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Question 1: Discuss the long-term regulation of mean arterial blood pressure

This is the rental mechanism for the regulation of blood pressure. It is called,"long-term" because it regulates the mean areterial blood pressure when the nervous mechanism loses sensitivity to alterations in pressure after it changes slowly over a long period. The kidneys regulate blood pressure by

1. Regulation of ECF volume: Increase in blood pressure causes excretion of large quantity of water in the urine excretion of excess amount of sodium in urine). These are called pressure diuresis and pressure natriuresis respectively. This action reduces blood and ECF volume, reducing blood pressure back to normal range. When reabsorption of water and sodium in the renal tubules is increased, it leads to increase in ECF and blood volume, leading to increase in blood pressure.
2. Renin-angiotensin mechanism: When ECF and blood pressure are reduced, renin is secreted from the kidneys and converts angiotensinogen to angiotensin 1. Angiotensin-converting enzyme(ACE) converts angiotensin1 to angiotensin 2, which does two things. The first is causing construction of arterioles leading to the increase in peripheral resistance, causing increase in blood pressure. It also constricts afferent arterioles in the kidney, leading to reduced glomerular filtration and retention of sodium and water, causing higher ECF, hence increasing blood pressure. The second effect of angiotensin 2 is triggering aldosterone release from the adrenal cortex,leading to reabsorption of sodium from the renal tubules, increasing water reabsorption and causing ECF increase, hence increasing blood pressure.

Question 2a: Write a short note on Pulmonary circulation

In the pulmonary circulation, blood is taken from the pulmonary artery, to its right and left branches which enter the lungs along with the primary bronchus to the capillary plexus in the lungs, where it is oxygenated. The lungs receive all the blood pumped out from the right ventricles(about 5L). This is emptied into the pulmonary veins, then taken to the left side of the heart. There's also a bronchial artery, arising from the the descending thoracic aorta that supplies the bronchi, connective tissue of the lungs. The lungs are drained by 2 bronchial veins from each lung. The veins from the right side drain into the azygos vein, while the vein from the left side drain into the superior hemiazygos or left superior intercostal veins.

Characteristics of pulmonary blood vessels

- Thin blood vessel wall
- Highly elastic
- Pulmonary capillaries are larger than systemic capillaries
- It carries blood at low pressure(low pressure bed). Systolic pressure is 25mmHg, diastolic pressure is 8mmHg hence mean arterial pressure is 16mmHg. Pulmonary capillary pressure stays around 7mmHg
- Has little vascular resistance
- Smooth muscle in the blood vessels aren't well developed
- Physiological shunt is present

Physiological shunt: This is a diversion through which venous and arterial blood are mixed. In pulmonary circulation, deoxygenated blood from bronchial circulation is carried into pulmonary veins without being oxygenated. This leads to venous admixture (mixing of oxygenated and deoxygenated blood). The fraction of venous blood which is not fully oxygenated is wasted blood. Physiological shunt is similar to physiological dead space in the sense that the former contains wasted blood and the latter contains wasted air. The normal shunt in the left side of the heart is about 1-5% of cardiac output. Abnormality may arise dues to acute pulmonary infections and bronchiectasis.

Regulation of pulmonary blood flow

- Cardiac output: There is a direct relationship between blood flow and cardiac output. Cardiac output is controlled by force of contraction, peripheral resistance, rate of contraction and venous return.
- Vascular resistance :This is inversely proportional with pulmonary blood flow. During inspiration, pulmonary vessels distend, reducing resistance and increasing blood flow.

The opposite happens during expiration. Drop in vascular resistance can also be due to exercise-induced hypoxia.

- Chemical factors: Lack of oxygen or excess carbon dioxide in the blood causes vasoconstriction. This directs blood from the part suffering hypoxia to the part that can still carry out gaseous exchange.
- Gravity and hydrostatic pressure: Blood pressure is higher in lower parts of the body than higher parts while standing, due to gravity. This applies to the lungs too. The topmost part is called the apical portion/Zone 1/area of zero blood flow). There, the pulmonary capillary pressure is very close to the alveolar pressure, allowing blood flow into the alveolar capillaries. However, if the pulmonary arterial pressure decreases or the alveolar pressure rises, the capillaries collapse, preventing blood flow into the alveoli. It is considered part of physiological dead space(ventilated but not perfused, hence higher ventilation:perfusion ratio). This makes the area more susceptible to tuberculosis, due to bacteria growth. In the second zone/mid portion/area of intermittent flow the alveolar pressure is lower than pulmonary systolic pressure but higher than diastolic pulmonary pressure, so when the heart is in systole, blood flow increases but decreases during diastole. The lowest part of the lung is the lower portion/zone 3/area of continuous blood flow, is where blood flows continuously because the pulmonary arterial pressure is higher than the alveolar pressure during both systole and diastole.

Question 2b: Write a short note on Circle of Willis

The Circle of Willis is a junction of several arteries at the bottom part of the brain. It helps blood flow from both the front and back sections of the brain. The brain recieves blood from the basilar artery and the internal carotid artery, which branches that give rise to the Circle of Willis. The arteries from the Circle of Willis traverse the brain to branch into pial arteries, which branch out into penetrating arteries and arterioles. It is therefore an important part of cerebral blood flow.

Measurement of cerebral blood flow

- Kety and Schmidt nitrous oxide method: This method is based on Fick's principle and makes use of nitrous oxide. Patient inhales the gas for 10 minutes, then concentration of gas in arterial blood and cerebral venous blood are used to find blood flow using this formula.

$$\text{Cerebral blood flow} = \frac{\text{Amount of } N_2O \text{ taken by brain}}{\text{Arteriovenous difference of } N_2O}$$

- Radioactive substances: Substances such as radioactive xenon are injected into the carotid artery and the radioactivity in the tissues is measured using a scintillation counter in order to determine blood flow to different parts of the brain.

Regulation of cerebral blood flow

- Autoregulation: The brain is capable of regulating its own blood flow but this depends on two things. The first is effective precision pressure; this is basically the same as mean arterial blood pressure as there's zero venous pressure in the brain. The second thing is cerebral vascular resistance; when the resistance is high, blood flow to the brain is lower. Resistance is controlled by intracranial pressure, cerebrospinal fluid pressure(increase in both cause lower blood flow) and viscosity of the blood(has inverse relationship with blood flow). Ischemia could result due to reduced blood flow, this is why Cushing reflex is important. It involves activation of the vasomotor center of the brain due to reduced blood flow, leading to peripheral vasoconstriction, hence higher arterial blood pressure and restoration of blood flow in the brain. This mechanism doesn't work if the intracranial pressure exceeds the arterial blood pressure . The brain volume doesn't change regardless of change in intracranial pressure or cerebrospinal fluid pressure. This is the Monro-Kellie principle.
- Chemical factors: The following factors can increase cerebral blood flow:decreased oxygen tension, reduced carbon dioxide tension, increased hydrogen ion concentration. Increased carbon dioxide tension and hydrogen concentration particularly , cause vasodilation.

- Nervous factors: These are only used in pathological conditions like hypertension, where cerebral blood vessels are constricted to reduce blood flow and prevent cerebral vascular hemorrhages and stroke.

Pathology:Stroke/Cardiovascular attack/CVA/Brain attack

This is the death of neurons in the Brian due to inadequate blood supply. It could cause paralysis that might either be temporary or permanent. It could be caused by heart disease, hypertension, high blood cholesterol, smoking, high sugar intake, etc. Symptoms include weakness, numbness of the body, speech impediment, loss of coordination and memory.

Types of stroke

- Ischemic: Interruption of blood flow due to a thrombus or embolus
- Hemorrhagic: Rupture of blood vessel in the brain

Question 2c:Write a short note on Splanchnic Circulation

Splanchnic circulation is also known as visceral circulation and consists of three portions

Mesenteric circulation(supplies blood to gastrointestinal tract):

The most amount of blood flow is to the pancreas while the least is to the stomach

Regulation

- Autoregulation
- Activity of Gastrointestinal tract: Contraction of the wall reduces blood flow while relaxation increases it.
- Nervous factor: Sympathetic nerves during fight or flight reactions cause vasoconstriction of mesenteric blood vessels to reduce blood flow to the GI(gastrointestinal)tract, so that more blood can be allocated to the brain, muscles and heart which need the blood more. Parasympathetic nerves don't directly affect the blood vessels but increases contraction of the GI tract, which compresses the blood vessels.

- Chemical factors: Hyperemia is the increase in mesenteric blood flow after food intake due to GI hormones, gastrin and cholecystokinin. The products of digestion trigger vasodilation, hence increasing mesenteric blood flow

Splenic circulation(supplying blood to spleen)

The spleen is important because it's the major reservoir of blood in the body. Blood is stored i the splenic venous sinuses and splenic pulp, which are both lines with reticuloendothelial cells. Blood enters the former when the spleen swells, from small arteries and arterioles. Blood enters the latter through their highly permeable membranes. Blood flow is regulated by sympathetic nerve fibers.

Hepatic circulation (supplying blood to the liver)

The liver receives blood from the hepatic artery and portal vein. The portal vein carries the most amount of blood from the heart, but less oxygen that's the hepatic artery as the blood it receives comes from the GI tract where exchanges have already been carried out. Together, the blood flow to liver is about 30% of cardiac output.

Regulation

- Systemic blood pressure: Hepatic blood flow is directly proportional to this.
- Splenic contraction:This increases blood flow to liver
- Movements of intestine: This increases blood flow
- Chemical factors:Vasodilators such as decrease in oxygen tension, and increased carbon dioxide tension and/or hydrogen ion concentration
- Nervous factors :Sympathetic fibers to the liver cause vasoconstriction and decrease blood flow.

Question 2d:Write a short note on Coronary Circulation

The right and left coronary arteries are the first branches of the aorta. The left artery supplies the anterior and lateral parts of the left ventricle, while the right artery supplies the right ventricle and the posterior part of the left ventricle. The branches stretch around the surface of the heart and are called epicardial arteries. They terminate as intramural arteries.

<u>Venous drainage</u>

- Coronary sinus: Drains 75% of blood from the heart. Drains blood from the left side of the heart into the right atrium.
- Anterior coronary vein: Drains blood from the right side of the heart into the right atrium.
- Thebesian veins: These veins drain blood from the myocardium into the corresponding part of the heart. Deoxygenated blood flowing from these veins into the cardiac chambers make up part of the physiological shunt.

<u>Coronary blood flow</u>

Coronary blood flow makes up 4% of cardiac output. It is measure by 4 methods:

- Direct method, using an electromagnetic flow meter.
- Fick's principle: Person inhales known quantity of nitrous oxide with atmospheric air. After a period of time, blood samples are collected from an artery and a coronary sinus. Blood flow is found with the following formula

$$\frac{\text{Amount of } N_2O \text{ taken up/minute}}{\text{Arteriovenous difference of } N_2O \text{ content}}$$

- Doppler's flow meter: This device has a probe that transmits and receives signals in the form of high frequency sound waves. The probe is placed at the opening of any of the coronary arteries to measure the velocity of flow of blood. Angiography is used to measure the cross sectional area of the blood vessel. Formula for blood flow= velocity of blood flow x cross sectional area of blood vessel.
- Video Densitometry: This technique measures both velocity of blood and cross sectional area of blood vessel.

Phasic changes in blood flow

When the heart contracts, intramural vessels are compressed, leading increase in blood pressure and drop in blood flow. This happens during systole in the left ventricle, countering the effect of rise in blood pressure in aorta. A similar thing also happens during isometric contraction, when intramural pressure is higher and aortic blood pressure is lower. During diastole, the vessels are decompressed so intramural blood pressure drops, increasing blood flow. However , towards the end of diastole, the blood flow drops due to decrease in aortic blood pressure. The right ventricle receives a small amount of blood during systole.

Factors regulating coronary circulation

- Oxygen: The need for oxygen increases blood flow to the heart via coronary vasodilation.
- Metabolic factors: Some metabolites have vasodilator effects. An example of adenosine, which is produced from the break down of ATP, then breakdown of ADP formed, in the muscles. Other such merabolites are potassium, hydrogen,carbon dioxide,etc.
- Coronary percussion pressure: The balance between mean arterial pressure and right atrial pressure. However, right atrial pressure is low, hence mean arterial pressure is the major factor influencing blood flow
- Nervous factors: Sympathetic and parasympathetic nervous system influence blood flow by their action in the heart. Sympathetic nerves increase rate and force of heart contraction, releasing vasodilator metabolites into the blood.

Coronary Heart Disease

This happens due to occlusion of the coronary artery/ies, either due to atherosclerosis(build up of cholesterol in the artery) that can lead to formation of an atherosclerotic plaques(formed from cholesterol, calcium and other substances). This plaque activates platelets leading to thrombosis. Fragments of the clot, called an embolus can detach from it and occlude smaller blood vessels(embolism). Occlusion of the coronary artery can lead to myocardial ischemia; a condition where the amount of oxygen reaching the heart muscles is very low. This could be resolved by the development of coronary collateral arteries. However, ischemia can lead to necrosis(cell or tissue death) if the damage is to a large part of the heart muscle or the occlusion involves many blood vessels. Necrosis is irreversible and can lead to a heart attack (myocardial infarction), which could cause death if ventricular fibrillation takes place. Symptoms of a heart attack include: chest pain, vomiting, palpitations , nausea, difficult breathing, weakness, and anxiety. If necrosis doesn't occur, myocardial stunning may take place. This only happens when there's a mild reduction in blood flow, and only ischemia occurs, and causes short term disturbance of the heart.

Cardiac pain/Angina pectoris

This is chest pain that is caused by myocardial infarction. It starts form below the sternum and stretches to the left arm and shoulder. It is due to metabolites and pain producing substances like substance P, stimulating sensory nerve endings. These substances are washed away if hypoxia of the hypothalamus is relieved. It can be chronic, arising from increased work load of the heart due to strenuous activity.

Sensory pathway: Inferior cervical sympathetic nerve fibers carry sensations of pain from the heart to the posterior gray horn of the first 4 thoracic segments of spinal cord and they synapse with the second order neurons of the lateral spinothalamic tract which is formed from fibers of the substantial gelatinosa of Rolando. These fibers reach the sensory cortex via thalamus.

Treatment

1. Drugs such as vasodilator drugs, calcium channel blockers, and sympathetic blocking agents. All these drugs primarily reduce workload on the heart.
2. Thrombolysis: This is the dissolution of a blood clot,especially as induced artificially by infusion of an enzyme into the blood.
3. Surgery: This could be a coronary bypass surgery, or a coronary angioplasty.

Question 2e: Write a short note on Cutaneous Circulation

Cutaneous circulation is important for the supply of nutrients to the skin and for regulation of temperature. Blood flow to the skin increase by about 10x normal blood flow during rise in temperature.

Arterioles reach the base of dermal papillae, then give rise to meta-arterioles from which capillary loops arise. These project an arterial limb that ascends vertically in the papillae, before turning and descending as a venous limb. Many venous limbs form a collecting venule, which anastomoses with another to form the subpapillary venous plexus. This drains into deep vein.

Regulation

This is done by the hypothalamus. Increase in temperature cause the it to trigger vasodilation of the blood vessels, increasing blood flow and promoting heat loss through the skin. When the temperature is lower than normal body temperature, vasoconstriction occurs to limit heat loss.

Vascular Reactions of the skin

- White reaction: Vasoconstriction of the cutaneous capillaries happens when the skin is lightly touched with a pointed object, creating a white line. This has nothing to do with the nervous system.
- Lewis Triple response : Named after Lewis Sir Thomas, who discovered that the reactions of skin to injuries happen in three reactions. First is the red reaction which happens due to dilation of cutaneous capillaries, when a pointed object is drawn across the skin firmly. It happens due to the release of 'H' substance from damaged tissues. When the stroke is more stronger, the red reaction spreads, causing a flare/spreading flush, due to dilation of arterioles. Unlike red reaction, it happens due to a nervous mechanism known as axon reflex, where the impulses move in a direction opposite from where they are supposed to. In the case of flare, the impulses move from pain receptors in the skin to sensory fibers to blood vessels (triggering dilation) instead of ending up at the posterior nerve root ganglion. A wheal forms if the stimulus is intense, leading to raised skin due to fluid leaking from the capillaries(local edema)

Question 3: Discuss the cardiovascular adjustment that occurs during excersise

During exercise, there's a rise in body's need for nutrients and oxygen due to higher rate of metabolism. There's also a need to maintain temperature for this reason. There are two types of exercise

- Dynamic exercise: This type of exercise involves movement of the joints and muscles, as well as external work. It leads to an increase in cardiac output, systolic pressure, heart rate and force of contraction. Examples include swimming.
- Static exercise: This doesn't involve joint movement, hence there's no external work. Unlike in dynamic exercise, diastolic pressure increases due to increase in peripheral resistance.

In terms of oxygen use, exercise could be aerobic or anaerobic. Exercise usually starts off as anaerobic for the first 3-5 minutes, when glycogen from the muscles is burned, before glycogen in the liver is used anaerobically, for about 20 minutes

- Aerobic excersise: This type of excersise low intensity work done for long time periods. Glycogen in the liver is oxidized to release energy, then body fat is used. Examples include running
- Anaerobic exercise: This involves high intensity exercise for short periods followed by rest, and burns glycogen from the muscles, without oxygen, causing fatigue due to lactic acid accumulation. These are endurance exercises such as push-ups, planks, etc.

<u>Effects of exercise on cardiovascular system</u>

- Blood pH is decreased due to increased carbon dioxide concentration in blood. Red blood cell(RBC) count increases due to erythropoietin release from the kidneys due to hypoxia. High RBC count along with increased water loss(due to sweating in order to regulate temperature) leads to hemoconcentration, dehydration and reduced blood blood volume.

- Heart rate: This increases during exercise due to reduction of vagal tone that starts even before the exercise(due to impulses going from the cerebral cortex and medullary centers of the brain), as well as increase in sympathetic tone. Proprioceptors in the muscles also play a role in sending impulses to the brain. Higher carbon dioxide tension triggers the medullary, while higher temperatures stimulate the hypothalamus and sinoatrial node of the heart. Catecholamines are secreted in large quantities into the blood during exercise.
- Cardiac output: This increases due to reduced vagal tone, that increases sympathetic activity. Heart rate and force of contraction increase for this reason, increasing stroke volume. The higher the amount of oxygen breathed in by the body, the higher the cardiac output
- Increased blood flow to muscles: This happens due to sympathetic nerve fibers (sympathetic cholinergic fibers)causing vasodilation in the muscles. Other factors include hypoxia, potassium ions,etc. However, blood flow stops when the muscles contract , but it resumes when they relax again.
- Blood pressure:There's an increase in systolic blood pressure due to higher heart rate. However, diastolic pressure only increases during isometric contraction, due to higher peripheral resistance. Otherwise, it reduces or doesn’t change at all. After exercise, blood pressure increases because the metabolites produced cause vasodilation.