The Circulatory System The circulatory system includes both the blood and lymphatic vascular systems. The blood vascular system is composed of the following structures:

- The heart, an organ whose function is to pump the blood.
- The **arteries**, a series of efferent vessels that become smaller as they branch, and whose function is to carry the blood, with its nutrients and oxygen, to the tissues.
- The capillaries, the smallest blood vessels, constituting a complex network of thin tubules that branch profusely in almost every organ and through whose walls the interchange between blood and tissues takes place.
- The **veins**, which result from the convergence of capillaries into a system of larger channels that continue enlarging as they approach the heart, toward which they convey the blood to be pumped again.

VESSELS OF THE BLOOD CIRCULATORY SYSTEM

•The heart is the principal organ of the blood circulatory system, pumping blood throughout the body and providing the force by which nutrients leave the capillaries and enter tissues.

•Large elastic arteries leave the heart and branch to form muscular arteries.

•These arteries branch further and enter organs, where they branch much further to form **arterioles**.

•These arterioles branch into the smallest vessels, the capillaries, the site of exchange between blood and surrounding tissue.

•Capillaries then merge to form **venules**, which merge further into small and then **medium-sized veins**.

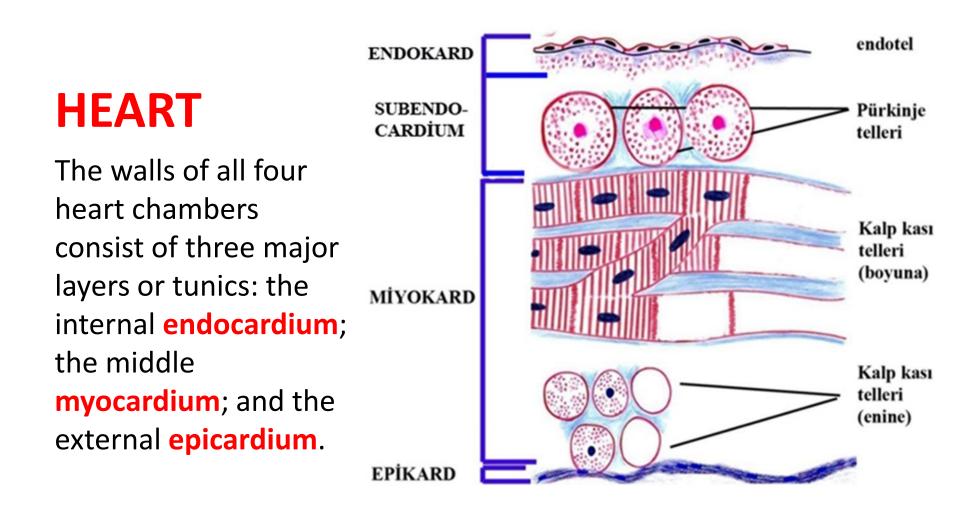
•These veins leave organs, form larger veins which eventually bring blood back to the heart.

HEART

•The heart is a muscular organ that contracts rhythmically, pumping the blood through the circulatory system.

- •The right and left **ventricles** pump
- blood to the lungs and the rest of the body respectively;

•right and left **atria** receive blood from the body and the pulmonary veins respectively.

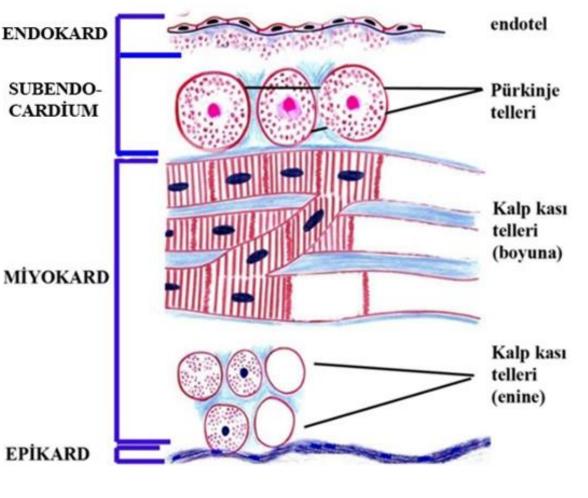


- Longitudinal view of heart showing the two atria and two ventricles.
 The ventricular walls are thicker than those of the atria, principally because of the much
- thicker myocardium.
- •The valves are basically flaps of connective tissue anchored in the heart's dense fibrous skeleton region, shown in white.
- •Other parts of the fibrous skeleton are the chordae tendinae, cords of dense connective tissue extending from the valves and attached to papillary muscles that help prevent valves from turning inside-out during ventricular contraction.

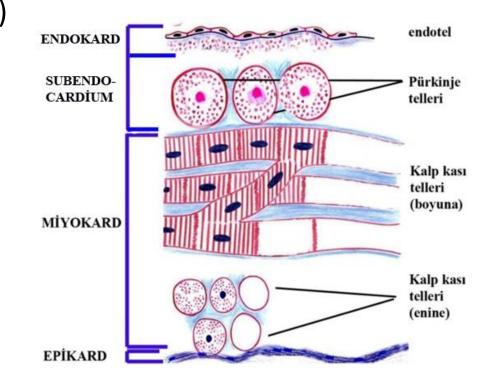
- •All these parts of the fibrous skeleton are covered by endothelium.
- •Shown in yellow are parts of the cardiac conducting system, which initiates the electrical impulse for heart's contraction (heartbeat) and spreads it through the ventricular myocardium.
- •Both the sinoatrial (SA) node (pacemaker), in the posterior wall of the right atrium, and the atrioventricular (AV) node in the floor of the right atrium consist of myocardial tissue that is difficult to distinguish histologically from surrounding cardiac muscle.
- •The AV node is continuous with specialized bundles of cardiac muscle fibers, the AV bundle (of His) which run along the interventricular septum to the apex of the heart, where they branch further as conducting (Purkinje) fibers which extend into myocardium of both ventricles.

•The endocardium

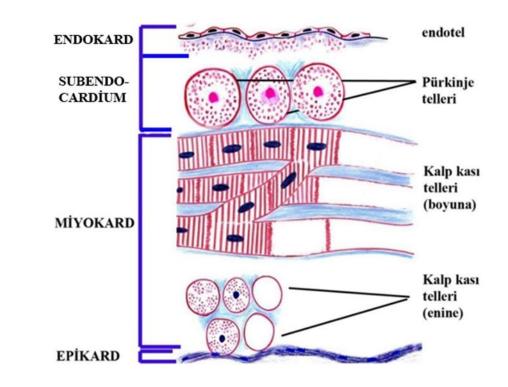
consists of a single layer of squamous endothelial cells on a thin layer of loose connective tissue containing elastic and collagen fibers as well as some smooth muscle cells.



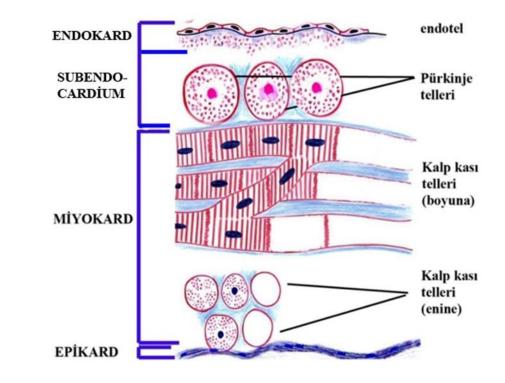
•Between the endocardium (En) and myocardium is a layer of variable thickness called the subendocardial layer (SEn) containing small nerves and in the ventricles the conducting (Purkinje) fibers (P) of the subendocardial conducting network.



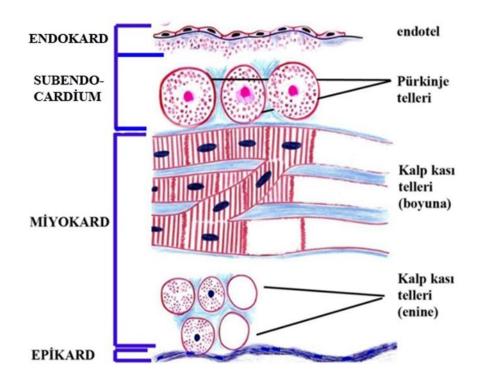
•These fibers are cardiac muscle cells joined by intercalated disks but specialized for impulse conduction rather than contraction.



•Purkinje fibers are usually larger than contractile cardiac muscle fibers with large amounts of lightly stained glycogen filling most of the cytoplasm and displacing sparse myofibrils to the periphery.

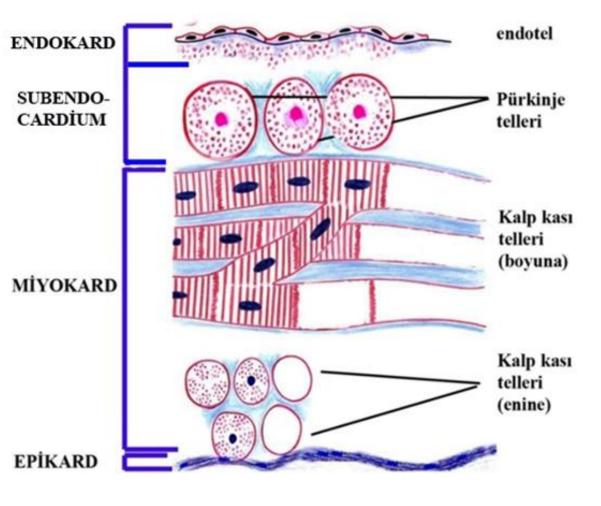


•The myocardium is the thickest of the tunics and consists of cardiac muscle cells arranged in layers that surround the heart chambers in a complex spiral.

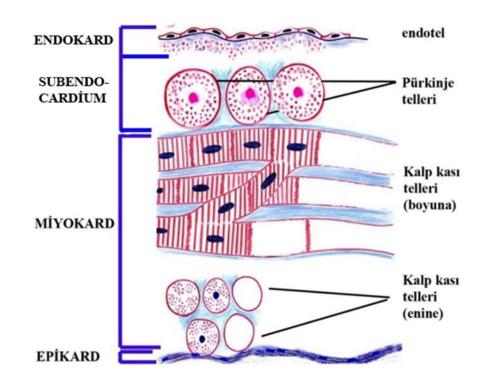


•The myocardium is much thicker in the ventricles than in the atria.

•The arrangement of these muscle cells is extremely varied, so that in sections cells are seen to be oriented in many directions.

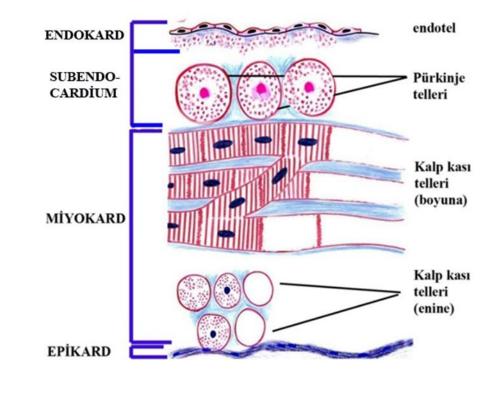


•The heart is covered externally by simple squamous epithelium (mesothelium) supported by a thin layer of connective tissue that constitutes the **epicardium**.



•A subepicardial layer of loose connective tissue contains veins, nerves, and many adipocytes.

•In the space between the pericardium's visceral layer (epicardium) and its parietal layer is a small amount of lubricant fluid that facilitates the heart's movements.



Major anatomical features of the heart.

•The cardiac valves consist of a central core of dense fibrous connective tissue (containing both collagen and elastic fibers), lined on both sides by endothelial layers.

•The bases of the valves are attached to strong fibrous rings that are part of the fibrous skeleton. This dense, fibrous region around the heart valves anchors the base of the valves and is the site of origin and insertion of the cardiac muscle fibers.

Epicardium

•The external tunic of the heart, the epicardium, is the site of the coronary vessels and contains considerable adipose tissue.

- •The epicardium consists of loose connective tissue containing both autonomic nerves and fat.
- •The epicardium is the visceral layer of the pericardium and is covered by the simple squamous-to-cuboidal epithelium that also lines the pericardial space.
- •These mesothelial cells secrete a lubricate fluid that prevents friction as the beating heart contacts the parietal pericardium on the other side of the pericardial cavity.

The fibrous skeleton of the heart consists of masses of dense connective tissue in the endocardium which anchors the valves and surrounds the two atrioventricular canals, maintaining their proper shape.

Section through a leaflet of the left atrioventricular valve (arrows) shows that valves are largely dense connective tissue (C) covered with a thin layer of endothelium.

The heart has a specialized system to generate a rhythmic stimulus for contraction that is spread to the entire myocardium. This system consists

of two nodes located in the right atrium—the sinoatrial (SA) node (pacemaker) and the atrioventricular (AV) node—and the atrioventricular bundle (of His).

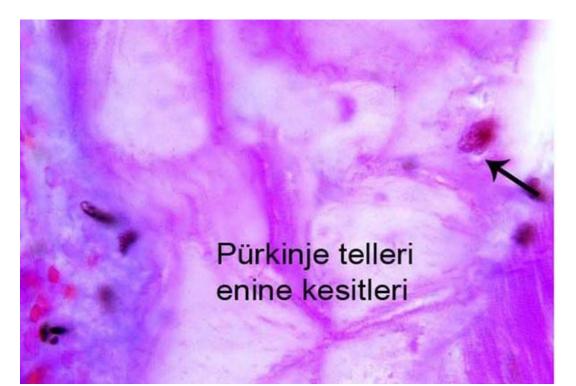
The SA node is a small mass of modified cardiac muscle cells that are fusiform, smaller and with fewer myofibrils than neighboring muscle cells.

The cells of the AV node are similar to those of the SA node but their cytoplasmic projections branch in various directions, forming a network.

The AV bundle originates from the node of the same name, passes along the interventricular septum and splits into left and right bundles, and then branches further to both ventricles.

The cells/fibers of the impulse-conducting system are modified cardiac muscle cells functionally integrated by gap junctions. Distally fibers of the AV bundle become larger than ordinary cardiac muscle fibers and acquire a distinctive appearance.

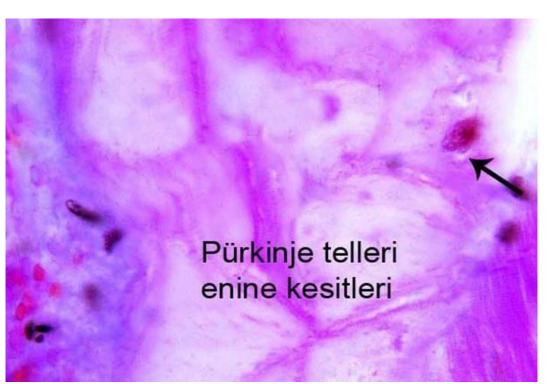
These conducting myofibers or Purkinje fibers have one or two central nuclei and their cytoplasm is rich in mitochondria and glycogen.



Myofibrils (Purkinje fibers) are sparse and restricted to the periphery of the cytoplasm.

After forming the subendocardial conducting network, these fibers penetrate the myocardial layer of both ventricles, an

important arrangement that allows the stimulus for contraction to reach the innermost layers of the ventricular musculature.



Both parasympathetic and sympathetic neural components innervate the heart.

Ganglionic nerve cells and nerve fibers are present in the regions close to the SA and AV nodes, where they affect heart rate and rhythm, such as during physical exercise and emotional stress.

Stimulation of the parasympathetic division (vagus nerve) slows the heartbeat, whereas stimulation of the sympathetic nerve accelerates the rhythm of the pacemaker.

Between the muscular fibers of the myocardium are afferent free nerve endings related to sensibility and pain. Partial obstruction of the coronary arteries reduces the supply of oxygen to the myocardium and causes pain (angina pectoris).

Walls of larger blood vessels contain three basic structural components:

-a simple squamous endothelium,

-smooth muscle, and --**connective tissue** with elastic elements in addition to collagen.

The amount and arrangement of these tissues in vessels are influenced by mechanical factors, primarily blood pressure, and metabolic factors reflecting local needs of tissues.

- The endothelium is a special type of epithelium that acts as a semipermeable barrier between two internal compartments: the blood plasma and the interstitial tissue fluid.
- Endothelium is highly differentiated to mediate and actively monitor the bidirectional exchange of small molecules and restrict the transport of some macromolecules.
- Besides their role in the exchanges between blood and tissues, endothelial cells perform several other functions, including production of vasoactive factors that affect the vascular tone, such as nitric oxide, endothelins, and vasoconstrictive agents, and conversion of circulating angiotensin I to angiotensin II.

Although morphologically similar, the endothelial cells of different blood vessels exert their various functional properties differently.

Smooth muscle cells or fibers occur in the walls of all vessels larger than capillaries and are arranged helically in layers.

Each muscle cell is enclosed by an external lamina and by various amounts of other extracellular material, all of which these cells produce.

In arterioles and small arteries the smooth muscle cells are frequently connected by communicating gap junctions.

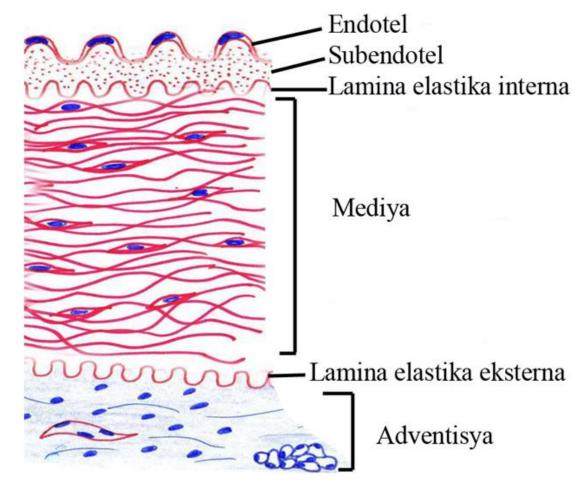
Connective tissue components are present in vascular walls in amounts and proportions that vary based on local functional requirements.

Collagen fibers are found throughout the wall:

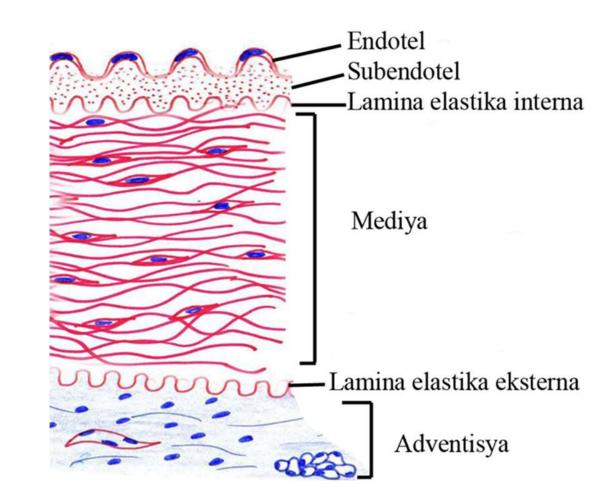
- -in the subendothelial layer,
- -between muscle layers, and
- -in the outer layers.
- **Elastic material** provides the resiliency for the vascular wall expanded under pressure.
- Elastin predominates in large arteries where it forms parallel lamellae regularly distributed between the muscle layers.

- All blood vessels greater than a certain diameter have many structural features in common and present a similar plan of construction.
- The distinction between different types of vessels often is not clear-cut because the transition from one type to another is gradual.

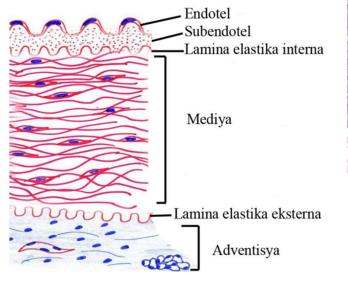
- The tunica intima has one layer of endothelial cells supported by a thin subendothelial layer of loose connective tissue with occasional smooth muscle cells.
- In arteries, the intima is separated from the media by an internal elastic lamina.

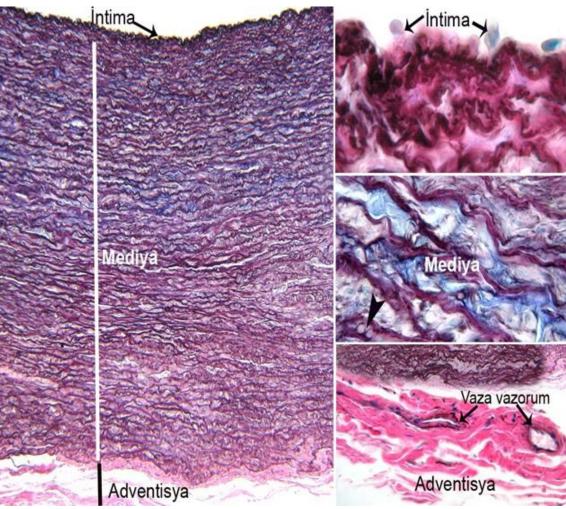


This lamina, composed of elastin, has holes (fenestrae) that allow the diffusion of substances to nourish cells deep in the vessel wall.

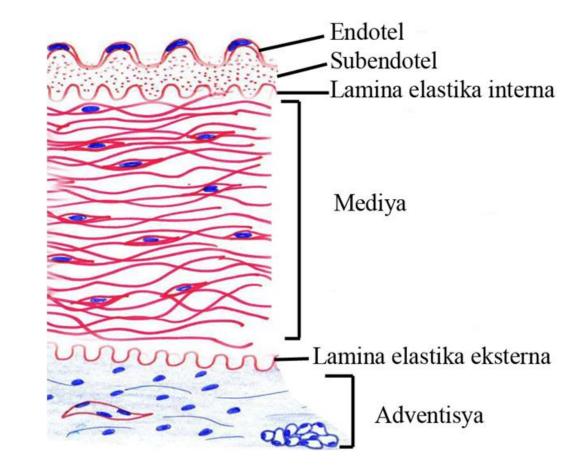


The **tunica media**, the middle layer, consists chiefly of concentric layers of helically arranged smooth muscle cells.

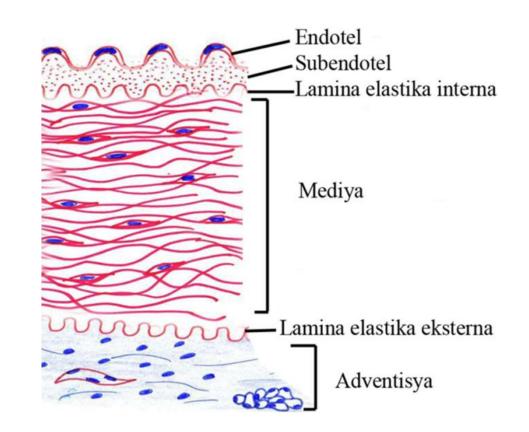




In arteries, the media has a thinner **external elastic lamina,** which separates it from the tunica adventitia.

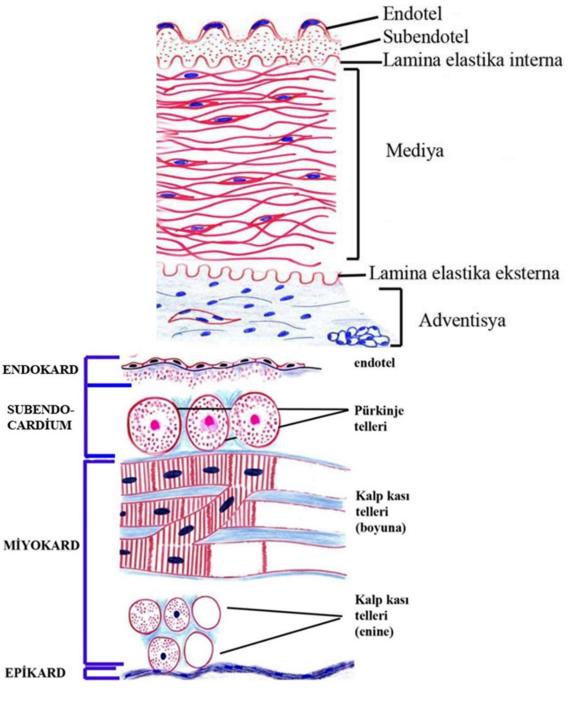


 The tunica adventitia or tunica externa consists principally of type I collagen and elastic fibers.



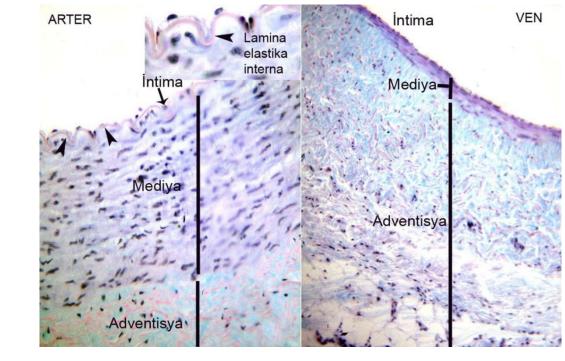
Walls of arteries, veins, and capillaries

Walls of both arteries and veins have a tunica intima, tunica media, and tunica externa (or adventitia), which correspond roughly to the heart's endocardium, myocardium and epicardium.



Walls of arteries, veins, and capillaries

- An artery has a thicker tunica media and relatively narrow lumen.
- A vein has a larger lumen and its tunica adventitia is the thickest layer.
- The tunica intima of veins is often folded to form valves.



Tunics of the vascular wall

- Simple squamous endothelial cells line the tunica intima which has subendothelial loose connective tissue and is separated from the tunica media by the internal elastic lamina, a prominent sheet of elastin.
- The media contains elastic lamellae and fibers and multiple layers of smooth muscle.
- The tunica media is much thicker in large arteries than veins, with relatively more elastin.
- Elastic fibers are also present in the outer tunica adventitia, which is relatively thicker in large veins.
- Vasa vasorum are seen in the adventitia of the aorta.
- The connective tissue of the adventitia always merges with the less dense connective tissue around it.

Walls of arteries, veins, and capillaries

- Large vessels usually have **vasa vasorum** ("vessels of the vessel"), which consist of arterioles, capillaries, and venules in the tunica adventitia and the outer part of the media.
- The vasa vasorum provide metabolites to cells of those layers, since in larger vessels the wall is too thick to be nourished solely by diffusion from the blood in the lumen.
- Luminal blood alone does provide nutrients and oxygen for cells of the tunica intima.
- Since they carry deoxygenated blood, large veins typically have more vasa vasorum than arteries.

Large Elastic Arteries

- Large elastic arteries help to stabilize the blood flow.
- The elastic arteries include the aorta and its large branches.
- The intima of the large elastic arteries is thicker than the corresponding tunic of a muscular artery.
- An internal elastic lamina, although present, may not be easily discerned, since it is similar to the elastic laminae of the next layer.
- The media consists of elastic fibers and a series of concentrically arranged, perforated elastic laminae whose number increases with age (there are about 40 in the newborn, 70 in the adult).
- Between the elastic laminae are smooth muscle cells, reticular fibers, proteoglycans, and glycoproteins.
- The tunica adventitia is relatively underdeveloped.

Large Elastic Arteries

- The several elastic laminae contribute to the important function of making blood flow more uniform.
- During ventricular contraction (systole), the elastic laminae of large arteries are stretched, reducing the force of the pressure somewhat.
- During ventricular relaxation (diastole), ventricular pressure drops to a low level, but the elastic rebound of large arteries helps to maintain arterial pressure.
- As a consequence, arterial pressure and blood velocity decrease and become less variable as the distance from the heart increases.

Muscular Arteries

- The muscular arteries can control blood flow to organs by contracting or relaxing the smooth muscle cells of the tunica media.
- The intima has a very thin subendothelial layer and the internal elastic lamina, the most external component of the intima, is prominent.
- The tunica media may contain up to 40 layers of more prominent smooth muscle cells which are intermingled with a variable number of elastic lamellae (depending on the size of the vessel) as well as reticular fibers and proteoglycans.
- An external elastic lamina, the last component of the media, is present only in the larger muscular arteries.

Muscular Arteries

- The adventitia consists of connective tissue.
- Lymphatic capillaries, vasa vasorum, and nerves are also found in the adventitia and these structures may penetrate to the outer part of the media.
- With distance from the heart arteries gradually have relatively less elastin and more smooth muscle in their walls.
- A transverse section through a muscular (medium caliber) artery shows multiple layers of smooth muscle in the media (M).
- The smooth muscle layers are more prominent than the elastic lamellae and fibers.
- Vasa vasorum are seen in the tunica adventitia.

Arterioles

- Muscular arteries branch repeatedly into smaller and smaller arteries, until reaching a size with only two or three medial layers of muscle.
- The smallest arteries branch as arterioles, which have one or two smooth muscle layers and indicate the beginning of an organ's microvasculature where exchanges between blood and tissue fluid occur.
- Arterioles are generally less than 0.5 mm in diameter, with lumens approximately as wide as the wall is thick.
- The subendothelial layer is very thin, the elastic laminae are absent and the media is generally composed of circularly arranged smooth muscle cells.
- In both small arteries and arterioles, the tunica adventitia is very thin and inconspicuous.

Arterioles

- In certain tissues and organs arteriovenous <u>shunts or</u> <u>anastomoses</u> regulate blood flow by allowing direct communication between arterioles and venules.
- These interconnections are abundant in skeletal muscle and in the skin of the hands and feet.
- When vessels of the arteriovenous anastomosis contract, all the blood must pass through the capillary network.
- When they relax, some blood flows directly to a venule instead of circulating in the capillaries.
- Their luminal diameters vary with the physiologic condition of the organ.
- Changes in diameter of these vessels regulate blood pressure, blood flow, temperature and heat conservation in affected areas.

Arterioles

- Arterioles are microvessels with a tunica intima that consists only of the endothelium, in which the cells may have rounded nuclei.
- They have tunica media with only one or two layers of smooth muscle, and usually thin, inconspicuous adventitia.
- Three arterioles of various sizes are shown here and a capillary.
- A large mesenteric arteriole is cut obliquely and longitudinally and clearly shows the endothelial cells (arrow heads) and one or two layers of smooth muscle cells cut transversely.
- Adventitia merges imperceptibly with neighboring connective tissue.

- Capillaries permit different levels of metabolic exchange between blood and surrounding tissues.
- They are composed of a single layer of **endothelial cells** rolled up in the form of a tube.
- Capillaries have only an endothelium, with no subendothelial layer or other tunics.
- The average diameter of capillaries varies from 5 to 10 μm and their individual length is usually not more than 50 $\mu m.$
- Altogether capillaries comprise over 90% of all blood vessels in the body, with a total length of nearly 96,000 km.
- •

- The total diameter of the capillaries is approximately 800 times larger than that of the aorta.
- The velocity of blood in the aorta averages 320 mm/s, but in capillaries blood flows only about 0.3 mm/s.
- Because of their thin walls and slow blood flow, capillaries are a favorable place for the exchange of water, solutes, and macromolecules between blood and tissues.
- Endothelial cells are functionally diverse according to the vessel they line.
- The capillaries are often referred to as exchange vessels, since it is at these sites that O₂, CO₂, substrates, and metabolites are transferred from blood to the tissues and from the tissues to blood.

- The mechanisms responsible for the interchange of materials between blood and tissue are not completely known.
- They depend on the kind of molecule and also on the structural characteristics and arrangement of endothelial cells in each type of capillary.
- Small molecules, both hydrophobic and hydrophilic can diffuse or be actively transported across the plasmalemma of capillary endothelial cells.
- These substances are then transported by diffusion through the endothelial cytoplasm to the opposite cell surface, where they are discharged into the extracellular space.

- Water and some other hydrophilic molecules, less than 1.5 nm in diameter and below 10 kDa in molecular mass, can cross the capillary wall by diffusing through the intercellular junctions (paracellular pathway).
- The pores of fenestrated capillaries, the spaces between endothelial cells of sinusoidal capillaries, and the pinocytotic vesicles are other pathways for the passage of large molecules.
- In general, endothelial cells are polygonal and elongated in the direction of blood flow.
- The nucleus causes that part of the cell to bulge into the capillary lumen.
- The cytoplasm contains a small Golgi appraratus, mitochondria, free ribosomes, and sparse cisternae of RER.

- Junctions of the tight zonula occludentes type are present between most endothelial cells, conferring the wall with variable permeability to macromolecules that plays significant roles in both normal and pathologic conditions.
- Capillaries have structural variations which permit different levels of metabolic exchange between blood and surrounding tissue.
- They can be grouped into three types, depending on the continuity of the endothelial cells and the external lamina.

- 1. The **continuous**, or tight, **capillary** allows regulated exchange of material and is characterized by the distinct continuity of the endothelial cells in its wall.
- This is the most common type of capillary and is found in all kinds of muscle tissue, connective tissue, exocrine glands, and nervous tissue.
- In some places, but not in the nervous system, numerous pinocytotic vesicles are present on both endothelial cell surfaces.
- Vesicles also appear as isolated vesicles in the cytoplasm of these cells and are responsible for transcytosis* of macromolecules in both directions across the endothelial cytoplasm.

*Macromolecules are captured in vesicles on one side of the cell, drawn across the cell, and ejected on the other side.

2. The **fenestrated capillary** allows more extensive molecular exchange across the endothelium and is characterized by the presence of small circular fenestrae through the very thin squamous endothelial cells. Each fenestra is usually covered by a very thin diaphragm containing heparan proteoglycans but no lipid bilayer.

- The basal lamina of the fenestrated capillaries is continuous, covering the fenestrae.
- Fenestrated capillaries are found in tissues where rapid interchange of substances occurs between the tissues and the blood, as in the kidney, the intestine, the choroid plexus and the endocrine glands.
- Macromolecules experimentally injected into the bloodstream can cross the capillary wall through the fenestrae to enter tissue spaces.

3. The **sinusoid** or **discontinuous capillary** permits maximal exchange of macromolecules as well as cells between tissues and blood and has the following characteristics: endothelial cells have large fenestrae without diaphragms; the cells form a discontinuous layer and are separated from one another by wide spaces; the basal lamina is also discontinuous.

- Sinusoids are irregularly shaped and have diamaters as large as 30-40 micrometer, much greater than thouse of other capillaries, properties which further slow blood flow at this site.
- Sinusoids are found in the liveri spleen, some endocrine organs, and bone marrow.

Venules

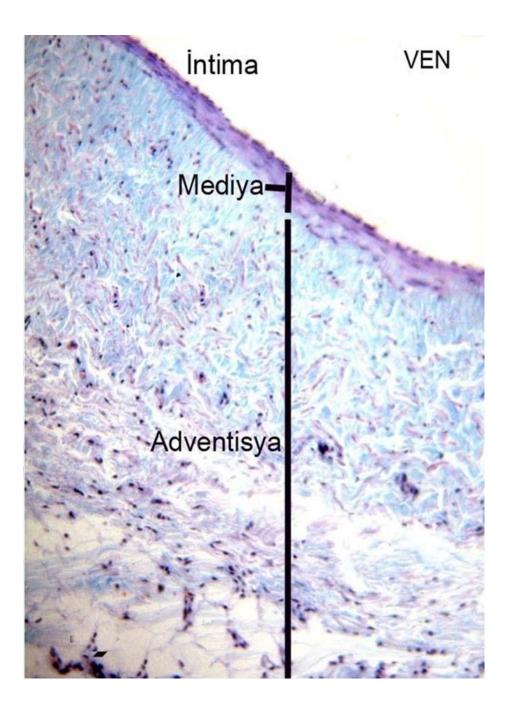
- The transition from capillaries to venules occurs gradually.
- The immediate **postcapillary venules** are similar structurally to capillaries, with pericytes, but range in diameter from 15 to 20 μm.
- These venules converge into larger **collecting venules** which have more contractile cells.
- With greater size the venules become surrounded by recognizable tunica media with two or three smooth muscle layers and are called **muscular venules**.
- A characteristic feature of all venules is the large diameter of the lumen compared to the overall thinness of the wall.

Venules

- Postcapillary venules resemble large capillaries, having only an endothelium with occasional pericytes (arrowhead).
- Their lumens and overall diameters are greater than those of nearby arterioles.
- Large **collecting venules** have much greater diameters than arterioles but the wall is still very thin, consisting of an endothelium with more numerous pericytes or smooth muscle cells.
- **Muscular venule** has a better defined tunica media, with as many as three layers of smooth muscle in some areas, a very thin intima of endothelial cells, and a more distinct tunica adventitia.

- Blood entering veins is under very low pressure and moves toward the heart by contraction of the tunica media and external compressions from surrounding muscles and other organs.
- Valves project from the tunica intima to prevent back-flow of blood. Most veins are small or medium veins, with diameters less than one centimeter.

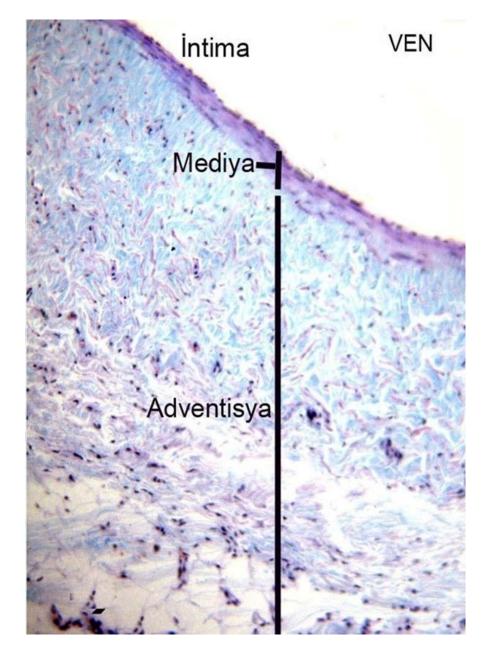
- Such veins are usually located in parallel with corresponding muscular arteries.
- The intima usually has a thin subendothelial layer and the media consists of small bundles of smooth muscle cells intermixed with reticular fibers and a delicate network of elastic fibers.
- The collagenous adventitial layer is welldeveloped.



- Veins usually travel near arteries and are classified as small, medium, or large based on size and development of the tunics.
- Micrograph of small vein shows a relatively large lumen compared to the small muscular artery with its thick media and adventitia.
- The wall of a small vein is very thin, containing only two or three layers of smooth muscle.
- Micrograph of a convergence between two small veins showing valves.
- Valves are thin folds of tunica intima projecting well into the lumen which act to prevent backflow of blood.

- Micrograph of a medium vein showing a thicker wall, but still less prominent than that of the accompanying muscular artery.
- Both the media and adventitia are better developed, but the wall is often folded around the relatively large lumen.
- Micrograph of a medium vein containing blood and showing valve folds (arrows).

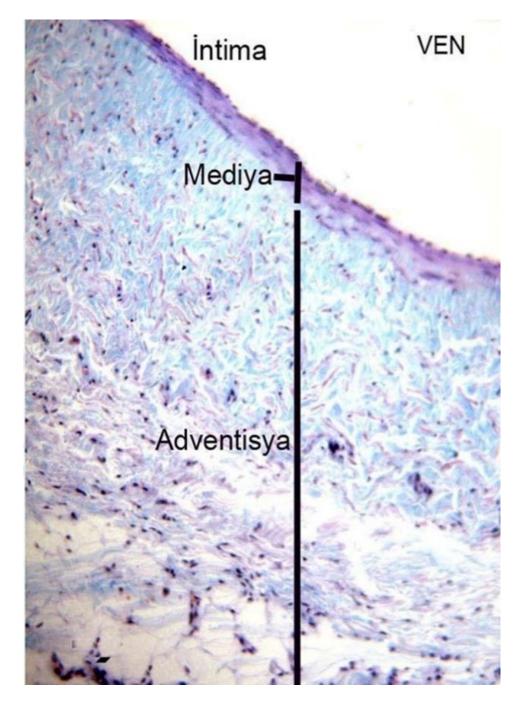
- Large veins have a welldeveloped tunica intima, but the tunica media is relatively thin, with few layers of smooth muscle and abundant connective tissue.
- The adventitial layer is thick in large veins and frequently contains longitudinal bundles of smooth muscle.
- Both the media and adventitia contain elastic fibers, but elastic laminae like those of arteries are not present.



- Most veins have valves, but these are most prominent in large veins.
- Valves consist of paired semilunar folds of the tunica intima projecting across part of the lumen.
- They are rich in elastic fibers and are lined on both sides by endothelium.
- The valves, which are especially numerous in veins of the legs, help keep the flow of venous blood directed toward the heart.

Wall of large vein with valve

- Large veins have a muscular tunica media that is very thin compared to the tunica adventitia composed of dense irregular connective tissue.
- The wall is often folded as shown here. The tunica intima here projects into the lumen as a valve, composed of the subendothelial connective tissue with endothelium on both sides.



LYMPHATIC VASCULAR SYSTEM

- In addition to blood vessels, the body has a system of thin-walled endothelial channels that collect excess interstitial fluid from the tissue spaces and return it to the blood.
- This fluid is called lymph; unlike the blood, it flows in only one direction, toward the heart.
- The lymphatic capillaries originate in the various tissues as thin, closed-ended vessels that consist of a single layer of endothelium and an incomplete basal lamina.
- Lymphatic capillaries are held open by bundles of anchoring filaments of the elastic fiber system which also bind the vessels firmly to the surrounding connective tissue.

LYMPHATIC VASCULAR SYSTEM

- The thin lymphatic capillaries converge into larger lymphatic vessels.
- Interposed in the path of these lymphatics are lymph nodes.
- Lymphatic vessels ultimately end up as two large trunks: the thoracic duct and the right lymphatic duct, which respectively empty lymph into the junction of the left internal jugular vein with the left subclavian vein and into the confluence of the right subclavian vein and the right internal jugular vein.

The structure of these lymphatic ducts is similar to that of large veins, with reinforced smooth muscle in the middle layer.

LYMPHATIC VASCULAR SYSTEM

- In this layer, the muscle bundles are longitudinally and circularly arranged, with longitudinal fibers predominating.
- The adventitia is relatively underdeveloped, but contains vasa vasorum and a neural network.
- Besides gathering interstitial fluid as lymph and returning it to the blood, the lymphatic system of vessels is a major distributor of lymphocytes, antibodies, and other immune components which it picks up at lymph nodes and other lymphoid tissues.

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