MSCU GROUP DISCUSSION ANSWERS TO ASSORTED PHYSIOLOGY ESSAYS FOR LEVEL 2

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5. Describe the regulation of blood pH

The normal blood pH is regulated between 7.35-7.45. Buffers, respiratory system and the kidneys are the key players in regulation of blood Ph. Buffers are molecules that take in or release ions in order to maintain H+ ion concentration at a certain level .Buffers in the blood include hemoglobin and phosphates and the carbonic acid bicarbonate buffer which are the first line of defense whenever sudden changes in blood pH occur. When blood becomes acidic, buffers mop up the excess H+ ions that are lowering the Ph levels. Lack of H+ ions leads to the blood becoming too basic and so the buffer release H+ ions. The hemoglobin protein can bind reversibly to hydrogen ions. The phosphate buffer only plays a minor role in the blood, however, because H_3PO_4 and $H_2PO_4^-$ are found in very low concentration in the blood. By far the most important buffer for maintaining acid-base balance in the blood is the carbonic-acid-bicarbonate buffer.

Buffers therefore maintain the blood Ph by either sacrificing or accepting H+ ions as necessary to maintain the number of free H+ ions in the blood. Another regulator of blood ph is the respiratory system where lungs are largely involved. When blood ph goes too low this is Corrected by hyperventilation while hypoventilation is used to lower ph in cases where blood ph has raised above 7.6. The basis of these mechanisms lies in the following equations;

HCO3 + H^+ ⇨ H2CO3 CO2 + H2O ……NOTE both reactions are reversible

The amount of CO2 expelled from the blood depends on how quickly you breathe. Hyperventilation will allow more CO2 to be passed from the bloodstream into the air and will therefore lower the level of CO2 in the blood. Hence no enough CO2 to react backwards to from H+ ions. So Ph is maintained by removal of H+ ions by the hydrogen carbonate buffer with the assurance that H+ ions won't be remade as the CO2 concentration was reduced by hyperventilation. Another regulator of blood PH are the kidneys. The kidneys can remove both H+ and HCO3 from the blood through various ways. About 85 percent of the basic HCO3 ions pass into the filtrate, but are selectively reabsorbed into the bloodstream depending on the blood Ph ,hence through the ability of renal system to determine the amount of the base to be reabsorbed in maintains blood ph. The HCO3 that remains in the tubule reacts with H+ ions secreted from the blood into the filtrate and passes out of the body as part of urine. Meanwhile another base Hydrogen phosphate also passes into filtrate. This allows the body to add unwanted H+ ions into the tubule since the hydrogen ions will react with hydrogen phosphate ions and leave the hydrogen carbonate ions to be reabsorbed at will. This further aids reabsorption of HCO3 ions hence raising the blood ph when need arises. Also the amino acid glutamine is held in the cells between the tubule and bloodstream and can be broken down by the body into acidic ammonium and basic hydrogen carbonate. Ammonium is secreted into the tubule and passed out as urine while HCO3 is moved into the bloodstream. This mechanism also helps to raise blood ph. Ammonium levels in urine can be used to detect respiratory acidosis.

6. Discuss the process of absorption and digestion of lipids

(a) Digestion.

Most fat digestion begins in the duodenum, pancreatic lipase being one of the most important enzyme. Though ebner glands secrete lingual lipase and the stomach secrets a lipase too they are of little quantitative significance for lipid digestion other than in the setting of pancreatic insufficiency. Now the pancreatic lipase in the duodenum hydrolyses the 1~ and 3~ bonds of the triglycerides with relative ease but acts on the 2~ bonds at a very low rate so the principal products of its action are free fatty acids and 2~monoglycerides. It acts on fats that have already been emulsified. Its activity is facilitated when an amphipathic helic that covers the active site is bent back. Colipase a protein also part of pancreatic juice binds a to ~COOH terminal domain of pancreatic lipase facilitating opening of the lid.colipase is secreted in an inactive from and is activated in the instestinal lumen by trypsin.colipase is also essential in the action of pancreatic lipase because it allows the lipase to remain associated with droplets of dietary lipids even in presence of bile acids. cholesterol esterase is another enzyme in the pancreatic juice that is activated by bile acids ,it catalyses hydrolysis of cholesterol esters,esters of fat soluble vitamins and phospholipids as well as tryglcerides .fats are relatively insoluble which limits their ability to cross the unstrirred layer and reach the surface of mucosal cells however they are finely emulsified in the small intestines by the detergent action of bile acids and monoglycerides .when concentration of bile acids is high lipids and bile acids interact to form micelles. These micelles solubilizes lipids and enable their transport to enterocytes.thus micelles move down their concentration gradient through unstirred layer to the brush border of mucosal cells .lipids collect in the micelles, with cholesterol in the hydrophobic centers ,phospholipids and monoglycerides lined up with their hydrophilic heads on the outside and hydrophobic tails in the centre.

(b) Absorption.

Inside the intestinal cells lipids are rapidly esterified, maintaining a favorable concentration gradient from the lumen into the cells.there are also carries that exert certain lipids back to the lumen like the cholesterol.the fate of fatty acids in the enterocytes depends on their size . Fatty acids with less than 10 to 12 carbon atoms are water soluble enough that they pass through the enterocytes unmodified and are actively transported into the portal blood.they circulate as free fatty acids .the fatty acids containing more than 10 to 12 are insoluble hence they undergo re-esterification to
tryglicerides in the enterocytes.in addition some cholesterol absorbed is esterified .they are then coated with a layer of protein,cholesterol and phospholipid to form chylomicrons that leave the cell and enter lymphatics because they are too large to pass through the junctions between capillary endothelial cells.in mucosal cells most triglycerides are formed by acylation of absorbed 2 monoglycerides ,primarily in the smooth endoplasmic reticulum .some triglycerides are made from glycerophosphate a product of glucose metabolism. Glycerophosphate is coverted to glycerophospholipid that participate in chylomicron formation that are extruded by exocytosis.

7. Discuss the upper gastrointestinal motility (i.e. mouth, esophagus and stomach)

Gut motility is the movement of food substances across the gastrointestinal tract. Motility grinds, mixes, and fragments ingested food to prepare it for digestion and absorption, and then it propels the food along the gastrointestinal tract. All of the contractile tissue of the gastrointestinal tract is smooth muscle, *except* for that in the pharynx, the upper one third of the esophagus, and the external anal sphincter, which is skeletal striated muscle. The smooth muscle of the gastrointestinal tract is **unitary smooth muscle,** in which the cells are electrically coupled via low-resistance pathways called **gap junctions**. Gap junctions permit rapid cell-to-cell spread of action potentials that provide for coordinated and smooth contraction. The circular and longitudinal muscles of the gastrointestinal tract have different functions. When circular muscle contracts, it results in shortening of a ring of smooth muscle, which decreases the diameter of that segment. When longitudinal muscle contracts, it results in shortening in the longitudinal direction, which decreases the length of that segment.
Contractions of gastrointestinal smooth muscle can be either phasic or tonic.
Phasic contractions are periodic contractions followed by relaxation. They are found in the esophagus, gastric antrum, and small intestine, all tissues involved in mixing and propulsion.
Tonic contractions maintain a constant level of contraction or tone without regular periods of relaxation. They are found in the orad (upper) region of the stomach and in the lower esophageal, ileocecal, and internal anal sphincters**.**
Upper gut motility covers the following;

(a) Mouth
Motility in the oral cavity is divided into mastication and swallowing.

- ***Mastication***- This is a behavioral semi-reflex which involves chewing and breaking down food substances into smaller particles. It is mediated by skeletal muscles of mastication such as masseter, temporalis, medial pterygoid and lateral pterygoid. The teeth, tongue and cheeks are also involved in the same. Proprioceptive receptors in the palate and muscles along with sensory receptors in oral mucosa are involved in determining the extent of mastication and the texture of the food bolus. The rhythmic jaw centers are controlled by the brainstem. It increases surface area of food substances which favors contact with digestive enzymes. It also allows mixing of food with saliva to allow chemical digestion of starch. It also helps in lubrication, moistening and formation of a food bolus.
- ***Swallowing (deglutition) -*** This is reflexly coordinated by the swallowing centres. It occurs in 3 phases;
  (1) Oral phase-This is initiated when the tongue forces a bolus of food back towards the pharynx, which contains many somatosensory receptors which then initiates voluntary swallowing reflex in the medulla via vagus and glossopharyngeal nerves (both afferent) and effected by pharyngeal muscles and upper esophageal muscles.

(2) Pharyngeal phase- Bolus is propelled from mouth to esophagus through the pharynx. The soft palate is pulled upwards, creating a narrow passage for food to move into the pharynx so that food can't reflux in nasopharynx. The epiglottis then covers the laryngeal opening and the upper esophageal sphincter relaxes allowing food to pass from pharynx to esophagus. Peristalsis is initiated in pharynx and breathing is inhibited.

(b) Esophagus

It begins with the esophageal phase of swallowing. This is controlled by both the ENS and swallowing reflex. Food is propelled through esophagus to stomach. Swallowing reflex opens upper esophageal sphincter in reception of food and closes it once bolus has passed through it to prevent reflux. A primary peristaltic wave coordinated by the swallowing reflex travels down propelling food. If it doesn't clear food, a secondary peristaltic wave, mediated by ENS, is initiated by the continued distention of the esophagus and travels downwards mediated by ENS. Temporary interruption of breathing occurs.

Successive contraction of the esophageal constrictor muscles aids in peristalsis. Distention of the wall of esophagus by a food bolus causes a reflex relaxation ahead of the bolus. Stretch releases serotonin which activates myenteric nerves. Cholinergic nerves behind bolus release substance P and acetylcholine which causes muscle contraction behind the bolus. Cholinergic neurons ahead of bolus activate neurons that secrete NO, VIP and ATP producing relaxation in front of the bolus. When in upright position, gravity contributes to the same. Lower esophageal sphincter opens mediated by peptidergic vagal fibres that release VIP as their neurotransmitter producing relaxation of smooth muscles of the sphincter. The orad region of stomach relaxes (receptive relaxation) allowing food to enter into stomach after which lower esophageal sphincter contracts.

(c) Stomach

The stomach has three muscle layers (outer longitudinal, the middle circular, and the inner oblique muscles.) Its surface area is increased by the rugae, plicae circulares. After receptive relaxation occurs to allow food entry from esophagus into stomach (up to 1.5 litres), mechanical digestion occurs; with the sphincters closed the contents are mixed with gastric juice, and to further reduce bolus size. Different foods have different gastric emptying time. After a liquid meal, the **gastric emptying time** is around 2 hours and 40 minutes. After a solid meal, the **gastric emptying time** is around 4 hours and 15 minutes. Fats, acids and amino acids strongly inhibit the gastric emptying time. When the gastric emptying time is reached, stomach wall contractions initiated by parasympathetic system begin to propel food from fundus to pylorus as the contractions grow gradually strong. The pyloric sphincter relaxes allowing food to move from stomach to small intestine. The migratory motor complex occurs every 90 minutes during fasting or inter-digestive period and begins from the stomach towards distal ileum to clear the digestive tract.

9. Write an essay on the renal counter-current mechanism.

Countercurrent mechanisms in the kidney help to create and maintain an osmotic gradient to reabsorb water from tubular fluid so as to produce a concentrated urine. The mechanisms are divided into; countercurrent multiplication and countercurrent exchange.

Countercurrent multiplication in the kidneys is the process of using energy to generate an *osmotic gradient* that enables the kidneys to reabsorb water from the tubular fluid and produce concentrated urine. This mechanism prevents one from producing litres and litres of dilute urine every day, and is the reason why one doesn't need to be continually drinking in order to stay hydrated. The kidneys contain two types of nephrons, superficial cortical nephrons (70-80%) and juxtamedullary nephrons (20-30%). While the loops of Henle of cortical nephrons penetrate only as far as the outer medulla of the kidney, those of the juxtamedullary nephrons penetrate deeply within the inner medulla. Although both cortical and juxtamedullary nephrons regulate the concentrations of solutes and water in the blood, *countercurrent multiplication in the loops of Henle of juxtamedullary nephrons* is largely responsible for developing the osmotic gradients that are needed to concentrate urine. The three segments of the loops of Henle have different characteristics that enable countercurrent multiplication.

- The *thin descending* limb is **passively permeable** to both water and small solutes such as sodium chloride and urea. As active reabsorption of solutes from the ascending limb of the loop of Henle increases the concentration of solutes within the interstitial space, water and solutes move down their concentration gradients until their concentrations within the descending tubule and the interstitial space have equilibrated. As such, water moves out of the tubular fluid and solutes to

move in. This means, the tubular fluid becomes steadily more concentrated or hyperosmotic (compared to blood) as it travels down the thin descending limb of the tubule.

- The *thin ascending* limb is **passively permeable** to small solutes, but impermeable to water, which means water cannot escape from this part of the loop. As a result, solutes move out of the tubular fluid, but water is retained and the tubular fluid becomes steadily more dilute or hyposmotic as it moves up the ascending limb of the tubule.
- The *thick ascending* limb actively reabsorbs sodium, potassium and chloride. This segment is also **impermeable to water**, which again means that water cannot escape from this part of the loop. This segment is sometimes called the "**diluting segment".**

Countercurrent multiplication moves sodium chloride from the tubular fluid into the interstitial space deep within the kidneys. Although in reality it is a continual process, the way the countercurrent multiplication process builds up an osmotic gradient in the interstitial fluid can be thought of in two steps:

1. *The single effect.* The single effect is driven by active transport of sodium chloride out of the tubular fluid in the thick ascending limb into the interstitial fluid, which becomes hyperosmotic. As a result, water moves passively down its concentration gradient out of the tubular fluid in the descending limb into the interstitial space, until it reaches equilibrium.
2. *Fluid flow.* As urine is continually being produced, new tubular fluid enters the descending limb, which pushes the fluid at

higher osmolarity down the tube and an osmotic gradient begins to develop.

As the fluid continues to move through the loop of Henle, these two steps are repeated over and over, causing the osmotic gradient to steadily multiply until it reaches a steady state. The length of the loop of Henle determines the size of the gradient - the longer the loop, the greater the osmotic gradient.

Countercurrent exchange- Absorbed water is returned to the circulatory system via the vasa recta, which surrounds the tips of the loops of Henle. The specialized blood capillary network (the vasa recta) that surrounds the loops are equally important. The vasa recta capillaries are long, hairpin-shaped blood vessels that run parallel to the loops of Henle. The hairpin turns slow the rate of blood flow, which helps maintain the osmotic gradient required for water reabsorption. Because the blood flow through these capillaries is very slow, any solutes that are reabsorbed into the bloodstream have time to diffuse back into the interstitial fluid, which **maintains** the solute concentration gradient in the medulla.

The concentration of urine is controlled by antidiuretic hormone, which helps the kidneys to conserve water. Its main effects in the renal tubules is to increase water permeability in the late distal tubule and collecting ducts, increase active transport of sodium chloride in the thick ascending limb of the loop of Henle, and enhance countercurrent multiplication and urea recycling, all of which increase the size of the osmotic gradient.

Urea recycling- urea recycling in the inner medulla also contributes to the osmotic gradient generated by the loops of Henle. Antidiuretic hormone increases water permeability, but not urea permeability in the cortical and outer medullary collecting ducts, causing urea to concentrate in the tubular fluid in this segment. In the inner medullary collecting ducts it increases both

water and urea permeability, which allows urea to flow passively down its concentration gradient into the interstitial fluid. This adds to the osmotic gradient and helps drive water reabsorption.

10. Describe and explain the mechanisms of the micturition reflex

- Filling

As the bladder fills since urine is continuously being formed, it collects at the base of the ureters then due to peristaltic waves in the ureters, urine is forced into the urinary bladder.

The backflow of urine is prevented by the horizontal course and the valvular arrangement of the openings into the urinary bladder.

The bladder fills drop by drop with little rise in intravesical pressure.

Although the urinary bladder may hold up to 1,000 ml of urine, micturition usually occurs long before that volume is attained. When 200 to 400 ml of urine has accumulated in the urinary bladder, sensory stretch receptors in the urinary bladder wall are usually stimulated and they trigger the micturition reflex.

Filling occurs due to the contraction of the external urethral sphincter which is supplied by the somatic pudendal nerves(S2,S3,S4), with sympathetic contraction of the inner urethral sphincter. The sympathetic nervous system also enables the detrusor to distend without reflex contractions, unlike that which happens in most voluntary muscles.

- Stretch receptors

They are present in the urinary bladder and the posterior urethra and stimulate afferent signals to the spinal cord

- Afferent impulses

These afferent impulses are transmitted through the pelvic nerve- nervous erigentes.

- Motor efferent impulses -parasympathetic

This supplies the detrusor muscle causing it to contract and supplies the internal urethral sphincter causing it to relax.

- Inhibition of the pudendal nerves

This occurs since the pudendal nerves cause contraction of the external urethral sphincter which would prevent voiding of urine.

- Regeneration

Once a micturition reflex begins, it is "self-regenerative." That is, initial contraction of the bladder activates the stretch receptors to cause a greater increase in sensory impulses from the bladder and posterior urethra, which causes a further increase in reflex contraction of the bladder; thus, the cycle is repeated again and again until the bladder has reached a strong degree of contraction. Then, after a few seconds to more than a minute, the self-regenerative reflex begins to fatigue and the regenerative cycle of the micturition reflex ceases, permitting the bladder to relax.

Once a micturition reflex has occurred but has not succeeded in emptying the bladder, the nervous elements of this reflex usually remain in an inhibited state for a few minutes to 1 hour or more before another micturition reflex occurs. As the bladder becomes more and more filled, micturition reflexes occur more and more often and more and more powerfully. Once the micturition reflex becomes powerful enough, it causes another reflex, which passes through the pudendal nerves to the external sphincter to inhibit it. If this inhibition is more potent in the brain than the voluntary constrictor signals to the external sphincter, urination will occur. If not, urination will not occur until the bladder fills still further and the micturition reflex becomes more powerful

- Influence from higher centers

The micturition reflex is an autonomic spinal cord reflex, but it can be inhibited or facilitated by centers in the brain. These centers include : strong facilitative and inhibitory centers in the brain stem, located mainly in the pons, and several centers located in the cerebral cortex that are mainly inhibitory but can become excitatory.

The higher centers normally exert final control of micturition as follows:

1. The higher centers keep the micturition reflex partially inhibited, except when micturition is desired.
2. The higher centers can prevent micturition, even if the micturition reflex occurs, by tonic contraction of the external bladder sphincter until a convenient time presents itself.

3. When it is time to urinate, the cortical centers can facilitate the sacral micturition centers to help initiate a micturition reflex and at the same time inhibit the external urinary sphincter so that urination can occur.

Voluntary urination is usually initiated in the following way: First, a person voluntarily contracts his or her abdominal muscles, which increases the pressure in the bladder and allows extra urine to enter the bladder neck and posterior urethra under pressure, thus stretching their walls. This stimulates the stretch receptors, which excites the micturition reflex and simultaneously inhibits the external urethral sphincter. Ordinarily, all the urine will be emptied, with rarely more than 5 to 10 milliliters left in the bladder.

11. Write an essay on water and electrolyte absorption in the GIT.

The GI system secretes nearly 8L of fluid into the GI tract which is combined with the nearly 2L of ingested fluid; however, only a 0.1-0.2L of fluid is excreted in the feces. Therefore, the GI system must absorb nearly 9L of fluid, composed of water and electrolytes, each day. Water and electrolyte absorption primarily occurs in the small and large intestines. Deregulation of this absorption can either lead to diarrhea or constipation.

- Water absorption

  Water is always absorbed in the alimentary tract through passive osmosis via a mostly paracellular route between enterocyte tight junctions. Consequently, water absorption is primarily actuated by active absorption of osmotic electrolytes, especially sodium. In cases where a high concentration of unabsorbable solutes remain in the GI lumen, water cannot be reabsorbed and thus causes an osmotic diarrhea.

- Sodium absorption

Overview

Luminal membrane Na^+ resorption occurs via a number of symporters and antiporters throughout the small and large intestines. In all cases, the luminal membrane resorption is powered by a sodium-potassium ATPase on the basolateral enterocyte membrane. This sodium-potassium ATPase actively transports Na^+ past the basolateral membrane, thus reducing intracellular Na^+ concentration, which subsequently creates an electrochemical gradient for inward Na^+ transport on the luminal membrane.

Duodenum and Jejunum:

Luminal resorption occurs on a variety of Na-Nutrient symporters, which include monosaccharides (Glucose and Galactose) in which Glucose and Galactose are transported by secondary active transport via Na^+-Glucose or Na^+-Galactose symporters. The energy for this resorption is provided by a sodium-potassium ATPase on the basolateral membrane of small intestine enterocytes which reduces the cytosolic concentration of Na^+ inside the cells and thus drives luminal resorption of sodium along with monosaccharides. , as well as amino acids, dipeptides, and tripeptides, are transported, by secondary active transport past the enterocytes luminal membrane by a variety of symporters. Once inside the enterocyte any dipeptides and tripeptides are cleaved to form individual amino acids by a variety of cytosolic peptidases. Individual amino acids are then passively transported past the basolateral membrane and into the blood. The end result of protein digestion is the production of single amino acids or dipeptides and tripeptides which are amenable to epithelial absorption. These mechanisms of sodium resorption are constitutively active and are not physiologically regulated.

Large Intestine

Na^+ absorption in the large intestine is very similar to that occurring in the Principal Cells during late distal tubule and collecting duct transport. Briefly, diffusion of Na^+ through luminal

membrane ion channels is powered by a basolateral sodium-potassium ATPase. As in the late distal tubule and collecting duct aldosterone significantly enhances sodium resorption in the large intestine by increasing expression of the basolateral sodium-potassium ATPase and luminal Na^+ ion channels.

- Chloride absorption

Absorption of Cl^- largely occurs through passive diffusion via a paracellular route. Substantial resorption of Na^+ may create a lumen negative charge, thus creating a strong electrochemical gradient for passive resorption of Cl^-. The majority of chloride is absorbed in the small intestine, especially the duodenum and jejunum.

- Bicarbonate absorption

A large amount of bicarbonate is secreted during pancreatic secretion and maintenance of proper acid-base balance requires that some must be absorbed. A CO_2 molecule is converted to H^+ and HCO_3^- by carbonic anhydrase in the enterocytes. The HCO_3^- is transported past the basolateral membrane while the H^+ is transported into the intestinal lumen on an Na^+-H^+ Antiporter. The H^+ probably then combines with luminal bicarbonate, and is then converted to CO_2 which then diffuses into the blood and is breathed off by the respiratory system. The net effect is resorption of a bicarbonate ion.

- Calcium absorption

Calcium ions are actively absorbed into the blood, especially from the duodenum, and the amount of calcium ion absorption is exactly controlled to supply the daily need of the body for calcium. One important factor controlling calcium absorption is parathyroid hormone secreted by the parathyroid glands, and another is vitamin D. Parathyroid hormone activates vitamin D, and the activated vitamin D in turn greatly enhances calcium absorption.

- Iron absorption

Iron is absorbed from all parts of the small intestine, mostly by the following mechanism. The liver secretes moderate amounts of apotransferrin into the bile, which flows through the bile duct into the duodenum. Here, the apotransferrin binds with free iron and also with certain iron compounds, such as hemoglobin and myoglobin from meat, two of the most important sources of iron in the diet. This combination is called transferrin. It, in turn, is attracted to and binds with receptors in the membranes of the intestinal epithelial cells. Then, by pinocytosis, the transferrin molecule, carrying its iron store, is absorbed into the epithelial cells and later released into the blood capillaries beneath these cells in the form of plasma transferrin.

- Potassium , magnesium and phosphate absorption

Potassium, magnesium, phosphate, and probably still other ions can also be actively absorbed through the intestinal mucosa. In general, the monovalent ions are absorbed with ease and in great quantities. Conversely, bivalent ions are normally absorbed in only small amounts; for example, maximum

absorption of calcium ions is only 1/50 as great as the normal absorption of sodium ions. Fortunately, only small quantities of the bivalent ions are normally required daily by the body.

12. Explain the mechanism of lung inflation and deflation and why in pneumothorax, lung inflation is not possible.

(a) Lung inflation

This is an increase in the volume of the lungs which occurs during inspiration. During quiet breathing, the diaphragm contracts to increase the thoracic volume for the lungs to occupy during inflation. The external intercostal muscles also help in this mechanism. During forced inspiration, accessory muscles of inspiration such as sternocleidomastoid and scalene help in increasing further the thoracic cavity volume. The ribs move upwards and outwards while the sternum moves upwards along with the ribs. These events lead to an increase in thoracic volume with a corresponding decrease in pressure as compared to atmospheric pressure thus facilitating lung inflation with air. The dorsal respiratory group of neurons in the medulla control inspiration, during which the apneustic centre of pons prevents inspiration turn off. The rate of inspiration and the volume of inspiration depends on several factors including volume of oxygen and carbon iv oxide in blood,as well as cortical influence. Important to note is the Herring Breuer reflex in limiting the degree of inspiration and prevents over inflation of the lungs. In infants, this reflex plays a role in regulating basic rhythm of breathing and prevents over inflation of lungs but in adults its important only when tidal volume is large >1L as in exercise. In this mechanism, pulmonary stretch receptors present in smooth muscles of the airways respond to excessive stretch of lung during large inspirations and send action potentials through vagus to medullary inspiratory centre and pons apneustic center. Inspiratory centre is inhibited directly and apneustic centre indirectly. The volume of air inspired during normal breathing (tidal volume) is about 500ml. During forced inspiration, an additional 3000 ml of air is inspired. Restrictive diseases such as pulmonary fibrosis reduce lungs compliance (ability of the lung to expand against its elastic properties). This leads to reduced capacity of the lung during inflation. Thus ultimately reducing the functional residual capacity and residual volume of the lung.

(b) Lung deflation

This is a decrease in the volume of the lungs which occurs during expiration. During quiet breathing, the diaphragm relaxes to reduce the thoracic volume while increasing pressure which forces air out of the lungs. The internal intercostal muscles, elastic recoil of lungs and elastic recoil of thoracic cavity also help in this mechanism. During forced expiration, accessory muscles of expiration such as rectus abdominis and oblique abdominis muscles help in decreasing further the thoracic cavity volume while increasing its pressure. The ribs move downwards and inwards while the sternum moves downwards along with the ribs. These events lead to an decrease in thoracic volume with a corresponding increase in pressure as compared to atmospheric pressure thus facilitating lung deflation as air is expired. The ventral respiratory group of neurons in the medulla control inspiration, during which the apneustic centre of pons prevents expiration turn off. The volume of air expired during normal breathing (tidal volume) is about 500ml. During forced expiration, an additional 1100 ml of air is expired.

Obstructive diseases such as asthma increases resistance to expiration thus increasing the residual volume and the functional residual capacity of the lung.

(c) Pneumothorax

A **pneumothorax** is an abnormal collection of air in the pleural space between the lung and the chest wall. It's often called collapsed lung. A pneumothorax can also be caused by physical trauma to the chest or as a complication of healthcare intervention, in which case it is called a traumatic pneumothorax. Normally the lungs are fully inflated within the cavity because the pressure inside the airways is higher than the pressure inside the pleural space. Despite the low pressure in the pleural space, air does not enter it because there are no natural connections to an air-containing passage, and the pressure of gases in the bloodstream is too low for them to be forced into the pleural space. Therefore, a pneumothorax can only develop if air is allowed to enter, through damage to the chest wall or damage to the lung itself, or occasionally because microorganism in the pleural space produce gas. Under normal conditions, lungs are filled with air when negative pressure is created by expanding the chest and thoracic cavity and air is sucked in through the nose or mouth. The pressure in the bronchial tube is greater than the alveoli sacs deeper in the lungs. A chest wound often breaks the vacuum seal of the chest surrounding the lungs (pneumothorax). The lack of a sealed chest prevents creating a vacuum when the chest expands. The leak often causes the lungs to collapse under the weight and pressure of surrounding muscles, bones and connective tissue. Breathing fails because the air cannot get pulled into the lungs. When air collects in the pleural space, the intrapleural pressure increases thus inhibiting lung inflation.

14. Discuss the enteric nervous system under the following subheadings;

(a) Anatomical location

The ENS consists of some about 100 million neurons, one-thousandth of the number of neurons in the brain, and about one-tenth the number of neurons in the spinal cord. The enteric nervous system is embedded in the lining of the gastrointestinal system, beginning in the esophagus and extending down to the anus.

The neurons of the ENS are collected into two types of ganglia: myenteric (Auerbach's plexus) and submucosal (Meissner's plexus). Myenteric plexuses are located between the inner and outer layers of the muscularis externa, while submucosal plexuses are located in the submucosa**.** The myenteric plexus is mainly organized as a longitudinal chains of neurons.

(b) Components

The enteric nervous system includes efferent neurons, afferent neurons, and interneurons, all of which make the enteric nervous system capable of carrying reflexes and acting as an integrating center in the absence of CNS input. For instance, the sensory neurons report mechanical and chemical conditions, while the motor neurons control peristalsis and the churning of intestinal contents through the intestinal muscles. Other neurons control the secretion of enzymes. The enteric nervous system also makes use of more than 30 neurotransmitters, most of which are identical to the ones

found in the CNS, such as acetylcholine, dopamine, and serotonin. More than 90% of the body's serotonin is in the gut, as well as about 50% of the body's dopamine. In addition, the ENS contains support cells that are similar to the astroglia of the brain, as well as a diffusion barrier around the capillaries that surround the ganglia, which is similar to the blood–brain barrier of the cerebral blood vessels. The neurons of the ENS are collected into two types of ganglia:

1. The myenteric (Auerbach's) plexus, located between the inner and outer layers of the muscularis externa. The myenteric plexus is mainly organized as a longitudinal chains of neurons.
2. The submucosal (Meissner's) plexus, located in the submucosa

(c) Its role in digestive Physiology

The enteric nervous system has been described as a second brain. There are several reasons for this. For instance, the enteric nervous system can operate autonomously; can operate independently of the brain and the spinal cord. It normally communicates with the central nervous system (CNS) through the parasympathetic (e.g., via the vagus nerve) and sympathetic (e.g., via the paravertebral ganglia) nervous systems. The enteric nervous system has the capacity to alter its response depending on factors such as bulk and nutrient composition.

The myenteric plexus increases the tone of the gut and the velocity and intensity of contractions. The submucosal plexus is involved with local conditions and controls local secretion, absorption, and muscle movements. When stimulated, the myenteric plexus increases the tone of the gut as well as the velocity and intensity of its contractions. This plexus is concerned with motility throughout the whole gut. Inhibition of the myenteric system helps to relax the sphincters. The submucosal plexus is more involved with local conditions and controls local secretion and absorption, as well as local muscle movements. The mucosa and epithelial tissue associated with the submucosal plexus have sensory nerve endings that feed signals to both layers of the enteric plexus. These tissues also send information back to the sympathetic pre-vertebral ganglia, the spinal cord, and the brain stem.

The enteric nervous system can be regulated by the parasympathetic and sympathetic divisions. The parasympathetic nervous system is able to stimulate the enteric nerves in order to increase enteric function. The parasympathetic enteric neurons function in defecation and provide a rich nerve supply to the sigmoid colon, the rectum, and the anus. Conversely, stimulation of the enteric nerves by the sympathetic nervous system will inhibit enteric function and capabilities. Neurotransmitter secretion and direct inhibition of the enteric plexuses cause this stall in function. If the gut tract is irritated or distended, afferent nerves will send signals to the medulla of the brain for further processing. The enteric nervous system also functions through the gastrointestinal reflexes. For instance, short reflexes to the digestive system provide shortcuts for the enteric nervous system (ENS) to act quickly and effectively, and form a sort of digestive brain. It reacts to digestive movement and chemical changes.

(d) Name one congenital defect nervous system malformation associated with the enteric

Hirschsprung disease- This is a birth defect in which enteric nerve cells are missing in the GIT tract. This is due to failure of migration of neural crest cells to the gastrointestinal tract during the fetal development. This defect causes blockages in the bowel because the stool does not move through the bowel normally.
Most often, the areas missing the nerve cells are the rectum and the sigmoid colon. However, in some cases, the nerve cells for the entire colon or part of the small intestine.

- In short-segment Hirschsprung disease, nerve cells are missing from the last part of the large intestine.
- In long-segment Hirschsprung disease, nerve cells are missing from most or all of the large intestine and sometimes the last part of the small intestine.
- Rarely, nerve cells are missing in the entire large and small intestine.

In a child with Hirschsprung disease, stool moves through the bowel until it reaches the part lacking nerve cells. At that point, the stool moves slowly or stops.

(e) Embryonic origin of the enteric nervous system.

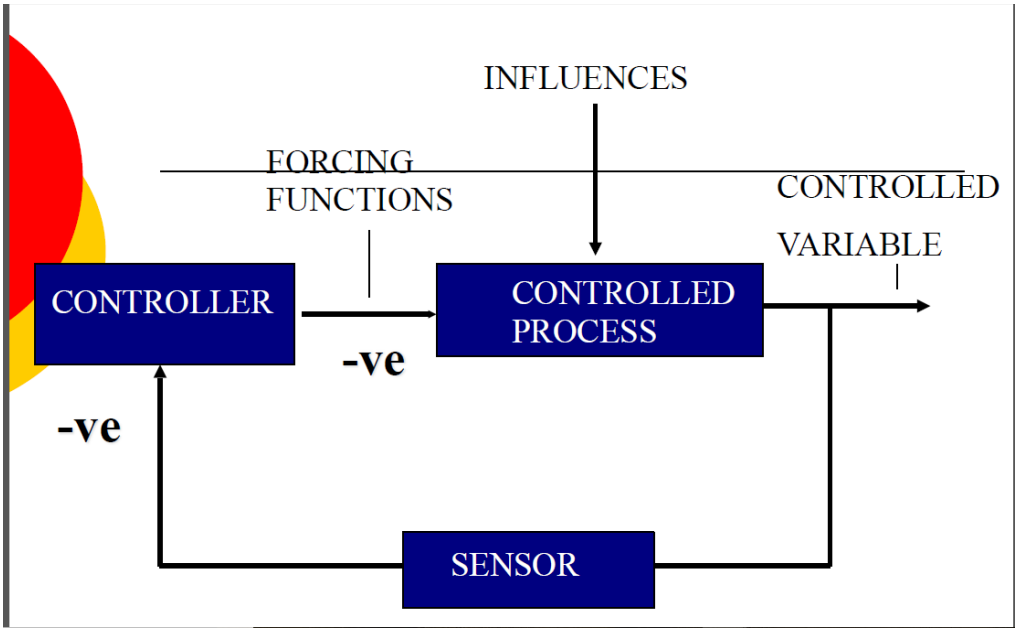
The neurons and glial cells of the enteric nervous system (ENS) are derived from the neural crest. Neural crest cells migrate to the developing gut. Vagal neural crest cells initially migrate into the foregut splanchnic mesoderm of the developing gastrointestinal tract, these cells then migrate caudally along the gut into the midgut. A second population of sacral neural crest cells have been identified as migrating into the region of the hindgut. During and following colonization of the gut by neural crest cells, massive proliferation of neural crest cells occurs, followed by differentiation into glial cells or into one of the many different types of enteric neurons
.

16. Write an essay on control of ventilation under the following headings.

a. The need for control.

The main goals of the respiratory control system: 1. Rate of alveolar ventilation sufficient to maintain the normal level of blood gases. 2. Changes in alveolar ventilation rate sufficient to acclimatize changing environments or metabolic needs e.g. jogging. 3. Adaptability to allow other activities such as talking or eating which share anatomical structures with the lung.

b. The theoretical control model



c. Control centers.

1. Medullary respiratory center. Is located in the reticular formation a. dorsal respiratory group - Is primarily responsible for inspiration and generates the basic rhythm for breathing. b. Ventral respiratory group - Is primarily responsible for expiration. - Is not active during normal quiet breathing when expiration is passive. - Is activated for example during exercise when expiration becomes an active process. 2. Apneustic center is located in the lower pons and it stimulates inspiration producing a deep and prolonged inspiratory gasp. 3. Pneumotaxic center is located in the upper pons and inhibits inspiration therefore regulating inspiratory volume and respiratory rate.

4. Cerebral cortex Breathing can be under voluntary control therefore a person can voluntarily hyperventilate or hypo ventilate.

d. The sensors

1. Central chemoreceptors in the medulla. They are sensitive to the pH of the csf. Decreases in the pH of the csf produces increases in breathing rate. 2. Peripheral chemoreceptors in the carotid and aortic bodies. Are sensitive to: a. Decreases in arterial PO2 - Stimulates peripheral chemoreceptor and cause increased breathing rate. B. Increases in arterial PCO2 - Stimulate peripheral chemoreceptors causing increased breathing rate. c. Increases in arterial H+ 3. Lung stretch receptors. Stimulated by distension of the lungs producing a reflex decrease in breathing frequency (Herring Breuer reflex). 4. Irritant receptors. Stimulated by noxious substances eg. Dust and pollen. 5. Juxtacapillary receptors. Engorgement of the pulmonary capillaries such as that may occur with left heart failure stimulates J receptors which then cause rapid shallow breathing. 6. Joint and muscle receptors. Activated during movement of limbs and involved in early stimulation of breathing during exercise.

e. The respiratory drives.

1. Hypercapnic ventilatory drive Hypercapnic drive is rise in arterial carbon dioxide more than normal, which is detected directly by peripheral chemoreceptors stimulating hyper ventilation. It is also detected

by central chemoreceptors by dissolving in the CSF combining with water molecules to form weak carbonic acid which is dissociated to bicarbonate and hydrogen ions in the presence of carbonic anhydrase. The hydrogen ions results to drop in pH of CSF which is detected by central chemoreceptors and interpreted as increased carbon dioxide in arterial blood stimulating hyper ventilation. 2. Hypoxic drive. Is a form of respiratory drive in which the body uses oxygen chemoreceptors instead of carbon dioxide receptors to regulate the respiratory cycle.

f. Response to exercise.

Parameter	Response
Oxygen consumption	Increase
Carbon iv oxide consumption	Increase
Ventilation rate	Increase
Arterial PO2 and PCO2	No change
Arterial pH	No change in moderate exercise
Venous PCO2	Increase
Pulmonary blood flow	Increase

20. Describe the pressure volume cycle of the human left ventricle under the following subheadings:

a) Ventricular filling

b) Isovolumetric contraction

c) Ventricular ejection

d) Isovolumetric relaxation

e) Heart Sound

A. Ventricular Filling

This occurs in three phases:

1. Rapid Ventricular Filling Phase - The ventricular pressure has

to a level lower than the left atrial pressure causing the mitral valve to open. The left ventricle fills with blood from the left atrium and the ventricular volume increases while pressure is low and constant. Lasts for about 0.11 seconds.

2. Diastasis - The ventricles relax and pressure increases slightly causing the final phase of ventricular filling. Lasts for about 0.19 seconds.

3. Last Rapid Filling Phase

It occurs due to atrial systole. The atria contract and push a small amount of blood into the ventricles. This is referred to as atrial kick.

B. Isovolumetric Contraction

This is the first phase of ventricular systole. It lasts for 0.05 second. There is an increase in tension, without any change in the length of muscle fibres. The atrio-ventricular valves are closed due to increase in pressure. The semilunar valves are already closed. The ventricle contract without change in volume causing a rapid increase in pressure. Thus causes the popping' opening of the semilunar valves.

C. Ventricular Ejection

Due to opening of the semilunar valves and contraction of the ventricle, blood is ejected out. This lasts for 0.22 seconds. It occurs in two phases, Rapid ejection (0.13sec) and slow ejection (0.09sec).

D. Isovolumetric Relaxation

This is decrease in tension without any change in the length of muscle fibres. All the valves are closed and the ventricle relaxes without change in volume or length of muscle fibres. This causes a decrease in intra ventricular pressure. It lasts 0.08 seconds.

E. Heart Sounds

1st Heart sound - Caused by the closure of the atrio-ventricular valves at the beginning of isovolumetric contraction. It coincides with the QRS complex in the electrocardiogram.

2nd Heart sound - Caused by the closure of semilunar valves in the beginning of ventricular diastole.

3rd Heart sound - Caused by the rushing of blood into the ventricles during Rapid Filling phase.

4th Heart sound - Caused by the contraction of atrial musculature during the end of the ventricular filling. It coincides with the P wave in the electrocardiogram.

21. DISCUSS THE MECHANISM OF RENAL EXCRETION OF DILUTE AND CONCENTRATED URINE.

Normal kidneys have tremendous capability to vary the relative proportions of solutes and water in the urine in response to various challenges. When there is excess water in the body and body fluid osmolarity is reduced, the kidney can excrete urine with an osmolarity as low as 50 mOsm/L.

•When there is a deficit of water and extracellular fluid osmolarity is high, the kidney can excrete urine with a concentration of 1200 to 1400 mOsm/L.

•There is a powerful feedback system for regulating plasma osmolarity and sodium concentration that operates by altering renal excretion of water independently of the rate of solute excretion. A primary effector of this feedback is antidiuretic hormone (ADH), also called vasopressin.

•LOOPS OF HENLE OF JUXTA MEDULLARY NEPHRONS establish hyperosmolality of interstitium of medulla. They are called COUNTER CURRENT MULTIPLIERS

•VASA RECTA maintain hyperosmolality established by counter current multipliers. They are called COUNTER CURRENT EXCHANGERS

•The medullary blood flow is low, accounting for less than 5 per cent of the total renal blood flow. This sluggish blood flow is sufficient to supply the metabolic needs of the tissues but helps to minimize solute loss from the medullary interstitium.

•The vasa recta serve as countercurrent exchangers, minimizing washout of solutes from the medullary interstitium unlike the cortical nephrons.

Urea has a major role in the concentration of urine. The renal countercurrent mechanisms are further expounded below;

Countercurrent mechanisms in the kidney help to create and maintain an osmotic gradient to reabsorb water from tubular fluid so as to produce a concentrated urine. The mechanisms are divided into; countercurrent multiplication and countercurrent exchange.

Countercurrent multiplication in the kidneys is the process of using energy to generate an osmotic gradient that enables the kidneys to reabsorb water from the tubular fluid and produce concentrated urine. This mechanism prevents one from producing litres and litres of dilute urine every day, and is the reason why one doesn't need to be continually drinking in order to stay hydrated. The kidneys contain two types of nephrons, superficial cortical nephrons (70-80%) and juxtamedullary nephrons (20-30%). While the loops of Henle of cortical nephrons penetrate only as far as the outer medulla of the kidney, those of the juxtamedullary nephrons penetrate deeply within the inner medulla. Although both cortical and juxtamedullary nephrons regulate the concentrations of solutes and water in the blood, countercurrent multiplication in the loops of Henle of juxtamedullary nephrons is largely responsible for developing the osmotic gradients that are needed to concentrate urine. The three segments of the loops of Henle have different characteristics that enable countercurrent multiplication.

- The thin descending limb is passively permeable to both water and small solutes such as sodium chloride and urea. As active reabsorption of solutes from the ascending limb of the loop of Henle increases the concentration of solutes within the interstitial space, water and solutes move down their concentration gradients until their concentrations within the descending tubule and the interstitial space have equilibrated. As such, water moves out of the tubular fluid and solutes to move in. This means, the tubular fluid becomes steadily more concentrated or hyperosmotic (compared to blood) as it travels down the thin descending limb of the tubule.

- The thin ascending limb is passively permeable to small solutes, but impermeable to water, which means water cannot escape from this part of the loop. As a result, solutes move out of the

tubular fluid, but water is retained and the tubular fluid becomes steadily more dilute or hyposmotic as it moves up the ascending limb of the tubule.

- The thick ascending limb actively reabsorbs sodium, potassium and chloride. This segment is also impermeable to water, which again means that water cannot escape from this part of the loop. This segment is sometimes called the "diluting segment".

Countercurrent multiplication moves sodium chloride from the tubular fluid into the interstitial space deep within the kidneys. Although in reality it is a continual process, the way the countercurrent multiplication process builds up an osmotic gradient in the interstitial fluid can be thought of in two steps:

1. The single effect. The single effect is driven by active transport of sodium chloride out of the tubular fluid in the thick ascending limb into the interstitial fluid, which becomes hyperosmotic. As a result, water moves passively down its concentration gradient out of the tubular fluid in the descending limb into the interstitial space, until it reaches equilibrium.

2. Fluid flow. As urine is continually being produced, new tubular fluid enters the descending limb, which pushes the fluid at higher osmolarity down the tube and an osmotic gradient begins to develop.

As the fluid continues to move through the loop of Henle, these two steps are repeated over and over, causing the osmotic gradient to steadily multiply until it reaches a steady state. The length of the loop of Henle determines the size of the gradient - the longer the loop, the greater the osmotic gradient.

Countercurrent exchange- Absorbed water is returned to the circulatory system via the vasa recta, which surrounds the tips of the loops of Henle. The specialized blood capillary network (the vasa recta) that surrounds the loops are equally important. The vasa recta capillaries are long, hairpin-shaped blood vessels that run parallel to the loops of Henle. The hairpin turns slow the rate of blood flow, which helps maintain the osmotic gradient required for water reabsorption. Because the blood flow through these capillaries is very slow, any solutes that are reabsorbed into the bloodstream have time to diffuse back into the interstitial fluid, which maintains the solute concentration gradient in the medulla.

The concentration of urine is controlled by antidiuretic hormone, which helps the kidneys to conserve water. Its main effects in the renal tubules is to increase water permeability in the late distal tubule and collecting ducts, increase active transport of sodium chloride in the thick ascending limb of the loop of Henle, and enhance countercurrent multiplication and urea recycling, all of which increase the size of the osmotic gradient.

Urea recycling- urea recycling in the inner medulla also contributes to the osmotic gradient generated by the loops of Henle. Antidiuretic hormone increases water permeability, but not urea permeability in the cortical and outer medullary collecting ducts, causing urea to concentrate in the tubular fluid in this segment. In the inner medullary collecting ducts it increases both water and urea permeability, which allows urea to flow passively down its concentration gradient into the interstitial fluid. This adds to the osmotic gradient and helps drive water reabsorption.

22. Write an essay on cardiovascular control mechanisms under the following headings;

a) Need for control

Conditions in the cardiovascular system need to be maintained within normal physiological range for instance during exercise. Thus it is necessary to control parameters such as heart rate and blood pressure through homeostasis.

b) Neural mechanisms of control

Consists of three components;

1. *Afferent nerve fibres*- from the heart baroreceptors and chemoreceptors. They carry information to the central nervous system.
2. *Vasomotor centre*- located in the brainstem (medulla/pons). Has 3 parts all controlled by the cerebral cortex and hypothalamus.
   (a). *Vasodilator area- cardioinhibitory as it causes vasodilation thus decreasing heart rate.*
   (b). Vasoconstriction area- cardioaccelerator area as it causes vasoconstriction and increases heart rate.
   (c). Sensory area- gets afferent from baroreceptors and chemoreceptors then controls vasodilator and vasoconstrictor centres.

3. Efferent nerve fibres- from the central nervous system to the heart. Sympathetic innervation to the heart comes from T1-T4 segments of the spinal cord while parasympathetic comes via the vagus nerve to the right sinoartrial node and left atrioventricular node.

(c) Hormonal mechanisms of control

Epinephrine and norepinephrine

Atrial natriuretic peptide

(d) Renal mechanism of control

The renin-angiotensin-aldosterone system (RAAS) plays an important role in regulating blood volume and systemic vascular resistance, which together influence cardiac output and arterial pressure.

Renin, which is released primarily by the kidneys, stimulates the formation of angiotensin in blood and tissues, which in turn stimulates the release of aldosterone from the adrenal cortex.

The release of renin is stimulated by:

- Sympathetic nerve activation (acting through β_1-adrenoceptors)
- Renal artery hypotension (caused by systemic hypotension or renal artery stenosis)
- Decreased sodium delivery to the distal tubules of the kidney.

When renin is released into the blood by granular juxtamedullary cells, it acts upon a circulating substrate, **angiotensinogen**, that undergoes proteolytic cleavage to form **angiotensin I**. Vascular

endothelium, particularly in the lungs, has an enzyme, **angiotensin converting enzyme (ACE)**, that cleaves off two amino acids to form the **angiotensin II**, although many other tissues in the body (heart, brain, vascular) also can form Angiotensin II.

Angiotensin II acts on the adrenal cortex to release **aldosterone** which causes the renal tubules to increase the reabsorption of sodium and water into the blood, while at the same time causing the excretion of potassium (to maintain electrolyte balance). This increases the volume of extracellular fluid in the body, which also increases blood pressure. It also stimulates thirst centres in the hypothalamus, stimulates secretion of ADH, and stimulates release of epinephrine and norepinephrine while inhibiting their re-uptake.

Therapeutic manipulation of this pathway is very important in treating hypertension and heart failure.

ACE inhibitors, angiotensin II receptor blockers and aldosterone receptor blockers, for example, are used to decrease arterial pressure, ventricular afterload, blood volume and hence ventricular preload, as well as inhibit and reverse cardiac and vascular hypertrophy

25. Describe the pressure volume loop of the left ventricle for a single cardiac cycle.

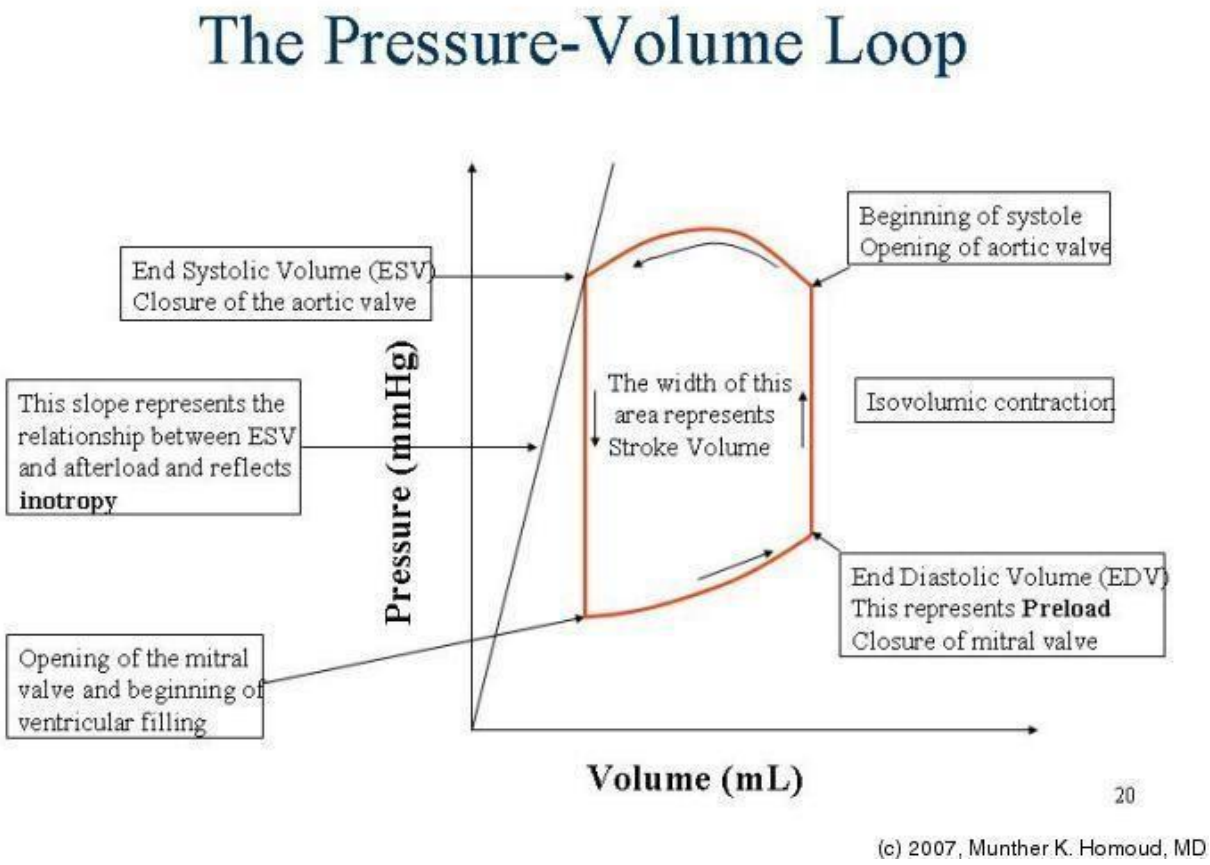
Left ventricular pressure-volume (PV) loops are derived from pressure and volume information found in the cardiac cycle diagram (upper panel of figure). To generate a PV loop for the left ventricle, the left ventricular pressure (LVP) is plotted against left ventricular volume (LV Vol) at multiple time points during a complete cardiac cycle. When this is done, a PV loop is generated.

To illustrate the pressure-volume relationship for a single cardiac cycle, the cycle can be divided into four basic phases: ventricular filling (phase a; diastole), isovolumetric contraction (phase b; systole), ejection (phase c; systole), and isovolumetric relaxation (phase d; diastole). Point 1 on the PV loop is the pressure and volume at the end of ventricular filling (diastole), and therefore represents the end-diastolic pressure and end-diastolic volume (EDV) for the ventricle. As the ventricle begins to contract isovolumetrically (phase b), the mitral valve closes and the LVP increases, but the LV volume remains the same, therefore resulting in a vertical line (all valves are closed). Once LVP exceeds aortic diastolic pressure, the aortic valve opens and ejection (phase c) begins. During this phase the LV volume decreases as LVP increases to a peak value (peak systolic pressure) and then decreases as the ventricle begins to relax. When the aortic valve closes, ejection ceases and the ventricle relaxes isovolumetrically - that is, the LVP falls but the LV volume remains unchanged, therefore the line is vertical (all valves are closed). The LV volume at this time is the end-systolic (i.e., residual) volume (ESV). When the LVP falls below left atrial pressure, the mitral valve opens and the ventricle begins to fill. Initially, the LVP continues to fall as the ventricle fills because the ventricle is still relaxing. However, once the ventricle is fully relaxed, the LVP gradually increases as the LV volume increases. The width of the loop represents the difference between EDV and ESV, which is by definition the stroke volume (SV). The area within the loop is the ventricular stroke work.

Ventricular filling occurs along the end-diastolic pressure-volume relationship (EDPVR), or passive filling curve for the ventricle. The slope of the EDPVR is the reciprocal of ventricular compliance. Therefore, changes in ventricular compliance alter the slope of the passive filling curve. For example, in ventricular hypertrophy the ventricle is less compliant (i.e., it is stiffer)

and therefore the slope of the filling curve in increased. This results in higher pressures during filling at a given ventricular volume. Another example of how the EDPVR can be altered is when a ventricle chronically dilates (remodels) as occurs in dilated cardiomyopathy or in valve disease. A dilated ventricle has a higher passive compliance and therefore the slope of the filling curve is reduced. This results in lower ventricular pressures during filling at any given ventricular volume. The maximal pressure that can be developed by the ventricle at any given left ventricular volume is defined by the end-systolic pressure-volume relationship (ESPVR), which represents the inotropic state of the ventricle. The slope and x-intercept of the ESPVR is generated experimentally by occluding the inferior vena cava (IVC), which reduces venous return to the heart (see figure). This decreases ventricular preload (EDV) and causes the PV loop to shift to the left and get smaller over several heart beats; decreased preload causes a reduction in SV (loop width). Peak systolic pressure (loop height) also decreases because arterial pressure falls as the cardiac output declines during IVC occlusion. Therefore, afterload is decreased along with the preload. The ESPVR is determined by the line intersecting the upper left corners of the loops. A linear relationship generally occurs within a narrow range of pressures and volumes (several beats). After several seconds the ESPVR becomes non-linear with a steeper slope as baroreflexes increase ventricular inotropy. It is important to note that the pressure-volume loop cannot cross over the ESPVR because that relationship defines the maximal pressure that can be generated at a given inotropic state.

The end-diastolic and end-systolic pressure-volume relationships are analogous to the passive and total tension curves used to analyze muscle function.



27. Discuss the structure, properties and functions of cell membrane.

Structure:

Phospholipids are a main component of the cell membrane.These are lipid molecules made up of a phosphate head and two fatty acid tails. The properties of phospholipid molecules allow them to spontaneously form a double-layered membrane. When in water or an aqueous solution, which includes the inside of the body, the hydrophilic heads of phospholipids heads will orient themselves to be on the outside, while the hydrophobic tails will be on the inside. The technical term for this double layer of phospholipids that forms the cell membrane is a phospholipid bilayer. Eukaryotic cells which make up the bodies of all organisms except bacteria and archaea, also have a nucleus that is surrounded by a phospholipid bilayer membrane.

In addition, the cell membrane contains glycolipids and sterols. One important sterol is cholesterol, which regulates the fluidity of the cell membrane in animal cells. When there is less cholesterol, membranes become more fluid, but also more permeable to molecules. The

amount of cholesterol in the membrane helps maintain its permeability so that the right amount of molecules can enter the cell at a time, not too many not too few.

The cell membrane also contains many different proteins. Proteins make up about half of the cell membrane. Many of these proteins are transmembrane proteins, which are embedded in the membrane but stick out on both sides. Some of these proteins are receptors which bind to signal molecules, while others are ion channels which are the only means of allowing ions into or out of the cell. Scientists use the **fluid mosaic model** to describe the structure of the cell membrane. The cell membrane has a fluid consistency due to being made up in large part of phospholipids, and because of this, proteins move freely across the surface. The multitude of different proteins and lipids in the cell membrane give it the look of a mosaic

Properties:

-**Amphipathic**; possession of both hydrophilic and hydrophobic properties makes it an amphipathic molecule.

-**Semipermeable**; the membrane is selectively permeable, allowing substances to pass through it and excluding others. However its permeability can also be varied because it contains numerous regulated ion channels and other transport proteins that can change the amounts of substances moving across it.

-**Sensitivity to pH**; the cell membrane is made up of a high percentage of protein molecules and thus pH change affects the nature of the proteins and hence the membrane

-**Sensitive to temperature**; the membrane being made up of proteins will be sensitive to temperatures that are not optimum range of temperatures.

-**Sensitive to electrical impulse**; the membrane contains various ion channels and they are responsible for the electrical excitability of the cells, and they mediate most of the electrical signaling in the nervous system.

Functions:

- Mechanical structure
  -Defense/encloses the cell
  -Cytoskeleton
  -Extracellular matrix
  -Protection
- Permeability for material exchange
- Active transport
- Bulk transport
  -Exocytosis and endocytosis
- Markers and signaling
  (For communication with other cells & external environment)
- Metabolic activities

31. Describe the similarities and differences of pulmonary and systemic blood circulation under the following subheadings;

(a) Systolic and diastolic blood pressure

Generally, pulmonary blood pressure is normally a lot lower than systemic blood pressure. This is because of the musculature of the left ventricle as compared to the right ventricle. This adaptation for systemic is based on the distance covered, having to circulate through the whole body as compared to the lungs which is just one organ. Normal pulmonary artery pressure is 8-20 mm Hg at rest while for systemic being around 100mmHg. If the pressure in the pulmonary artery is greater than 25 mm Hg at rest or 30 mmHg during physical activity, it is abnormally high depicting pulmonary hypertension. Venous blood pressure for systemic circulation is lower than in pulmonary; having a value of 2mmHg as compared to pulmonary with a value of 6mmHg venous blood pressure. Pulmonary blood pressure is at 25mmHg systolic pressure and 8mmHg diastolic pressure. Systolic systemic blood pressure always ranges around 100mmHg while diastolic ranges around 80mmHg.
However both must carry blood flow volume equivalent to cardiac output since the cardiac output for both are almost equivalent; with 6.0 L/min for systemic and 5.9L/min for pulmonary. Pulmonary system is able to accommodate this blood flow despite small blood pressure due to decreased vascular resistance that occurs after pulmonary capillaries open further during lung dilation.
Pulmonary system has a higher compliance compared to systemic circulation. Thus during increased blood pressure, pulmonary circulation is able to reduce resistance by distending the already present blood vessels to increase their caliber and recruiting more blood vessels which open up markedly. Additionally, pulmonary arterioles have much less smooth muscle than systemic arterioles and, thus, pulmonary arterioles generate much less resistance than systemic arterioles. The resistance created by systemic smooth muscles is essential to increase blood pressure so that blood may reach peripheral tissues. Due to this, the resistance in systemic circulation is higher at a value of 16.3 P/Flow while pulmonary has 1.7 P/flow.

(b) Oncotic pressure

- The critical capillary opening pressure of a pulmonary capillary is considerable less than that of a systemic capillary. This is because the metarterioles and precapillary sphincters in the pulmonary circuit have less smooth muscle, and are therefore less resistant to blood flow, than their counterparts in the systemic circulation. Recruitment of pulmonary capillaries begins in the 3-5 mmHg pressure range while recruitment of systemic capillaries begins in the 8 mmHg range. The pulmonary capillaries have very thin walls as compared to systemic which minimizes the barrier to diffusion. Capillary hydrostatic pressure is lower as compared to systemic. In pulmonary, (Pc) is 13 mmHg (arteriolar end) to 6 mmHg (venous end) but variable because of the hydrostatic effects of gravity especially in the erect lung. Whereas in systemic circulation, arteriolar end of capillary has a hydrostatic pressure of 35mmHg and 15mmHg in venous end. The interstitial oncotic pressure is high in pulmonary circulation due to significant leak of protein (mostly albumin) across the thin capillary walls under normal circumstances. However Capillary oncotic pressure = 25 mmHg (Same as in systemic capillaries), and in both the Starling's law is applicable. The pulmonary system has however devised ways to prevent pulmonary edema; Increased lymph flow:
- Increased fluid filtration causes increased lymph flow which tends to remove the fluid.

- Decrease in interstitial oncotic pressure (oncotic buffering mechanism): When filtration increases, the albumin loss in the filtrate decreases. This combined with the increased lymph flow washes the albumin out of the interstitium and interstitial oncotic pressure decreases. This protection does not work if the capillary membrane is damaged e.g. by septic mediators.
- High interstitial compliance: A large volume of fluid can accumulate in the gel of the interstitium without much pressure rise. Finally, the interstial tissues become full of fluid, the pressure rises and alveolar flooding occurs. This has been called the bathtub effect: the analogy is that the tub can take a lot of fluid but there comes a point when it is full and suddenly overflows.

(c) Partial pressure of carbon iv oxide and oxygen

In pulmonary circulation the partial pressures for oxygen in arterial blood ranges between 95-100 (P_aO_2) mmHg, and in venous blood 40-50mmHg. Whereas in systemic arterial blood partial pressure of oxygen ranges between 75-100mmHg, and 30-40mmHg in venous blood. For carbon iv oxide, pulmonary has 40mmHg in arteriole and 50mmHg in venous blood while systemic has 35-45mmHg in arteriole, 41-51mmHg in venous blood. Contrary to all other systemic arteries, pulmonary artery is unique since it conveys deoxygenated blood while the other arteries convey oxygenated blood. The pulmonary vein also carries highly oxygenated blood back to the heart as opposed to other systemic veins which carry deoxygenated blood back to the heart. Unique feature in pulmonary circulation is the phenomenon of hypoxic vasoconstriction. In systemic circulation, if a tissue becomes hypoxic, blood flow to the same tissue is increased to cater for the deficiency and thus the response to hypoxia is vasodilation. In pulmonary, if an alveolar is hypoxic, the response is vasoconstriction to reduce blood flow and thus blood is redirected to the alveoli with higher partial pressures of oxygen. This is to help match perfusion with ventilation. This mechanism is due to the oxygen sensitive potassium channels in the smooth muscle membrane which close at low oxygen concentration, thus raising the membrane potential to threshold, depolarizing and leading to contraction.

(d) Factors that affect the affinity of hemoglobin for oxygen and carbon iv oxide.

Bohr and Haldane effects affect the affinity of hemoglobin. Bohr effect is relevant in tissues while Haldane effect is relevant in the lungs. Within the tissues there are high levels of carbon iv oxide, low levels of oxygen, low pH, high temperature and presence of 2,3-biphosphoglycerate(a negative allosteric effector of hemoglobin). These conditions favour dissociation of oxyhemoglobin to release oxygen to the tissues and bind carbon iv oxide. On the pulmonary end, within the lungs there is a need to release carbon iv oxide and bind oxygen. The following conditions favour this; high levels of oxygen, low carbon iv oxide levels, high Ph, low temperature, and absence of 2,3-biphosphoglycerate. Bohr effect facilitates transportation of oxygen from lungs and release into tissues whereas Haldane effect facilitates conveyance of carbon iv oxide from tissues and release in the lungs. Within the tissues, systemic circulation is in effect whereas pulmonary circulation is in effect in the lungs for both.

30. Write an essay on the control of respiration

Done to maintain partial pressures of oxygen and carbon iv oxide at normal range.

Components of the control system

1. **Chemoreceptors-** . *Central chemoreceptors* are found in the brainstem. They detect changes in the ph of cerebrospinal fluid. Blood brain barrier is impermeable to most ions but not to carbon iv oxide. Thus carbon iv oxide crosses and combines with water in the presence of carbonic anhydrase forming H_2CO_3 and finally dissociates into hydrogen ions and HCO_3^- . The hydrogen protons decrease the ph of cerebrospinal fluid. *Peripheral chemoreceptors* are found in carotid and aortic bodies. Mostly detect changes in arterial oxygen partial pressures but also carbon iv oxide and ph changes.
2. **Mechanoreceptors-** found in the lungs and in joints. The lungs have stretch receptors which facilitate the Herring Breuer reflex which controls the distention of the lung during inspiration. Joint and muscle receptors detect limb movement thus inspiratory centre instructed to increase breathing in a feedforward loop.
3. **Other receptors** include the airway irritant receptors and juxtacapillary receptors which respond to chemicals in pulmonary circulation, pulmonary stretch receptors, and atrial stretch receptors.
4. **Control centres-** located in the brainstem(medulla and pons);
   - **Medullary respiratory centre-** has a dorsal respiratory group of neurons to control inspiration and a ventral respiratory group to control expiration.
   - **Pontine centres-** the apneustic centre causes prolonged inhalation. In experimental setup it will cause long inspiration and short exhalation. Thus prevents turn off of inhalation. The pneumotaxic centre on the other hand turns off inspiration to limit the size of tidal volume.
5. **Cerebral cortex-** this can override the brainstem centres in intances such as voluntary hyperventilation.
6. **Respiratory muscles-** respond accordingly to signals from the central nervous system.

The basis of rhythmic ventilation, during inspiration, activity of inspiratory neurons ramp up and increases steadily and at the end of the activity, it shuts off abruptly;

(a) **Starting inspiration-** medullary respiratory neurons are continuously active. The centres receive stimulation from receptors and from the parts of the brain involved with voluntary respiratory movements and emotions. Combined efforts from all sources causes action potentials to stimulate respiratory muscles.
(b) **Increasing inspiration-** more and more inspiratory neurons are activated
(c) **Stopping inspiration-** the neurons stimulating inspiration re also responsible for stopping inspiration and receive input from pontine group of neurons and lung stretch receptors. Inhibitory neurons activated and relaxation of respiratory muscles results in expiration.

Modification of ventilation

(a) Cerebral and limbic system- respiration can be voluntarily controlled for instance during making a speech, playing wind instruments and modified by emotions.
(b) Chemical control- carbon iv oxide is the major regulator (hypercapneic ventilatory drive); increase or decrease in pH can stimulate chemosensitive areas causing greater rate and depth of respiration. Oxygen levels affect respiration when a 50% or greater decrease from normal exist (hypoxic ventilatory drive)

Input to respiratory centres in the brainstem

1. Higher centres of the brain (speech, emotions, voluntary control of breathing and action potentials in motor pathways)
2. Medullary receptors
3. Carotid and aortic body chemoreceptors
4. Herring Breuer reflex from the stretch receptors in lungs
5. Proprioceptors in muscle and joints
6. Receptors for touch, pain, and temperature stimuli.

Herring Breuer reflex

This limits the degree of inspiration and prevents over-inflation of lungs. In infants it plays a role in regulating the basic rhythm of breathing and prevents over-inflation of lungs but in adults it's only important when tidal volume is large such as during exercise .1L.

Pulmonary stretch receptors present in smooth muscle of airways respond to excessive stretch of lung during large inspirations and send action potentials through vagus to medullary inspiratory centre and pons apneustic centre. Inspiratory centre is directly inhibited and apneustic centre indirectly.

TRIBUTE TO THE LATE PROFFESOR HASSAN SAIDI

PROF. SAIDI WAS A CELEBRATED GENERAL AND LAPARASCOPIC SURGEON AT KENYATTA NATIONAL HOSPITAL AND AGA KHAN HOSPITALS, A FELLOW OF THE AMERICAN COLEGE OF SURGEONS AND MEMBER OF THE KENYA MEDICAL ASSOCIATION. CHAIRMAN DEPARTMENT OF HUMAN ANATOMY, PRESIDENT SURGICAL SOCIETY OF KENYA, EDITOR IN CHIEF OF THE ANNALS OF AFRICAN SURGERY JOURNAL, ASSOCIATE DEAN SCHOOL OF MEDICINE UNIVERSITY OF NAIROBI, BOARD CHAIR NARIOBI SURGICAL SKILLS CENTRE.

We celebrate his life legacy for being an excellent teacher of Anatomy, with a thirty-year experience in instruction and teaching Human Anatomy at the University of Nairobi, Aga Khan University Nairobi and University of Pennsylvania. He has mastery of Embryology, Gross Anatomy, Histology and molecular biology, with surgical anatomy as his pet subject. Having taught over 4000 undergraduate medical students, supervised over 40 B.Sc. Anatomy students, 30 Master of Medicine Surgery students, and 4 Master of Anatomy students. He mentored many renowned surgeons, doctors and clinical officers.

Prof. Hassan Saidi was able to publish over 60 high impact peer reviewed articles in local and international journals. His research activity focused on clinical anatomy in all its aspects, trauma, oncology and surgery of the digestive tract. He published a book on histology and was in the process of publishing a text book of Surgical Anatomy. Prof. Hassan Saidi held many leadership roles in the University of Nairobi, initially as a course coordinator and rising to become the chairman of thematic areas within the department. He was the substantive Chairman of the Department of Human Anatomy until the time of his death. Prof. Hassan Saidi was also the associate dean, Preclinical departments of the University of Nairobi. During his tenure as a chairman, he shepherded the establishment of the Nairobi Surgical Skills Centre, publication of the Kimani's Histology Text and Atlas, Establishment of the Anatomy Journal of Africa, supported staff development, training and promotion as well as supporting many local and international staff retreats.

Prof Hassan indeed had many friends. He definitely did not know all of them, but yet he would never deny any genuine person seeking assistance. Taking time to engage with different age groups and this he did effortlessly. An opportunity to watch football, play some basketball or just have a 'chat' (always very insightful and refreshing) over some coffee snack was a sought-after opportunity by many. In his 36hr day, he would still find time to call up and catch up with his friends, his objective to savour every moment with friends to improve them in one way or another. What better HE WAS!

Prof. Hassan Saidi was married, with three sons. He was actively involved in charity and volunteer activities through HAIBA foundation and other charity groups. He was a mentor, a great teacher, researcher and a surgeon.He surely fought a good fight and finished the race. He will be missed by many but his legacy lives on forever in our hearts and lives, till always and forever!!!

TRIBUTE TO THE LATE PROFFESOR HASSAN SAIDI

WHAT ARE YOU DOING TO EMULATE THE KIND OF LIFE PROF. SAIDI LIVED? IN ALL THE ABOVE CITED ACHIEVEMENTS, AND THE IMPACT HE GENERATED IN ALL WALKS OF LIFE, DO YOU THINK IT'S POSSIBLE TO LEAVE A TRAIL OF THE SAME MAGNITUDE OF EXQUISITION?

YES IT IS! START WITHIN YOUR SPHERE OF INFLUENCE. LOOK FOR A WAY TO BLESS AND MOULD YOUR FELLOW MEDICS. STUDY MEDICINE WITH PASSION, TRANSFORMATIVE PURPOSE AND PURSUE EXCELLENCE WITH DISTINCTIONS IN ALL YOU DO. ABOVE IT ALL, PURSUE GOD WITH ALL OF YOUR BEING, WHILE PLUGGING INTO HIS SOURCE TO HELP YOU ACHIEVE IT ALL IN KEEPING PROF. SAIDI'S LEGACY ALIVE!!!

ALL THE BEST IN YOUR STUDIES AND UPCOMING EXAMS AS GOD LEADS YOU INTO THE GREAT DOCTORS HE ORCHESTRATED YOU TO BE!!!

WHERE GOD LEADS, HE PROVIDES. WHERE HE GUIDES, HIS GRACE IS SUFFICIENT!