CV 3. CIRCULATORY SYSTEM

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Learning Objectives

1. Describe how blood flows within the systemic and pulmonary circulation.
2. Describe the functions of arteries, arterioles, capillaries, venules and veins.
3. Describe the relationship between pressure, flow, and resistance in regulating peripheral circulation.
4. Define systolic, diastolic, and mean arterial pressure.
5. Explain the myogenic response, hyperemia and reactive hyperemia. Name two reflexes that control blood pressure.
6. Explain the factors that alter transcapillary movement (filtration and reabsorption).
7. Explain capacitance vessel versus distributing vessels and the relationship between lymphatic and blood circulations.

BLOOD VESSELS

Blood ejected from the left ventricle flows into the **aorta** (Fig 1), which branches into arteries, arterioles, and eventually capillaries.

Arteries are low resistance vessels that serve as pressure reservoirs to maintain blood flow during diastole. All **arteries** have muscular walls. In response to pressure, to paracrines, and to nervous activity, the smooth muscle of the artery can either constrict or relax and thereby change the diameter of the vessel. The arteries regulate which organ receives blood (i.e., is perfused).

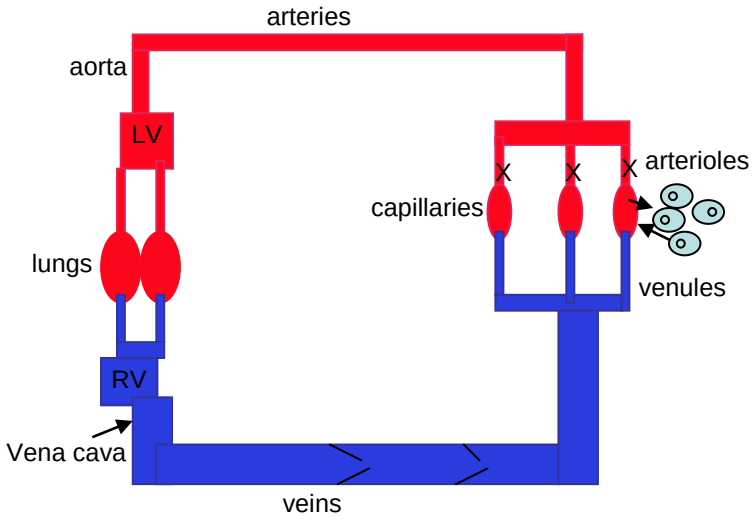

Figure 1. Model of the the systemic and pulmonary circulations.

Arterioles are located downstream of the arteries. They have smaller diameters and have the highest ratio of smooth muscle to lumen size. The arterioles act as spigots (sphincters) to increase or decrease local perfusion (i.e., delivery of blood to the tissues).

Capillaries are very thin walled vessels and are the site of gas, solute, and fluid exchange between the blood and tissues.

Venules receive the blood draining out of the capillaries. Venules converge into larger diameter vessels called **veins**, and finally into the **vena cava,** the major vessel that empties into the right atrium. The **veins are low resistance vessels that serve as capacitance or volume reservoirs**.

On the right side of the heart, blood ejected from the **right ventricles flows into the pulmonary arteries**, the pulmonary capillaries, and finally into the pulmonary vein, which empties into the left atrium, which drains into the left ventricles.

The walls of blood vessels are composed of a layer of simple squamous epithelium (flat cells) called **endothelium** which in the larger vessels is surrounded by layer(s) of smooth muscle and connective tissue. The smooth muscle in arteries and arterioles is arranged concentrically around the lumen permitting control of the luminal diameter. The smooth muscle in the large veins is arranged parallel to the lumen permitting peristaltic contraction (shortening of the length). The large veins also have valves which prevent backflow. In most blood vessels, the smooth muscle is partially contracted at all times (**muscle tone**). This basal tone is maintained by the sympathetic nervous system. Contraction of smooth muscle can be modulated by ligands (neural transmitters, hormones, and paracrines) or by stretch.

Angiogenesis is the process by which new blood vessels develop. This occurs in normal growth, in exercise, and in response to injury (wound healing). Angiogenesis is controlled by proliferative and anti-proliferative factors that regulate mitosis. Growth factors that promote angiogenesis include vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF). Anti-angiogenesis factors are two cytokines, angiostatin and endostatin.

PRESSURE, VOLUME, & FLOW

Bulk flow is the movement of blood from a region of high pressure to a region of low pressure ($P_2 - P_1$). In the systemic circulation the highest pressure is in the aorta. The pressure in the aorta oscillates from the **systolic pressure, usually 120 mmHg, to the diastolic pressure, usually 80 mm Hg**. The pressure within the aorta and arterial system is called the **after load.** To eject blood, the heart develops pressure equal to or greater than the after load.

Hydrostatic pressure is that which is exerted on the walls of the vessel by the fluid within the vessel. The rapid ejection of blood into the aorta can be felt as a **pulse** (pressure wave). The **pulse pressure** is systolic pressure – diastolic pressure. Pulse pressure is usually 120- 80 = 40 mmHg.

PP = SP - DP

Once fluid begins to flow through the cardiovascular system, pressure decreases because energy is lost due to friction exerted by the vessel walls and from friction between blood cells. This friction is called **resistance.**

Flow rate is expressed as volume per time (ml/min) and is directly proportional to driving pressure (delta P) and inversely proportional to **resistance**. Blood flow is abbreviated Q with a dot above it. Note that flow is not velocity. **Velocity** is expressed in distance per time (mm/sec).

$$\dot{Q} = \frac{P_2 - P_1}{\text{Resistance}}$$

Resistance is the opposition to fluid movement and is determined by the radius and length of the vessel and the viscosity of the blood. The primary way that

$$\text{Resistance (R)} = \frac{8\,\eta\,l}{\pi\,r^4}$$

resistance is changed in the cardiovascular system is by changing the vessel radius. Radius can be changed by altering the amount of contraction of the smooth muscle in the arteries and arterioles. Also, resistance can be increased when vessels are plugged by plaques of fatty lipids; this disease is known as **atherosclerosis,** or hardening of the arteries.

Because the arterial pressure is pulsatile, we use the **mean arterial pressure** (MAP) to represent the driving pressure. Mean arterial pressure is estimated as diastolic pressure plus 1/3 of the pulse pressure (SP-DP).

MAP = DP + 1/3 (PP)

For a person with a SP of 120 and DP of 80, MAP = 93 mmHg.

The MAP is closer to DP than SP because diastole lasts longer than systole. MAP is determined by the balance of blood flow into the arteries and blood flow out of the arteries into the tissues. If the **flow in is greater than the flow out**, blood will collect in the arteries and **MAP will rise**. If the **flow out exceeds the flow in, MAP will decrease**.

Blood flow into the arteries is determined by the cardiac output (CO). Blood flow out is determined by the **total peripheral resistance (TPR)**, which is the total resistance of the circulatory system.

$CO \times TPR = MAP - P_{\text{vena cava}}$

Note: because pressure in the vena cava is ~ zero, the equation used is as follows:

CO = MAP/TPR or CO x TPR = MAP

In **hypotension**, the blood pressure falls too low and the driving force for blood flow will be unable to overcome the opposition of gravity. Blood will pool in the feet. Delivery of blood and oxygen to the brain will decrease; the person will become "light headed" or faint.

In **hypertension (>139 SP or >89 DP)**, the blood pressure is chronically raised. This can lead to rupture of a weak vessel wall (**hemorrhage**) and bleeding into the tissue. If this occurs in the brain it is called a **stroke**. Rupture of a major artery can be fatal.

We estimate blood pressure with a sphygmomanometer (inflatable pressure cuff and pressure gauge). The cuff encircles the arm, is inflated until the pressure exerted exceeds the systolic pressure and collapses the artery. The pressure in the cuff is gradually released. When the cuff pressure is less than the arterial pressure then flow resumes in the artery. The blood squeezing through a partially collapsed vessel makes a sound (Korotkoff sound) which can be heard by a stethoscope. The pressure when the sound starts is systolic pressure. The pressure when the sound disappears is the diastolic pressure.

Total peripheral resistance (TPR) is determined by several factors: (1) length of the blood vessels, (2) radius of the blood vessels, and (3) viscosity of the blood. Normally the length of the blood vessels and the viscosity of blood remain fixed. Therefore the most important of these factors is the radius of the vessel. As the radius (r) of a tube increases, the resistance (R) of the tube to fluid flow decreases dramatically because R is proportional to $1/r^4$.

BLOOD FLOW AND CONTROL OF BLOOD PRESSURE

The distribution of blood flow is regulated by changes in vascular resistance. The **arterioles are the primary site of variable resistance** in the systemic circulation. Arterioles are small in diameter and few in number so their total cross sectional area is the smallest. Arteriolar resistance is primarily affected by sympathetic regulation although local regulatory mechanisms match blood flow to the metabolic needs of the tissue. For example, at rest, skeletal muscles receive approximately 20% of the cardiac output, but during exercise the metabolic demands of the muscle increases and they receive as much as 85% of cardiac output.

Resistance of the arterioles is regulated by local control (paracrines, metabolites) and by reflex control (sympathetic innervation, hormones).

Local control of BP includes:

1. Hyperemia = increased blood flow to organs. The paracrine factors that are active in hyperemia are increased **CO2, H+ and K+** in interstitial fluid.

- **active hyperemia** is due to increased metabolism.
- **reactive hyperemia** is due to reperfusion.

2. Myogenic response = contraction or dilation of arteriolar smooth muscle in response to a change in stretch (transmural pressure).

Reflex control of BP includes: mediated by epinephrine (Epi) and norepinephrine (NorEpi).

1. Sympathetic innervation

- **expl. vasoconstriction by NorEpi** acting on the **alpha 1 adrenergic receptors** (AR) of blood vessels.

2. Hormones

- **expl. vasoconstriction by either epinephrine or by vasopressin**

Variation in blood flow to individual tissues/organs is possible because the arterioles are arranged in parallel not in series. Total blood flow through all of the arterioles of the body **always** equals cardiac output. [Question: Will the blood flow in the left arm increase when you apply a tourniquet to the right arm?]

TRANS - CAPILLARY EXCHANGE OF SOLUTES & FLUIDS

The transport of materials to the organs is only one part of the circulatory system. Once blood reaches the capillaries, the plasma and cells exchange materials across the endothelium of the capillary. Transport can occur via bulk flow across patent openings (fenestrated capillary found in the liver, endocrine glands, and kidney), via diffusion, or via vesicle transport (sealed capillary of the brain, testes, and thymus).

Dynamic changes in arterioles (vasodilation or vasoconstriction) regulate downstream *pressures* and *flow rates* across capillary beds.

Recall that velocity of blood flow is dependent on the cross sectional area. Although the capillaries are the smallest blood vessel in diameter, **blood flow through the capillary bed is slow**. This is because the capillaries are more numerous than any other blood vessel hence their total cross sectional area is large. The slow flow rate enables time for the exchange (filtration and reabsorption) of solutes and fluid across the endothelium of the capillary with the interstitial fluid.

Filtration is the net movement of solutes out of the capillary into the interstitial fluid (IF).

Reabsorption is the net movement of solutes and fluid into the capillary from the IF.
Two pressure gradients dictate net movement across this endothelium. The first is the difference in the hydrostatic pressures (P) of the plasma and of the interstitial fluid (IF) (Fig 2). The second is the difference in the oncotic pressures (π) (attraction of water by protein) between these two fluid compartments.

$$\textbf{Net filtration} = (P_{plasma} - P_{IF}) - (\pi_{plasma} - \pi_{IF})$$

***** The hydrostatic pressure and the oncotic pressure of the IF are usually zero.

The hydrostatic pressure decreases from the arteriole side (35 mm Hg) to the venule side (15 mm Hg) of the capillary due to resistance of the vessel walls but the oncotic pressure of the plasma (28 mm Hg) does not change. Therefore **filtration occurs at the arteriole end** of the capillary and **reabsorption at the venule end** of the capillary.

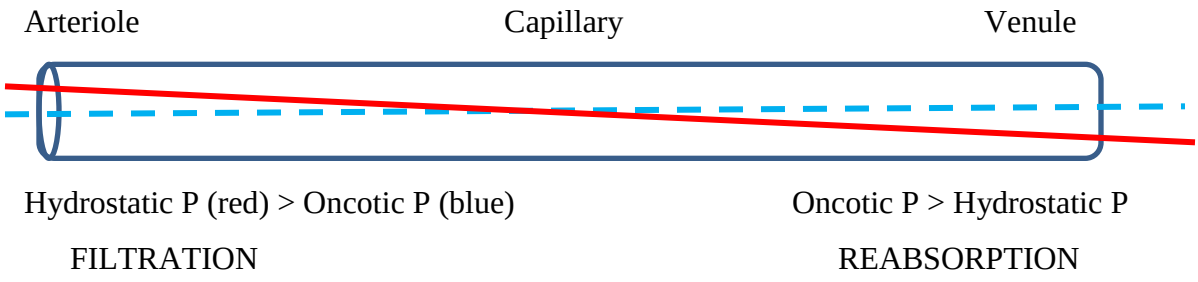

Figure 2. Filtration and reabsorption of solutes and fluid across the capillary endothelium determined by differences in hydrostatic pressure (solid line) and oncotic pressure (dotted line).

What happens if the upstream arteriole dilates? This will raise the hydrostatic pressure in the capillary increasing filtration but decreasing reabsorption so more fluid will remain in the IF. This accumulation of fluid is called **edema**. Edema can result if there is an increase in capillary hydrostatic pressure; a decrease in plasma protein concentration (oncotic pressure); or an increase in the interstitial protein content (oncotic pressure).

Under some circumstances (such as hemorrhage or severe dehydration) the balance between filtration and reabsorption favors reabsorption and fluid moves into plasma. This **auto-transfusion** helps to maintain blood volume.

VENOUS RETURN

The amount of blood returned to the heart dictates EDV. In exercise when the oxygen demands of the body increase, venous return is increased to increase stoke volume and cardiac output. This is accomplished by:

1. Increased sympathetic drive = constriction of large veins.
2. Respiratory pump = increased depth of breathing expands the chest and thereby lower pressure within the thoracic cavity.
3. Skeletal pump = contraction of the skeletal muscles “squeezes” the veins.

The importance of venous return is that the heart can only pump out what enters. Recall that a stretched heart has a greater force of contraction (Frank Starling’s law).

LYMPHATIC SYSTEM

In a normal body, there is a mis-match of filtration to reabsorption causing some fluid to remain in the interstitium (IF). This is called **lymph.** Lymph is drained by a separate series of thin walled vessels called the lymphatics. The lymphatic system is designed for one-way transport of interstitial fluid from the tissues to the circulation. Small lymph vessels in the tissues coalesce to form larger lymphatic vessels that progressively increase in size. Interposed along the lymphatic vessels are filters called lymph nodes which help to capture and destroy foreign pathogens.

The lymphatics have no pump analogous to the heart, instead fluid is moved by contraction of skeletal muscles which compress the lymphatic vessels. Uni-directional movement is insured by valves. The return of filtered fluid to the circulation is important because: (1) it recycles plasma proteins thereby maintaining a low oncotic pressure within the interstitial space, and (2) it maintains hydrostatic pressure by returning as much as **3L per day** to the circulation.

KEY CONCEPTS

- Heart consists of two pumps. The pressure generated by the heart drives the unidirectional flow of blood through the pulmonary circulation where gas exchange occurs and through the systemic circulation where exchange of nutrients metabolites, heat, and hormones occurs.
- The vascular system is both a conduit for the flowing blood and a dynamic system that controls the distribution of the blood to the organs of the body.
- Arteries are low resistance conduits and pressure reservoirs for maintaining blood flow during diastole. Arterioles are the dominant site of resistance to flow.
- Capillaries are the site of exchange. The balance of hydrostatic and oncotic forces determines the direction of fluid movement into or out of the capillaries.
- Veins are the low resistance conduits for venous return and volume reservoirs. Sympathetic NS constriction of veins can increase venous return, thereby increasing SV and CO.
- The lymphatic system provides a one-way route for the return of interstitial fluid to the cardiovascular system.
- Disease states that alter the hydrostatic and oncotic pressures can result in edema. These disease states include heart failure, liver disease, kidney disease and protein malnutrition.

QUESTIONS

1. Which of the following arterial blood pressures (mmHg) has the largest pulse pressure?
    A. 130/85
    B. 120/90
    C. 115/75
    D. 125/70

2. If blood pressure doubled at the same time that peripheral resistance doubled, the blood flow through a vessel would be:
    A. doubled
    B. halved
    C. 16 times greater
    D. unchanged

3. Which of the following promote edema formation?
    A. decreased blood protein concentration
    B. lymphatic blockage
    C. venous blockage (clot)
    D. A and C
    E. A, B, and C

ANSWERS

1. D
2. D
3. E