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THE CIRCULATORY SYSTEM

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INTRODUCTION

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.

The lymphatic vascular system begins with the lymphatic capillaries, which are closed-ended tubules that merge to form vessels of steadily increasing size; these vessels terminate in the blood vascular system emptying into the large veins near the heart. One of the functions of the lymphatic system is to return the fluid of the tissue spaces to the blood.

The internal surface of all components of the blood and lymphatic systems is lined by a single layer of a squamous epithelium, called endothelium.

The circulatory system is considered to consist of the macrovasculature, vessels that are more than 0.1 mm in diameter (large arterioles, muscular and elastic arteries, and muscular veins), and the microvasculature (arterioles, capillaries, and postcapillary venules) visible only with a microscope. The microvasculature is particularly important functionally, being the site of interchanges between blood and the surrounding tissues both under normal conditions and during inflammatory processes.

HEART

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

1- The right and left ventricles pump blood to the lungs and the rest of the body respectively.
2- The right and left atria receive blood from the body and the pulmonary veins respectively.

The walls of all four heart chambers consist of three major layers or tunics: the internal endocardium; the middle myocardium; and the external epicardium.

1- **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. Connecting this subendothelial layer to the myocardium is additional connective tissue (often called the subendocardial layer) containing veins, nerves, and branches of the impulse-conducting system of the heart.
2- **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.
3- **The external epicardium** is 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 . The epicardium corresponds to the visceral layer of the pericardium, the serous membrane in which the heart lies. 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.

TISSUES OF THE VASCULAR WALL

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.

Endothelial cells, especially those of arteries, contain unique very small, elongated vesicles called Weibel-Palade bodies, which contain selectin and von Willebrand factor involved in blood coagulation.
Growth factors such as vascular endothelial growth factor (VEGF) help maintain the vasculature, regulate the formation of the vascular system from embryonic mesenchyme (vasculogenesis) and promote capillary outgrowth from existing vessels (angiogenesis) under normal and pathologic conditions in adults.

STRUCTURAL PLAN OF BLOOD VESSELS

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. Blood vessels are usually composed of the following layers, or tunics (L. *tunica,* coat).

1- **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, the most external component of the intima. This lamina, composed of elastin, has holes (fenestrae) that allow the diffusion of substances to nourish cells deep in the vessel wall. As a result of the loss of blood pressure and contraction of the vessel at death, the tunica intima of arteries may have a slightly folded appearance in tissue sections

2- **The tunica media** the middle layer, consists chiefly of concentric layers of helically arranged smooth muscle cells . Interposed among the smooth muscle cells are variable amounts of elastic fibers and lamellae, reticular fibers of collagen type III, proteoglycans, and glycoproteins, all of which is produced by these cells. In arteries, the media has a thinner external elastic lamina, which separates it from the tunica adventitia.
3- **The tunica adventitia or tunica externa** consists principally of type I collagen and elastic fibers . This adventitial layer is gradually continuous with the stromal connective tissue of the organ through which the blood vessel runs.

VASCULATURE

For didactic purposes vessels of the macrovasculature are classified arbitrarily as the types indicated in the following discussion.

Large Elastic Arteries

Large elastic arteries help to stabilize the blood flow. The elastic arteries include the aorta and its large branches. Freshly dissected, they have a yellowish color from the elastin in the media. The intima 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.

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. 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.

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.

Capillaries

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. The average diameter of capillaries varies from 5 to 10 µm and their individual length is usually not more than 50 µm.

Altogether capillaries comprise over 90% of all blood vessels in the body, with a total length of nearly 96,000 km (60,000 miles). 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 O_2, CO_2, 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.

2- **The fenestrated capillary** allows more extensive molecular exchange across the endothelium and is characterized by the presence of small circular fenestrae (L, *fenestra*, perforation) 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 diameters as large as 30–40 m, much greater than those of other capillaries, properties which further slow blood flow at this site. Sinusoidal capillaries are found in the liver, 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 m. Postcapillary venules participate in the exchanges between the blood and the tissues are the primary site at which white blood cells leave the circulation at sites of infection or tissue damage. 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

Veins

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 well-developed.

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