The circulatory system (part I/II)

Functions of capillaries:

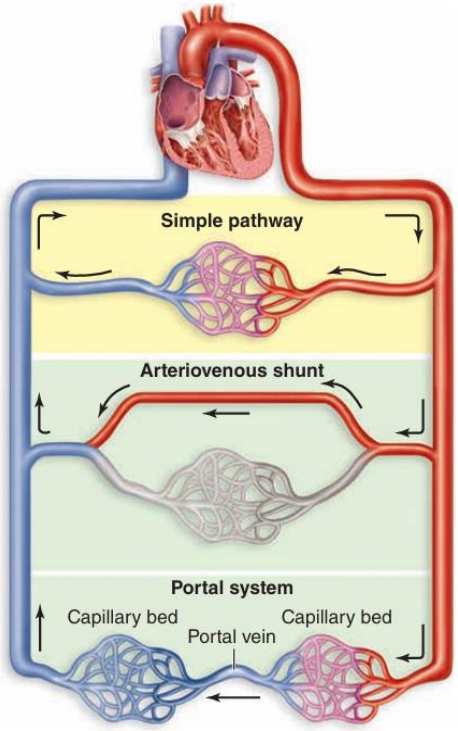
1. Permeability of capillaries is dependent on morphology of endothelial cells, size, charge and shape pf traversing molecules. Permeability is changed during inflammatory response by histamine and bradykinin.
    - Some substances diffuse, others are actively transported across capillary endothelium.
    - Other substances move across capillary wall via small pores (intercellular junctions) or large pores (fenestrae & pinocytic vesicles).
    - Leukocytes leave blood into interstitial spaces by penetrating intercellular junctions by a process called **diapedesis**, and then migrate into the target location via a process of migration by chemotactic stimuli.
2. Metabolic functions of capillaries are carried out by the endothelial cells:
    A. Conversion of inactive angiotensin I to active angiotensin II (especially in the lungs).
    B. Deactivation of bradykinin, serotonin, thrombin and prostaglandins into inactive forms.
    C. Breakdown of lipoproteins to yield triglycerides and cholesterol.
    D. Release of the following substances:
        - **Prostacyclin**; a potent vasodilator and anti-platelet aggregation factor.
        - **Nitric oxide** (NO) a relaxing factor, and **endothelin 1** a contracting factor.
        - **Tissue factor** responsible for coagulation.
    E. Regulation of transendothelial migration of leukocytes (diapedesis).
3. Antithrombogenic function: in addition to the release of endothelial cells some antithrombotic factors (prostacyclin, antithrombin etc.), the integrity of endothelial cells by itself is an important factor to prevent thrombosis, however, injured endothelial cells and exposure of subendothelial connective tissue induces the process of platelets aggregation and subsequent thrombosis.
    - The endothelial cells contain storage granules called **Weible-Palade granules**, theses granules contain two important factors; **von Willbrand's factor** (vWF) an essential glycoprotein that facilitates platelets adhesion and aggregation to injured blood vessel.
    - Other factor is **P-selectin** that plays a role in regulating leukocytes adhesion to endothelium and diapedesis during inflammation.
    - Deficiency of von Willbrand's factor results in impaired platelet adhesion to injured endothelium and in prolonged bleeding (von Willbrand's disease).

Arteriovenous anastomosis

In certain tissues and organs, arterioles bypass capillary beds to accommodate special functions, where arterioles connect directly to venules. The media and adventitia are thicker in AV anastomoses and richly innervated by sympathetic and parasympathetic nerve fibers. Changes in the diameter of these vessels regulate blood pressure, flow, and temperature especially in the peripheral areas of the skin (finger tips, tip of the nose), high blood flow in the skin allows more heat dissipation from the body and vice versa.

Another important alternative microvascular pathway is a **venous portal system** in which blood flows through two successive capillary beds separated by a portal vein. This arrangement allows for hormones or nutrients picked up by the blood in the first capillary network to be delivered most efficiently to cells around the second capillary bed before the blood is returned to the heart for general distribution. The best examples are the hepatic portal system of the liver and the hypothalamic hypophyseal portal system in the anterior pituitary gland.

An **arterial portal system** is present in kidney in which an arteriole gives capillary (glomerulus) which drains into another arteriole that gives off another capillary network which drains into a venule.



Carotid bodies and Aortic bodies

Are chemoreceptors sensitive to high CO2 and low O2 concentration as well as low pH level in the blood located near the bifurcation of carotid artery and arch of the aorta. These structures are richly irrigated by fenestrated capillaries that surround type I (glomus) cells and smaller type II (satellite) cells, type II are supportive, type I glomus cells contain numerous vesicles that store dopamine, acetylcholine and other neurotransmitters. These neurotransmitters are released in response to low O2 (hypoxia), high CO2 (hypercapnia) and low pH (acidosis). Most of the nerves of the carotid bodies are afferent nerve fibers of the CN IX.

Carotid sinuses

Are slight dilatations of internal carotid artery, these sinuses are baroreceptors that detect changes in blood pressure and relay information to the CNS, the arterial media is thinner to allow it to respond to changes to blood pressure, the intima and adventitia are very rich in nerve endings. The afferent nerve impulses of the CN IX are processes in the brain's vasomotor center to maintain normal blood pressure. Functionally similar baroreceptors present in the aortic arch transmit signals related to blood pressure via CN X.

Veins

Veins carry blood back to the heart from microvasculature all over the body. Blood entering veins is under very low pressure and moves toward the heart by contraction of the smooth muscle fibers in the media and by external compressions from surrounding skeletal muscles and other organs. When considered as a functional unit, the veins can be classified as capacitance vessels because more than 70 % of the total blood volume is in this portion at any time. The transition from capillaries to venules occurs gradually, the immediate **postcapillary venule** (**pericyte venule**) characterized by the presence of pericytes, these blood vessels have several features in common with capillaries e.g. inflammatory processes and exchange of cells and molecules between the blood and tissues. Postcapillary venules are the primary site at which white blood cells adhere to endothelium and

leave the circulation at sites of infection or tissue damage. Junctions between endothelial cells of postcapillary venules are the loosest of the microvasculature. *This facilitates transendothelial migration of leukocytes at these locations during inflammation, as well as a characteristic loss of fluid here during the inflammatory response, leading to tissue **edema**.*

Venules: are further subclassified into postcapillary venules (have no smooth muscles in their walls) and muscular venules (surrounded by 2-3 smooth muscle layers in t. media).

Small veins: are less than 1 mm in diameter and are continuous with muscular venules.

Medium veins: represent most of the named veins in this category. They usually are accompanied by arteries and have a diameter of as much as 10 mm. The tunics are most evident. e.g: radial, popliteal veins.

Large veins: usually have a diameter greater than 10 mm. Examples of such veins include the superior and inferior vena cava and hepatic portal vein.

In large vein (close to the heart) the intima is well developed has few longitudinal bundles of smooth muscle cells and abundant connective tissue but the media is thinner and, the adventitia is the thickest and best developed in large veins.
An important feature of large and medium veins are **valves**, which consist of thin, paired folds of the tunica intima projecting across the lumen, rich in elastic fibers and covered 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.

The Heart

The heart is a four-chambered pump composed of two atria and two ventricles and is surrounded by a fibroserous sac called the pericardium. It contracts rhythmically to propel blood into the circulation, *it also secrets natriuretic (losing sodium in urine) factors; atrial natriuretic peptide (**ANP**) from atria and brain natriuretic peptide (**BNP**) from ventricles in response to volume overload or myocardial strain (such as heart failure)*.

Its wall consists of three tunics: endocardium, myocardium and epicardium (from inside toward the outside), the fibrous central region of the heart called the fibrous skeleton which serves as the base of the valves and as the site of origin and insertion of cardiac muscle.

The endocardium

It consists of lining endothelium supported by underlying subendothelial fibroelastic connective tissue and a deeper layer of connective tissue that is continuous with that of myocardium called subendocardial layer that contains branches of the impulse conducting system of the heart (Purkinje fibers).

The myocardium

It consists mainly of typically contractile cardiac muscle fibers arranged spirally around each heart chamber, most of the myocardium is inserted into the fibrous skeleton of the heart. Because strong force is required to pump blood through the systemic and pulmonary circulations, the myocardium is much thicker in the walls of the ventricles, particularly the left, than in the atrial walls.

The epicardium

It is a simple squamous mesothelium supported by a layer of loose connective tissue containing blood vessels and nerves. It corresponds to the visceral layer of the pericardium (the membrane surrounding the heart), the epicardium is reflected back as a parietal layer of the pericardium lining the fibrous pericardial sac leaving a small pericardial cavity between the visceral and parietal layer that contains thin film of pericardial fluid that help prevents friction produced by cardiac movements.

Cardiac skeleton is a dense irregular fibrous connective tissue that separates the myocardium of the atria from that of the ventricles, forming part of the interventricular and interatrial septa and extends into the valve cusps and the chordae tendineae to which they attached. Its main functions:

1. Surround, anchor and support heart valves.
2. Provide insertion from cardiac muscles in all chambers.
3. Act as electrical insulator between atria and ventricles to help coordinate the heartbeat.

The cardiac valves consist of a central core of dense C.T. (have collagen and elastic fibers) lined on both sides by endothelial layers, the bases of valves are attached to the fibrous skeleton.

Conducting system of the heart

The heart generates rhythmic stimulus that is spread to the entire myocardium by special system consist from the Sinoatrial node (S.A. node), atrioventricular node (A.V. node) and the atrioventricular bundles.

The SA node is region of modified cardiac muscle that is less well-stained and smaller size fusiform cardiac muscle, contains fewer myofibrils & fewer intercalated discs than adjacent contractile myocardial fibers. It acts as peacemaker which rhythmically generate an impulse that spreads to the atria and reach the AV node. From the AV node, an AV bundle emerges to spread the impulse into the ventricles.

The AV node is located in the floor of the right atrium near the AV valve and composed of cells similar to those of the SA node.

AV bundles are originated from AV node and branches to both ventricles. Distally the cells of AV bundles become larger than ordinary cardiac muscle and acquire special appearance, these so called (**Purkinje fibers**), these are pale-staining fibers, larger than the adjacent contractile fibers, with sparse, peripheral myofibrils, and much glycogen. The myofibrils are restricted to the periphery of the cytoplasm. Purkinje fibers travel the subendocardial layer and penetrate the myocardium to become intramyocardial to allow the stimulus to go into the inner most layer of the ventricular musculature.

Both sympathetic and parasympathetic system innervate the heart, stimulation of parasympathetic system (vagus nerve) slows the heartbeat, whereas stimulation of sympathetic system accelerates the rhythm of the pacemaker (SA node).

Lymphatic Vascular system:

A system of very thin-walled channels, the **lymphatic capillaries** (are close-ended vessels that consist of single layer of endothelium and an incomplete basal lamina with fine anchoring filaments of collagen extend from the basal lamina to the surrounding connective tissue, preventing collapse of the vessels), which collect excess interstitial fluid from the tissue spaces as **lymph** and return it to the blood in a unidirectional way. With

exceptions such as the bone marrow and most of the CNS, most tissues with blood microvasculature also contain lymphatic capillaries (or lymphatics).

The thin lymphatic vessels gradually converge and become larger as they approach the heart. In the path of the lymphatic vessels are lymph nodes. The lymphatic vessels have a structure similar to that of veins except that they have thinner walls and lack clear cut separation between layers (intima, media and adventitia), they have also numerous valves keeping lymph flow in one direction. Lymphatic vessels ultimately converge as two large trunks; the thoracic duct and the right lymphatic duct which empty lymph back to the blood.

Atherosclerosis *(Gr. athero, gruel or porridge, and scleros, hardening) is a disease of elastic arteries and large muscular arteries that may play a role in nearly half of all deaths in developed parts of the world. It is initiated by damaged or dysfunctional endothelial cells oxidizing low-density lipoproteins (LDLs) in the tunica intima, which induces adhesion and intima entry of monocytes/macrophages to remove the modified LDL. Lipid-filled macrophages (called foam cells) accumulate and, along with the free LDL, produce a pathologic sign of early atherosclerosis called fatty streaks. During disease progression these develop into fibro-fatty plaques, or atheromas, consisting of a gruel-like mix of smooth muscle cells, collagen fibers, and lymphocytes with necrotic regions of lipid, debris, and foam cells. Predisposing factors include dyslipidemia (> 3:1 ratios of LDL to HDL [high-density lipoprotein]), hyperglycemia of diabetes, hypertension, and the presence of toxins introduced by smoking. In elastic arteries atheromas produce localized destruction within the wall, weakening it and causing arterial bulges or* ***aneurysms*** *which can rupture. In muscular arteries such as the coronary arteries, atheromas can occlude blood flow to downstream vessels, leading to* ***ischemic heart disease****.*