MSCU GROUP DISCUSSION ANSWERS TO ASSORTED PHYSIOLOGY SAQ'S FOR LEVEL 2

A TRIBUTE TO THE LATE PROF. HASSAN SAIDI. BSc (Anatomy), MBChB, MMed (Surg), FACS.

(a)RENAL PHYSIOLOGY

1. State the principles used in measuring renal clearance

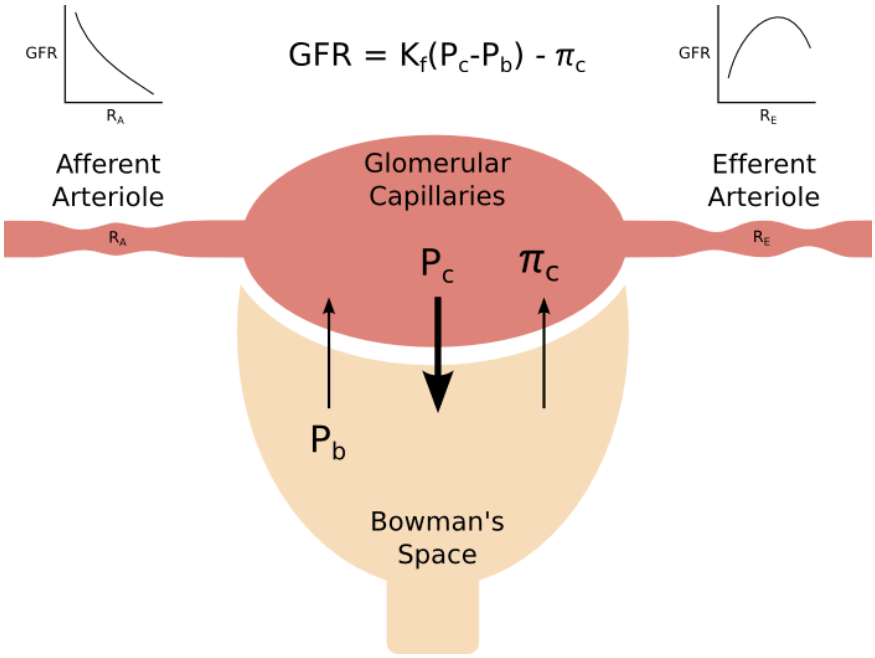
Renal clearance is the volume of plasma from which substance has been removed and excreted into urine per unit time (volume/time). Renal clearance can be calculated for any substance. Depending on the characteristics of the substance and its renal handling, renal clearance can vary from zero to greater than 600 mL/min. The Fick's principle is used in determining clearance (The total uptake of a substance by peripheral tissue is equal to the product of blood flow to peripheral tissue and arterio-venous concentration gradient).

$C = U \times V / P_A$

- U = [solute] in urine (mg/ml)
- V = volume of urine/min (ml/min)
- P_A = [solute] in arterial plasma (mg/100 ml plasma)

Renal clearance of **albumin** is approximately zero because, normally, albumin is not filtered across the glomerular capillaries. The renal clearance of **glucose** is also zero, although for a different reason: Glucose is filtered and then completely reabsorbed back into the bloodstream. Other substances such as Na^+, urea, phosphate, and Cl^- have clearances that are higher than zero because they are filtered and partially reabsorbed. **Inulin,** is freely filtered across the glomerular capillaries, but it is neither reabsorbed nor secreted; therefore, its clearance measures the glomerular filtration rate. Creatinine clearance shares the same concept as inulin and used in measuring GFR. Organic acids such as ***para*-aminohippuric acid** (**PAH**) have the highest clearances of all substances because they are both filtered and secreted thus its clearance is used in measuring renal blood flow.

2. With a diagram, describe the interaction of various forces in glomerular filtration



Glomerular filtration rate is the product of Kf (ultrafiltration coefficient) and the net ultrafiltration pressure. The **net ultrafiltration pressure,** sum of the three Starling pressures (omitting the oncotic pressure in Bowman's space since it is considered to be zero because filtration of protein is negligible). For glomerular capillaries, the net ultrafiltration pressure **always favors filtration,** so the direction of fluid movement is always *out* of the capillaries. The greater the net pressure, the higher the rate of glomerular filtration.

3. Explain the role of urea in the production of concentrated urine

Urea is reabsorbed by the nephron and concentrated by the medulla. Urea recycling in the inner medulla, contributes to 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 tubular fluid in this segment. In inner medullary collecting ducts, it increases both water and urea permeability. This allows urea to flow passively down its gradient into interstitial fluid and thus adds to osmotic gradient and helps drive water reabsorption. The urea transporters involved are UT1 and UT3 which are activated by ADH.

4. Write short notes on erythropoietin

> Erythropoietin is one of the endocrine secretions of the kidney

> It's a glycoprotein cytokine secreted by the kidney in response to hypoxia

> Stimulates red blood cell production in the bone marrow

>It increases mRNA formation and protein synthesis

> Erythropoietin is produced by interstitial fibroblasts in the kidney in adults and in liver perisinuisoidal cells during neonatal and perinatal period.

> Other functions include vasoconstriction-dependent hypoconstriction, and angiogenesis.

5. Write short notes on the nerve of filling and the nerve of emptying

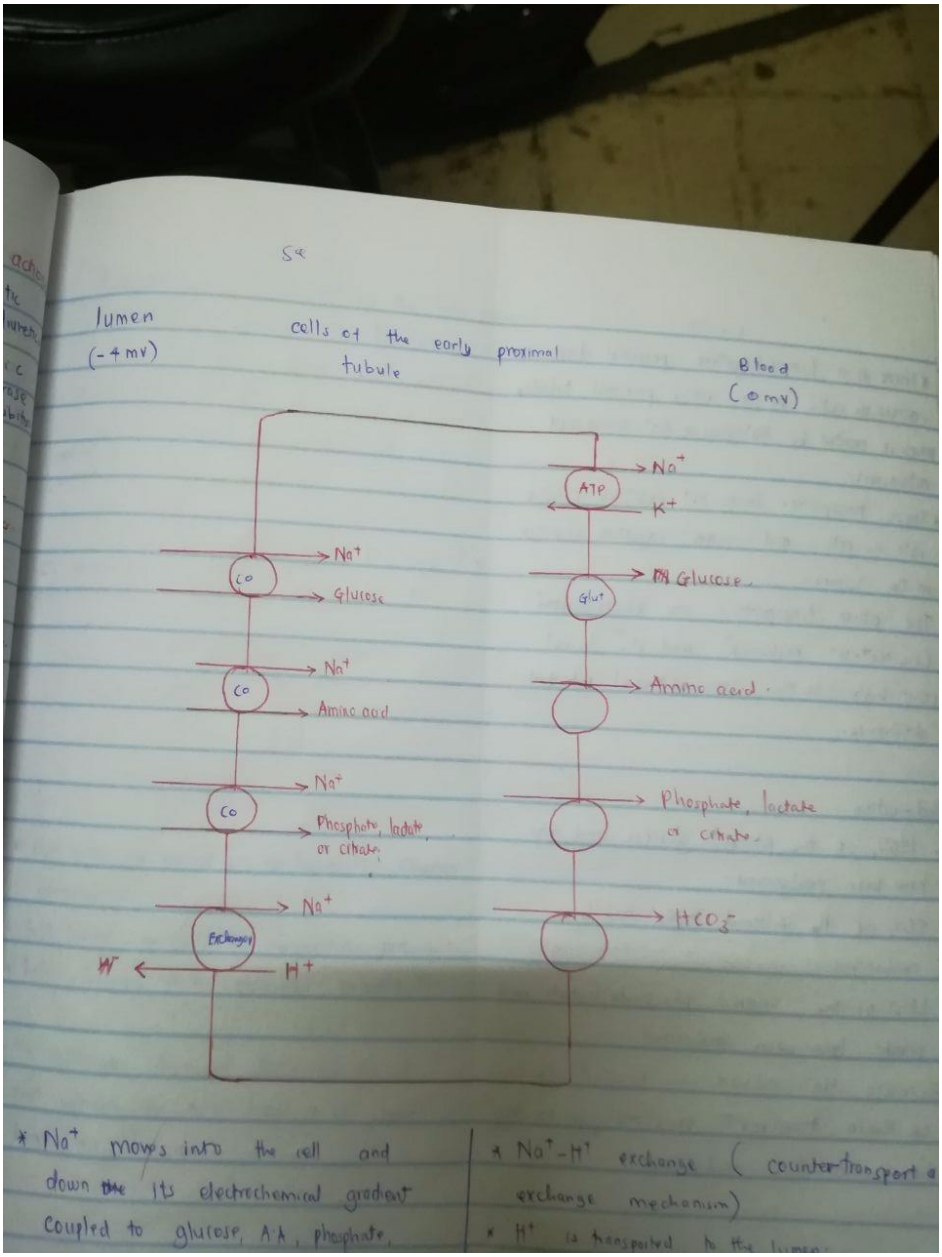
The nerve of filling and nerve of emptying are referred as such with regards to bladder filling and emptying. The nerve of filling is the sympathetic division to the bladder. The preganglionic nerve arise from (L1, L2) which synapse at the hypogastric ganglion from which postganglionic nerves come from and innervate urinary bladder as the hypogastric nerve. It relaxes the detrusor muscles of the bladder and contracts internal urethral sphincter to allow urine to collect and fill the bladder. The nerve of emptying is the parasympathetic division to the bladder which comes from S2,S3,S4 segments of the spinal cord which combine with the pelvic nerve (S1,2,3) which passes through the hypogastric ganglion and synapses at a ganglion near the urinary bladder from which post ganglionic fibres arise. It contracts the bladder detrusor muscles and relaxes the internal urethral sphincter to initiate emptying the bladder of urine to allow micturition. Afferent fibers from the stretch receptors of bladder to CNS also pass through the pelvic nerve.

6. List the five factors which determine the net glomerular filtration rate

- The surface area of the filter- directly proportional.
- The thickness or permeability of the glomerular capillary.
- Changes in renal blood flow.
- Magnitude of any forces favoring or opposing filtration.
- Tubuloglomerular feedback
- Glomerular capillaries pressure
- Systemic blood pressure
- Contraction or relaxation of mesangial cells
- Changes in concentration of plasma proteins.

7. List five substances reabsorbed in the proximal convoluted tubule and their mechanism of reabsorption.

- Glucose- Active transport
- Water- passive osmosis
- Bicarbonate ions (HCO_3^-)- direct reabsorption
- Amino acids - secondary active transport with sodium
- Lactate and phosphate- secondary active transport with sodium
- Chloride ions- passive diffusion
- Sodium hydrogen exchanger.



8. List five symptoms or signs of renal failure and for any three outline why they occur.

Recall classification of renal failure into pre-renal, renal and post-renal when tackling this question.

- Facial puffiness
- Leg swelling

Damage to the glomeruli in can result in nephrotic syndrome. In nephrotic syndrome, declining levels of albumin in your blood can lead to fluid accumulation thus leading to edema.

- Pain in the loins
- Anemia

The cause of the anemia is decreased renal secretion of erythropoietin, which stimulates the bone marrow to produce red blood cells. If the kidneys are seriously damaged, they are unable to form adequate quantities of erythropoietin, which leads to diminished red blood cell production and consequent anemia.

- Hypertension

Presence of renal lesions that either decrease glomerular filtration rate or increase tubular reabsorption usually lead to hypertension.

>Acidosis- due to retention of metabolic end products. Severe acidosis leads to coma.

9. Outline four events that occur at the distal convoluted tubule of the kidney.

- Hormonal control

Sodium ions are only reabsorbed when aldosterone is present. Water follows passively and potassium and hydrogen ions are secreted into the tubular lumen by the sodium-potassium ATPase pump.

- Feedback control of GFR.

The first portion of the distal tubule forms the macula densa, a group of closely packed epithelial cells that is part of the juxtaglomerular complex and provides feedback control of GFR and blood flow in this same nephron.

- Calcium regulation

The DCT also participates in calcium regulation by reabsorbing Ca^{2+} in response to parathyroid hormone. PTH effect is mediated through phosphorylation of regulatory proteins and enhancing the synthesis of all transporters within the distal convoluted tubule.

10. Describe the renin-angiotensin-aldosterone system.

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.

11. Describe 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.

12. What are the causes of post-renal kidney failure?

Post-renal acute renal failure in particular is caused by **anything that interferes with the flow of urine out of the kidneys.** Kidney stones or tumors in the ureters can block waste from passing into the bladder. Also, anything that causes an obstruction in the bladder itself, such as an enlarged prostate, a bladder stone, or a blood clot, may stop urine from properly passing out of the kidneys and through the bladder.

13. Describe how nephrons handle urea

Movement of large amounts of urea across cell membranes is made possible by urea transporter proteins (UT1 and UT4).

Urea allows the kidneys to create hyperosmotic urine. Preventing the loss of water in this manner is important if the person's body must save water in order to maintain a suitable blood pressure or in order to maintain a suitable concentration of sodium ions in the blood plasma.

About 40% of the urea filtered is normally found in the final urine, since there is more reabsorption than secretion along the nephron.

It is regulated by antidiuretic hormone, which controls the amount reabsorbed in the collecting duct system and secreted into the loop 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.

14. Define shock, giving 4 examples and for each describe their mechanisms.

Shock is a life-threatening condition of low blood perfusion to tissues resulting in cellular injury and inadequate tissue function. It's basically when tissue perfusion doesn't match up the tissue requirement. **The main types of shock include;**

- Cardiogenic shock (due to heart problems- the heart is unable to circulate enough blood volume to maintain adequate tissue perfusion. This can happen after a heart attack or during an acute episode of heart failure.)
- Hypovolemic shock (caused by too little blood volume from blood loss or excessive fluid loss)
- Obstructive shock – can be caused by an obstruction in the cardiovascular system. Examples include a pulmonary embolism and pneumothorax.
- Distributive shock – occurs as a result of poor distribution of blood to the tissues, leading to inadequate tissue perfusion. This type of shock is seen in spinal/neurogenic shock (caused by damage to the nervous

system), septic (due to infections), and anaphylactic shock (caused by allergic reaction). This is also known as relative hypovolemia.

15. Describe water reabsorption from the collecting ducts of the kidney.

The permeability of the collecting ducts for water lead to a concentration of the urine up to the fivefold osmolarity of the plasma. The permeability of the collecting ducts is regulated with ADH (antidiuretic hormone, Vasopressin). ADH causes the incorporation of additional water channels (aquaporins) into the luminal membrane. The high osmotic pressure of the renal medulla is the responsible force for the urine concentration. ADH can control 10% of the primary urine volume, thus can regulate the diuresis between 1–20 l/d.

In the absence of ADH, the permeability of the collecting ducts for water is low, the urine will not be concentrated. A deficiency of ADH secretion leads to diabetes insipidus, a disorder with massive diuresis and excessive thirst.

Additional sodium reabsorption takes place in the collecting ducts via luminal sodium channels. The energy for the sodium reabsorption derives from the basolateral sodium-potassium pump. Aldosterone regulates the sodium and water reabsorption and potassium secretion via expression of the sodium channels and the basolateral sodium-potassium pump. The luminal sodium channels can be inhibited by amiloride, a potassium-sparing diuretic.

16. Briefly describe renal glucose reabsorption and its tubular maximum.

Glucose moves from tubular fluid into the cell on the **Na^+-glucose cotransporter** (called **SGLT**) in the luminal membrane. Two Na^+ ions and one glucose bind to the cotransport protein, the protein rotates in the membrane, and Na^+ and glucose are released into the ICF. In this step, glucose is transported against an electrochemical gradient; the energy for this *uphill* transport of glucose comes from the *downhill* movement of Na^+. The Na^+ gradient is maintained by the Na^+-K^+ ATPase in the peritubular membrane. Because ATP is used *directly* to energize the Na^+-K^+ ATPase and *indirectly* to maintain the Na^+ gradient, Na^+-glucose cotransport is called **secondary active transport.** Glucose is transported from the cell into peritubular capillary blood by **facilitated diffusion.** In this

step, glucose is moving down its electrochemical gradient and no energy is required. The proteins involved in facilitated diffusion of glucose are called **GLUT 1** and **GLUT 2,** which belong to a larger family of glucose carriers. The tubular maximum of glucose is 375mg/min. This is the concentration of glucose in tubular fluid beyond which no more can be reabsorbed.

17. Briefly explain the factors that influence net filtration pressure at the glomerulus

This net pressure is the combination of three other pressures acting on the glomerulus:
1. Glomerular capillary blood pressure - 55 mmHg.
This is the pressure inside the capillaries of the glomerulus. This hydrostatic pressure is created by the contraction of the heart. It is regulated by many factors including dilating and constricting the afferent and efferent arterioles of the glomerulus.
2. Bowman's capsule hydrostatic pressure - 15 mmHg- this is a hydrostatic pressure just like the preceding one, however it is in the opposite direction. The Bowman's capsule isn't a vacuum, so the fluid in the capsule exerts a pressure on its surroundings. This is going to encourage the fluid to move in the opposite direction as the glomerular capillary blood pressure.
3. Plasma colloid osmotic pressure - 30 mmHg – This is a pressure established by osmosis. In other words, the plasma contains lots of proteins, whereas the fluid in the Bowman's capsule doesn't. Therefore, water (fluid) wants to move in the direction of the proteins to dilute the high concentration.

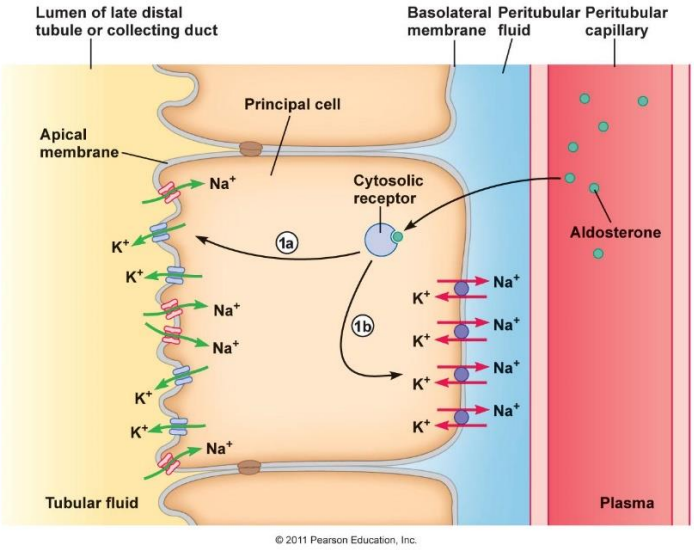
Therefore to obtain the net pressure we subtract the forces opposed to filtration from the forces favoring filtration:
Net filtration = 55mmHg - (30mmHg + 15mmHg)
Net filtration = 10 mmHg

18. Explain the pathophysiology associated with any two symptoms due to renal failure

- Facial puffiness, Leg swelling- Damage to the glomeruli in can result in nephrotic syndrome. In nephrotic syndrome, declining levels of albumin in your blood can lead to fluid accumulation thus leading to edema.
- Anemia- The cause of the anemia is decreased renal secretion of erythropoietin, which stimulates the bone marrow to produce red blood cells. If the kidneys are seriously damaged, they are unable to form adequate quantities of erythropoietin, which leads to diminished red blood cell production and consequent anemia.
- Hypertension- Presence of renal lesions that either decrease glomerular filtration rate or increase tubular reabsorption usually lead to hypertension.

19. List ions secreted at the distal convoluted tubule and for each, the transport process.

Na^+/K^+ ATPase transporter- Principal cells make up the majority of the tubular cells. They are mainly involved in the uptake of sodium ions and extrusion of potassium ions. The hormone aldosterone affects this cell by stimulating it to produce additional sodium/potassium pumps (moving 3Na from filtrate into peritubular capillaries in exchange for 2K). This exchange is driven by a Na^+/K^+ ATPase on the basolateral membrane, which sets up a gradient for sodium to enter the cell through the epithelial sodium channel. Sodium ions are positively charged, so as they are extruded an electrical gradient is formed. Additionally, potassium ions accumulate within the cell due to the **Na^+/K^+-ATPase**. Both of these factors promote secretion of potassium ions into the lumen of the tubule through a potassium uniporter which are increased in number by aldosterone as well.

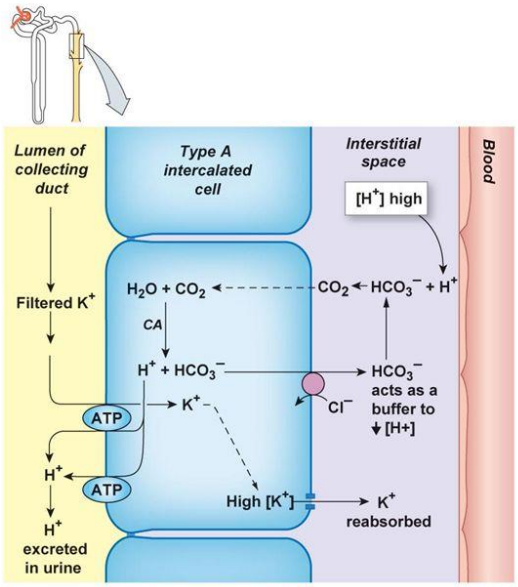


The intercalated cells- play a role in acid-base control, by controlling the levels of hydrogen (H^+) and bicarbonate ions (HCO_3^-). The bicarbonate ions cross the basolateral membrane into the extracellular fluid through the anion exchanger channel, in exchange for chloride. The hydrogen ions are secreted into the lumen via a **K^+/H^+ ATPase** antiporter and H^+-ATPase.

To prevent an accumulation of chloride ions and potassium ions within the cell, a **K^+/Cl^- symporter** on the basolateral membrane allows leakage of these ions back into the extracellular fluid.

Intercalated Cells

- Type A intercalated cells function in acidosis



(a) Type A intercalated cell function in acidosis.

Figure 20-22a

20. Briefly explain how the renal clearance of a substance is measured.

Renal clearance is the volume of plasma per minute needed to excrete the quantity of solute appearing in the urine in a minute. The concentration in urine and arterial plasma of the substance are measured. The volume of urine is also measured and the three are equated as follows.

$$C = U \times V / P_A$$

- U = [solute] in urine (mg/ml)
- V = volume of urine/min (ml/min)
- P_A = [solute] in arterial plasma (mg/100 ml plasma)

Clearance ratios can be obtained by comparing it with the clearance of inulin.

21. Briefly describe the function of the thick ascending loop of Henle

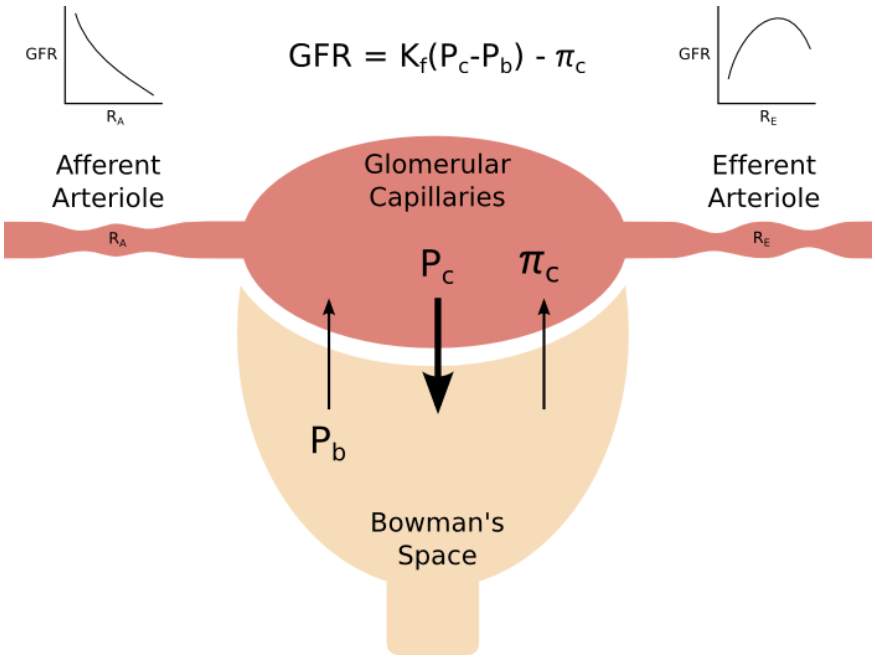
The thick ascending loop of Henle is a major resorptive segment of the nephron and accounts for resorption of nearly a quarter of the filtered load of sodium, chloride, and potassium ions. In addition, Henle's thick segment is a major location of magnesium and calcium ion resorption. Importantly, the tight junctions of this segment are virtually impermeable to water. Given the large amount of solute resorption that occurs in the absence of water resorption, the tubular fluid becomes progressively dilute as it travels through the thick ascending loop. This feature is why this segment is frequently referred to as the "Diluting Segment" of the nephron. Thick Ascending Loop of Henle Transport is characterized by a Na-2Cl-K symporter on the luminal surface that allows for resorption of large amounts of these ions. Resorption is powered by a basolateral Na-K

ATPase. Importantly, the ascending Henle is highly impermeable to water and the resorption of large amounts of sodium in the absence of water results in significant dilution of the tubular fluid. A small amount of potassium back-leak into the lumen via a potassium channel yields a positive luminal charge that powers paracellular resorption of positive ions, including magnesium and calcium.

22. Briefly describe the role of autonomic nervous system in the control of micturition

Bladder and urethra are supplied by autonomic nervous system. Sympathetic arises from T12, L1, L2 and travel through the presacral nerve to innervate ureter, bladder and internal urethral sphincter. This causes the relaxation of bladder and contraction of internal sphincter. Pain impulses from the bladder and urethra are carried by parasympathetic. Parasympathetic arises from S2, S3, S4, segments of spinal cord and fibres travel in the pelvic nerve. The stimulation of the pelvic nerve causes bladder contraction and relaxation of internal sphincter.

23. With a diagram, illustrate the interaction of various forces in glomerular filtration.



(b) GASTROINTESTINAL PHYSIOLOGY

1 .State the constituents of a good healthy diet

Components of a balanced diet include: Carbohydrates, Fats, Proteins, Vitamins, Minerals and Water

2. Describe the role of secretions in the digestive system

a) Ions e.g. Na+, K+, H+, HCO-3 and Cl- create acidic/basic conditions necessary for the digestion of different nutrients

b) Water- lubricates and dissolves food nutrients for easier digestion

c) Digestive Enzymes-break down food molecules to particles which are easier to absorb

d) Mucus- Lubricate and protect inner mucosa of tract

e) Bile- emulsifies lipid molecules in water making it easier for absorption

(f) Hormones (gastrin, cholecystokinin, glucose-dependent insulinotropic peptide and secretin) and paracrine (somatostatin and histamine) - stimulate and inhibit various secretions in the GIT.

(g) Neurocrines (acetylcholine, norepinephrine, substance P) - alter contractions and relaxation of GIT smooth muscles.

3. Describe the absorption and end products of carbohydrate digestion.

Salivary amylase in the mouth breaks them down into shorter polysaccharides, pancreatic amylase in the duodenum breaks down polysaccharides into mono-, di-, and oligosaccharides. They are further broken down in the small intestines by brush border enzymes to the end product; monosaccharaides i.e. glucose, fructose and galactose .Glucose form 80% of the end products while fructose and galactose form the remaining 20%. Absorption occurs at the small intestines. Glucose is transported from lumen to mucus membrane of small intestines via Na+ cotransporter (SGLT1). The energy required for this process is obtained from the binding process of Na+ and glucose molecules to carrier proteins. From the epithelial cells glucose molecules reach the portal system via facilitated diffusion (using GLUT2). Na+ ions move laterally to the intracellular spaces then move to blood via active transport using energy derived from ATP breakdown.

Galactose uses similar mechanism to glucose. Fructose is absorbed into the enterocyte via GLUT5 through facilitated diffusion and to the blood via facilitated diffusion using GLUT2 while some is converted to glucose first then follows similar path as glucose.

4. Actions of insulin in glucose regulation

Insulin helps control blood glucose levels by signaling the liver, muscles and fat cells to take in glucose from the blood. Insulin therefore helps cells take in glucose to be used for energy. If body has sufficient energy and blood glucose level is high, insulin signals liver to take up glucose and store it as glycogen. It increases catabolism of glucose (glycogenesis) and increases anabolism of glycogen.

5. List the carbohydrate 'brush border' enzymes and state their functions.

Brush border enzymes are present in brush border of microvilli in the small intestines. These enzymes breakdown disaccharides and starches to monosaccharide that are easy to absorb. They include:

a) Sucrase -breaks down sucrose to fructose and glucose
b) Lactase- breaks down lactose to galactose and glucose
c) Maltase- breaks down maltose and maltriose to glucose molecules
d) Dextrinase - breaks down dextrins, maltose and maltriose into glucose molecules
e) Trehalase – breaks trehalose to two glucose molecules

6. Explain the neuromyogenic control of gut function.

The gastrointestinal tract is regulated, in part, by the autonomic nervous system, which has an extrinsic component and an intrinsic component. The extrinsic component is the sympathetic and parasympathetic innervation of the gastrointestinal tract. The intrinsic component is called the enteric nervous system. The enteric nervous system is wholly contained within the submucosal and myenteric plexuses in the wall of the gastrointestinal tract. The intrinsic or enteric nervous system is located in ganglia in the myenteric and submucosal plexuses and controls the contractile, secretory and endocrine functions of the gastrointestinal tract.

Postganglionic nerve fibers of the sympathetic nervous system are adrenergic (i.e., release norepinephrine) and synapse with either Meissner's or Myenteric plexuses. Short preganglionic sympathetic neurons synapse at ganglia; celiac, hypogastric, superior and inferior mesenteric. Postganglionic neurons of the parasympathetic nervous system are classified as either cholinergic or peptidergic. Cholinergic neurons release acetylcholine (ACh) as the

neurotransmitter. Peptidergic neurons release one of several peptides including substance P and vasoactive inhibitory peptide (VIP); in some in stances, the neuropeptide has not yet been identified. The preganglionic neurons synapse with Myenteric or Meissner's plexuses. The regions from esophagus to ascending colon are innervated parasympathetically by vagus and lower GIT by the pelvic nerve.

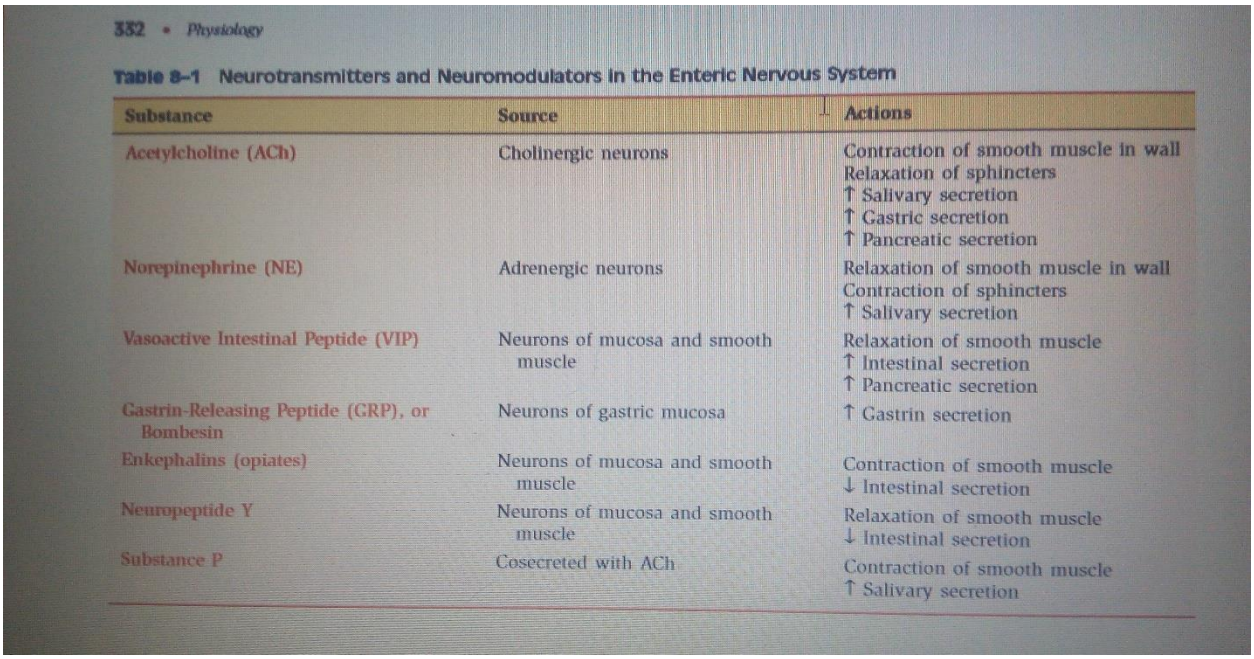


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Table 8–1 Neurotransmitters and Neuromodulators in the Enteric Nervous System

Substance	Source	Actions
Acetylcholine (ACh)	Cholinergic neurons	Contraction of smooth muscle in wall Relaxation of sphincters ↑ Salivary secretion ↑ Gastric secretion ↑ Pancreatic secretion
Norepinephrine (NE)	Adrenergic neurons	Relaxation of smooth muscle in wall Contraction of sphincters ↑ Salivary secretion
Vasoactive Intestinal Peptide (VIP)	Neurons of mucosa and smooth muscle	Relaxation of smooth muscle ↑ Intestinal secretion ↑ Pancreatic secretion
Gastrin-Releasing Peptide (GRP), or Bombesin	Neurons of gastric mucosa	↑ Gastrin secretion
Enkephalins (opiates)	Neurons of mucosa and smooth muscle	Contraction of smooth muscle ↓ Intestinal secretion
Neuropeptide Y	Neurons of mucosa and smooth muscle	Relaxation of smooth muscle ↓ Intestinal secretion
Substance P	Cosecreted with ACh	Contraction of smooth muscle ↑ Salivary secretion

Reference; Linda Costanzo BRS Physiology, 5thEdition

7. Using a diagram, illustrate how enterocytes absorb glucose and fructose.

Glucose and galactose are absorbed by mechanisms involving Na+-dependent cotransport. Fructose is absorbed by facilitated diffusion.

Glucose and galactose are absorbed across the apical membrane by secondary active transport mechanisms similar to those found in the early proximal convoluted tubule. Both glucose and galactose move from the intestinal lumen into the cell on the Na+-Glucose cotransporter (SGLT 1), against an electrochemical gradient. The energy for this step does not come directly from adenosine triphosphate (ATP) but from the Na+ gradient across the apical membrane; the Na+ gradient is created and maintained by the Na+-K+-ATPase on

the basolateral membrane. Glucose and galactose are extruded from the cell into the blood, across the basolateral membrane, by facilitated diffusion (GLUT 2).

Fructose absorption does not involve an energy requiring step or a cotransporter in the apical membrane. Rather, fructose is transported across both the apical and basolateral membranes by facilitated diffusion; in the apical membrane, the fructose-specific transporter is called GLUT 5, and in the basolateral membrane, fructose is transported by GLUT 2. Because only facilitated diffusion is involved, fructose cannot be absorbed against an electrochemical gradient.

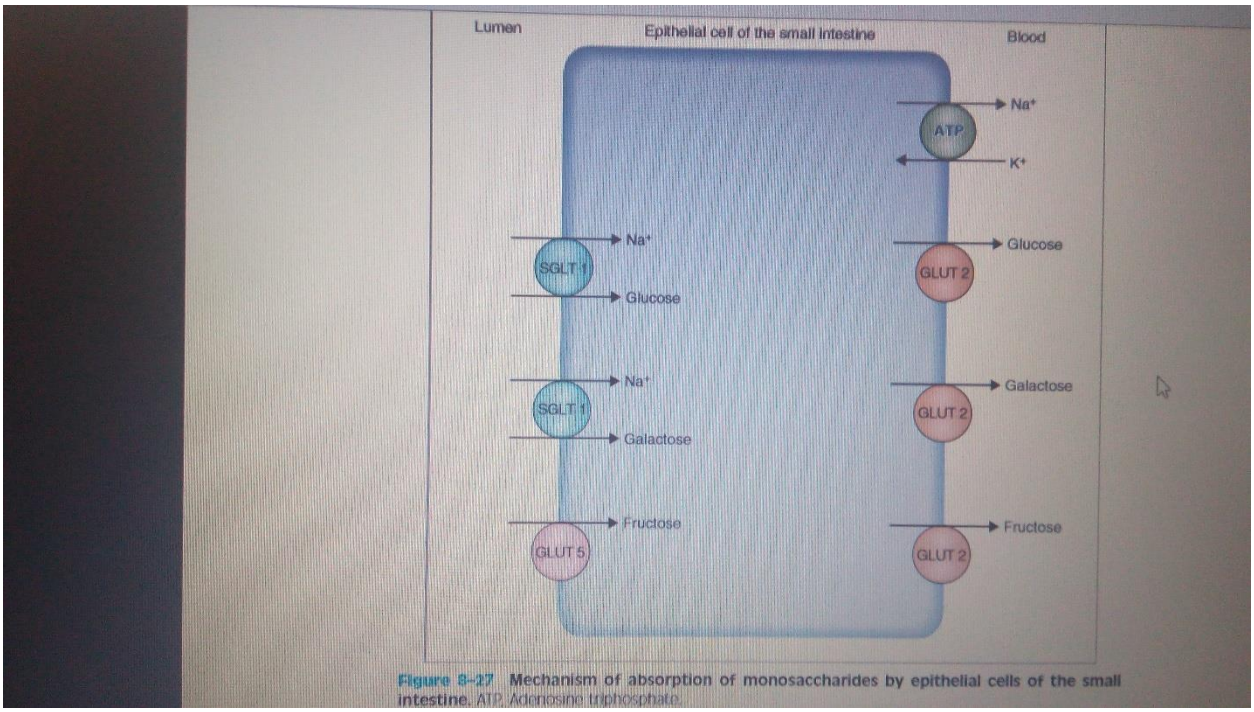


Figure 8–27 Mechanism of absorption of monosaccharides by epithelial cells of the small intestine. ATP, Adenosine triphosphate.

Reference; Linda S.Costanzo BRSPhysiology, 5thEdition

8. Describe the stimulation and effects of duodenogastric reflux. *

Biliary reflux, bile reflux or duodenogastric reflux is a condition that occurs when bile flows upward from the duodenum into the stomach and esophagus. Normally, the pyloric sphincter prevents bile from entering the stomach, when damaged or fails to work correctly, bile can enter the stomach and then transported into the esophagus as in gastric reflux. Small amounts of bile in the stomach are asymptomatic but excessive amounts cause irritation and

inflammation. It is not to be confused with acid reflux or gastroesophageal reflux disease (GERD), which is the backflow of stomach acid into the esophagus.

9. Using a diagram, illustrate how enterocytes absorb oligopeptides.

They are not directly absorbed. During digestion of proteins, pancreatic proteases, trypsin, chymotrypsin, elastase, carboxypeptidase A, and carboxypeptidase B, released in the small intestines, hydrolyze dietary protein to amino acids, dipeptides, tripeptides, and larger peptides called oligopeptides. Only the amino acids, dipeptides, and tripeptides are absorbable. The oligopeptides are further hydrolyzed by brush-border proteases, yielding the smaller absorbable molecules.

At least seven different transport systems transport amino acids into enterocytes. Five of these require Na^{2+} and cotransport amino acids and Na^{2+} in a fashion similar to the cotransport of Na^{2+} and glucose. Two of these five also require Cl –. In two systems, transport is independent of Na+. The L-amino acids are absorbed by mechanisms analogous to those for monosaccharide absorption. The amino acids are transported from the lumen into the cell by Na+ amino acid co-transporters in the apical membrane, energized by the Na+ gradient. There are four separate cotransporters: one each for neutral, acidic, basic, and imino amino acids. The amino acids then are transported across the basolateral membrane into the blood by facilitated diffusion, again by separate mechanisms for neutral, acidic, basic, and imino amino acids. Most ingested protein is absorbed by intestinal epithelial cells in the dipeptide and tripeptide forms rather than as free amino acids.

Di- and tri-peptides are transported into enterocytes by a system known as PepT1 (or peptide transporter 1) that requires H+ instead of Na+. In the apical membrane transport dipeptides and tripeptides from the intestinal lumen into the cell, utilizing an H+ ion gradient created by a Na+-H+ exchanger in the apical membrane. Once inside the cell, most of the dipeptides and tripeptides are hydrolyzed to amino acids by cytosolic peptidases, producing amino acids that exit the cell by facilitated diffusion; the remaining dipeptides and tripeptides are absorbed unchanged.

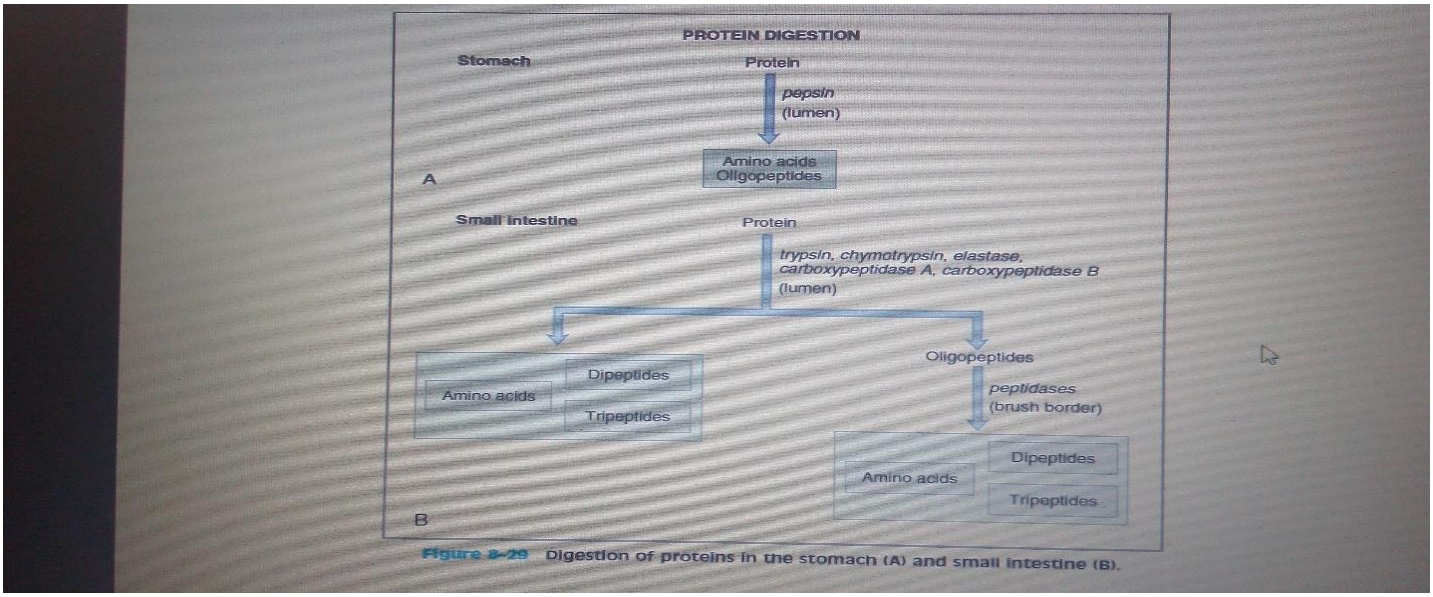


Figure 8–29 Digestion of proteins in the stomach (A) and small intestine (B).

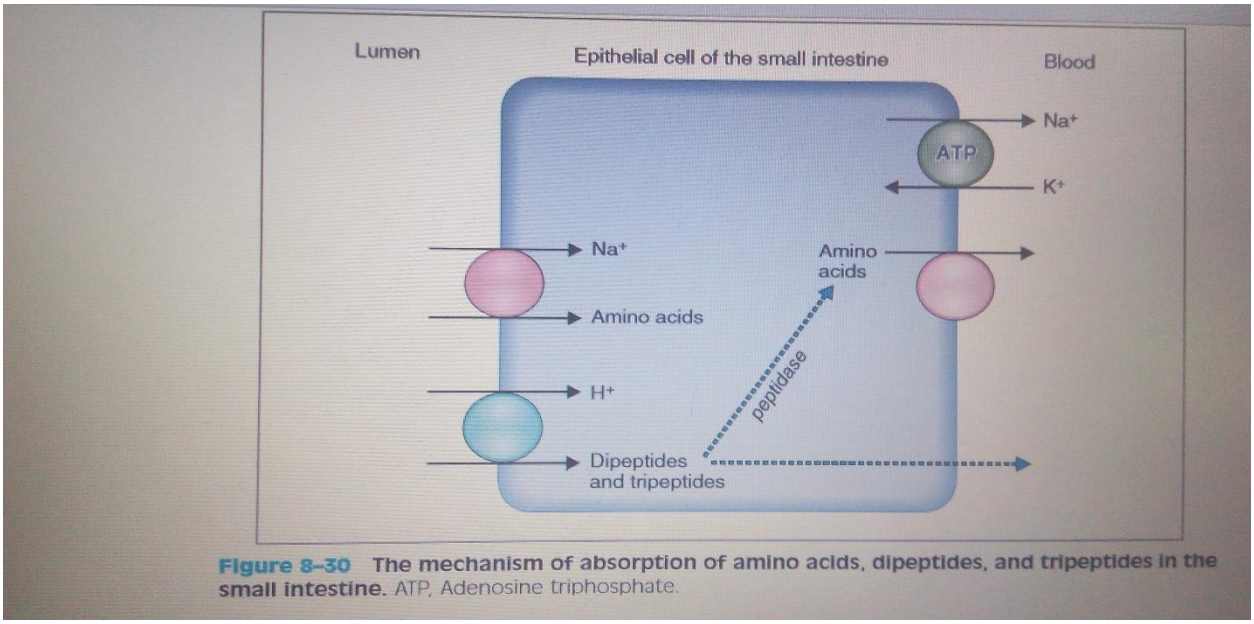


Figure 8–30 The mechanism of absorption of amino acids, dipeptides, and tripeptides in the small intestine. ATP, Adenosine triphosphate.

Reference; Linda S.Costanzo BRSPhysiology, 5thEdition

10. Describe enterohepatic circulation and state its function.

Enterohepatic circulation refers to the circulation of biliary acids, bilirubin, drugs and other substances from the liver to the bile, followed by entry into the small intestines, absorption by the enterocyte and transport back to the liver. The blood from the intestines, pancreas, and spleen drains via the hepatic portal vein to the liver and from the liver via the hepatic veins to the inferior vena cava.

The enterohepatic circulation are as follows:

1. In the ileum, the bile salts are transported from the intestinal lumen into the portal blood by Na+-bile salt cotransporters. Significantly, this recirculation step is located in the terminal small intestine (ileum), so bile salts are present in high concentration for the entire length of small intestine to maximize lipid digestion and absorption.

2. The portal blood carries bile salts to the liver.

3. The liver extracts the bile salts from portal blood and adds them to the hepatic bile salt/bile acid pool. Therefore, the liver must replace, by synthesis, only the small percentage of the bile salts that is not recirculated (i.e., excreted in feces); the fecal loss is about 600 mg/day (out of the total bile salt pool of 2.5 g). This is via a negative feedback control by the bile salts. The rate-limiting enzyme in the biosynthetic pathway, cholesterol 7α-hydroxylase, is inhibited by bile salts. When greater quantities of bile salts are recirculated to the liver, there is decreased demand for synthesis and the enzyme is inhibited. When smaller quantities of bile salts are recirculated, there is increased demand for synthesis and the enzyme is stimulated.

FUNCTIONS: 1. Deconjugated bilirubin are metabolized to urobilinogen, some of which is absorbed via the enterohepatic circulation and delivered back to the liver while the remainder is converted to urobilin and stercobilin, which are excreted in the feces.

2. Approximately 95% of bile acids are recirculated to the liver via the enterohepatic circulation. The recirculation of bile salts to the liver reduces the demand to synthesize new bile salt. The liver must replace only the small percentage of the bile salt pool that is excreted in feces.

3. It is important in toxicology as many lipophilic xenobiotics undergo this process causing repeated liver damage.

4. Recirculation of bile salts to the liver also stimulates biliary secretion, which is called a choleretic effect.

Reference; Linda S.Costanzo BRSPhysiology, 5thEdition

11. Describe the mechanism of vitamin B12 absorption.

The fat-soluble vitamins are vitamins A, D, E, and K. In the intestinal lumen, fat-soluble vitamins are incorporated into micelles and transported to the apical membrane of the intestinal cells. They diffuse across the apical membrane into the cells, are incorporated in chylomicrons, and then are extruded into lymph, which delivers them to the general circulation.

The water-soluble vitamins include vitamins B1, B2, B6, B12, C, biotin, folic acid, nicotinic acid, and pantothenic acid. In most cases, absorption of the water-soluble vitamins occurs via a Na+-dependent cotransport mechanism in the small intestine. The exception is the absorption of vitamin B12 (cobalamin).

Absorption of vitamin B12 requires intrinsic factor and occurs in the following steps:

1. Dietary vitamin B12 is released from foods by the digestive action of pepsin in the stomach.
2. Free vitamin B12 binds to R proteins (trasncobalamin), which are secreted in salivary juices.
3. In the duodenum, pancreatic proteases degrade the R proteins, causing vitamin B12 to be transferred to intrinsic factor, a glycoprotein secreted by the gastric parietal cells.
4. The vitamin B12-intrinsic factor complex is resistant to the degradative actions of pancreatic proteases and travels to the ileum, where there is a specific transport mechanism for its absorption. Within the enterocytes the vitamin B12 dissociates from intrinsic factor then binds to transcobalamin2 and leave the enterocytes to the liver. A consequence of gastrectomy is loss of the source of intrinsic factor, the parietal cells. Therefore, after a gastrectomy, patients fail to absorb vitamin B12 from the ileum, eventually become vitamin B12 deficient, and may develop pernicious anemia. To prevent pernicious anemia, vitamin B12 must be administered by injection; orally supplemented vitamin B12 cannot be absorbed in the absence of intrinsic factor.

Reference; Linda S.Costanzo BRSPhysiology, 5thEdition

12. Describe the motility of colon

Three prominent patterns of motility are observed the colon:

- **Segmentation contractions** which chop and mix the ingesta, presenting it to the mucosa where absorption occurs. These contractions are quite prominent forming sacculations in the colon known as *haustra*.
- **Antiperistaltic contractions propagate toward the ileum**, which serves to retard the movement of ingesta through the colon, allowing additional opportunity for absorption of water and electrolytes. Peristaltic contractions, in addition to influx from the small intestine, facilitate movement of ingesta through the colon.
- **Mass movements** constitute a type of motility not seen elsewhere in the digestive tube. Known also as giant migrating contractions, this pattern of motility is like a very intense and prolonged peristaltic contraction which strips an area of large intestine clear of contents.

In periods between meals, the colon is generally quiescent. Following a meal, colonic motility increases significantly, due to signals propagated through the enteric nervous system - the so called *gastrocolic and duodenocolic reflexes*, manifestation of enteric nervous system control. The signal is stimulated almost exclusively by the presence of fat in the proximal small intestine. Additionally, distension of the colon is a primary stimulator of contractions.

Several times each day, mass movements push feces into the rectum, which is usually empty. The gastrocolic reflex mentioned above is a stimulus for this. Distension of the rectum stimulates the defecation reflex. This is largely a spinal reflex mediated via the pelvic nerves, and results in reflex relaxation of the internal anal sphincter followed by voluntary relaxation of the external anal sphincter and defecation.

Defecation can be prevented by voluntary constriction of the external sphincter. When this happens, the rectum soon relaxes and the internal sphincter again contracts, a state which persists until another bolus of feces is forced into the rectum.

13. Describe entero-gastric reflex. State its stimulus and describe its effects

The **enterogastric reflex** is one of the three extrinsic **reflexes** of the gastrointestinal tract. The enterogastric reflex is stimulated in the duodenum by a pH of 3-4 and in the stomach by a pH of 1.5. Upon initiation of the reflex, the release of gastrin by G-cells in the antrum of the stomach is shut off. This in turn inhibits gastric motility and the secretion of gastric acid (HCl). It leads to inhibition of the vagal nuclei in the medulla, inhibition of the local reflexes and activate the sympathetic fibres that cause the pyloric sphincter to tighten and prevents further chyme entry into the small intestine. It is a feedback mechanism to regulate the rate at which partially digested food (chyme) leaves the stomach and enters the small intestine. Receptors in the duodenal wall detect distension of the duodenum caused by the presence of chyme and also raised acidity (i.e. low pH) of the duodenal contents due to excess gastric acid. They send signals via the parasympathetic nervous system, causing reflex inhibition of stomach-wall muscles responsible for the stomach emptying.

14. For protein digestion, list the enzymes involved, their source of secretion and their site of action.

>**Pepsinogen**, the inactive form of **pepsin**, is secreted by **chief cells** that line the gastric glands and they digest proteins in the stomach.

Within the small intestine, the pancreatic juice contains proteases which digest proteins. These are; pro-carboxypeptidase, chymotrypsinogen and trypsinogen. The enzyme **enterokinase** is membrane-bound along the lining of the small intestine. It converts **trypsinogen** into its active form **trypsin**.

> **Trypsin**- Trypsin catalyzes the conversion of both **pro-carboxypeptidase** and **chymotrypsinogen** into their active forms, **carboxypeptidase** and **chymotrypsin**, respectively

> **Carboxypeptidase- Carboxypeptidase** specifically hydrolyzes the amino acid from the carboxyl end of peptide chains to yield individual **amino acids.**

> **Chymotrypsin-** The enzyme **chymotrypsin**, like pepsin, hydrolyzes peptides in various size smaller amino acid chains finally producing **dipeptides & tripeptides.**

15. Briefly describe the role of intrinsic factor in vitamin B12 absorption

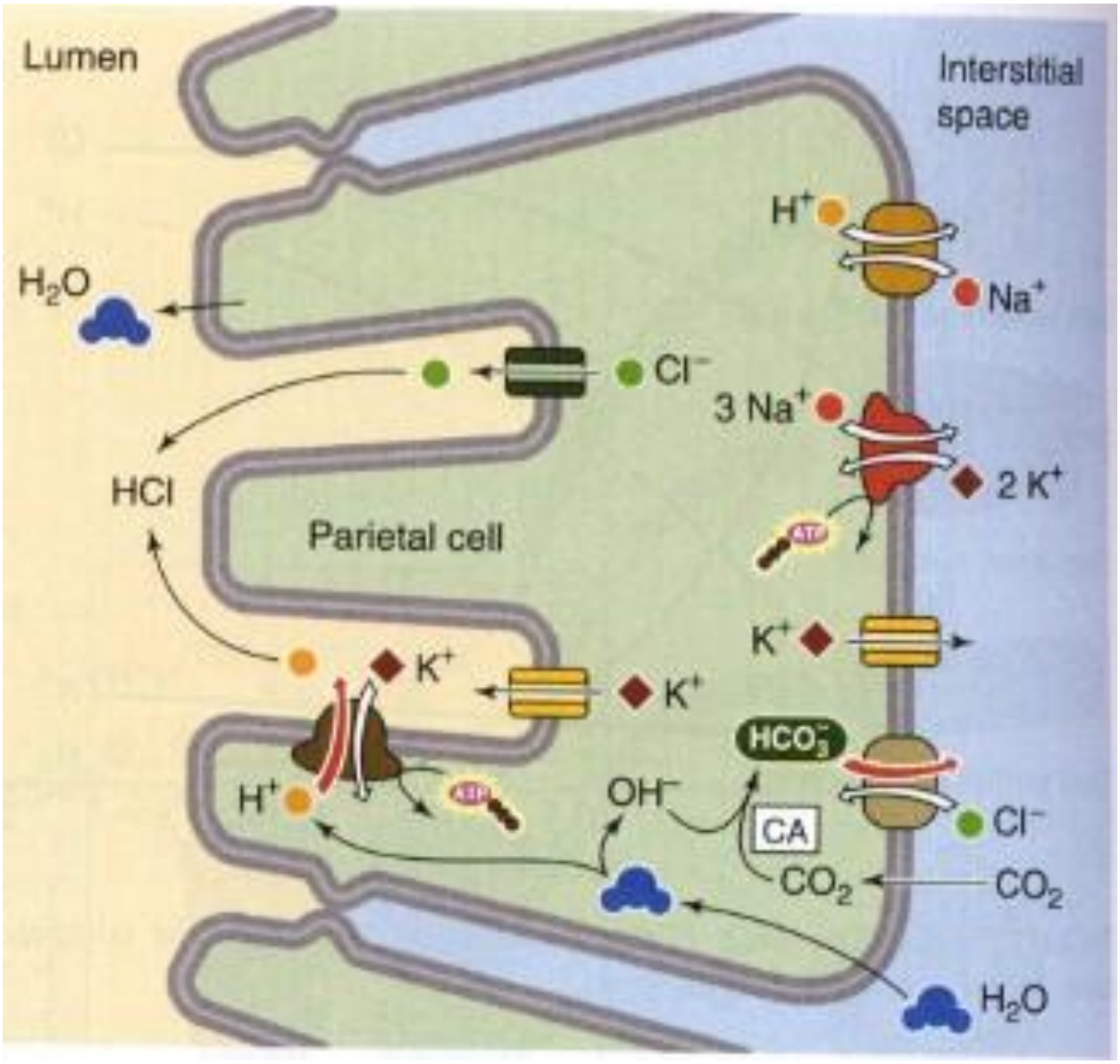
Intrinsic factor is a glycoprotein secreted by parietal of the gastric mucosa. It has an important **role** in the absorption of vitamin B12 (cobalamin) in the intestine, and failure to produce or utilize **intrinsic factor** results in the condition pernicious anemia.

Dietary vitamin B_{12} is released from ingested proteins in the stomach through the action of pepsin and gastric acid. It is rapidly bound by one of two vitamin B_{12}-binding proteins such as haptocorrin that are present in gastric juice; at acid pH, these binding proteins have a greater affinity for the vitamin than does intrinsic factor. In the small intestine, pancreatic proteases digest the binding proteins, releasing vitamin B_{12} which then becomes bound to intrinsic factor forming an intrinsic factor- vitamin B12 complex. Finally, there are receptors for intrinsic factor on the ileal mucosa which bind the complex, allowing vitamin B_{12} to be absorbed into portal blood. Vitamin B_{12} is necessary for maturation of erythrocytes, and a deficiency of this vitamin leads to development of anemia. Since efficient absorption of vitamin B_{12} depends on intrinsic factor, diseases which decrease the secretion of intrinsic factor (e.g. atrophic gastritis), interfere with cleavage of the binding proteins (e.g. pancreatic exocrine insufficiency) or decrease binding and absorption of the intrinsic factor-vitamin B_{12} complex (e.g. ileal disease or resection) can result in this type of anemia.

16. Briefly describe the formation of HCL in the gastric mucosa

The hydrogen ion concentration in parietal cell secretions is roughly 3 million fold higher than in blood, and chloride is secreted against both a concentration and electric gradient. Thus, the ability of the parietal cell to secrete acid is dependent on active transport. The key player in acid secretion is an H+/K+ ATPase or "proton pump" located in the basolateral membrane. This ATPase is magnesium-dependent. The current model for explaining acid secretion is as follows:

- Hydrogen ions are generated within the parietal cell from dissociation of water. The hydroxyl ions formed in this process rapidly combine with carbon dioxide to form bicarbonate ion, a reaction catalyzed by carbonic anhydrase.
- Bicarbonate is transported out of the basolateral membrane in exchange for chloride. The outflow of bicarbonate into blood results in a slight elevation of blood pH known as the "alkaline tide". This process serves to maintain intracellular pH in the parietal cell.
- Chloride and potassium ions are transported into the lumen of the canaliculus by conductance channels, and such is necessary for secretion of acid.
- Hydrogen ion is pumped out of the cell, into the lumen, in exchange for potassium through the action of the proton pump; potassium is thus effectively recycled.
- Accumulation of osmotically-active hydrogen ion in the canaliculus generates an osmotic gradient across the membrane that results in outward diffusion of water - the resulting gastric juice is 155 mM HCl and 15 mM KCl with a small amount of NaCl.



17. Briefly explain the process of carbohydrate digestion.

In the Mouth

Carbohydrate digestion begins in the mouth. The salivary glands in the mouth secrete saliva, which helps to moisten the food. The food is then chewed while the salivary glands also release the enzyme salivary amylase, which begins the process of breaking down the polysaccharides in the carbohydrate food.

In the Stomach

After the carbohydrate food is chewed into smaller pieces and mixed with salivary amylase and other salivary juices, it is swallowed and passed through the esophagus. The mixture enters the stomach where it is known as chyme. There is no further digestion of chyme, as the stomach produces acid which destroys bacteria in the food and stops the action of the salivary amylase.

In the Pancreas and Small Intestine

After being in the stomach, the chyme enters the beginning portion of the small intestine, or the duodenum. In response to chyme being in the duodenum, the pancreas releases the enzyme pancreatic amylase, which breaks the polysaccharide down into a disaccharide, a chain of only two sugars linked together. Brush border enzymes are present in brush border of microvilli in the small intestines. These enzymes breakdown disaccharides and starches to monosaccharide that are easy to absorb. They include:

a) Sucrase -breaks down sucrose to fructose and glucose

b) Lactase- breaks down lactose to galactose and glucose

c) Maltase- breaks down maltose and maltriose to glucose molecules

d) Dextrinase - breaks down dextrins, maltose and maltriose into glucose molecules

e) Trehalase – breaks trehalose to two glucose molecules.

The monosaccharides are single sugars that are then absorbed in the small intestine.

In the Large Intestine (Colon)

Carbohydrates that were not digested and absorbed by the small intestine reach the colon where they are partly broken down by intestinal bacteria. Fiber, which cannot be digested like other carbohydrates, is excreted with feces or partly digested by the intestinal bacteria

(c)RESPIRATORY PHYSIOLOGY

1. Describe 1 cause and 1 corrective response to respiratory alkalosis.

Respiratory alkalosis is a disturbance in acid and base balance due to alveolar hyperventilation. Alveolar hyperventilation leads to a decreased partial pressure of arterial carbon dioxide. In turn, the decrease in PaCO2 increases the ratio of bicarbonate concentration to PaCO2 and thereby increases the pH level. Respiratory alkalosis is caused by hyperventilation in cases such as during anxiety moments. The response to respiratory is primarily aimed to offset the alkalosis. First, the buffer systems other than the bicarbonate buffer system respond by releasing hydrogen ions. The renal system then seeks to compensate by reducing reabsorption of hydrogen ions and finally respiratory compensation occurs.

2. Explain the phenomena of hypoxic vasoconstriction and contrast it with systemic hypoxic response.

Hypoxic pulmonary vasoconstriction is a phenomenon in which small pulmonary arteries constrict in the presence of alveolar hypoxia. This causes redirection of blood flow from poorly ventilated lung regions to well ventilated lung regions. This phenomenon of hypoxic vasoconstriction differs with systemic hypoxic response in that in systemic hypoxic response there is vasodilation. By widening the blood vessels, the tissue allows greater perfusion.

3. Outline and explain some of the possible complications of extracorporeal circulation.

Extracorporeal circulation is circulation outside the body. Examples occur such as during pulmonary bypasses, dialysis procedures. Some of the complications include;

a. Oliguria

this is due to development of acute kidney injury characterized by decreased diuresis volume and increased creatinine especially in patients under cardiopulmonary bypass.

b. Hyperglycemia

This due to increased need for exogenous insulin to keep up the same glucose homeostasis levels.

c. Neurosensory alterations characterized by agitation, cognitive deficit or convulsive crises.

This could be due to the small clots released, during the intraoperative phase, into small arteries and cerebral capillary vessels.

d. Abnormal pH changes

e. Abnormal temperature changes

f. Abnormal blood pressures

g. Damage of blood cells due to turbulent flow of blood

h. Formation of clots

4. Briefly describe the use of feedforward control mechanisms in exercise.

As exercise begins, proprioceptors in the muscles and joints send information to motor cortex of the brain. Descending signals from the motor cortex go not only to the exercising muscles but also along

parallel pathways to the CVS and respiratory control centers and to the limbic system. Output from the limbic and cardiovascular control center triggers generalized sympathetic discharge. As a result, an immediate slight increase in blood pressure marks the beginning of exercise. Sympathetic discharge causes widespread vasoconstriction, increasing blood pressure. Once exercise has begun, this increase in blood pressure compensates for decreases in blood pressure resulting from muscle vasodilatation.

5. Describe the 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.

6) DESCRIBE AND EXPLAIN COMPLIANCE IN RESPIRATORY PHYSIOLOGY

-Compliance is the measurement of the ability to stretch against elastic properties. Compliance in the slope of pressure-volume curve is the volume change per unit pressure. In respiratory physiology, the lung and blood vessels exhibit compliance.

In normal expanding range (2-10mm water) the lung is very dispensable, compliant C=Volume difference/Pressure difference (this is due to the additional energy required during inspiration to recruit and inflate additional alveoli. In Compliance, curves are not linear and the difference between inspiration and exploratory curves is called HYSTERESIS.

For comparison; Vein=0.04L/cm of water

Artery=0.002L/cm of water

In pulmonary blood vessels, they have higher compliance as compared to systemic blood vessels. Following increased blood pressure, they respond by distending the vessels and recruiting more blood vessels to reduce resistance.

7) OUTLINE CIRCUMSTANCES WHERE OXYGEN THERAPY IS ESSENTIAL AND ONE CIRCUSMSTANCE WHERE IT CAN BE DETRIMENTAL

Essential

- During low blood oxygen (hypoxaemia)
- Carbon dioxide toxicity (hypercapneia)
- During hypoxic hypoxia
- Treating gas gangrene
- During cluster headaches
- Chronic conditions e.g. Chronic Obstructive Pulmonary Disease (COPD), chronic bronchitis

Detrimental

In patients suffering from pulmonary fibrosis and Histotoxic hypoxia.

8**. List the common types of hypoxia and state whether oxygen therapy would be useful in each**

•Hypoxic hypoxia- Partial pressure of arterial oxygen is reduced. For instance, breathing oxygen poor air or at reduced atmospheric pressure. Oxygen therapy not useful

•Anemic hypoxia- Essentially low hemoglobin content and thus transport of oxygen to tissues is inhibited. Also in carbon monoxide poisoning, effective hemoglobin content is reduced by HbCO coupling. Oxygen therapy is Useful.

•Stagnant Hypoxia- Due to circulation that is slow that tissue doesn't receive its necessary "flow" of oxygen. It can be due to shock, congestive heart failure, or localized constrictions. Oxygen therapy is Useful.

•Histotoxic hypoxia- Inhibition of tissue oxidative processes by poisons like cyanide. Oxygen therapy is not useful

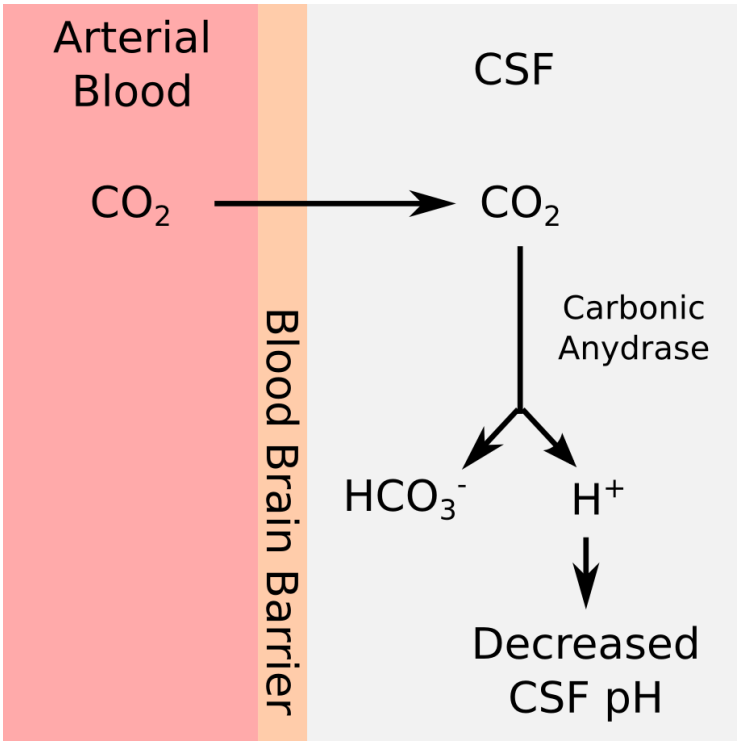
9. Describe the indirect measurement of blood pH by central chemoreceptors

The Central Chemoreceptors are an anatomical collection of neuronal chemoreceptors located just beneath the ventral surface of the brainstem's medulla. The central chemoreceptors are critical sensors of arterial carbon dioxide and are the key sensory component of a negative feedback loop which controls respiratory activity in an attempt to maintain relatively constant levels of arterial carbon dioxide.

Sensory Mechanism

The central chemoreceptors are most directly sensitive to changes in their surrounding extracellular fluid pH, which given their anatomical location would mean the CSF. However, the blood brain barrier is relatively impermeable to hydrogen and bicarbonate ions; consequently, the central chemoreceptors cannot respond quickly to changes in the blood pH. Although blood pH is not closely linked to the CSF pH, the partial pressure of arterial carbon dioxide displays a tight relationship with the CSF pH through a notable mechanism. Dissolved CO_2 within the arterial blood can readily diffuse through the blood brain barrier into the CSF where it is converted by carbonic anhydrase into carbonic acid (H_2CO_3).

Carbonic Acid spontaneously releases a free hydrogen ion which reduces the pH of CSF. Consequently, changes in the arterial partial pressures of CO_2 indirectly modulate the pH of the CSF through CO_2 diffusion and conversion to carbonic acid. When arterial carbon dioxide increases above normal, CSF pH decreases and the central chemoreceptors send stimuli above their basal rate. Conversely, when arterial carbon dioxide decreases below normal, CSF pH increases and the central chemoreceptors reduce their activity below their basal rate.



Effects-The central chemoreceptors send signals to the brainstem respiratory centers, especially the Inspiratory Center, and thus aid in control of respiration by modifying the respiratory drive. When CSF pH lowers, due to increased arterial carbon dioxide partial pressures, stimuli sent by the central chemoreceptors activates the Inspiratory Center to increase the respiratory drive, thus enhancing alveolar ventilation and aiding in elimination of accumulated CO2. When CSF pH rises due to decreased arterial carbon dioxide partial pressures, decreased stimuli sent by the central chemoreceptors lowers basal stimulation of the Inspiratory Center, thus reducing respiratory drive which in turn reduces alveolar ventilation and pulmonary elimination of CO2.

10) EXPLAIN RESPIRATORY-PERFUSION RATIOS

Ventilation-perfusion ratio is a ratio comparing the rates of alveolar ventilation and cardiac output.

Alveolar Ventilation (VA) =Tidal Volume (VT)-Dead space Volume (VD) × Respiratory rate:

4.2ml/min= (0.5-0.15) × 12

Cardiac output= stroke volume × heart rate:

6.0 ml/min=0.086 × 70

VA/Q= Approximately 0.8

Ideally it should be 1:1, however the normal range is 0.63-3.3

Theoretically; If there is no ventilation, but normal perfusion: V/Q=0 and if there is normal ventilation but no perfusion, V/Q=∞ (infinity)

It is regional V/Q and not overall V/Q that's crucial.

11. Describe acute mountain sickness.

Altitude sickness, also known as acute mountain sickness (AMS), is a negative health effect of high altitude, caused by acute exposure to low amounts of oxygen at high altitude. It presents as a collection of nonspecific symptoms, acquired at high altitude or in low air pressure. It occurs above 2,400 metres (8,000 ft.). It can progress to high altitude pulmonary oedema or high altitude cerebral oedema, both of which are potentially fatal, and can only be cured by immediate descent to lower altitude or oxygen administration. It's a delayed response to high altitude change as it develops over time. As altitude increases, the available amount of oxygen to sustain mental and physical alertness decreases with the overall air pressure. Mild AMS does not usually interfere with normal activity and symptoms generally subside within 2-4 days as the body acclimatizes. As long as symptoms are mild, and only a nuisance, ascent can continue at a moderate rate. It is basically a mild form of high altitude cerebral oedema. Moderate AMS includes severe headache (not relieved by medication), nausea, vomiting, increasing weakness and fatigue, shortness of breath, and decreased coordination. Normal activity is difficult. At this stage, only advanced medications or descent can reverse the problem. Severe AMS presents as an increase in the severity of the symptoms, including greater shortness of breath at rest, inability to walk, decreasing mental status, and fluid build-up in the lungs.

12. Describe and explain what respiratory drive is.

Respiratory drive refers to the process by which detected changes in the body's pH and PCO2 and PO2 levels are responded to by the central nervous system's corrective stimulation of the rhythm, effort and rate of breathing. Carbon IV oxide is the major regulator of respiration (hypercapnic ventilatory drive); increase or decrease in pH can stimulate chemo-sensitive areas causing greater rate and depth of respiration. Oxygen levels affect respiration when a 50% or greater decrease from normal exist (hypoxic ventilatory drive).

Hypercapnic drive occurs when there is rise in arterial carbon dioxide more than normal, which is detected directly by peripheral chemoreceptors stimulating hyperventilation. 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.

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.

13. Describe the non-respiratory functions of the lung.

-Immune functions- the lungs have dust cells which are professional macrophages from the mononuclear phagocytic system.

- Important endocrine functions of the lung include: Release of inflammatory mediators such as histamine, endothelin, and eicosanoids, release of nitric oxide to regulate smooth muscle and ACE metabolizes angiotensin I to angiotensin II

- Modification of circulating levels of a range of biologically active materials.

- Filtration of blood- The entire cardiac output passes through the 7µm pulmonary capillaries, which act as an effective sieve for particulate matter. Complementing this role, the lungs are able to clear thrombi more rapidly than other organs as pulmonary endothelium has a high concentration of plasmin activator and heparin.

- Serving as a reservoir of blood for rapid adjustment of input to the left atrium when needed- The highly compliant pulmonary circulation contains a reservoir of ~500ml of blood which acts as a volume reserve for the left ventricle.

- Drug Delivery- The same properties that optimise the lung for gas exchange optimise it for delivery of inhaled agents. Drugs absorbed in the pulmonary circulation are; Lipophilic and alkaline (pKa >8)

14. Describe the role of intrapleural pressure in lung inflation and deflation.

Intrapleural pressure is the pressure within the pleural space. Due to the elastic forces of the lung (tending to contract) and the chest wall (tending to expand) under normal conditions intrapleural pressure is negative. The magnitude of this pressure varies with each phase of ventilation. During inspiration as the chest wall expands, the intrapleural pressure decreases (more negative). During expiration as the chest wall recoils it increases (less negative). The air coming into the lung is driven by these pressure gradients. The negativity of intrapleural pressure allows the outside pressure (alveolar pressure) to exert force and maintain proper background inflation of the lungs to prevent complete collapse.

15. Explain chloride shift as it occurs in lung tissue.

The chloride shift is an exchange of ions that takes place in our red blood cells in order to ensure that no build-up of electric change takes place during gas exchange. Within our tissues, the cells produce a bunch of carbon dioxide molecules that are ultimately expelled by the cell and travel to the blood plasma. Once inside the blood plasma, the majority of carbon dioxide moves into the red blood cells, where they are converted into bicarbonate ions with the help from carbonic anhydrase. Unlike carbon dioxide, bicarbonate is very soluble in the blood plasma and therefore must return there by moving out of the red blood cell. However, as it moves across a special ion-exchange membrane protein, a chloride ion is brought into the cell (in a one-to-one ratio). This is known as the chloride shift and it takes place in order to maintain electric neutrality so that there is no build-up of charge. The same thing happens in our lungs just the process is reversed (i.e. bicarbonate ions are brought into the red blood cell while the chloride ions are moved out of the cell).

16. Describe the factors that affect Hemoglobin's affinity for oxygen.

- **pH**

The body may undergo change in blood pH during maximal exertion that forces cells into anaerobic metabolism. In exercising muscles, anaerobic metabolism generates lactic acid, which in turn releases H^+ into the cytoplasm and extracellular fluid.

As the cells generate more hydrogen ions, $[H^+]$ rises and pH falls, the affinity of Hb for oxygen declines making the O_2-Hb dissociation curve to shift to the right.

Consequently, Hb, in blood, releases more oxygen at the tissues as blood becomes more acidic

- **Temperature**

A rise in temperature shifts the O_2-Hb curve to the right and hence causes HbO_2 to release more of its oxygen at any given $\mathbf{Po_2}$.When the exercising muscles warm(due to heat production),the local rise in temperature promotes the oxygen release from HbO_2.Thus,an elevated temperature diminishes hemoglobin's affinity for oxygen.

- **Pco_2**

Pco_2 increases in the tissue capillary blood because of the carbon dioxide entering the blood from the tissues. Elevated Pco_2 and the release of metabolically produced acids like lactic acid together elevate the $[H^+]$ of blood

- **BPG**

2,3-bisphosphateglycerate or 2,3-BPG is a compound made by red blood cells in particularly large amounts whereas only trace amounts of it occur in other human cells.

BPG binds reversibly with Hb making it to have a lower affinity for oxygen. Whenever erythrocytes produce more BPG, Hemoglobin's affinity for oxygen falls and hence enhances unloading of oxygen from Hb as blood flows through the tissues. Such increase in BPG levels can occur in several conditions associated with insufficient oxygen supply to tissues to maintain oxygen delivery.

Extended periods of low oxygen (chronic hypoxia), for example, triggers the increased production of BPG in red blood cells. Increase in BPG levels during exposure to low oxygen is important because it enhances the unloading of oxygen at tissue capillaries.

17. Briefly describe and explain the significance of physiological dead space.

This is the volume of air which is inhaled that does not take part in the gas exchange, either because it remains in the conducting airways, or reaches alveoli that are not perfused or poorly perfused. It increases during diseases that negatively affect pulmonary blood flow. It is measured by Fowler's method. Anatomical dead space is the portion of the airway that doesn't

have alveoli and thus doesn't take part in gaseous exchange. It totally amounts to 150ml. alveolar dead space is the alveoli bearing areas which don't participate in gaseous exchange. (Pathological). Physiological dead space is a sum of both anatomical and alveolar dead space.

Benefits do accrue to a seemingly wasteful design for ventilation that includes dead space;

-Carbon dioxide is retained, making a bicarbonate-buffered blood interstitium possible.

-Inspired air is brought to body temperature, increasing the affinity of hemoglobin for Oxygen, improving O_2 uptake.

-Particulate matter is trapped on the mucus that lines the conducting airways, allowing its removal by mucociliary transport.

-Inspired air is humidified, improving the quality of airway mucus.

18. Describe the cause, effect and response in metabolic acidosis.

Cause;

Metabolic acidosis is a condition that occurs when the body produces excessive quantities of acid or when the kidneys are not removing enough acid from the body. It occurs in kidney diseases, diabetic metabolic ketoacidosis and in excess exercise leading to accumulation of lactic acid.

Effects;

If unchecked metabolic acidosis leads to **acidemia** i.e low blood pH(less than 7.35) due to increased production of hydrogen ions by the body or the inability of the body to form bicarbonate (HCO_3^-) in the kidney .Its consequences can be serious including comma and death.

Compensatory mechanisms;

-Bicarbonate buffering systems

-Intracellular buffering by absorption of hydrogen atoms by various molecules, including proteins, phosphates and carbonate in bone.

-Respiratory compensation; Hyperventilation will cause more carbon dioxide to be removed from the body and thereby increase pH

-Renal compensation; Kidneys regulate the plasma pH

19. List the functions of the airway.

-Heat and moisture exchange

-Thermoregulation

-Filtration

-Humidification

-Olfaction

-Air conditioning

-Voice production

-Immune functions

20. Explain how a rise in CO2 may be detected by central chemoreceptors.

An increase in carbon dioxide causes tension of the arteries, often released from decreased CO_2 output(hypercapnia),indirectly causes the blood to become more acidic; the cerebrospinal fluid PH is closely comparable to plasma, as carbon dioxide easily diffuses across the blood-brain barrier. This system utilizes negative feedback system, therefore if the pH of the cerebrospinal fluid does not compare to an ideal set level, then the receptor will send an error signal to the effectors and appropriate action may be executed. The Central Chemoreceptors are an anatomical collection of neuronal chemoreceptors located just beneath the ventral surface of the brainstem's medulla. The central chemoreceptors are critical sensors of arterial carbon dioxide and are the key sensory component of a negative feedback loop which controls respiratory activity in an attempt to maintain relatively constant levels of arterial carbon dioxide.

Sensory Mechanism

The central chemoreceptors are most directly sensitive to changes in their surrounding extracellular fluid pH, which given their anatomical location would mean the CSF. However, the blood brain barrier is relatively impermeable to hydrogen and bicarbonate ions; consequently, the central chemoreceptors cannot respond quickly to changes in the blood ph. Although blood pH is not closely linked to the CSF pH, the partial pressure of arterial carbon dioxide displays a tight relationship with the CSF pH through a notable mechanism. Dissolved CO2 within the arterial blood can readily diffuse through the blood brain barrier into the CSF where it is converted by carbonic anhydrase into carbonic acid (H2CO3).

Carbonic Acid spontaneously releases a free hydrogen ion which reduces the pH of CSF. Consequently, changes in the arterial partial pressures of CO2 indirectly modulate the pH of the CSF through CO2 diffusion and conversion to carbonic acid. When arterial carbon dioxide increases above normal, CSF pH decreases and the central chemoreceptors send stimuli above their basal rate. Conversely, when arterial carbon dioxide decreases below normal, CSF pH increases and the central chemoreceptors reduce their activity below their basal rate.

21. What factors determine the rate of gas transfer across the alveolar capillary membrane?

> Surface area of the membrane- this is directly proportional to the rate.

> Thickness of the membrane- inversely proportional

> Pressure gradient- between partial pressure of a gas in the alveoli and the pulmonary capillary.

> Solubility of gas in fluid medium- directly proportional

> Molecular weight of the gas- inversely proportional.

22. Describe briefly the functions of the larynx

> Phonation- production of sound

> Respiration- entry to the airway
> Protection- ensures food particles and particulate matter don't enter the trachea.
> Deglutition

23. Describe the work of breathing

Work of breathing is the energy expended to inhale and exhale a breathing gas. It is usually expressed as work per unit volume, for example, joules/litre, or as a work rate, such as joules/min or equivalent units, as it is not particularly useful without a reference to volume or time. It can be calculated in terms of the pulmonary pressure multiplied by the change in pulmonary volume, or in terms of the oxygen consumption attributable to breathing. In a normal resting state the work of breathing constitutes about 5% of the total body oxygen consumption. It can increase considerably due to illness or constraints on gas flow imposed by breathing apparatus, ambient pressure, or breathing gas composition.

The energy expended during breathing is used to facilitate lung compliance, to counter the airway resistance and to counter the viscosity of the lungs and chest wall.

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!