

Histology

The Cardiovascular System

eMODULE TUTORIAL

CLICK TO BEGIN

H8 The Histology of the Cardiovascular System

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Western University Virtual Slide Box

University of Michigan Virtual Microscopy

University of Minnesota Histology Guide

University of Leeds Histology Guide

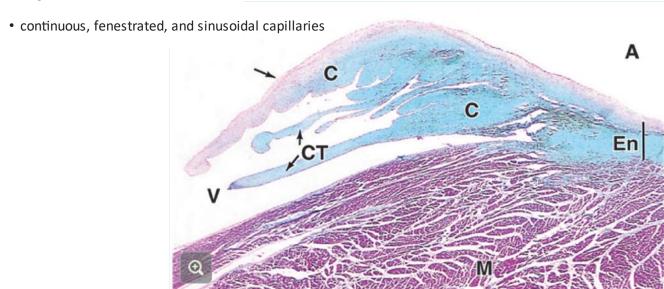
University of Illinois Cell and Tissue Biology

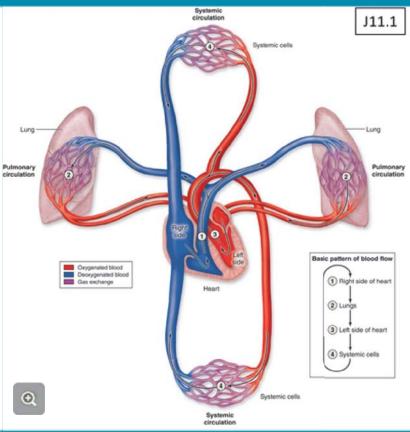
PREVIOUS

H8 Objectives 1

When you have learned the material presented here, you will be able to describe the histological features of the following structures. Furthermore, you will be able to describe the functional implications of their histological structure.

- · the heart
- larger vessels



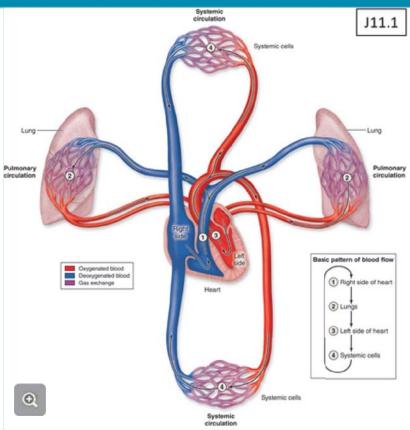


The heart pumps blood, **simultaneously**, through two distinct systems of vessels.

The right side of the heart pumps blood through the vessels of the **pulmonary circulation**. In the lungs, carbon dioxide is eliminated and blood is oxygenated.

The left side of the heart pumps blood through vessels of the **systemic circulation**. In the peripheral tissues, oxygen is delivered, and waste products of cellular metabolism, including carbon dioxide are carried away.

H8 Part I: The Heart



The heart consists of four chambers: two atria and two ventricles. The atria receive blood from **veins**, and the ventricles propel blood into **arteries**.

The right atrium receives deoxygenated blood from systemic veins via the superior and inferior venae cavae (SVC and IVC). It propels blood into the right ventricle, which, in turn, propels this deoxygenated blood into the arteries of the pulmonary circulation.

The left atrium receives oxygenated blood from the lungs via the pulmonary veins. It propels blood into the left ventricle, which, in turn, propels this oxygenated blood into the arteries of the systemic circulation.

All surfaces in contact with circulating blood, i.e. the luminal surfaces of the heart chambers, of blood vessels, and, indeed, of lymphatic vessels, are lined by a simple squamous epithelium called **endothelium**.

Endothelium is critically important in **controlling molecular exchange between blood and subendothelial CT**, but, in addition, it is **antithrombogenic**, it controls the **diapedesis** of white blood cells, and it controls **vascular resistance** and the **growth of adjacent cells** through the release of paracrine factors.

The Functions of Endothelium

- it is a **selectively permeable barrier** (simple diffusion, active transport, pinocytosis, receptor-mediated endocytosis)
- it is nonthrombogenic, i.e. smooth, nonturbulent, secretion of anticoagulants (thrombomodulin), antithrombogenic agents (TPA)
- it can modulate vascular resistance, and therefore blood flow, through release of nitric oxide, and the action of membrane-bound enzymes, eg. ACE
- it regulates immune responses by expression of leukocyte adhesion molecules which control leukocyte adhesion & transmigration (diapedesis)
- it can, when appropriately stimulated, produce growth factors, such as vascular endothelial
 growth factor (VEGF), that promote the proliferation of the cellular components of the vessel wall
 during the processes of vasculogenesis and angiogenesis

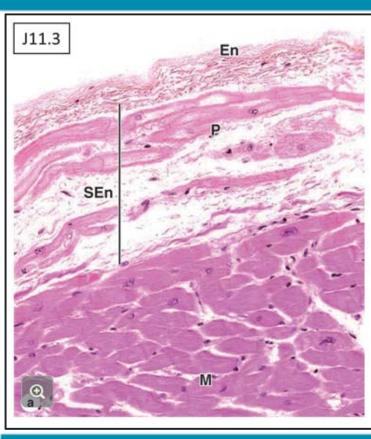
The walls of the heart chambers are composed of **three histological layers**. The innermost is the **endocardium**. The bulk of the chamber walls is the **myocardium**. The outer surface of the heart is the **epicardium**, which in gross anatomy, is called the **visceral layer of the serous pericardium**.

The endocardium consists of 1) the endothelium and its underlying lamina propriation, 2) an intermediate myoelastic layer consisting of smooth muscle fibres and CT, and 3) the subendocardial layer consisting of CT that merges with the subadjacent myocardium. Components of the conducting system of the heart, consisting of specialized cardiac muscle fibres, occupy the subendocardial layer.

The intermediate layer, the myocardium, is the thickest layer of the heart wall. In it, cardiac muscle fibres are arranged spirally around each heart chamber, thus contributing to the functional efficiency of myocardial contraction. The myocardium is thicker in the walls of the ventricles than the atria because greater pressure must be generated by these chambers in order to overcome the vascular resistance of the pulmonary and systemic circulations. Because the systemic circulation has a higher vascular resistance than the pulmonary circulation, the greatest pressure must be generated by the left ventricle, and the myocardium is thickest in the walls of this chamber. You saw this in the gross anatomy lab.

The epicardium is a serous membrane consisting of a simple squamous mesothelium and underlying loose CT. This loose CT contains nerves and blood vessels, as well as a variable amount of adipose.

Again, you studied this layer in the gross anatomy lab, where it was referred to as the visceral layer of the serous pericardium. At the origins of the great vessels, it reflects onto the inner surface of the fibrous pericardium, becoming the parietal layer of the serous pericardium; together they form the pericardial sac. Both layers of the serous pericardium produce the serous fluid, the pericardial fluid, which lubricates the movement of the heart relative to the pericardial sac.



The Endocardium and Myocardium 💢



Luminal surface of the ventricular wall. showing the layers of the endocardium:

- 1) the endothelium (En)
- 2) the thin **myoelastic layer** (not labeled)
- 3) the subendocardial layer (SEn).

In the subendocardial layer are found Purkinje fibres (P) of the conducting system of the heart. Purkinje fibres are specialized cardiac muscle fibres, joined by intercalated discs, that function in impulse conduction rather than contraction.

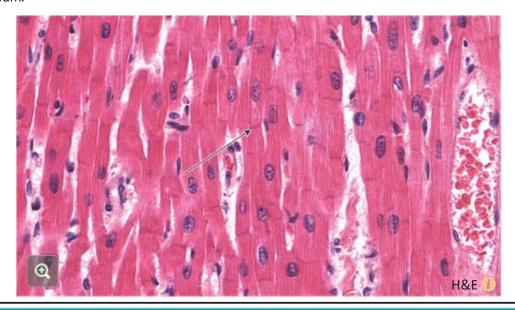
Deep to the endocardium is the myocardium (M).

H&E

The Myocardium



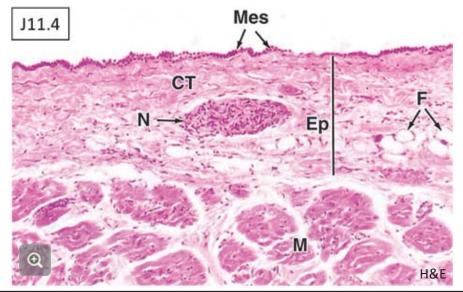
Depicted is a longitudinal section of the myocardium. Recall that cardiac muscle is a **functional syncytium**, which allows for rapid coordinated contraction of cardiomyocytes along their entire length. This property is mediated by the presence of **intercalated discs** (labelled with an arrow) that join cardiomyocytes within the myocardium.



The Epicardium



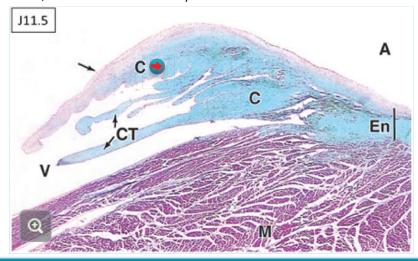
The external layer of the heart is the **epicardium** (Ep). It consists of a simple squamous epithelium, the **mesothelium** (Mes) and underlying **CT**. Embedded in this CT is a variable number of fat cells (F), autonomic nerves (N) and blood vessels. **Interstitial fluid** within the CT serves as the source for the production of **pericardial fluid** secreted across the mesothelium into the pericardial space. The myocardium (M) can be seen deep to the epicardium.



The **cardiac skeleton** is composed of **dense fibrous CT** that forms the following structures and performs the following functions:

- it contributes to the formation of the interatrial and interventricular septae
- it surrounds the four valves of the heart; in doing so, it provides anchorage for the valve leaflets as well as for the myocardium of the chamber walls
- it extends into the leaflets of the valves and into the chordae tendineae of the atrioventricular valves
- it acts as an electrical insulator, preventing direct spread of electrical impulses from the cardiomyocytes of the atria to the cardiomyocytes of the ventricles

A section through an atrioventricular valve cusp (arrow) demonstrates the fibrous skeleton of the heart. It is composed of dense irregular connective tissue (C), which stains blue in this preparation. It is found largely in the endocardium (En), where it forms rings that surround the valves and physically and electrically separate the myocardium of the atria from that of the ventricles. Because dense irregular connective tissue is inextensible, these rings control the size and shape of the openings. As shown, it extends into the valve leaflets, forming much of its core, and into the chordae tendineae (CT) that attach the valve cusps to the papillary muscles of the ventricular walls. Indeed, valve leaflets and chordae tendineae largely consist of a core of dense connective tissue covered by endothelium. The lumena of the atrium (A) and the ventricle (V) are labeled, as is the ventricular myocardium.



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Histological section through the tricuspid valve and right ventricle. The valve is comprised largely of dense irregular connective tissue (C) and anchored to the papillary muscle of the ventricular wall by chordae tendinae (CT). The valve and CT are lined by endothelium.

The endocardium of the right ventricle is also shown in this image.

H&E



The conducting system of the heart is composed of modified cardiac muscle fibres that are specialized for the generation of depolarizing impulses and their propagation throughout the myocardium. It stimulates and coordinates the contraction of the chamber walls, and therefore, the rhythmic propulsion of blood. The components of the conducting system of the heart are located in the subendocardium and extend into the subadjacent myocardium.

Within the walls of the right atrium are two nodes of specialized myocardial cells, the **sinoatrial (SA) node** and the **atrioventricular (AV) node**. The SA node acts as the pacemaker, setting the basic rate of contraction of the heart. Other components of the conducting system of the heart are the **AV bundle** and the **subendocardial conducting network**.

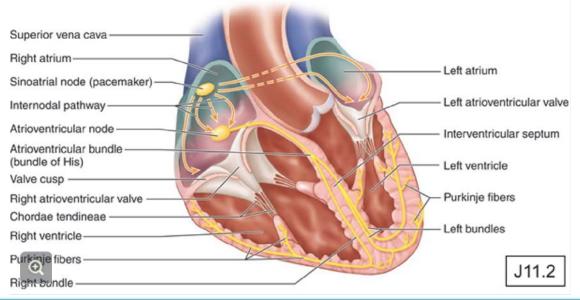
In the gross anatomy lab, you found the location of the **SA node** in the wall of the right atrium where this chamber meets the SVC, at the apex of the crista terminalis. It is a 6-7 mm³ knot of modified myocardial cells. These cells have an unstable resting potential, which leads to the **regular generation of action potentials** that **spread via the internodal pathway to the AV node**. In doing so, these impulses cause the coordinated contraction of the atrial myocardium, **atrial systole**.

In the gross anatomy lab, you found the location of the **AV node** in the interatrial septum, superior to the coronary sinus and adjacent to the AV valve. The cells of the AV node are depolarized by the incoming signal from the SA node. The signal in the AV node is delayed, due to the electrical properties of these cells, and therefore, atrial contraction is complete, before the signal for contraction spreads to the ventricles.

H8 The Conducting System of the Heart II

From the AV node, the signal is conducted through the **AV bundle** in the **membranous portion** of the interventricular septum. The fibres of the AV bundle bifurcate and form the **left and right bundle branches** in the subendocardium of the muscular portion of the interventricular septum.

At the apex of the heart, the right and left bundles disperse throughout the walls of the ventricles to form the **subendocardial conducting network**, commonly referred to as Purkinje fibres. It coordinates the simultaneous contraction of myocardium of the right and left ventricular walls.



Pain interpreted as originating in distribution of somatic sensory nerves

As you learned in gross anatomy, the heart receives autonomic input from the sympathetic cardiac nerves, originating as preganglionic fibres from the upper thoracic spinal cord segments, and descending as postganglionic fibres from the cervical sympathetic chain ganglia in the neck. It also receives parasympathetic preganglionic input from the vagus nerve. These two arms of the ANS meet at the cardiac plexus, located anterior and posterior to the aortic arch.

Parasympathetic ganglionic cells and sympathetic postganglionic fibres are located in the regions of the SA and AV node. Their input influences heart rate, the parasympathetic input decreasing heart rate, and the sympathetic input increasing heart rate. Since the SA node develops from structures on the right side of the embryo and the AV node develops from structures on the left side of the embryo, the right vagus and right sympathetic cardiac nerves are distributed primarily to the SA node, while the left vagus nerve and left

sympathetic cardiac nerves are distributed primarily to the AV node.

Nociceptive sensory nerve endings within the myocardium respond to stimuli such as ischemia, as may occur during angina pectoris, and conduct their impulses centrally via the sympathetic cardiac nerves, back to the upper thoracic segments of the spinal cord. Overlap here with incoming sensory fibres from the corresponding dermatomes leads to the common referral of cardiac pain to the medial arm and upper chest, as illustrated in the accompanying slide.

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Patient perceives diffuse pain in

T1-4 dermatomes

Visceral

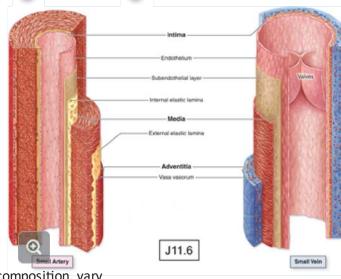
sensory nerve

H8 Part II: Blood Vessels

H8 The Structure of Larger Blood Vessels I

The walls of arteries and veins (but not the smallest blood vessels, capillaries) consist of three layers. From the lumen outward, these are the tunica intima , tunica media and tunica adventitia

(externa).



The thickness of each layer, and the details of its composition, vary between different vessels, determined largely by blood pressure.

Vessels branch frequently and along with their caliber, their structure changes gradually with each branching. Thus, there is a smooth transition in structure and function from one class of vessel to another. **Elastic arteries**, as they branch, become **muscular arteries**, which, as they branch, become **arterioles**. A description of the **structural features and functional implications** of these classes of vessels follows.

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- 2. the **tunica media**, the intermediate layer: χ
- consists of concentric layers of smooth muscle cells that spiral around the vessel lumen
- SyNS input controls vascular tone and therefore vessel diameter
- in some arteries, smooth muscle alternates with layers of elastin, elaborated by the smooth muscle cells, which form fenestrated elastic layers
- in some arteries, an external elastic lamina is present

External elastic lamina J11.6 Small Vein

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- 3. the tunica externa (adventitia):
- CT sheath connecting BV to surrounding structures, it is composed largely of type I collagen fibres and elastic fibres
- in larger vessels, contains vasa vasorum o, small blood vessels within the tunica externa and outer tunica media that supply blood to the tissues of the vessel that are too far from the lumen to be nourished by the blood within the vessel lumen; not surprisingly, large systemic veins that carry deoxygenated blood have more vasa vasorum than similarly-sized arteries

External elastic lamina J11.6 Small Vein

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H8 Elastic Arteries are the Largest Arteries

Elastic arteries are the largest arteries, closest to heart, such as the aorta and its main branches (brachiocephalic trunk, common carotids, subclavians, common iliac arteries) and the pulmonary trunk and its main branches (left and right pulmonary arteries). Their primary function is to distribute blood to smaller arteries.

The thickest of their three layers is the tunica media, which contains **abundant elastin** in the form of **fenestrated sheets** between layers of smooth muscle cells; the aorta of an adult contains about 50 elastic lamellae, although this number is greater in the hypertensive individual.

Elastic arteries modulate changes in blood pressure during the cardiac cycle. The abundant elastin in their walls allows them to stretch in response to the increase in pressure that occurs during systole; the extent of this stretch is limited by the vessel's collagen content. When blood pressure drops during diastole, the vessel wall "bounces back", which helps to maintain arteriolar blood pressure. The aortic and pulmonary semilunar valves prevent regurgitation of blood back into the ventricles, and the blood is therefore propelled forward during diastole. As the distance from the heart increases, arteriolar blood pressure becomes less variable (the peaks and troughs of systole and diastole even out) and blood velocity decreases.

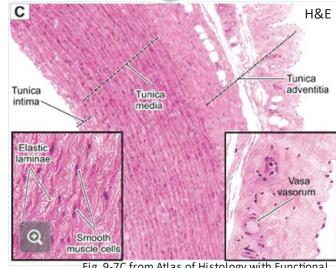
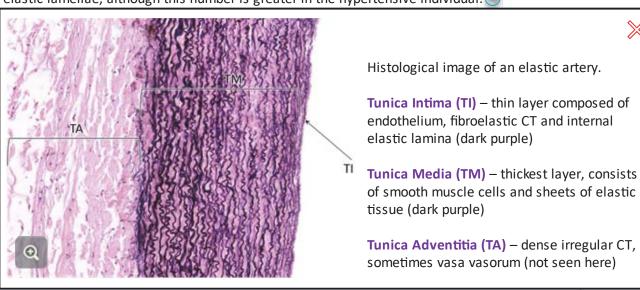


Fig. 9-7C from Atlas of Histology with Functional & Clinical Correlations, by Cui, © 2011.

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As elastic arteries branch, their structure changes and they become muscular arteries. Muscular arteries distribute blood to body organs; thus examples are the renal arteries, gastric arteries and arteries that supply skeletal muscles. In muscular arteries, the thick tunica media contains a higher proportion of smooth muscle fibres, and less elastin than elastic arteries, although in the largest muscular arteries, well-developed layers of elastin, the internal and external elastic lamellae, are present at the junctions between the three layers.

The smooth muscle is under the control of the sympathetic nervous system. Sympathetic input regulates blood flow to organs according to tissue requirements.

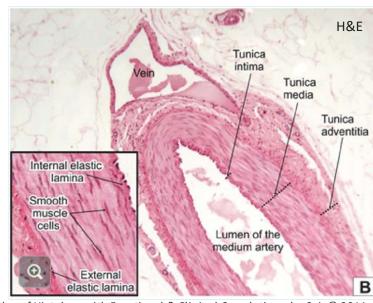
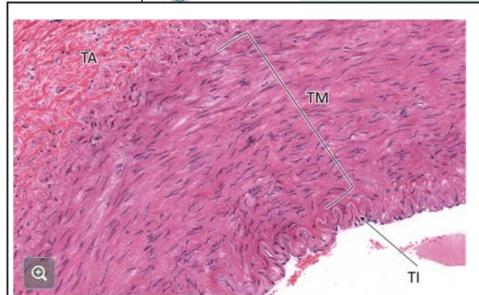


Fig. 9-8B from <u>Atlas of Histology with Functional & Clinical Correlations</u>, by Cui, © 2011.

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Histological image of a muscular artery.

TI – Prominent internal elastic lamina (light pink)

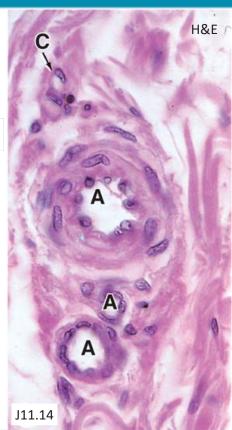
TM – Less elastin and more smooth muscle fibres

TA – Dense irregular CT

The branching of muscular arteries gives rise to progressively smaller vessels, ultimately with 3-4 layers of smooth muscle in their media. These smallest arteries give rise to vessels with 1-2 layers of medial smooth muscle, arterioles (A), which lack elastic laminae. Arterioles are characterized by a thin, ill-defined tunica externa. They function to control blood flow into capillary beds through changes in vascular resistance, controlled by the SyNS, local conditions and hormones.

Arterioles give rise to capillary beds, networks of capillaries (C) that anastomose within the parenchyma of an organ. It is across the walls of these smallest vessels that molecular exchange between blood and interstitial fluid take place. The metabolic activity of an organ or tissue is directly related to the density of its capillary network. Thus, myocardium, skeletal muscle and the kidney have dense capillary networks, dense CT structures, such as ligaments and tendons, do not. Recall that cartilage lacks a blood supply and has a very slow metabolic rate, thus illustrating the limit of this relationship.

Vasoconstriction and vasodilatation of arterioles occurs in a pulsatile manner; it controls the flow of blood into capillary beds in response to tissue requirements. Vascular resistance in arterioles is the major determinant of systemic blood pressure.



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Arteriole (A) with two layers of SMCs, and lacking an elastic laminae

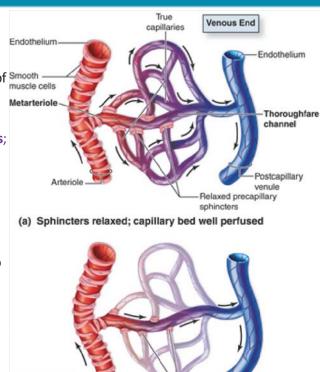
Venule (V) with an endothelium, one layer of smooth muscle and thin adventitia

H8 Capillary Beds

Terminal branches of arterioles, called **metarterioles**, deliver blood to capillary beds. Metarterioles **become thoroughfare channels**, which drain the capillary bed into **postcapillary venules**; the latter are the first part of the venous network.

Metarterioles have scattered smooth muscle fibres in their walls that are arranged as precapillary sphincters; these function to control the volume of blood that enters the true capillaries. Like arterioles, the contraction and relaxation of precapillary sphincters is pulsatile, occurring 5-10 times per minute. True capillaries are the smallest of blood vessels and lack smooth muscle in their walls. The thoroughfare channel is the continuation of the metarteriole which opens into the postcapillary venule; it lacks smooth muscle.

Perfusion of the capillary bed, and therefore molecular exchange between blood and interstitial fluid, is controlled by the precapillary sphincters.



(b) Sphincters contracted; blood bypasses capillary bed

Contracted precapillary

sphincters

Structurally, capillaries are very simple, consisting of endothelium and basement membrane rolled into a tube. Capillaries may be smaller in diameter than an red blood cell, which makes the flexibility of red blood cells critical in their ability to move through capillary beds. The thin walls of capillaries allow for the rapid exchange of fluids, gases, metabolites & waste products between blood and interstitial fluid.

Pericytes are relatively undifferentiated cells associated with capillaries that may contribute to blood vessel remodeling and wound healing. When appropriately stimulated, they may proliferate and differentiate to form the cellular components of the walls of new blood vessels.

The structure, and therefore permeability, of capillaries varies between organs and tissues with different functions. They are classified into three histologic types, based on their structural properties:

- 1. Continuous capillaries
- 2. Fenestrated capillaries
- 3. Sinusoidal capillaries

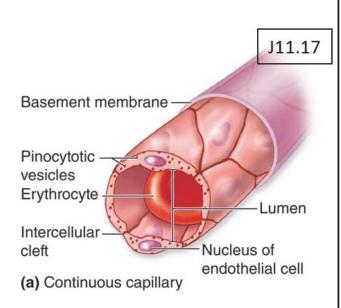
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Continuous Capillaries



Continuous capillaries are the least permeable and most common type of capillary. They are found, for instance, in the lung, muscle, brain and exocrine glands.

Molecular passage across the walls of these vessels is highly regulated. They have a complete ("continuous") endothelial lining, which includes numerous tight junctions & desmosomes joining the endothelial cells across the intercellular cleft. Tight junctions, you will recall from the histology module on epithelia, limit paracellular molecular transfer, allowing the epithelial cells to control molecular passage by active, transcellular means, such as pinocytosis. Lipid-soluble molecules may diffuse passively through the membrane of all cells, including the endothelial cells that line capillaries. These capillaries have a continuous basement



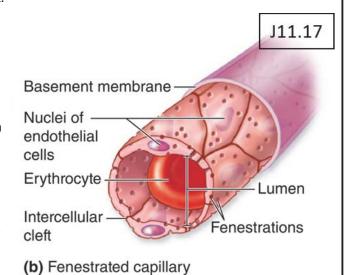
membrane.

Fenestrated Capillaries



Fenestrated capillaries are more permeable than continuous capillaries. They are found, for instance, in endocrine tissue, the small intestine, the choroid plexus of the brain (which secretes cerebrospinal fluid), and in the kidney. These are examples of tissues and organs in which the exchange of molecules, including larger molecules, is functionally important.

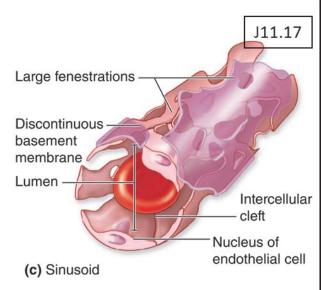
In fenestrated capillaries, pores (fenestrae) in endothelial cell walls permit rapid exchange of peptides & small proteins between blood and the interstitial fluid surrounding the vessel. Fenestrae may form when pinocytotic vesicles span the cytoplasm of the endothelial cell, and open on both surfaces of the cells, thus creating a passage for exchange of these larger molecules. Evidence for this is the observation that the number and size of fenestrae varies with tissue activity level, for instance, in the small intestine before and after a meal. These capillaries, too, have a continuous basement membrane.



Sinusoidal Capillaries or Sinusoids



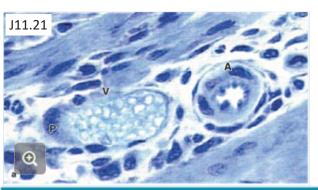
Sinusoids, sometimes called "discontinuous capillaries", have larger pores in their walls and a thinner or discontinuous basement membrane. In addition, there are gaps between the endothelial cells. Sinusoids permit the most rapid exchange of the largest solutes. They are often larger-diameter vessels, as compared to continuous and fenestrated capillaries, which slows blood flow, maximizing molecular exchange, and even the exchange of cells, between blood and the surrounding interstitial fluid. They are found, for instance, in the liver, bone marrow and spleen.



Postcapillary venules receive efferent blood from capillary beds. There is no abrupt change in the structure of the vessels; **postcapillary venules are endothelium and basal lamina**, although they have more associated **pericytes** and their **diameters are larger** than those of capillaries.

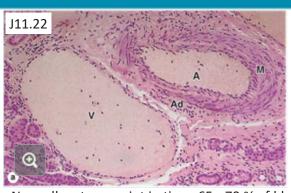
Postcapillary venules are the primary site of action of vasoactive agents such as histamine and serotonin, released by mast cells during the inflammatory response. Postcapillary venules are therefore the primary site of the extravasation of tissue fluid that causes edema. They are also the primary site at which white blood cells exit the circulation and enter the subadjacent CT via diapedesis, both under normal conditions, and, at higher rates, during inflammation.

The convergence of postcapillary venules forms **venules** with associated smooth muscle, which ultimately have defined tunicae media and adventitia. Convergence of venules forms **small veins**, then **medium** and **large**, each with three defined layers in their walls. All venules and veins characteristically have thinner walls and larger diameters as compared to their companion arteriole or artery.



This image is of a postcapillary venule (V) and its companion arteriole (A). A pericyte (P) is associated with the postcapillary venule. Notice the larger lumen and thinner wall of the venous vessel.

FYI, the stain is toluidine blue.



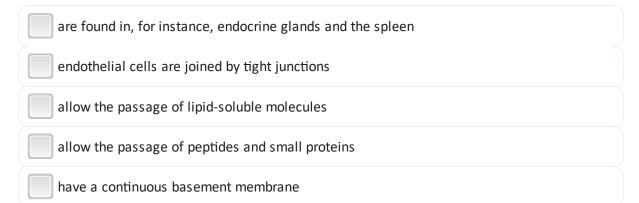
This image is of a small vein (V) and its companion, a small muscular artery (A). Again, notice the larger lumen and thinner wall of the venous vessel. The artery has a more well-developed tunica media (M) and a tunica adventitia (Ad) than the vein, with the media being the thickest of the three layers.

Normally, at any point in time, 65 - 70 % of blood volume, or about 3.5 L, is in the venous systems of various tissues and organs. Sympathetic stimulation of venous smooth muscle causes **venoconstriction**, which moves blood out of this **blood reservoir** into the arteriolar / capillary systems.

Venous blood is under **very low pressure**, as compared to arteriolar blood, which results in modifications in the structure of veins as compared to arteries. Because their intraluminal pressure is low, veins have **thinner walls**, as compared to their companion arteries; the thick walls of the latter are built to withstand their high intraluminal pressures. Because the pressure in veins is too low to propel the contained blood back to the heart, veins rely on compression from adjacent organs, such as skeletal muscle in the limbs, to exert pressure on the contained blood. This mechanism is referred to as the **skeletal muscle pump**. In order to control the direction of movement of venous blood, larger **veins have valves** which ensure the one-way flow of blood back to the heart. These valves are **better developed in the lower limbs**, as compared to the upper limbs and head and neck. This is because it is within the lower limbs that the venous blood is most challenged by gravity.

H8 Question 1

From the following options, choose all statements that correctly describe continuous capillaries.



Individuals with Marfan syndrome have mutations in a gene involved in collagen production. They often develop aortic aneurisms. What layer of the arterial wall is most affected by this mutation?

Endothelium	
Tunica intima	
Tunica media	
Tunica adventitia	
External elastic lamina	

In which layer of the heart wall are the major components of the conducting system of the heart located?



Which layer of the heart wall produces pericardial fluid?

the lamina propria of the endothelial layer

the myocardium

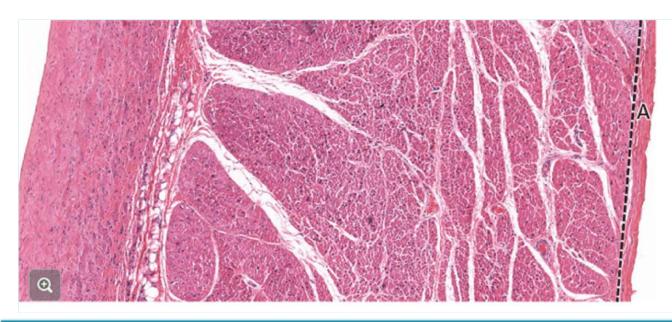
the subendocardial layer

the epicardium

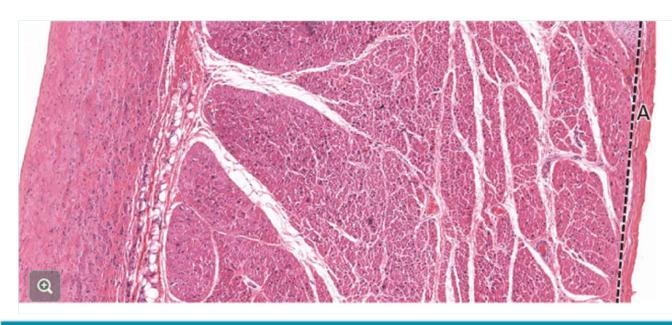
In which layer of the heart wall are nociceptive nerve endings that respond to ischemia primarily located?



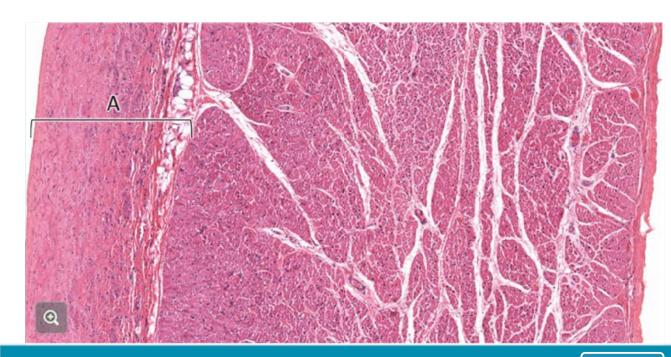
Identify the layer indicated by A.



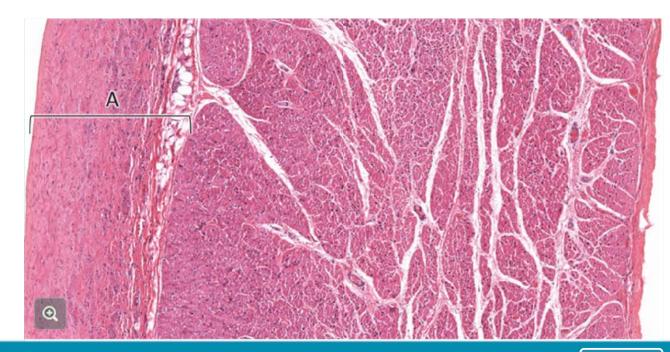
The cells lining layer A produce _____ fluid.



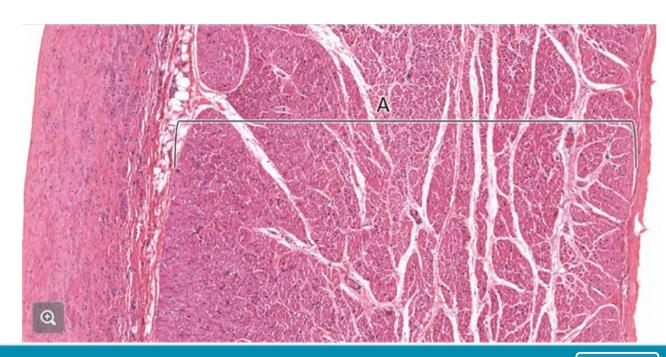
Identify layer. Be specific.



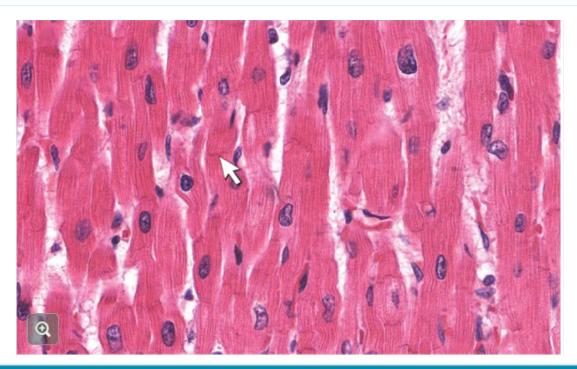
Specialized fibres are present within this layer, what are they?



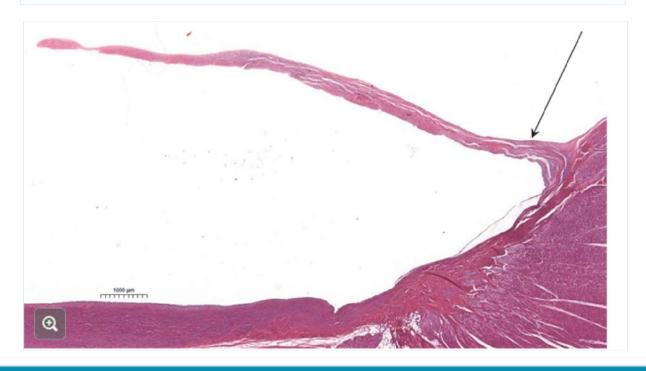
Identify layer A. Be specific.



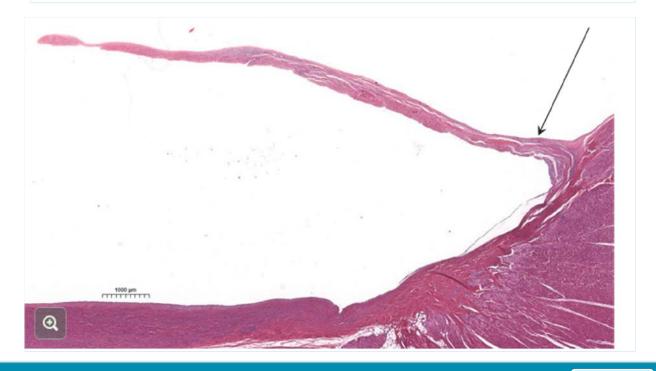
Identify the structure indicated. Be specific.



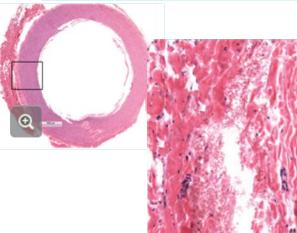
Identify the structure indicated. Be specific.

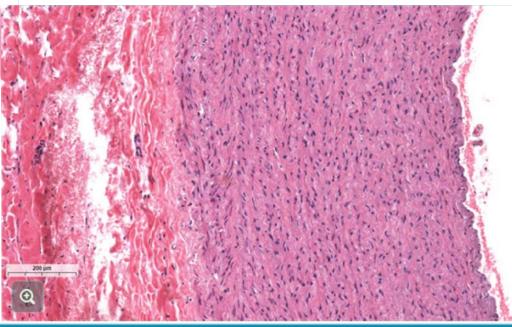


This structure adheres to the ventricular wall via _____ muscles.

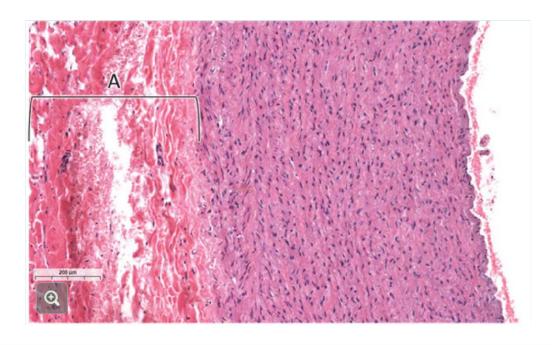


What vessel type is depicted. Be specific. (hint: look at the tunica media!)

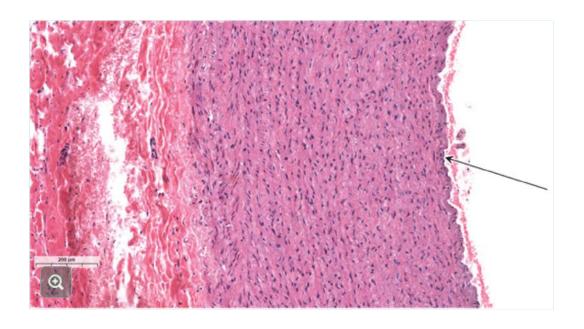




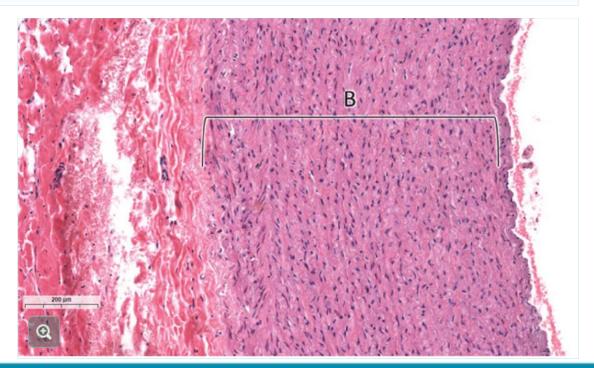
Identify the blood vessel layer indicated by A. Be specific.



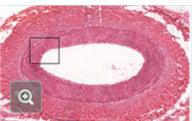
Identify the blood vessel layer indicated. Be specific.

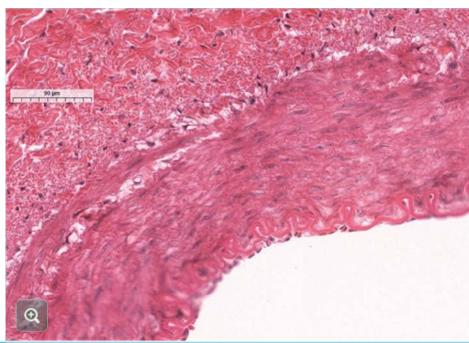


Identify the blood vessel layer indicated by B. Be specific.

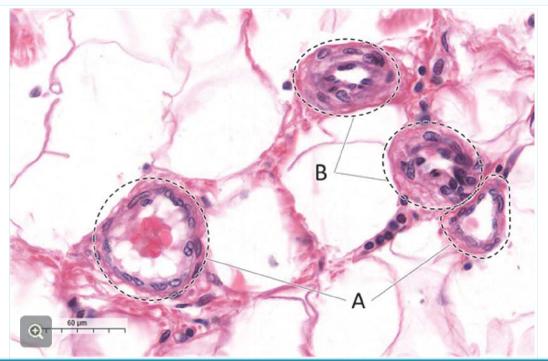


What vessel type is depicted. Be specific. (Hint: look at the tunica media!)

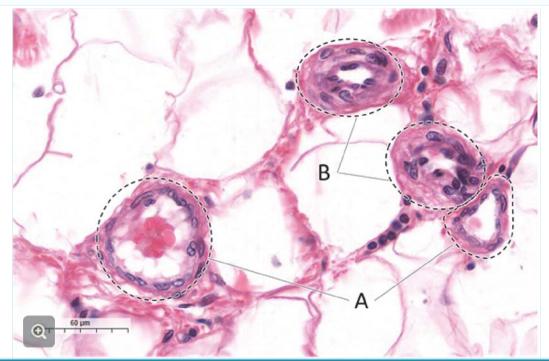




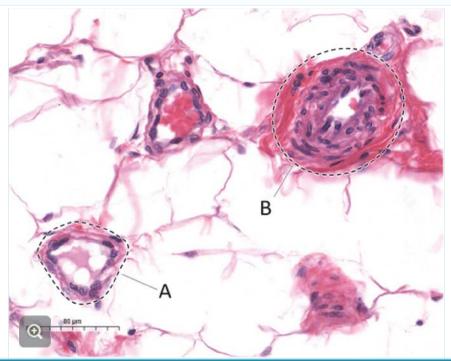
Identify the vessel type A.



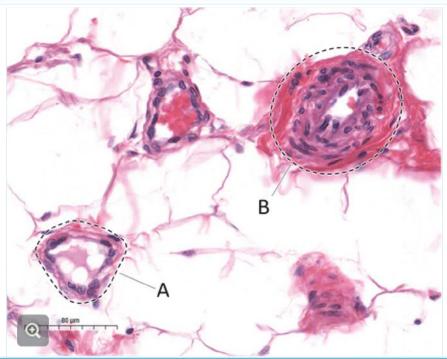
Identify the vessel type B.



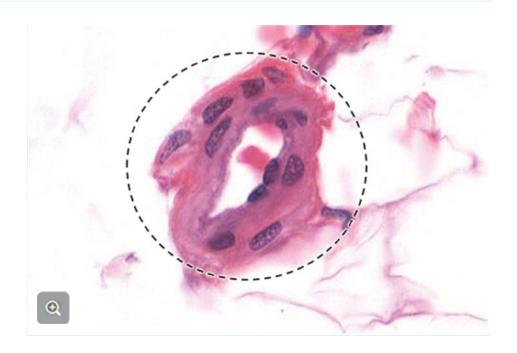
Identify the vessel type A.



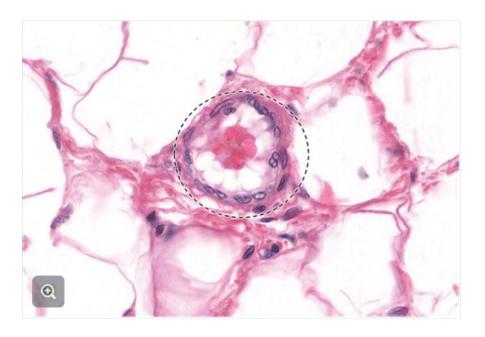
Identify the vessel type B.



Identify the structure outlined. Be specific.



Identify the structure outlined. Be specific.



Congratulations on Finishing H8 The Cardiovascular System!

REVIEW H8