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ANSWERS TO THE ASSIGNMENT

1. LONG-TERM REGULATION OF MEAN ATERIAL BLOOD PRESSURE

There are several physiological mechanisms that regulate blood pressure in the long-term, the first of which is the renin-angiotensin-aldosterone system (RAAS).

- **Renin-Angiotensin-Aldosterone System (RAAS):** Renin is a peptide hormone released by the granular cells of the juxtaglomerular apparatus in the kidney. It is released in response to:
 - Sympathetic stimulation:
- ✓ Reduced sodium-chloride delivery to the distal convoluted tubule
- ✓ Decreased blood flow to the kidney
- ✓ Renin facilitates the conversion of angiotensinogen to angiotensin I which is then converted to angiotensin II using angiotensin-converting enzyme (ACE).

Angiotensin II is a potent vasoconstrictor. It acts directly on the kidney to increase sodium reabsorption in the proximal convoluted tubule. Sodium is reabsorbed via the sodium-hydrogen exchanger. Angiotensin II also promotes release of aldosterone. ACE also breaks down a substance called bradykinin which is a potent vasodilator. Therefore, the breakdown of bradykinin potentiates the overall constricting effect.

Aldosterone promotes salt and water retention by acting at the distal convoluted tubule to increase expression of epithelial sodium channels. Furthermore, aldosterone increases the activity of the basolateral sodium-potassium ATP-ase, thus increasing the electrochemical gradient for movement of sodium ions. More sodium collects in the kidney tissue and water then follows by osmosis. This results in decreased water excretion and therefore increased blood volume and thus blood pressure.

- Anti-Diuretic Hormone (ADH): Anti Diuretic Hormone (ADH) is released from the OVLT of the hypothalamus in response to thirst or an increased plasma osmolarity. ADH acts to increase the permeability of the collecting duct to water by inserting aquaporin channels (AQP2) into the apical membrane. It also stimulates sodium reabsorption from the thick ascending limb of the loop of Henle. This increases water reabsorption thus increasing plasma volume and decreasing osmolarity.
 Further control of blood pressure: Other factors that can affect long-term regulation of blood pressure are natriuretic peptides and these include;
 - Atrial natriuretic peptide (ANP) is synthesised and stored in cardiac myocytes. It is released when the atria are stretched, indicating of high blood pressure. ANP acts to promote sodium excretion. It dilates the afferent arteriole of the glomerulus, increasing blood flow (GFR). Moreover, ANP

inhibits sodium reabsorption along the nephron. Conversely, ANP secretion is low when blood pressure is low. Prostaglandins act as local vasodilators to increase GFR and reduce sodium reabsorption. They also act to prevent excessive vasoconstriction triggered by the sympathetic nervous and renin-angiotensin-aldosterone systems.

Clinical Relevance - Hypertension

Hypertension is defined as a sustained increase in blood pressure. It may be primary (of an unknown cause) or secondary to another condition such as chronic renal disease or Cushing's syndrome. It causes damage to the walls of blood vessels, making them weaker. This leads to a number of pathologies including atherosclerosis, thromboembolism and aneurysms.

2. a. <u>PULMONARY CIRCULATION</u>

Pulmonary circulation moves blood between the heart and the lungs. It transports deoxygenated blood to the lungs to absorb oxygen and release carbon dioxide. The oxygenated blood then flows back to the heart. Muscles in the vessels are not strong and there is also low pressure and resistance. **Pathway:** Oxygen-depleted blood from the body leaves the systemic circulation when it enters the right atrium through the superior and inferior vena cava. The blood is then pumped through the tricuspid valve into the right ventricle. From the right ventricle, blood is pumped through the pulmonary valve and into the pulmonary artery. The pulmonary artery splits into the right and left pulmonary arteries and travel to each lung. At the lungs, the blood travels through capillary beds on the alveoli where gas exchange occurs, removing carbon dioxide and adding oxygen to the blood. Gas exchange occurs due to gas partial pressure gradients across the alveoli of the lungs and the capillaries interwoven in the alveoli. The oxygenated blood then leaves the lungs through pulmonary veins, which returns it to the left atrium, completing the pulmonary circuit.

<u>Pulmonary Vessels:</u> The artery extends only 5cm beyond the apex of the right ventricle and then divides into right and left main branches that supply blood to the two respective lungs. The arteries are thin, with a wall thickness one third that of the aorta. The pulmonary arterial branches are very short, and all the pulmonary arteries, even the smaller arteries and arterioles, have larger diameters than their counterpart systemic arteries. The vessels are thin and distensible, giving the pulmonary arterial tree a large compliance, averaging almost 7ml/mmHg. This large compliance allows the pulmonary arteries to accommodate the stroke volume output of the right ventricle. The pulmonary veins, like the arteries are also short. They immediately empty their effluent blood into the left atrium, to be pumped by the left heart through the systemic circulation.

Bronchial Vessels: They are small bronchial arteries that originate from the systemic circulation, amounting to about 1-2% of the total cardiac output. They carry oxygenated blood, supply the supporting tissues of the lungs, including the connective tissue of the lungs, including that of the septa, and large and small bronchi. After these bronchial and arterial blood have passed through the supporting tissues, it empties into the pulmonary veins and enters the left atrium, rather than passing back to the right atrium.

Pressures in the pulmonary system include; pulmonary artery, right ventricular, left atrial and pulmonary capillary pressures.

Pulmonary circulation Superior vena cava Pulmonary artery Right lung Pulmonary veins Heart

DIAGRAM OF PULMONARY CIRCULATION

b. CIRCLE OF WILLIS

This is the movement of blood through the network of blood vessels to supply the brain. The circle of Willis is a ring of interconnecting arteries located at the base of the brain around the optic chiasm or chiasma, infundibulum of the pituitary stalk and the hypothalamus. The brain receives blood from the basilar artery and internal carotid artery. Venous drainage is by sinuses, which open into internal jugular vein. Normally, brain receives 750 to 800 mL of blood per minute. It is about 15% to 16% of total cardiac output and about 50 to 55 mL/100 g of brain tissue per minute.

Measurement of Cerebral blood flow:

- Kety and Schmidt nitrous oxide method
- <u>Using radioactive substances</u>: Radioactive substances method is used to determine the amount of blood flow to different regions of the cerebral cortex. Radioactive substance is injected into the carotid artery.
- <u>Computerized axial tomography</u>: is a process which combines many two dimensional X-ray images to generate cross sectional pictures of different organs or regions of the body. CT scan of brain is useful to determine brain damage and local changes in cerebral blood flow, while the subject performs a task.
- Regulation of cerebral blood flow: cererebral circulation is regulated by three factors:
- <u>Autoregulation</u>: Like any other vital organ, the brain also regulates its own blood flow. However, the autoregulation in brain has got its own limitations. It depends upon; effective perfusion pressure and cerebral vascular resistance.
- <u>Chemical factors</u>: O₂ and CO₂, hydrogen ion concentration.
- Neural factors

Clinical significance: Aneurysm, stroke, cerebral hemorrhage, ischaemic attack.

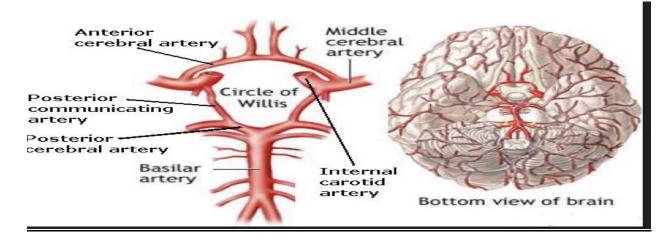


DIAGRAM OF THE CIRCLE OF WILLIS

a. **SPLANCHNIC CIRCULATION**

The splanchnic circulation is composed of gastric, small intestinal, colonic, pancreatic, hepatic, and splenic circulations, arranged in parallel with one another. It constitutes of three portions; mesenteric circulation supplying blood to GI tract, splenic circulation supplying blood to spleen and the hepatic circulation supplying blood to liver. The unique feature of splanchnic circulation is that the blood from mesenteric bed and spleen forms a major amount of blood flowing to liver. Blood flows to liver from GI tract and spleen through portal system.

<u>Mesenteric circulation</u>: the distribution of blood flow is as stomach: 35mL/100g/min, intestine:50 mL/100g/min and the pancreas:80mL/100g/min. Mesenteric blood flow is regulated by the following factors:

- Local Autoregulation (is the primary factor regulating blood flow through mesenteric bed)
- Activity of Gastrointestinal
- Nervous Factor (mesenteric blood flow is regulated by sympathetic nerve fibers)
- Chemical Factors ,,

Splenic circulation: the spleen is the main reservoir for blood. Due to the dilatation of blood vessels, a large amount of blood is stored in spleen. And the constriction of blood vessels by sympathetic stimulation releases blood into circulation. In the spleen, two structures are involved in storage of blood, namely splenic venous sinuses and splenic pulp. Small arteries and arterioles open directly into the venous sinuses. When spleen distends, sinuses swell and large quantity of blood is stored. Capillaries of splenic pulp are highly permeable. So, most of the blood cells pass through capillary membrane and are stored in the pulp. Venous sinuses and the pulp are lined with reticuloendothelial cells. Blood flow to spleen is regulated by sympathetic nerve fibers. Hepatic circulation: the liver receives blood from two sources; hepatic artery and the portal vein. It receives maximum amount of blood as compared to any other organ in the body since, most of the metabolic activities are carried out in the liver. Blood flow to liver is 1,500 mL/min, which forms 30% of the cardiac output. It is about 100 mL/100 g of tissue/min. Normally, about 1,100 mL of blood flows through portal vein and remaining 400 mL of blood flows through hepatic artery. However, portal vein carries only about 25% of oxygen to liver. It is because it

carries the blood, which has already passed through the blood vessels of GI tract, where oxygen might have been used. Hepatic artery transports 75% of oxygen to the liver. Blood flow to liver is regulated by the following factors; systemic blood pressure, splenic contraction, movements of intestine, chemical (e.g. excess CO₂, lack of O₂, increase in H⁺ ion concentration), nervous factors.

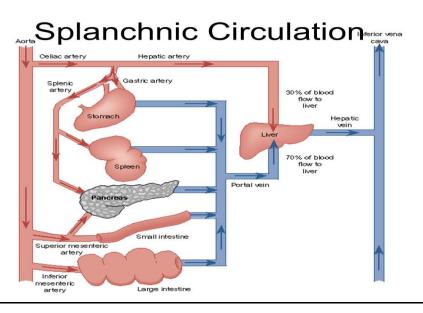


DIAGRAM OF SPLACHNIC CIRCULATION

b. CORONARY CIRCULATION

This is a part of the systemic circulatory system that supplies blood to and provides drainage from the tissues of the heart. Heart muscle is supplied by two coronary arteries, namely right and left coronary arteries, which are the first branches of aorta. 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. Coronary arteries divide and subdivide into smaller branches, which run all along the surface of the heart. Smaller branches are called epicardiac arteries and give rise to further smaller branches known as final arteries or intramural vessels. Final arteries run at right angles through the heart muscle, near the inner aspect of wall of the heart. Venous drainage from heart muscle is by 3 types of vessels; coronary sinus, anterior coronary veins, thebesian veins. The normal coronary blood flow in a resting human averages 70 ml/min/100g of the heart weight, or about 225ml/min, which is about 4-5% of the total cardiac output. Measurement of coronary blood flow is done by direct method and indirect. Factors regulating coronary blood flow include:

- Autoregulation: Like any other organ, heart also has the capacity to regulate its own blood flow.
- Metabolic Products: which increase the coronary blood flow.
- Nervous factors.

<u>Clinical significance:</u> Coronary artery disease, myocardial ischemia and necrosis.

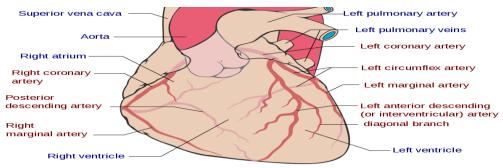


DIAGRAM OF CORONARY CIRCULATION

c. CUTANEOUS CIRCULATION

The cutaneous circulation is the circulation and blood supply of the skin. The skin is not a very metabolically active tissue and has relatively small energy requirements, so its blood supply is different to that of other tissues. Cutaneous blood flow performs functions such as; supply of nutrition to skin and the regulation of body temperature by heat loss.

Blood flow to the skin: Under normal conditions, the blood flow to skin is about 250 mL/m²/min. When the body temperature increases, cutaneous blood flow increases up to 2,800 mL/m²/min because of cutaneous vasodilatation.

Cutaneous Vascular response of the Skin

Vascular responses of the skin are the reactions developed in blood vessels of skin when mechanical stimulus is applied over the surface of it. There are namely two types of vascular responses of skin including the;

- i. White reaction: is the response of blood vessels in skin to a mechanical stimulus when the surface of skin is stroked lightly with a pointed object, with a pale line appearing within 20s. Maximum intensity of the line is obtained in 1 minute and it fades away after 5 minutes. White reaction is due to the contraction of precapillary sphincters and blood drains out of capillaries and small veins and there is usually no nervous factor involved in this process.
- ii. <u>Lewis triple response</u>: as discovered by Lewis Sir Thomas in 1927, it occurs when the skin is stroked more firmly with pointed objects and it includes three consecutive reactions of blood vessels to a mechanical stimulus. The three consecutive reactions are as follows:
 - Red reaction: is the appearance of a red line when a pointed instrument is drawn firmly over the surface of the skin as a result of the dilatation of capillaries due to mechanical stimulus with the reaction occurring over the line of the stroke. Its time of appearance is within 15s after the stroke, and it obtains the maximum intensity at the end of 1 minute and disappears later gradually. Red reaction does not depend upon nervous factors and there is a local release of bradykinin.
 - Flare: If the stroke is applied with little more force or if the stroke is repeated on the same line, the red reaction spreads around the line of stroke. It spreads for about 10 cm from the line of stroke, depending upon the force applied. This is called flare or spreading flush, flare appears within 30 seconds after appearance of red line and it is due to dilatation of arterioles. It depends upon nervous mechanism and is due to axon reflex. Axon reflex is a response elicited by peripheral nerve stimulation; attributed to impulses travelling proximally from the stimulation site along motor axons, encountering a branch point and then passing distally down the other branch to activate local arterioles or muscles.

• Wheal: When intensity of stimulus is severe, the surface of skin on the line of stroke is interrupted. A small elevation or swelling is seen in the surrounding area up to a height of 2 mm. It is called wheal or local edema and it appears within 3 minutes after the stimulus, replacing the red line. Maximum height is obtained within 5 minutes and it disappears after several hours. Wheal appears due to the leakage of fluid from capillaries and does not depend upon nervous mechanism.

<u>Clinical significance:</u> Cold vasodilation, reactive hyperemia, dermatographia (a striking triple response that occurs as an unusual reaction and is caused by anything drawn on the skin due to excessive release of histamine).

3. THE CARDIOVASCULAR ADJUSTMENT THAT OCCURS DURING EXERCISE

Exercising is an event that when it occurs, it leads to changes in the body system one of which is in the cardiovascular system. In order for the body system to complement whatever changes may have occurred, some physiologic events take place. The first is the activation of the sympathetic nervous system. During the course of the exercise, muscles are stretched and are activated via the mechanism of their contraction resulting in the transfer of signals to the medulla (in the brain). The vasomotor centre is initiated and causes a sympathetic discharge to stimulate the S-A node of the heart. The heart is stimulated to a greatly increased heart rate and increased pumping strength which it increases the cardiac output. The heart is stimulated to supply the increased blood flow required by the muscles while at the same time blood flow to most nonmuscular regions of the body, is temporarily reduced thereby lending blood to supply the muscles. It is important that the cardiac output is increased as sufficient cardiac output helps keep blood pressure at the levels needed to supply oxygen-rich blood and nutrients to the brain, vital organs and to the muscles during exercise.

Clinical Significance: Muscle pull.