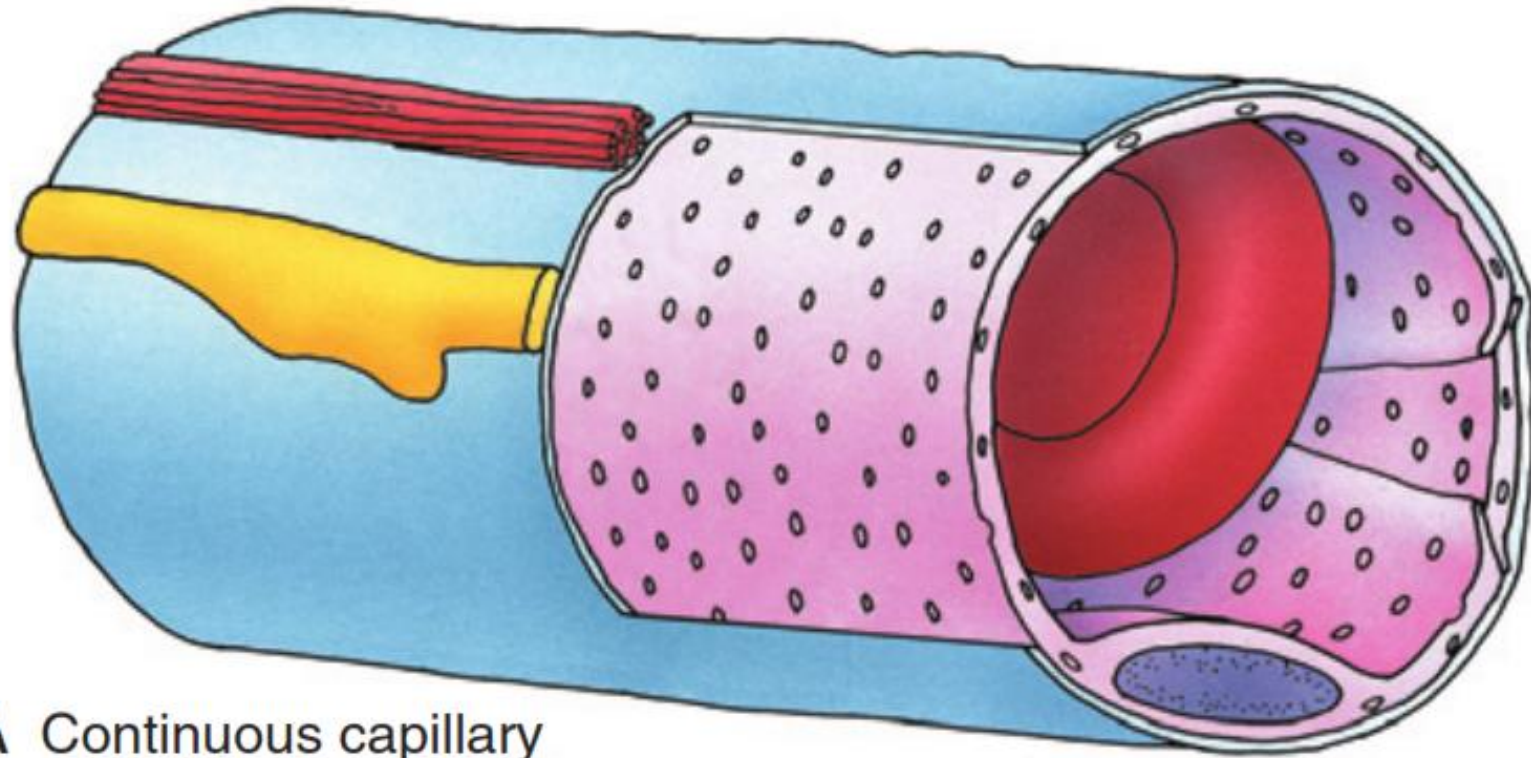
The cells exhibit a polarity with the transport systems, such that $\text{Na}^+\text{-K}^+$ ATPase is located in the adluminal cell membrane only.



In the CNS, the **blood–brain barrier** regulation resides within the endothelial cells but is **influenced by signaling** molecules formed by the astrocytes associated with the capillaries.

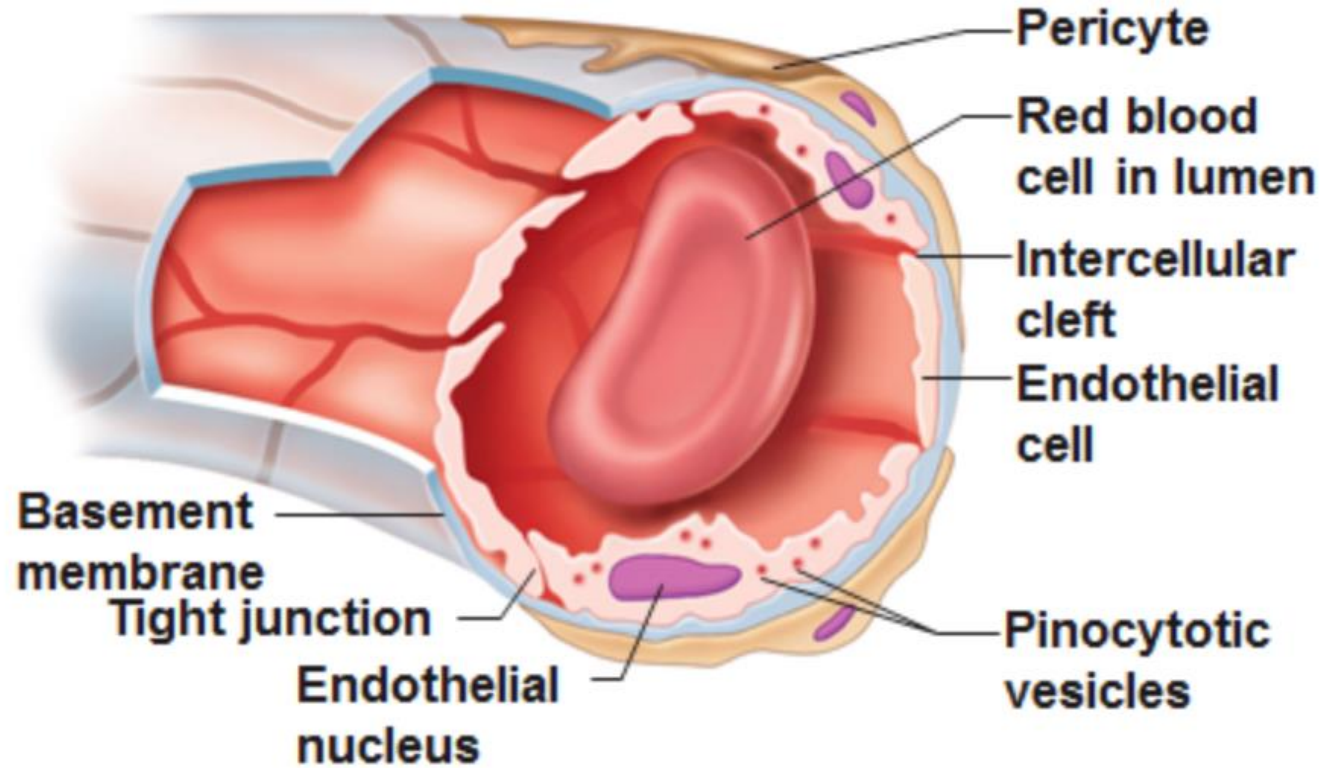
It is interesting to note that continuous capillaries of the CNS have a much reduced number of pinocytotic vesicles.





A Continuous capillary





(a) Continuous capillary. Least permeable, and most common (e.g., skin, muscle).



Fenestrated Capillaries (Visceral Capillaries)

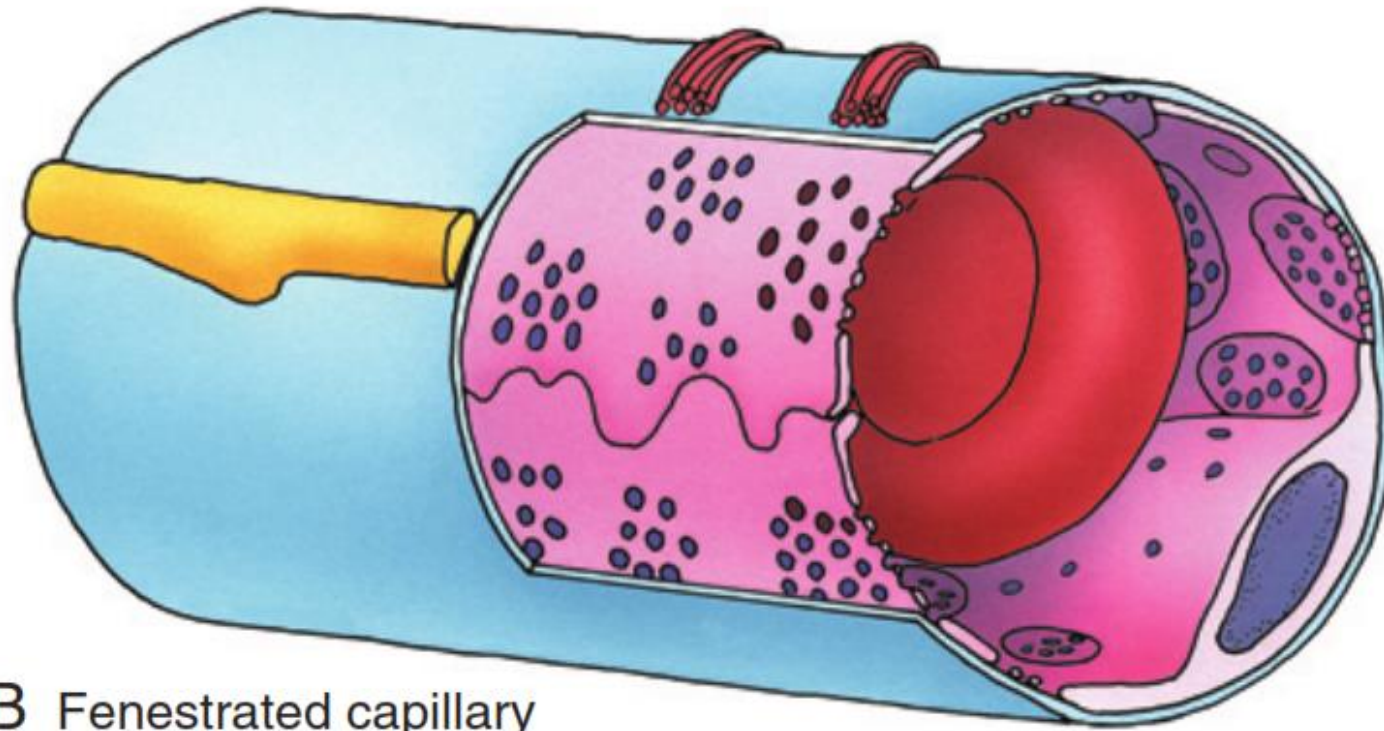
These capillaries are found in the **pancreas, intestines, kidneys, and endocrine glands**.

They possess pores (fenestrae) in their walls that are covered by pore diaphragms (except renal glomerulus)

the diaphragm displays eight fibrils radiating out from a central area and forming wedge-like channels, each with an opening of about 5.5 nm.

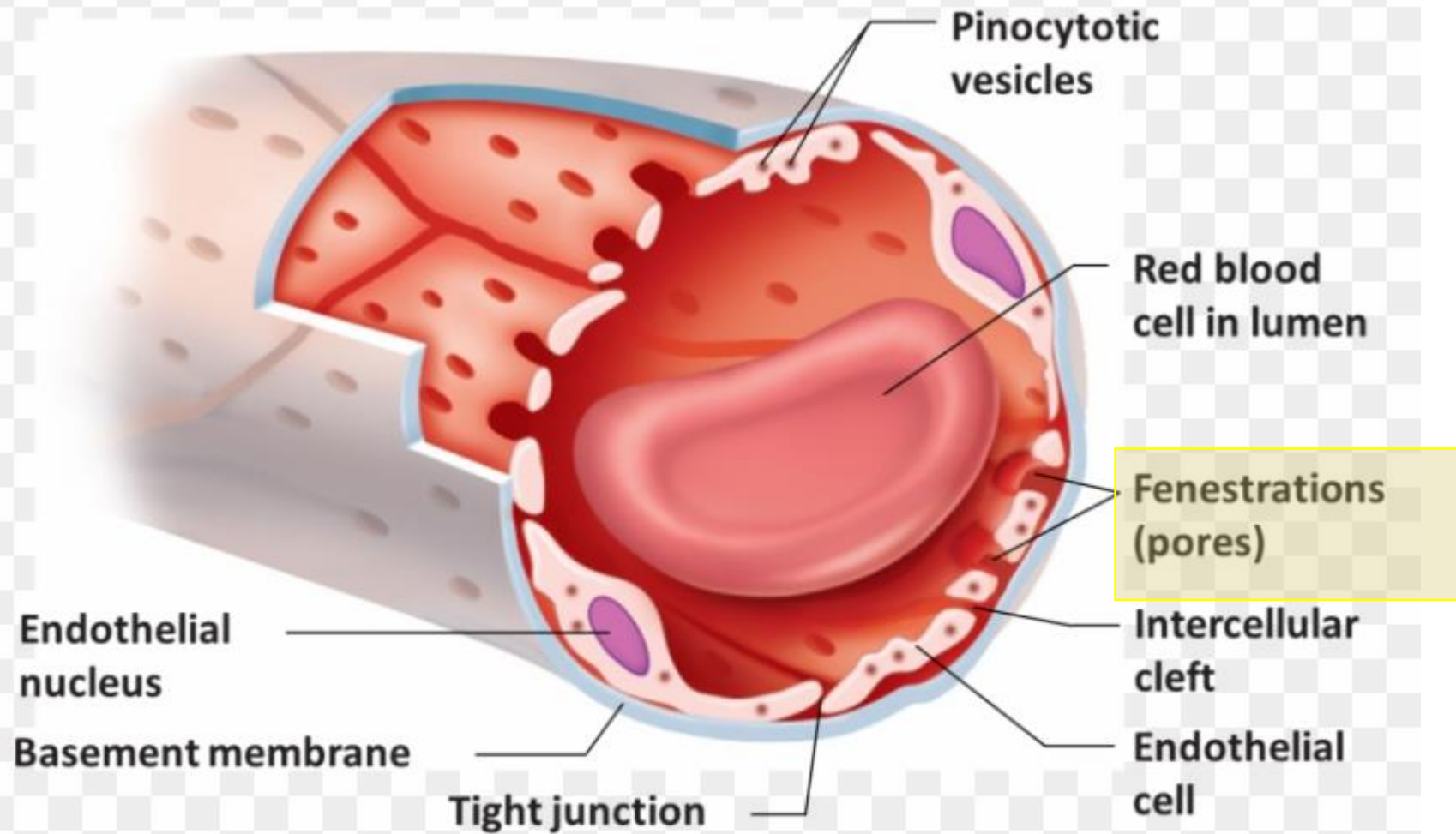
These pore–diaphragm complexes are **regularly spaced** about 50 nm apart but are **located in clusters**; thus, most of the endothelial wall of the fenestrated capillary is without fenestrae (see Fig. 11–12B).





B Fenestrated capillary





(b) Fenestrated capillary: Large fenestrations (pores) increase permeability. Occurs in special locations (e.g., kidney, small intestine).



Sinusoidal Capillaries

They are called ***sinusoids, irregular blood pools or channels that conform to*** the shape of the structure in which they are located.

discontinuous endothelial cells and basal lamina and contain many ***large fenestrae without diaphragms***, enhancing exchange between blood and tissue.

They are present in certain organs of the body, including the **bone marrow, liver, spleen, lymphoid organs, and some endocrine glands**

In certain organs, the endothelium is thin and **continuous (as in some lymphoid organs)**; in others, it may have continuous areas intermingled with **fenestrated areas (as in endocrine glands)**. Macrophages may be located either in or along the outside of the sinusoidal wall.

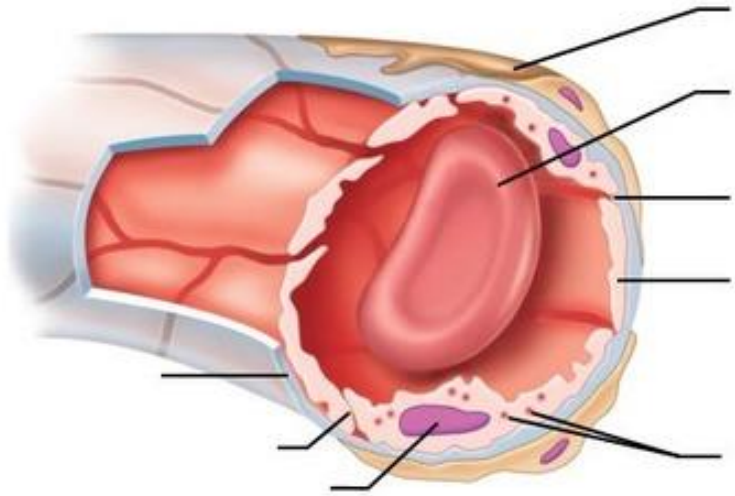




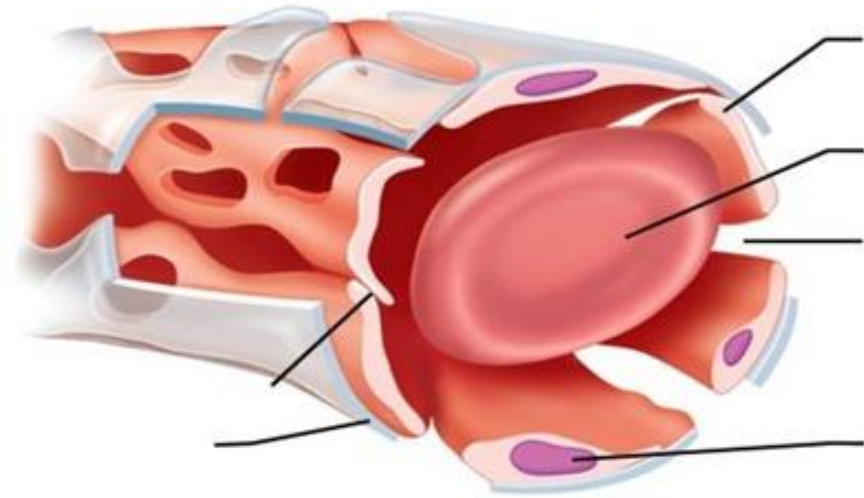
C Sinusoidal (discontinuous) capillary



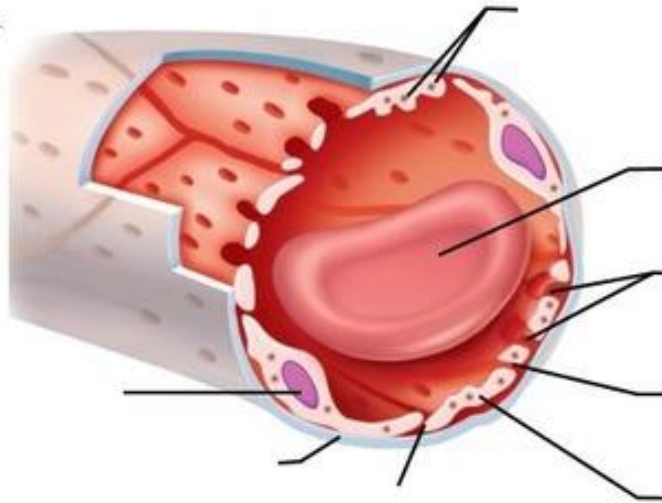
Figure 19.3 Capillary structure.



Continuous capillary. Least permeable, and most common (e.g., skin, muscle).



Sinusoid capillary. Most permeable. Occurs in special locations (e.g., liver, bone marrow, spleen).



Fenestrated capillary. Large fenestrations (pores) increase permeability. Occurs in areas of active absorption or filtration (e.g., kidney, small intestine).

