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ASSIGNMENT TITLE: assignment on Cardiovascular Physiology for MBBs 200L

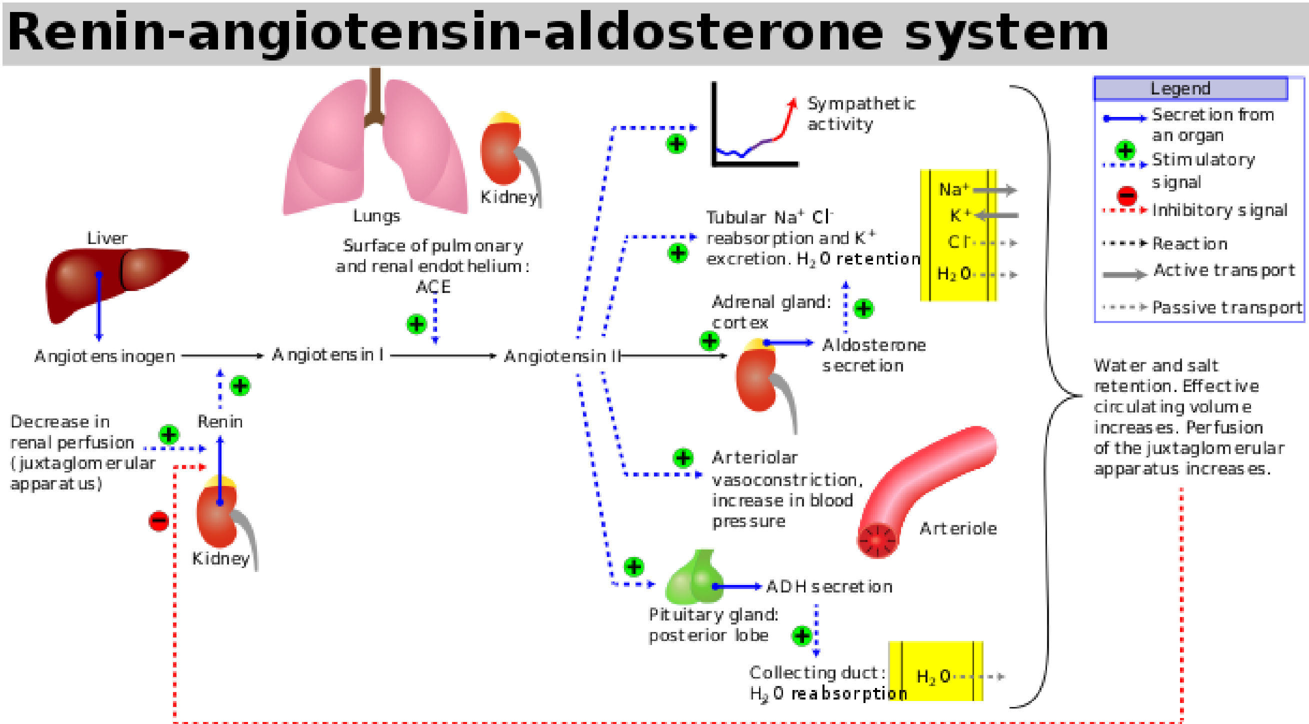
1. Discuss the long-term regulation of mean arterial blood pressure?

The long-term regulation of blood pressure is by the Renin- Angiotensin-aldosterone system.

Renin-Angiotensin-Aldosterone System (RAAS)

The endocrine system helps regulate blood pressure. To understand the RAAS I will explain a typical instance. When you do not drink water for like 5-6 hours, plasma volume goes down and blood pressure goes low. As a result, perfusions to the kidney will go down, when the kidney senses a reduction in perfusion, it will secrete an enzyme called renin. The liver secretes an inactive enzyme angiotensinogen. Renin converts Angiotensinogen to Angiotensinogen I which is still inactive. Angiotensinogen I is converted to Angiotensinogen II by Angiotensinogen converting enzyme (ACE), found on the surface of pulmonary and renal endothelium. Angiotensinogen II reacts with receptors on various target organs;

- It will first promote sympathetic nerves, increasing the release of epinephrine and norepinephrine from adrenal medulla, increasing the increase and reuptake of norepinephrine at adrenergic nerve terminals.
- Tubular reabsorption and excretion- increase reabsorption of sodium ions. Anywhere sodium ions go water follows and potassium ions are excreted, there is water retention.
- Angiotensinogen II causes the adrenal cortex to secrete aldosterone, which also promotes reabsorption of sodium ions, excretion of potassium ions and water retention.
- It also helps arteriolar vasoconstriction which helps increase blood pressure
- It also acts on the pituitary gland which releases antidiuretic hormone which also helps with water retention.

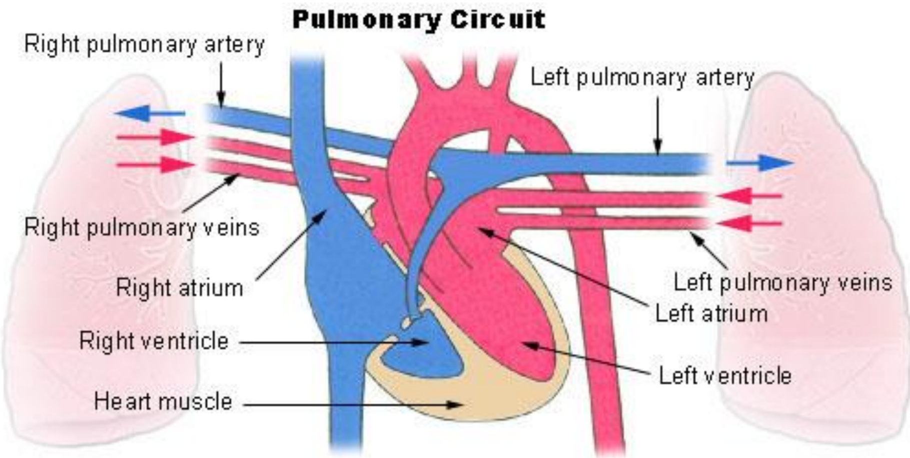


Clinical application

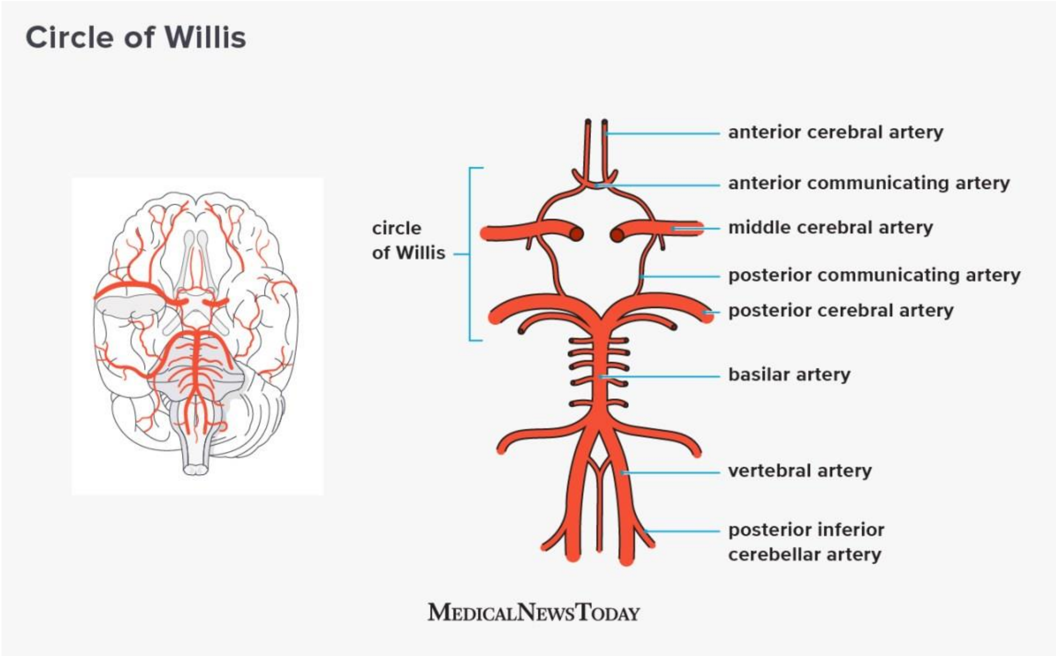
- <u>Renin inhibitor:</u> inhibits the enzyme which converts angiotensinogen into angiotensinogen II, the rate limiting step in the RAAS. An example is the Alliskiren. Adverse effects include; Hyperkalemia, renal impairment, hypotension.
- <u>ACE inhibitors (ACEIs):</u> this blocks ACE resulting in decreased conversion of angiotensinogen I to angiotensinogen II. ACE is also very important for degradation of bradykinin to an inactive metabolite. Bradykinin is an inflammatory substance and promotes the release of nitric oxide, prostaglandins etc. examples are: enalapril, captopril, lisinopril.
- <u>Angiotensinogen receptor blockers (ARBs):</u> blocks the activity of angiotensinogen II at the receptor sites. Examples of such drugs are: losartan, valsartan, candesartan.

2. Write short notes on the following:

a. Pulmonary circulation: this is also known as lesser circulation. It occurs between the heart and the lungs; the heart carries deoxygenated blood from the heart to the lungs to be oxygenated. The right ventricle pumps out deoxygenated blood through the pulmonary artery for blood to be oxygenated, then it pumped back to the heart, the left atrium through the pulmonary vein.



b. Circle of Willis: the arteries which supply blood to the brain are derived from two terminal internal carotid arteries and basilar artery (formed by union of the right and left vertebral arteries). Branches of the internal carotid arteries and basilar artery anastomose on the inferior surface of the brain to form the circle of Willis. The circle of Willis is thus basically a free anastomosis between two internal carotid arteries and the two vertebral arteries which equalize pressure on the arteries of the two sides. In this way, the circulus arteriosus allows blood that enters by either internal carotid or vertebral artery to be distributed to any part of both cerebral hemispheres. Six large arteries take part in the formation of the circle of Willis supply by their central and cortical branches to the brain substance.



c. Splanchnic circulation: the blood vessels of the gastrointestinal system are apart of a more extensive system called the splanchnic circulation. It includes the gut, pancreas, liver, and spleen. Splanchnic blood flow courses through the gut, spleen and pancreas and then flows immediately into the hepatic circulation by way of the portal vein. This complex secondary flow of blood allows the reticuloendothelial system of the sinusoids to remove harmful bacterial and other substances that could potentially enter the systemic circulation. maintenance of an adequate blood supply to the intestines is important in insuring normal intestinal homeostasis.

Splanchnic blood flow is influenced by several factors including the status of the normal systemic circulation, the degree of collateral blood flow and the exposure to exogenous and endogenous neuro-humoral factors

Splanchnic circulation consists of three portions:

1. Mesenteric circulation supplying the GI tract
2. Splenic circulation supplying blood to spleen
3. Hepatic circulation supplying blood to the liver.

Unique feature of splanchnic circulation is that the blood from the mesenteric bed and spleen forms a major amount of blood flowing to liver. Blood flows to liver from GI tract and spleen through the portal system.

The mesenteric circulation is regulated by local autoregulation, activities of gastrointestinal tract and nervous factor. Blood flow in the spleen is regulated by sympathetic nerve fibers. The blood flow to the liver is regulated by systemic blood pressure, splenic contraction, movements of the intestine, chemical factors and neural factors.

d. Coronary circulation: This is the circulation of blood in the blood vessels of the heart muscle (myocardium),the vessels that deliver oxygen-rich blood to the myocardium are known as coronary arteries while the vessel that remove the deoxygenated blood from the heart muscle are known as cardiac veins, these include the great cardiac veins, the middle cardiac veins, the small and the anterior cardiac veins. As the left and right coronary arteries run on the surface of the heart, they can be called epicardial coronary arteries. These arteries when healthy are capable of auto regulation to maintain coronary blood flow at levels appropriate to the needs of the heart muscle.

These relatively narrow vessels are commonly affected by atherosclerosis and can become blocked, causing angina or a heart attack.

The coronary arteries that run deep within the myocardium are referred to as subendocardial artery. Heart muscle is supplied by two coronary arteries,

namely right and left coronary arteries, which are the first branches of aorta. Arteries encircle the heart in the manner of a crown, hence the name coronary arteries

(Latin word corona = crown).

Right and Left Coronary Arteries

Right coronary artery supplies whole of the right ventricle and posterior portion of left ventricle. Left coronary artery supplies mainly the anterior and lateral

parts of left ventricle. There are many variations in diameter of coronary arteries.

VENOUS DRAINAGE

Venous drainage from heart muscle is by three types of vessels.

- 1. *Coronary Sinus*

Coronary sinus is the larger vein draining 75% of total coronary flow. It drains blood from left side of the heart and opens into right atrium near tricuspid valve.

- 2. *Anterior Coronary Veins*

Anterior coronary veins drain blood from right side of the heart and open directly into right atrium.

3. *Thebesian Veins*

Thebesian veins drain deoxygenated blood from myocardium, directly into the concerned chamber of the heart

CORONARY BLOOD FLOW

AND ITS MEASUREMENT

- NORMAL CORONARY BLOOD FLOW

Normal blood flow through coronary circulation is about 200 mL/minute. It forms 4% of cardiac output. It is about 65 to 70 mL/minute/100 g of cardiac muscle.

- MEASUREMENT OF CORONARY

BLOOD FLOW

- *Direct Method*

Coronary blood flow is measured by using an electromagnetic flowmeter. It is directly placed around any coronary artery. Coronary blood flow is regulated mainly by local vascular response to the needs of cardiac muscle.

Factors regulating coronary blood flow:

1. Need for oxygen

2. Metabolic factors

3. Coronary perfusion pressure

4. Nervous factors.

Cutaneous circulation: This is the circulation of blood through the skin. The primary function of the skin circulation is to help maintain body temperature. blood vessels constrict to prevent heat loss and dilate to facilitate transfer of heat from the body core to the body surface .the skin comprises 4% to 5% of the total body weight and receives about 2% of the cardiac output .The arterio-venous oxygen difference is small (3vol%), indicating that most of the blood flow is non nutrient flow. Skin blood vessels (arterioles) are of two types. The most numerous are composed of smooth muscle, supply capillary beds and are innervated with sympathetic constrictor fibers, like arterioles in skeletal muscle beds, they provide nutrient flow to the skin. Veins draining these vascular beds comprise large venous plexuses with slow blood flow in the fore arm, legs and thigh. These plexuses provide a large surface area for heat exchange with the environment. The second type of vessel is composed almost exclusively of smooth muscle. these provide a direct connection between arteries and the venous plexuses described above. They are known as arterio- venous anastomosis and are numerous in the palms, soles and skin of the ears, nose and lips. Flow is non nutrient because there are few exchange vessels. These vessels have a low level of basal tone and are innervated by sympathetic fibers, to which they are responsive.

FUNCTIONS OF CUTANEOUS CIRCULATION

Cutaneous blood flow performs two functions:

1. Supply of nutrition to skin
2. Regulation of body temperature by heat loss.

NORMAL BLOOD FLOW TO SKIN

Under normal conditions, the blood flow to skin is about 250 mL/square meter/minute. When the body temperature increases, cutaneous blood flow increases up to 2,800 mL/square meter/minute because of cutaneous vasodilatation.

REGULATION OF CUTANEOUS BLOOD FLOW

Cutaneous blood flow is regulated mainly by body temperature. Hypothalamus plays an important role in regulating cutaneous blood flow. When body temperature increases, the hypothalamus is activated. Hypothalamus in turn causes

cutaneous vasodilatation by acting through medullary vasomotor center. Now, blood flow increases in skin. Increase in cutaneous blood flow causes the loss of heat from the body through sweat. When body temperature is low, vasoconstriction occurs in the skin. Therefore, the blood flow to skin decreases and prevents the heat loss from skin.

3. Discuss the cardiovascular adjustment that occurs during exercise.

Muscular exercise constitutes the strongest physiologic stress on the human CVS. It demands a huge increase in the supply of O_2 and nutrients to the exercising muscles and a proportionate increase in the removal of metabolic waste products and excess heat generated during the exercise. Certain cardiovascular adjustments are made to enable the body cope with the above increased demands.

The changes could be grouped into:

- Changes in cardiac function
- Changes in arterial blood pressure
- Redistribution of cardiac output
- Increased O_2 delivery to the tissues
- Temperature regulation

Changes in cardiac function: The cardiac function changes include; increase in stroke volume, heart rate and cardiac output. In exercise, cardiac output can increase from 5L to 30L per minute. It is important to note that change in stroke volume alone will increase cardiac output by only 50%. Hence, increased HR is the main mechanism by which increase of up to 60% in C.O is achieved in exercise. The changes in force of contraction of the heart, the heart rate {HR} and C.O are brought about by increase sympathetic discharge to the heart, reduced parasympathetic tone to the heart, increase in level of adrenaline and noradrenaline in the blood and as exercise progresses, increase in temperature. Also, venoconstriction, muscle pump, thoracic pump, mobilization of blood from the viscera and increased pressure transmitted through the dilated arterioles to the veins increase venous return to the heart. An increased venous return will raise cardiac output.

Changes in arterial blood pressure: There is usually an increase in arterial pressure in exercise. The increase can be as little as 20mmHg or as great as 80mmHg depending on the type of exercise and condition under which the exercise is performed. The increase in arterial pressure in exercise is due to a number of factors:

a. Vasoconstriction of the arterioles and small arteries in most tissues of the body, except in the exercising skeletal muscles.

b. Increased pumping activity of the heart. Both heart rate and stroke volume increase in exercise, leading to tremendous increase in C.O.

c) There is mixed venoconstriction leading to a great increase in venous return.

The effects in a, b and c above are due to increased release of adrenaline and noradrenaline from the adrenal medulla.

When exercise is performed under tense conditions, the MAP can increase to as high as 170mmHg. The reason for such a high increase in blood pressure is that only a few muscles are used in this tense exercise situation and vasodilation occurs in only the few muscles that are active.

Increased oxygen delivery to the tissues: This is achieved by the combined effects of the following:

a) Increased pulmonary ventilation-The rate and depth of breathing is increased
b) Increased CO-This ensures that more blood gets to the tissues. The combined effect of a and b bring about an enormous increase in the O_2 load transported to the tissues.
c) At the tissue level, the following adjustments ensure increased O_2 delivery to the tissues.

i)More capillaries are open and the capillaries are dilated.

ii)The dilated vessels reduce the distance of diffusion between the capillary walls and the body cells.

iii)Because the muscle cells are very active,PO_2 inside them could be 15mmHg or less. Since arterial PO_2 is 97mmHg, the diffusion gradient for O_2 is increased and this leads to a more rapid diffusion of O_2 to the tissues.

Temperature regulation:

This is achieved through increased heat loss via the lungs {due to increased pulmonary ventilation} and the skin. Most of the heat produced in the body is generated in the deep organs, especially in the liver, brain, heart& skeletal muscles during exercise. This heat is transferred from the deeper organs and tissues to the skin, where heat is lost to the air and other objects in the surrounding of the body. The rate at which heat is lost is determined by two factors:

i) How rapidly the heat produced in the core of the body can be carried to the skin and
ii) How rapidly heat can be transferred from the skin to the surroundings.

Blood vessels are distributed profusely immediately beneath the skin. There is a continuous venous plexus beneath the skin that is supplied by inflow of blood from the skin capillaries. The rate of blood flow into the venous plexus can vary tremendously. When the vessels are fully dilated,30% of C.O can supply the skin. A high rate of blood flow to the skin causes heat to be conducted from the core of the body to the skin with great efficiency, whereas reduction in skin blood flow decreases heat transfer from the core to the skin.

The skin is therefore a well-controlled “heat radiator” system in which blood flow to the skin determines how much heat is transferred to the skin.