Case 3: Path of the Heart

COMPONENTS OF THE VASCULATURE				
ARTERIES	**ARTERIOLES**	**CAPILLARIES**	**VENULES**	**VEINS**
• A series of vessels that transport blood away from the heart by branching into vessels of smaller and smaller diameter, eventually branching into capillaries to supply all regions of the body with oxygenated blood • Have smaller diameter than their venous counterparts • Are thick-walled and under high pressure • The blood volume contained in arteries is called the stressed volume	• Are the smallest branches of the arteries with a diameter of less than 0.1 mm • The width of the wall is approximately equal to the diameter of its lumen • The endothelium of the tunica intima is supported by a thin subendothelial connective tissue layer consisting of type III collagen and a few elastic fibers embedded in ground substance • A thin, fenestrated internal elastic lamina is absent in small and terminal arterioles but present in larger arterioles. • Do not have external elastic lamina • In small arterioles, the tunica media is composed of a single smooth muscle cell layer that completely encircles the endothelial cells. • In larger arterioles, the tunica media consists of 2-3 layers of smooth muscle cells. • The tunica adventitia is scant and is represented by fibroelastic connective tissue housing a few fibroblast • Are the site of highest resistance in the CVS • Have a smooth muscle wall that is extensively innervated by autonomic fibers • Arteriolar resistance is regulated by the autonomic nervous system	• Have the largest total cross-sectional and surface area. • The smallest blood vessels, approximately 50 um in length with a diameter of 8-10 um. • Are formed by a single layer of squamous endothelial cells rolled into a tube, with the long axis of these cells lying in the same direction as the blood flow • The cytoplasm contains a Golgi complex, a few mitochondria, some rough endoplasmic reticulum (RER), and free ribosomes • Intermediate filaments located around the perinuclear zone vary in filament composition. These filaments (desmin and vimentin) provide structural support to the endothelial cells, but the significance of their variation is unclear. • The large number of pinocytotic vesicles associated with the entire plasmalemma is an identifying characteristic of capillaries • The external surfaces of the endothelial cells are surrounded by a basal lamina secreted by the endothelial cells • Endothelial cells are joined together by fasciae occludentes, or tight junctions • Are the site of exchange of nutrients, water, and gases	• Their walls are similar to but larger than capillaries, with a thin endothelium surrounded by reticular fibers and pericytes but larger venules possess smooth muscle cells instead of pericytes. • The endothelial cells of venules located in certain lymphoid organs are cuboidal rather than squamous and are called high – endothelial venules. ○ These function in lymphocytic recognition and segregation by type-specific receptors on their luminal surface, ensuring that specific lymphocytes migrate into the proper regions of the lymphoid parenchyma. • Are innervated by autonomic fibers.	• Large veins include the vena cavae and the pulmonary, portal, renal, internal jugular, iliac, and azygos veins • Progressively merge to form large veins, eventually, the venae cavae (inferior and superior), to return blood to the heart from the extremities, head, liver, and body wall • Contain the highest proportion of the blood in the CVS. • The blood volume contained in the veins is called unstressed volume

LAYERS OF THE ARTERY

- **Tunica Intima**
  - innermost layer made up of:

Endothelium	• Composed of a single layer of flattened squamous epithelial cells, which form a tube lining the lumen of the vessel • Endothelial cells not only provide an exceptionally smooth surface but also function in secreting types II, IV, and V collagens, lamin, endothelin, nitric oxide, and Von Willebrand factor. • Also possess membrane-bound enzymes, such as angiotensin- converting enzyme (ACE), which cleaves angiotensin I to generate angiotensin II, as well as enzymes that inactivate bradykinin, serotonin, prostaglandins, thrombin, and norepinephrine. • They also bind lipoprotein lipase, the enzyme that degrades lipoproteins. • Von Willebrand factor facilitates the coagulation of platelets during clot formation and is stored only in arteries
Subendothelial Layer	• Lies immediately beneath the endothelial cells • Composed of loose connective tissue and a few scattered smooth muscle cells, both arranged longitudinally
Internal Elastic Lamina	• ·Especially well developed in muscular arteries • Marks the boundary between the tunica intima and tunica media • Composed of elastin, which is a fenestrated sheet that permits the diffusion of substances into the deeper regions of the arterial wall to nourish the cells there.

- **Tunica Media**
  - The thickest layer of the vessel wall
  - Composed of mostly helically arranged smooth muscle cells
  - Interspersed within the layers of smooth muscles are some elastic fibers, type II collagen, and proteoglycans
  - External elastic lamina is present in larger muscular arteries which is more delicate than the internal elastic lamina and separates the tunica media from the overlying tunica adventitia
  - Capillaries and postcapillary venules do not have a tunica media, in these small vessels pericytes replace the tunica media
- **Tunica Adventitia**
  - The outermost layer of the blood vessel wall, blends into the surrounding connective tissue
  - Composed mostly of fibroblasts, type I collagen fibers and longitudinally oriented elastic fibers.

LAYERS OF THE VEIN

- Greater diameter than arteries
- Diameter increase at each convergence while arterial diameter continue to decrease at each branching
- Larger lumen, slit-like in appearance
- Walls are thinner and less elastic than arterial wall
- The 3 layers lack distinct boundaries particularly the boundaries between the tunica intima and the tunica media
- Only a few major vessels (such as pulmonary veins) have a well-developed smooth muscle layer and most large veins are without a tunica media; in its place is a well-developed tunica adventitia, an exception are the superficial veins of the legs, which have a well-defined muscular wall, perhaps to resist the distension caused by gravity.
- The muscular and elastic layers are not well developed but the connective tissue components are more pronounced than in arteries
- The thickest layer is the tunica adventitia and in large veins, this layer contain many elastic fibers, abundant collagen fibers, and vasa vasorum whereas the inferior vena cava has longitudinally arranged smooth muscle cells in its adventitia
- Veins with little or no smooth muscle in their walls are found in the retina, meninges, placenta, and penis.
- Have valves (medium vein) that function to prevent backflow of blood

DIFFERENTIATING THE FEATURES OF ARTERIES AND VEINS

	ARTERIES	VEINS
Overall diameter	• Lesser	• Greater
Thickness of the Wall and Shape of Lumen	• Thicker • More elastic and less likely to collapse after death • Lumen is more regular	• Thinner • Less elastic that's why it collapses during death • Lumen is slit-like or irregular in shape
Diameter of lumen in relation to the thickness of the wall	• Lesser than the thickness of the wall except in large arteries • The smaller the artery the thicker the wall is compared to the size of lumen	• Relatively thin wall and relatively larger lumen
Three coats	• Well demarcated and distinguishable from each other	• More loosely constructed that's why the 3 coats lack distinct boundaries
Internal elastic lamina	• Present and well developed in medium sized arteries	• Present only in large veins
Thickest coat	• Tunica media	• Tunica adventitia
Muscle and Tissue	• More of smooth muscles and elastic tissue	• Lesser amount of smooth muscles and elastic fibers • More connective tissues
Valves	• Absent	• Present especially in the lower extremities (medium veins)
Vasa vasorum	• Fewer and prominent in tunica media and tunica adventitia of elastic artery	• More prevalent in the walls (Tunica adventitia of large veins)
Blood Content	• Because of agonal contraction at the moment of death, it is usually empty • Internal elastic membrane appears scalloped	• Because of weaker agonal contraction the lumen may contain blood

TYPES OF ARTERIES AND THEIR CHARACTERISTICS

ARTERY	TUNICA INTIMA	TUNICA MEDIA	TUNICA ADVENTITIA
1. Elastic Artery (conducting) e.g. Aorta	• Endothelium with Weibel-Palade bodies, basal lamina, subendothelial layer, incomplete internal elastic lamina	• 40 to 70 striated elastic membranes • Smooth muscle cells interspersed between elastic membranes • Thin external elastic lamina • Vasa vasorum in outer half	• Thin layer of fibroelastic connective tissue • Vasa vasorum • Lymphatic vessels • Nerve fibers
2. Muscular Artery (distributing) e.g. Femoral Artery	• Endothelium with Weibel-Palade bodies, basal lamina, subendothelial layer, thick internal elastic lamina	• Up to 40 layers of smooth muscle cells • Thick external elastic lamina	• Thin layer of fibroelastic connective tissue • Vasa vasorum not very prominent • Lymphatic vessels • Nerve fibers
3. Arteriole	• Endothelium with Weibel-Palade bodies, basal lamina, subendothelial layer not very prominent, some elastic fibers instead of defined internal elastic lamina	• One or two layers of smooth muscle cless	• Loose connective tissue • Nerve fibers
4. Metarteriole	• Endothelium, Basal Lamina	• Smooth muscle cells form Precapillary sphincter	• Sparse • Loose connective tissue

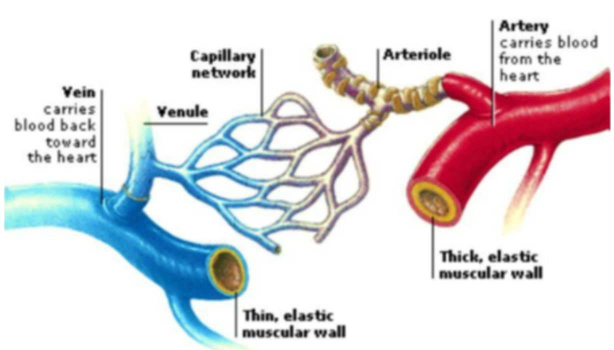
TYPES OF VEINS AND THEIR CHARACTERISTICS

VEINS	TUNICA INTIMA	TUNICA MEDIA	TUNICA ADVENTITIA
1. Large Veins	• **Endothelium:** basal lamina, valves in some, subendothelial connective tissue	• Connective tissue: smooth muscle cells	• Smooth muscle cells oriented in longitudinal bundles: cardiac muscle cells near their entry into the heart; collagen layers with fibroblasts
2. Medium and Small veins	• **Endothelium:** basal lamina, valves in some, subendothelial connective tissue	• Reticular and elastic fibers, some smooth muscle cells	• Collagen layers with fibroblasts
3. Venules	• **Endothelium**: basal lamina (pericytes, postcapillary venules)	• Sparse connective tissue and a few smooth muscle cells	• Some collagen and a few fibroblasts

CAPILLARIES

- The smallest blood vessels
- Composed of a single layer of squamous endothelial cells
- The large number of pinocytotic vesicles associated with the entire plasmalemma is an identifying characteristic of capillaries.
  - These vesicles may be in singular array, two singles may be fused together, or several vesicles may be fused, forming a transient channel
- The external surface of the endothelial cells are surrounded by a basal lamina.
- Pericytes are located along the outside of the capillaries and small venules, and appear to be surrounding them.
  - Pericytes share the basal lamina of the endothelial cells.

1.Continuous capillaries	• Have no pores/fenestrae in their walls • Present in muscle, nervous, and connective tissues, whereas in the brain tissue they are classified as modified continuous capillaries. • The intercellular junctions between their endothelial cells are a type of fasciae occludentes, which prevent passage of many molecules. • Substances such as amino acids, glucose, nucleosides, and purines move across the capillary wall via carrier-mediated transport
2. Fenestrated capillaries	• Have pores (fenestrae) in their walls that are covered by pore diaphragm. • Found in the pancreas, intestines and endocrine glands. • The pores are bridged by an ultrathin diaphragm. • These pore-diaphragm complexes are located in clusters, thus, most of the endothelial wall of the fenestrated capillary is without fenestrae – an exception is the renal glomerulus, composed of fenestrated capillaries that lack diaphragm
3. Sinusodial capillaries	• May possess discontinuous endothelial cells and basal lamina and many contain many large fenestrae without diaphragms, enhancing exchange between blood and tissue. • Because of their location, sinusoidal capillaries have an enlarged diameter of 30 - 40 um. • Are lined by endothelium • The vascular channels in certain organs of the body, including the bone marrow, liver, spleen, lymphoid organs, and certain endocrine glands are called sinusoids, irregular blood pools, or channels that conform to the shape of the structure in which they are located



STRUCTURAL CHARACTERISTICS OF THE VASCULAR SYSTEM AND THEIR FUNCTIONAL SIGNIFICANCE

CAPACITIES, PERCENTAGE DISTRIBUTION OF BLOOD IN THE VASCULAR TREE

Capacitance (Compliance)

- Describes the distensibility of blood vessels
- Can be expressed by the following equation: C= V/P
  - C- capacitance (ml/mmHg)
  - V- volume (ml)
  - P- pressure (mmHg)
- Is directly proportional to volume and inversely proportional to pressure.
- Is much greater for veins than arteries.
  - As a result, more blood volume is contained in the veins (unstressed volume) than in the arteries (stressed volume)
- Changes in the capacitance of the veins produce changes in unstressed volume.
  - For example, a decrease in venous capacitance decreases the unstressed volume and increase stressed volume by shifting blood from the veins to the arteries.
- Capacitance of the arteries decreases as a person ages; therefore, the arteries becomes less distensible.

VELOCITY OF BLOOD FLOW AND CROSS-SECTIONAL AREA

- Can be expressed by the following equation:
  - V = Q/A
    - V - velocity (cm/sec)
    - Q - Blood flow (ml/min)
    - A - cross-sectional area (cm2)
- Velocity is directly proportional to blood flow and inversely proportional to the cross-sectional area at any level of the CVS.
- For example, blood velocity is higher in the aorta (small cross-sectional area) than in the sum of all the capillaries (large cross-sectional area).
- The lower velocity of blood flow in the capillaries optimizes the exchange of substances across the capillary wall.
- Blood flow:
  - Can be expressed by the following equation:

$$Q = \Delta P / R \quad \text{or} \quad \text{Cardiac output} = \frac{\text{Mean arterial pressure} - \text{right atrial pressure}}{\text{Total peripheral resistance (TPR)}}$$

Q – Flow - cardiac output (ml/min)
ΔP – pressure gradient - pressure gradient (mmHg)
R – resistance - total peripheral resistance (mmHg / ml/min)

- The equation for blood flow (or cardiac output) is analogous to Ohm's law for electrical circuits (I = V / R), where blood flow is analogous to current and pressure is analogous to voltage.
- The pressure gradient (AP) drives blood flow.
  - It is the pressure difference (P1-P2) between the two ends of the vessel.
- Thus, blood flows from high pressure to low pressure, and flow is inversely proportional to the resistance of the blood vessels.

RESISTANCE

- Is directly proportional to the viscosity of the blood.
  - For example, increasing viscosity by increasing hematocrit will increase resistance and decrease flow.
- Is directly proportional to length of vessel.
- Is inversely proportional to the fourth power of the vessel radius.
  - This is a powerful relationship.
  - For example, if blood vessel radius decreases by a factor of 2, then resistance will increase by a factor of 16 (24) and flow will therefore decrease by a factor of 16.

Resistance in Parallel or Series:

- **Parallel Resistance**
  - is illustrated by the systemic circulation: each organ is supplied by an artery that branches off the aorta. The total resistance of this parallel arrangement is expressed in the following equation:

$$\frac{1}{R_{total}} = \frac{1}{R_a} + \frac{1}{R_b} + \cdots \frac{1}{R_n}$$

R_a, R_b, & R_n are the resistance of the renal, hepatic, and ....arteries, respectively. The total resistance is less than the resistance of any of the individual arteries.

- **Series Resistance**
  - Is illustrated by the arrangement of blood vessels within a given organ. Each organ is supplied by a large artery, smaller arteries, then arterioles, capillaries, and veins arranged in series.
  - The total resistance is the sum of the individual resistance, as expressed in the ff equation:

<u>**R total = R artery + R arterioles + R capillaries**</u>

POISEUILLE'S EQUATION

- Poiseuille equation - gives factors that change the resistance of blood vessels

$$R = \frac{8nl}{\pi r^4}$$

R – resistance
n - viscosity of blood
l – length of blood vessel
r^4 – radius of blood vessel to the 4^{th} power

DIFFERENCE BETWEEN LAMINAR & TURBULENT FLOW

- **Laminar Flow**
  - Blood flows at a steady rate through a long, smooth vessel, it flows in streamlines, with each layer of blood remaining the same distance from the wall. The central portion of the blood stays in the center of the vessel.
- **Turbulent Flow**
  - Blood flowing in all directions in the vessel and continually mixing within the vessel.
- Laminar flow is streamlined (in a straight line), turbulent flow is not.

CAUSES OF TURBULENT BLOOD FLOW

- High blood flow velocity
- Obstruction in a vessel
- Sharp turn
- Rough surface
- Eddy currents - adds to friction

FACTORS AFFECTING TURBULENT FLOW

- Velocity of Blood flow (v) - cm/s
- Diameter of Blood vessel (d)
- Viscosity of Blood (n) + density (p) (poise)
- Formula:

$$Re = \frac{v \bullet d}{n/p}$$

REYNOLD'S EQUATION

- Reynold's number predicts whether blood flow will be laminar or turbulent
- **Reynold's Equation**
  - Re (Reynold's no.) = measure of the tendency for turbulence to occur
    - Re > 200 - 400 : turbulent flow at branches of vessels
    - Re > 2000 : turbulence even in straight smooth vessel
  - When Reynold's number is increased, there is a greater tendency for turbulence, which causes audible vibrations called bruits. Reynolds number (and therefore turbulence) is increased by the following factors:
    - ↓ blood viscosity (e.g. ↓ hematocrit, anemia)
    - ↑ blood velocity (e.g. narrowing of a vessel)

FLOW CONTINUITY EQUATION

Velocity of blood flow and cross-sectional area

- Can be expressed by the flow continuity equation:
  - v = Q/A
    - v - velocity (cm/sec)
    - Q - Blood flow (ml/min)
    - A - cross-sectional area (cm2)
- Velocity is directly proportional to blood flow and inversely proportional to the cross-sectional area at any level of the CVS.
- For example, blood velocity is higher in the aorta (small cross-sectional area) than in the sum of all the capillaries (large cross-sectional area).
- The lower velocity of blood flow in the capillaries optimizes the exchange of substances across the capillary wall.

BERNOULLI'S PRINCIPLE

- The greater the velocity of flow in a vessel, the lower the lateral pressure distending its wall.
- Clinical Significance:
  - When a vessel is narrowed by a pathologic process such as an arteriosclerotic plaque, the lateral pressure at the constriction is decreased and the narrowing tends to maintain itself.

LAW OF LAPLACE

- Law of Laplace states that tension is proportional to radius.
- The smaller the radius of a blood vessel, the lower the tension in the wall necessary to balance the distending pressure.
- Clinical Significance:
  - A dilated heart must do more work than a non-dilated heart. When the radius of a cardiac chamber is increased, a greater tension must be developed in the myocardium to produce any given pressure.

MECHANISM OF CRITICAL CLOSING PRESSURE IN BLOOD VESSELS AND THE FACTORS AFFECTING IT

- When pressure in a small blood vessel is reduced, a point is reached at which there is no flow of blood even though the pressure is not zero. The pressure at which flow ceases is called the critical closing pressure.
- This is in part a manifestation of the fact that it takes some pressure to force red cells through capillaries which have smaller diameter than the red cells.
- Also, the vessels are surrounded by tissues that exert a small but definite pressure on the vessels and when the intraluminal pressure falls below the tissue pressure, the vessels collapse