Structure and Function of Blood Vessels

Scientific Foundations

Learning objectives

- Students should be able to list the differences in structure and permeability between the three types of endothelia.
- Students should be able to list the components of endothelium that determine its permeability.
- Students should be able to describe two molecular mechanisms that increase the permeability of endothelium.
- Given a histological image, students should be able to identify the different types of blood vessels and explain the role each plays in the conduction of blood and distribution of nutrients.
- Given an histological image of a large artery, students should be able to describe the function of each layer of the wall of the artery and the components and cells in each layer.
- Given an electron micrograph of a capillary, students should be able to determine whether the capillary is continuous, fenestrated or discontinuous.

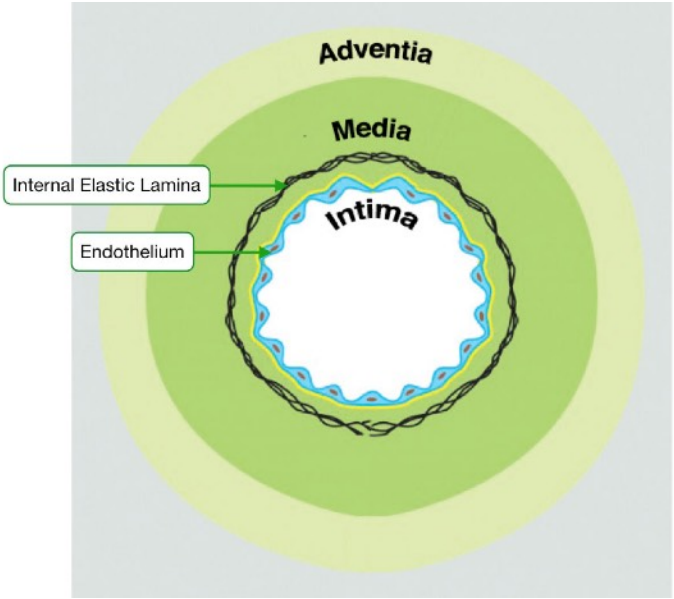
Introduction

The vascular system is a continuous network of tubes or vessels that distributes blood throughout the body and returns it the heart. An endothelium lines the inner surface of the entire network of vessels but the walls of the vessels differ depending on the size of the vessel and their position along the length of the system. The walls of large arteries and veins contain three distinct layers, tunica adventitia, tunica media and tunica intima (from outside to inside), whereas capillaries and small venules may contain only endothelia cells and the occasional support cell.

Below we describe the structural features of the different types of vessels and how those structures facilitate the functions of the vessels. The vessels are presented in order as blood travels from the heart to the peripheral tissues and returns to the heart.

Walls of a Blood Vessel

The wall of the aorta illustrates the three layers of a blood vessel.

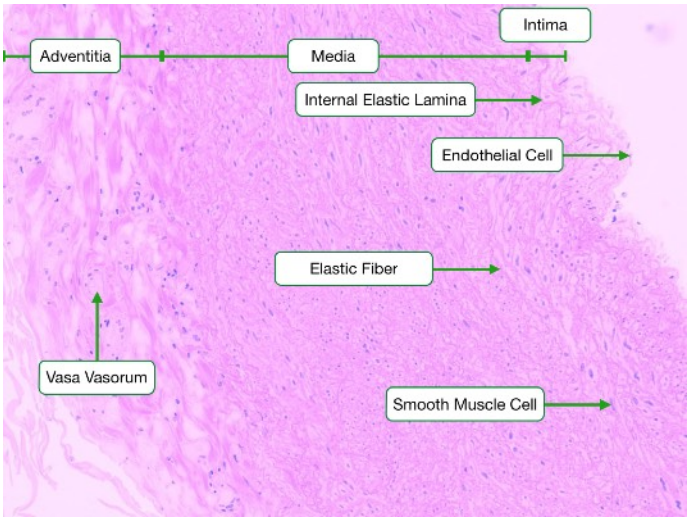


- The **tunica intima** is thin and composed of endothelial cells and their underlying supporting tissue, which includes the basement membrane and internal elastic lamina. The internal elastic lamina is composed of elastic fibers.
- The **tunica media** is the largest portion of the wall and is composed of elastic fibers, smooth muscle and collagenous tissue.
- The **tunica adventitia** is the outermost component of the arterial wall. It contains mostly connective tissue in the form of collagen and a few small blood vessels called vasa vasorum that supplies the cells that make up the arterial wall.

These three layers will be visible in large arteries and veins, but as the diameter of the vessel decrease, the intima and media layers become thinner. In the smallest blood vessels, capillaries, only endothelial cells and an occasional support cell are found.

Elastic Artery: Aorta Wall

Elastic arteries are notable for the numerous elastic fibers in their tunica media. The elastic fibers allow the aorta to stretch during systole to accommodate a large volume of blood, and then contract during diastole to push the blood downstream through cardiovascular system. Note the internal elastic lamina that separates the media from intima layer.



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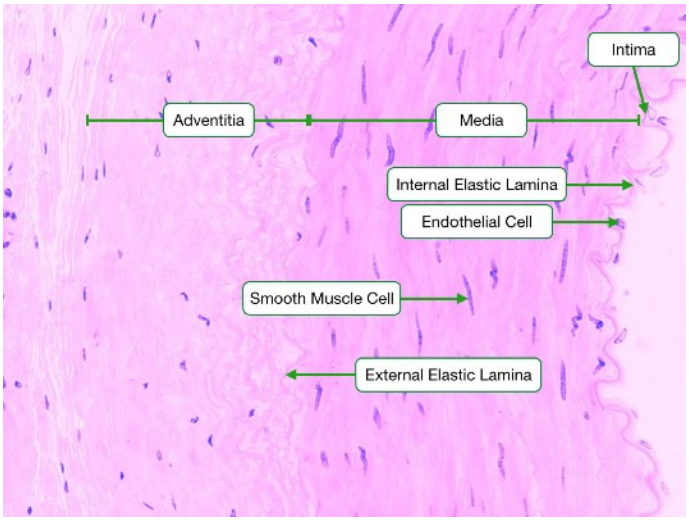
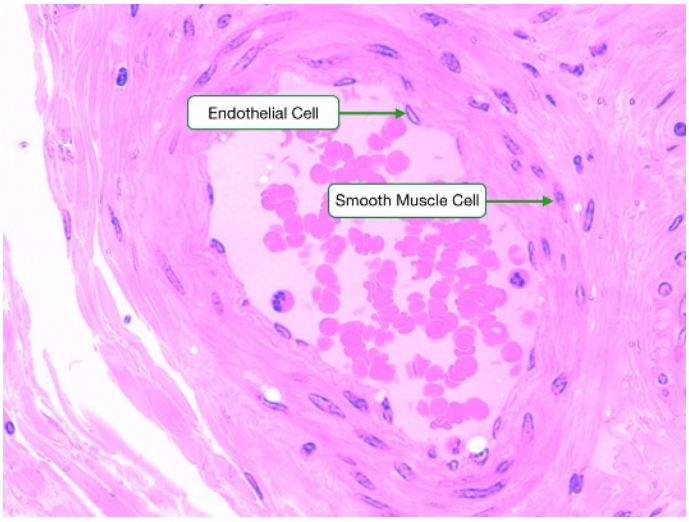


Muscular Artery Wall

Muscular arteries continue from elastic arteries and control the distribution of blood throughout the body. The tunica media of muscular arteries contains fewer elastic fibers and more smooth muscle cells than elastic arteries. Note the prominent internal elastic lamina and external elastic lamina which separates the tunica media from tunica adventitia and is also composed of elastic fibers.

Muscular arteries control the distribution of blood to different parts of the body. The smooth muscle cells in the medial layer contract to decrease the lumen of the artery and decrease blood flow or relax to increase the diameter of the lumen and the amount of blood flow. Smooth muscle cells are also responsible for synthesizing all the protein components in the walls of blood vessels, including collagen, elastic fibers and proteoglycans.

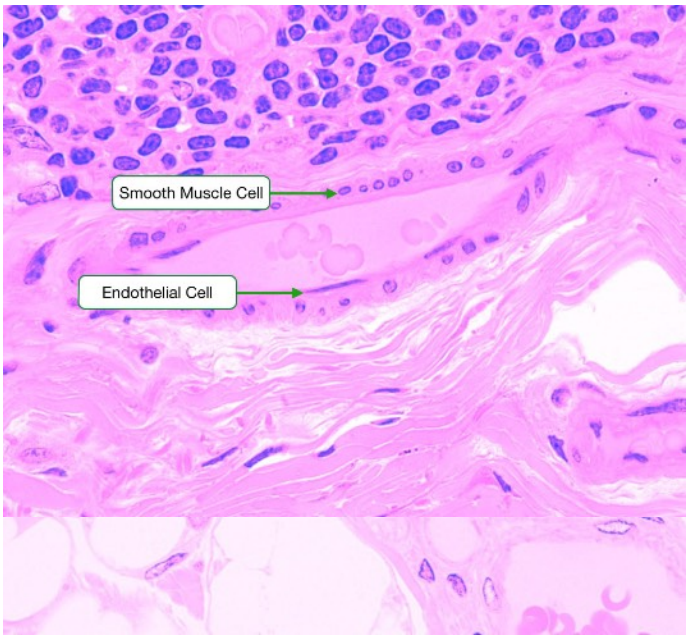


Small Muscular Artery

As muscular arteries branch and decrease in size, the number of layers of smooth muscle cells in the tunica media decreases. Also, the internal and external elastic laminae become much less prominent.

Arterioles

In arterioles, the tunica media contains only one or two layers of smooth muscle cells. Contraction of the smooth muscle cells constricts the lumen of the arteriole, increasing vascular resistance and reducing the flow of blood into capillary beds.

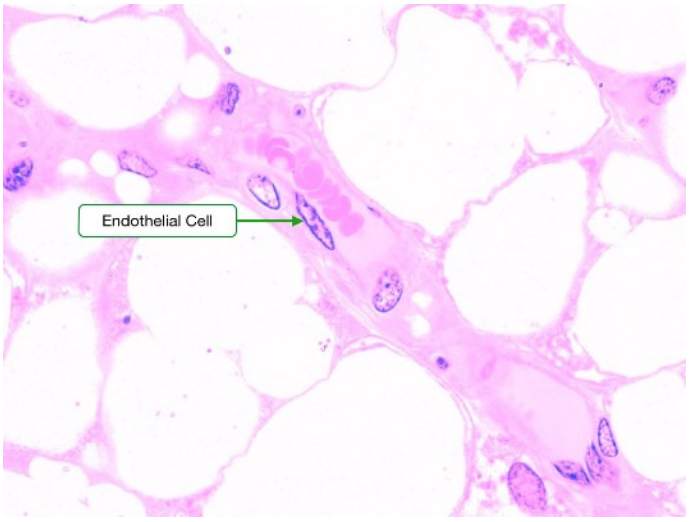


Arteriole, Longitudinal Section

This image shows an arteriole in longitudinal section. The arteriole has a single layer of smooth muscle cells. Note the orientation of the smooth muscle cells in longitudinal section versus cross section.

Capillary

Capillaries contain a single layer of endothelial cells and their basement membrane. The lumen of capillaries is so narrow that red blood cells have to pass in single file. The thin walls of capillaries facilitate exchange of gases and small molecules between the bloodstream and surrounding tissue. Capillaries are often wrapped with pericytes which are contractile cells that regulate the activity of endothelial cells through cell adhesion proteins and gap junctions.



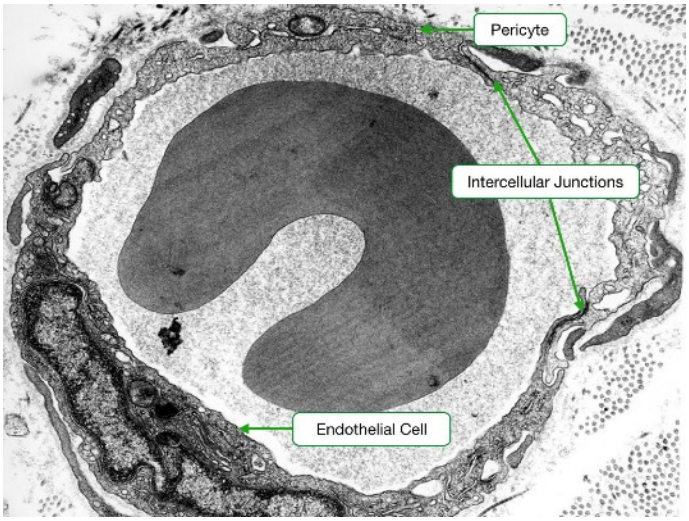
Permeability of Capillaries

One of the most important roles of the capillary wall is to control what passes from the blood into the surrounding tissue and fluid. There are three primary components that restrict the diffusion of material between the blood and interstitial fluid: endothelial cells, junctional complexes and basement membrane.

Because endothelial cells line the entire wall of capillaries, their structure plays a critical role in controlling the movement of molecules and proteins across capillaries. There are three structural types of capillaries: continuous, fenestrated and discontinuous.

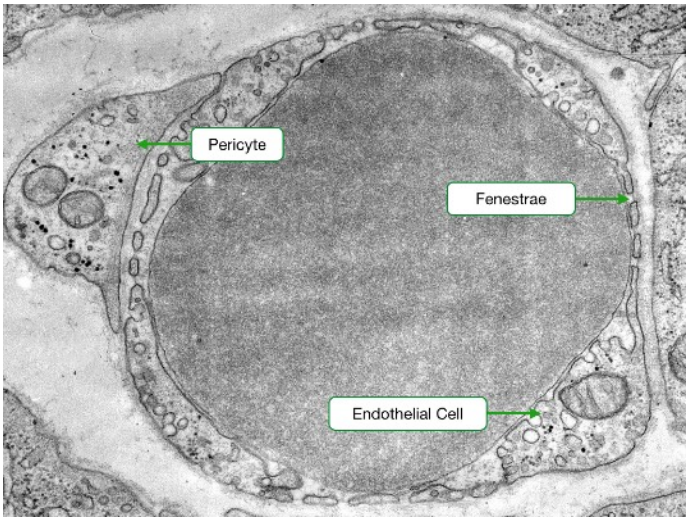
Continuous Capillary, Electron Micrograph

Endothelial cells in continuous capillaries completely enclose the lumen of the blood vessel. The only gaps are the junctions between adjacent endothelial cells where small molecules can diffuse between the bloodstream and surrounding tissue. Consequently, continuous capillaries are the most restrictive. Continuous capillaries are prominent in adipose and muscle tissue and in the brain.

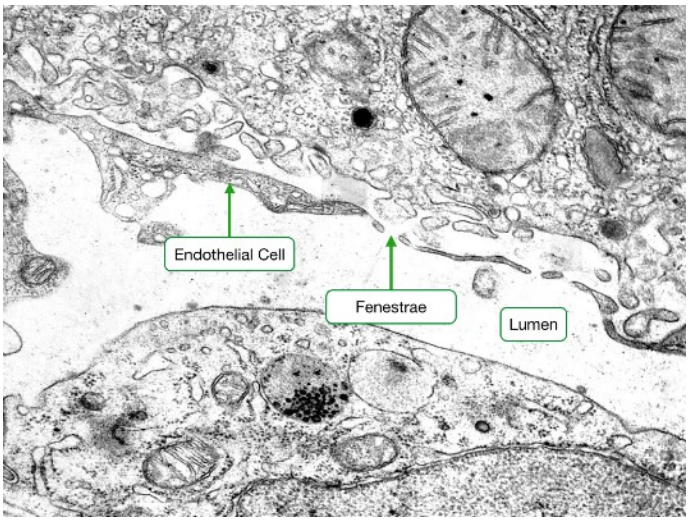


Fenestrated Capillary, Electron Micrograph

Fenenstrated capillaries are more permeable than continuous capillaries because the endothelial cells contain holes or fenestrae that allow small molecules and certain proteins to pass through the endothelium. Barely visible in the fenestrae is an electron-dense line known as the diaphragm that functions as a filtration barrier. Fenestrated capillaries are prominent in the kidney, intestine and endocrine glands.

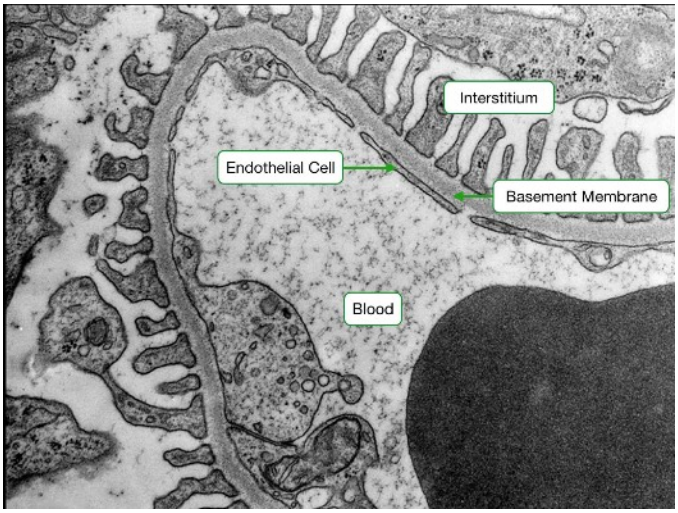


Discontinuous Capillary, Electron Micrograph



Discontinuous capillaries are the leakiest of the three types of capillaries. Similar to fenestrated capillaries, discontinuous capillaries contain gaps, but the gaps here are larger than in fenestrated endothelia and lack diaphragms. These gaps allow proteins to diffuse freely across the endothelium. Note also that there is no basement membrane beneath discontinuous endothelia, whereas both continuous and fenestrated capillaries contain a basement membrane. The lack of a basement membrane removes another barrier to protein diffusion (see below). Discontinuous endothelia are prominent in the liver, spleen and bone marrow and are often called sinusoids in these organs.

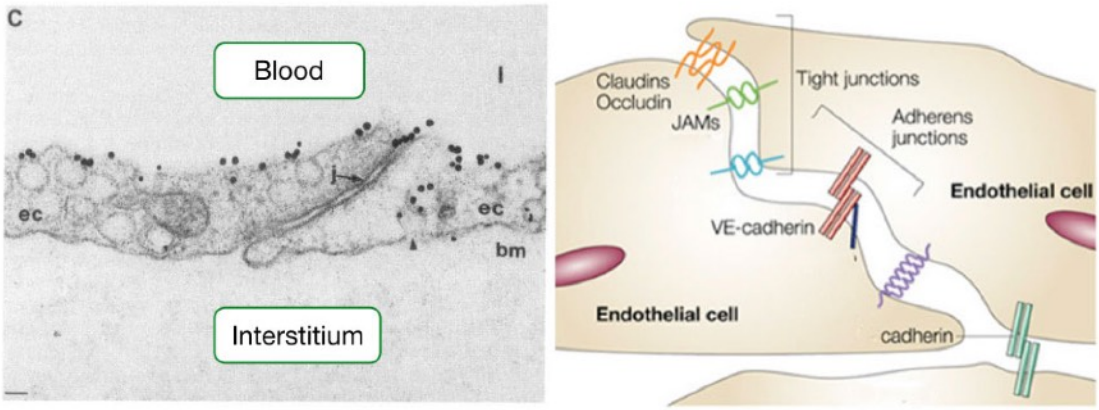
Basement Membrane



Besides providing structural support and organization to endothelial cells, the basement membrane also restricts the passage of protein from blood into the interstitium. Basement membrane contains numerous proteoglycans that contain long sugar side chains that are negatively charged. Consequently, the basement membrane is a negatively charged structure that repels other negatively charged molecules. Recall that the major protein in the blood, albumin, is negatively charged at physiological pH and is repelled by the basement membrane. Only continuous and fenestrated capillaries have a basement membrane.

Junctional Complexes

Endothelial cells are a type of epithelium and have the same junctional complexes as other epithelial cells, including adhering junctions and tight junctions. Because in continuous capillaries the only gaps in the endothelium is where two adjacent endothelial cells meet, the junctional

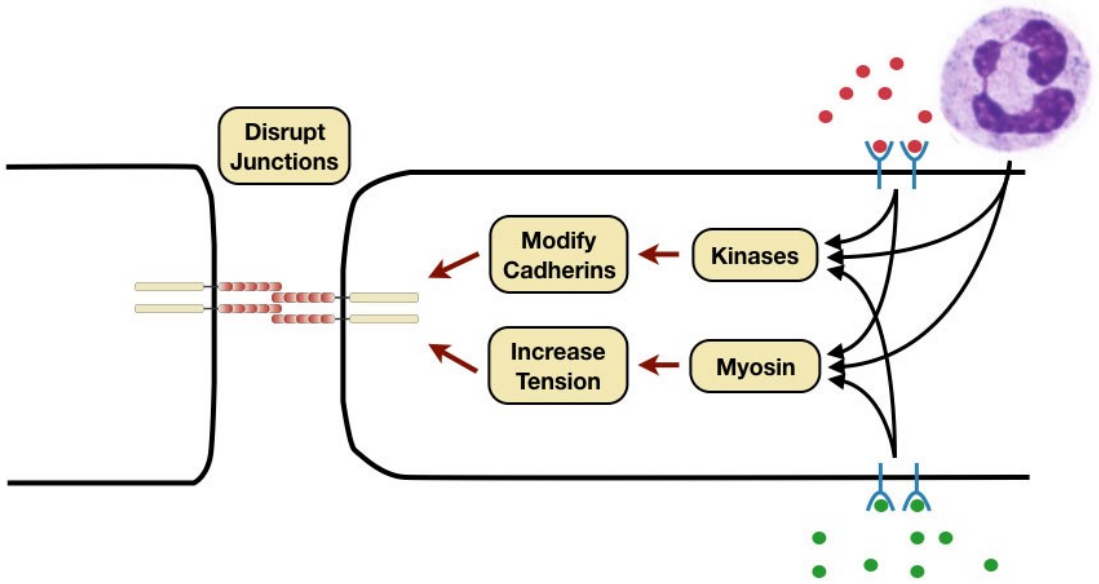


complexes are critical for regulating the passage of material across capillaries. Similar to other epithelial cells, tight junctions are primarily responsible for determining the paracellular permeability of endothelium. Endothelial in different organs will express different types of claudins to tailor the permeability of the endothelium to the function of the organ.

Mechanisms to Loosen the Junctional Complexes

Occasionally, the junctional complexes need to be loosened to allow fluid, protein and other molecules to diffuse more freely from blood into surrounding tissue. For example, during an infection of a tissue or organ, an immune response requires fluid, protein and even cells to flow from blood into the site of infection. To increase permeability, endothelial cells loosen their junctional complexes by at least two mechanisms.

The first mechanism involves weakening the interactions between cadherins in adhering junctions. Endothelial cells activate pathways that modify (via phosphorylation) cadherins that cause them to dissociate from actin filaments. Recall that association with actin filaments clusters cadherins to

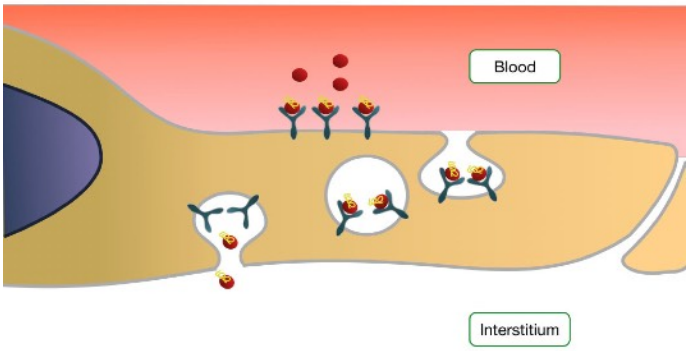


create strong intercellular connections. Endothelial cells also modify cadhreins so that they become targets for endocytosis. Consequently, the number of cadherins on the cell surface is reduced.

The second mechanism to weaken interactions between endothelial cells involves increasing intracellular tension that pulls apart endothelial cells. Recall that in smooth muscle cells tension generated by myosin filaments pulling on actin filaments causes the cells to shrink leading to contraction of the tissue. Endothelial cells employ a similar process, to a lesser extent, to create gaps between adjacent endothelial cells. Endothelial cells activate muscle myosin which pulls on filaments anchored to the cell membrane. The tension created pulls the cell membrane away from the adjacent cell, increasing the size of the gap between endothelial cells.

During an immune response, immune cells in the tissue and circulatory system release signaling molecules that activate both pathways in endothelial cells, increasing the permeability of the endothelium to allow fluid, protein and eventually cells to cross the endothelium.

Transcytosis

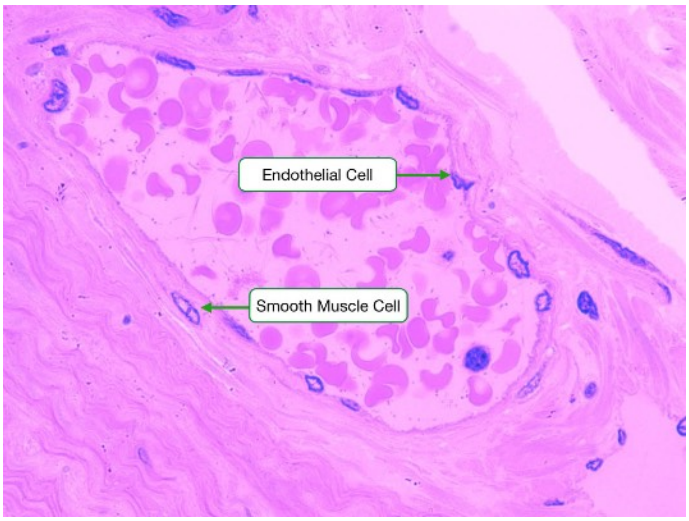


Certain proteins must be able to cross from the blood into the surrounding tissue. For example, albumin, which the body wants to keep in the blood to maintain oncotic pressure, is a carrier for certain hydrophobic molecules, such as cholesterol. To get cholesterol from the blood into tissues, the endothelium must allow passage of albumin that is bound to cholesterol while preventing free albumin from crossing. The endothelium accomplishes this through transcytosis.

Transcytosis is a process through which cells internalize material through endocytosis on one side and release that material on the opposite. Endothelia cells use transcytosis to move specific proteins from the blood into the surrounding tissue. For example, endothelial cells express on their surfaces that face blood (abluminal) a receptor that binds albumin only when it is associated with cholesterol. Endothelial cells endocytose the receptor-albumin complex into vesicles. The pH of the vesicles decreases to dissociate albumin from its receptor. The vesicle then fuses with the basal surface to release albumin into the surrounding tissue.

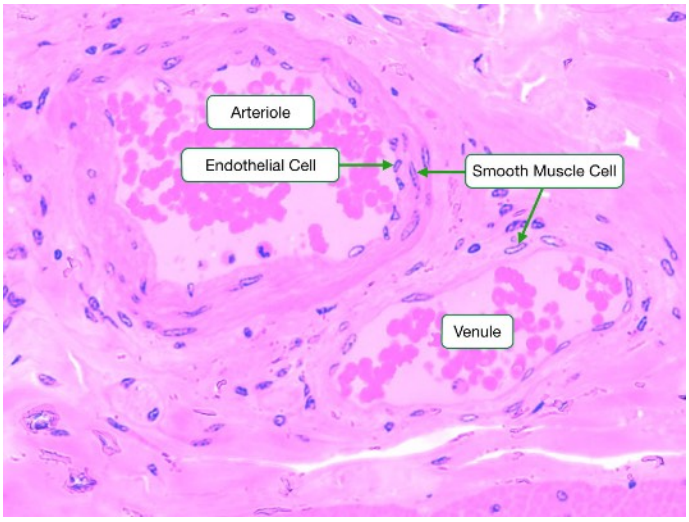
Venule

This image of a venule shows several of its characteristic features. Identify its endothelium and narrow layer of smooth muscle cells. Small venules are usually surrounded by pericytes, and larger venules are surrounded by smooth muscle. Venules collect blood from the capillary beds and play a critical role in immune responses to infection as they are the sites where immune cells cross from the blood into the surrounding tissue.



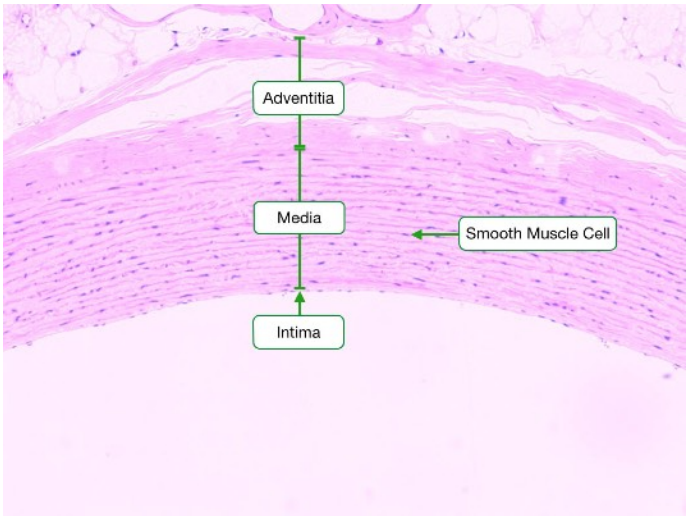
Artery and Venule

In many tissues and organs, arteries and venules often run together. This image compares the structure of a venule to that of the small artery and highlights the differences. The lumens of the vessels are similar in size but the artery has a thicker medial layer with more smooth muscle. Venule, with thinner walls, are more compliant and capable of holding more blood. Consequently, arteries tend to maintain their round shape better than veins in histological sections. Veins also contain valves to prevent back flow of blood but these are infrequent and are not reliably seen in histological samples.



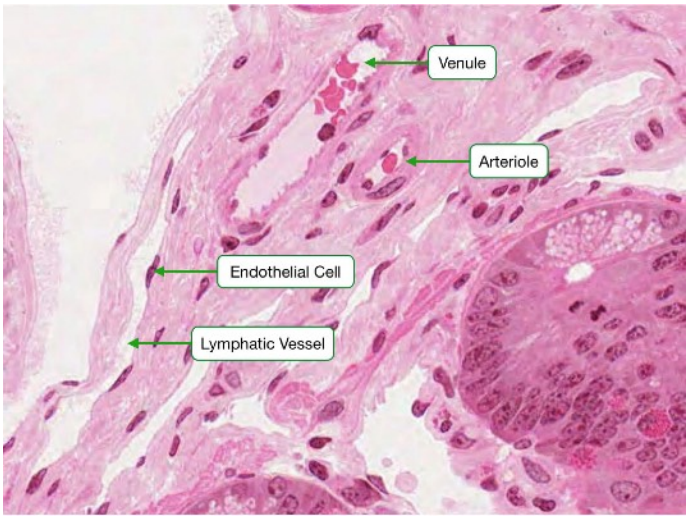
Vena Cava

This image shows the wall of the vena cava, which is the largest vein in the body. Note the relatively thin media compared to the aorta. The media layer contains primarily smooth muscle cells and collagen with very few elastic fibers.



Lymphatic Vessel

Lymphatic vessels are responsible for draining interstitial fluid and returning it to the bloodstream. These vessels are lined by endothelial cells and have a very thin layer of smooth muscle. Like veins, lymphatic vessels have valves that prevent back flow. Lymphatic vessels notably lack red blood cells, which help distinguish them from veins. The lymphatic system also plays an important role in generating immune responses.



Response to Damage

The endothelium is prone to damage due to the shear forces generated by flowing blood. Like other epithelia, endothelium have mechanisms to repair damage and regenerate endothelia cells. Surprisingly, it appears that the smooth muscle cells in the media play a prominent role repairing the endothelium. Upon, damage to the endothelium certain smooth muscle cells migrate from the media into the intimal layer. These cells can produce collagen and other connective tissue proteins to repair damage and can differentiate into endothelial cells.