

Digestive

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July 2023

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1 Introduction

The gastrointestinal (GI) tract plays a pivotal role in the intake, absorption, and processing of nutrients and water, while also contributing to the overall balance of the body. Its intricate mechanisms and functions are crucial for maintaining bodily homeostasis and ensuring optimal health. In this handout guide, we will explore the fascinating complexities of the GI tract, unraveling its anatomy, functions, and significance in our overall well-being.

2 Layers and Physiology of the GI Tract

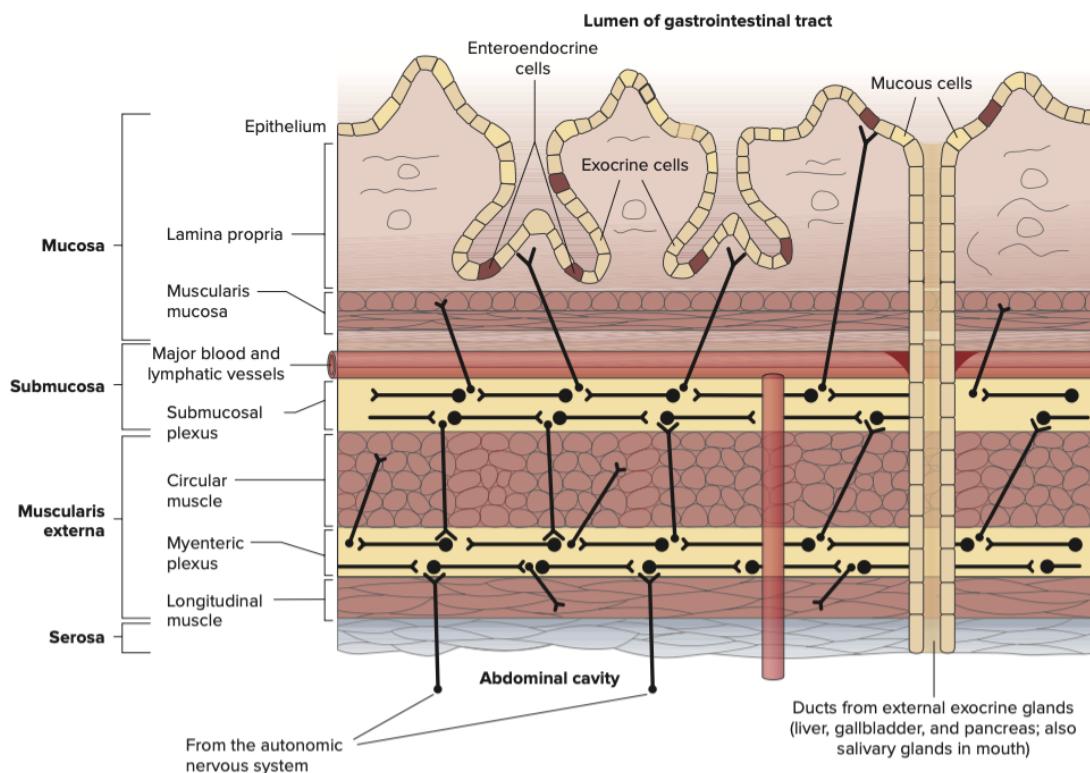


Figure 1: Layers of the GI tract. (Source: Vander's Human Physiology)

- The **muscosa** is composed of epithelium connected via tight junctions. It consists of the **lamina propria**, which contains connective tissue and small lymphatic and blood vessels, and the **muscularis mucosa**. Both are involved in small movements of the surface layer of the tract.
- The **submucosa** contains major blood vessels and lymphatic vessels, along with the **submucosal (Meissner's) plexus**, a collection of neurons part of the enteric nervous system.
- The **muscularis externa** is composed of **circular muscle** involved in the narrowing of the tube, the **myenteric (Auerbach's) plexus** that contains sympathetic and parasympathetic innervation, and longitudinal muscle involved in the lengthening of the tube.
- The **serosa** consists of thin sheets of connective tissue that connect the GI tract to the abdominal wall.

- **Villi** and **microvilli** increase the surface area for nutrient absorption in the small intestine. The cells at the base of the villi rise up to replace cells at the tip of the epithelium, which release digestive enzymes when they break. **Enteroendocrine cells** are found at the base of the villi. These cells secrete hormones that regulate intestinal processes.
- **Plexi** are intricate networks of nerves through which neural input from upstream the GI tract can travel laterally downstream. In a **short reflex**, signals detected by receptors in the GI travel through the plexus, where they travel to effector cells that carry out the response. In a **long reflex**, stimuli detected by receptors in the GI travel to the CNS, then back through the plexus and finally to effector cells.

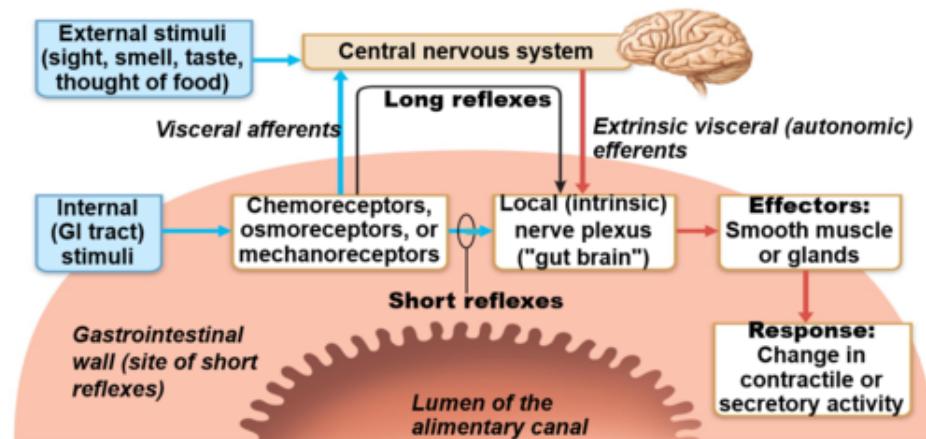


Figure 2: Reflexes. (Source: lamission.edu)

3 GI Hormones

GI hormones respond to the chemical environment and modulate absorption, motility, and digestive processes of the tract.

- Concentration of food molecules, distension, osmolarity, and acidity all control GI hormone release.
- **Cholecystokinin (CCK)** is a peptide hormone whose release is triggered by fatty acids and amino acids in the small intestine. Note that CCK potentiates secretin's effect on bicarbonate (HCO_3^-) in the pancreas and liver but does not directly control it. CCK is released by I cells in the duodenum and jejunum.
- **Secretin** is a peptide hormone created in the small intestine. It responds to acidity in the small intestine and results in bicarbonate secretion from the pancreas and liver into the small intestine. Secretin also potentiates CCK's enzymatic secretion activity. Secretin is produced by S cells in the duodenum and jejunum.
- **Glucose-dependent insulinotropic polypeptide (GIP)** is an *incretin*, meaning it causes a decrease in blood glucose levels by activating insulin secretion. It also plays a minor role in inhibiting gastrin secretion from the stomach. As such, it used to be known as gastrin inhibiting peptide. It is produced by K cells in the duodenum.

- **Gastrin** is produced by **G cells** in the antrum, or lower portion, of the stomach. It is secreted in response to parasympathetic stimulation, as well as peptides and amino acids found in chyme. Gastrin is directly inhibited by acidity and somatostatin.

	Gastrin	CCK	Secretin	GIP				
<i>Chemical class</i>	Peptide	Peptide	Peptide	Peptide				
<i>Site of production</i>	Antrum of stomach	Small intestine	Small intestine	Small intestine				
<i>Stimuli for hormone release</i>	Amino acids, peptides in stomach; parasympathetic nerves	Amino acids, fatty acids in small intestine	Acid in small intestine	Glucose, fat in small intestine				
<i>Factors inhibiting hormone release</i>	Acid in stomach; somatostatin							
<i>Target Organ Responses</i>								
<i>Stomach</i>								
Acid secretion	Stimulates	Inhibits	Inhibits					
Motility	Stimulates	Inhibits	Inhibits					
<i>Pancreas</i>								
HCO ₃ ⁻ secretion		Potentiates secretin's actions	Stimulates					
Enzyme secretion		Stimulates	Potentiates CCK's actions					
Insulin secretion				Stimulates				
<i>Liver (bile ducts)</i>								
HCO ₃ ⁻ secretion		Potentiates secretin's actions	Stimulates					
<i>Gallbladder</i>								
Contraction		Stimulates						
<i>Sphincter of Oddi</i>								
		Relaxes						
<i>Small intestine</i>								
Motility	Stimulates ileum							
<i>Large intestine</i>								
	Stimulates mass movement							

Figure 3: GI hormone chart. (Source: Vander's Human Physiology)

4 Swallowing

Saliva is a fluid found in the mouth and is secreted by the *extrinsic salivary glands*: the parotid, submandibular, and sublingual glands. Salivary secretion is always present at a basal level by the *intrinsinc salivary glands*, which are located in the cheek, tongue and inner lip. However, parasympathetic stimulation increases blood flow to the extrinsic salivary glands, making saliva more watery. Meanwhile, sympathetic stimulation results in more solid saliva by decreasing blood flow.

1. Saliva contains *bicarbonate*, which buffers the acidity of food and bacterial secretions.
2. Saliva also contains water, which moistens and lubricates the food.

3. Mucus, a glycoprotein-rich protective substance secreted by epithelial cells throughout the GI tract, is also found in saliva.
4. **Lysozymes**, antimicrobials vital to innate immunity, are found in tears and saliva.
5. Saliva also contains **salivary amylase**, an enzyme that begins the digestion of carbohydrates.
6. It also contains *salivary lipase*, which begins the digestion of triglycerides.

The swallowing center is found in the **medulla oblongata** and mediates the following steps of swallowing:

1. The tongue shapes the food and pushes it to the back of the throat in the form of a **bolus**.
2. The soft palate of the mouth rises, blocking food from entering the nose.
3. The food travels through the upper pharynx, resulting in the closure of the glottis and the tilting of the epiglottis, a flap of tissue, backward to cover the glottis. This prevents the aspiration of the food into the lungs.
4. The upper esophageal sphincter relaxes, allowing the food to pass through it. Afterward, the food passes through the lower esophageal sphincter, which remains relaxed.
 - Stomach pressure is slightly greater than atmospheric pressure, while the opening of the pharynx is equal to atmospheric pressure. However, the intrathoracic region of the esophagus is subatmospheric due to the inspiration of the lungs. Thus, the lower and upper esophageal sphincters are to prevent air from being forced downward and food from being forced upward.

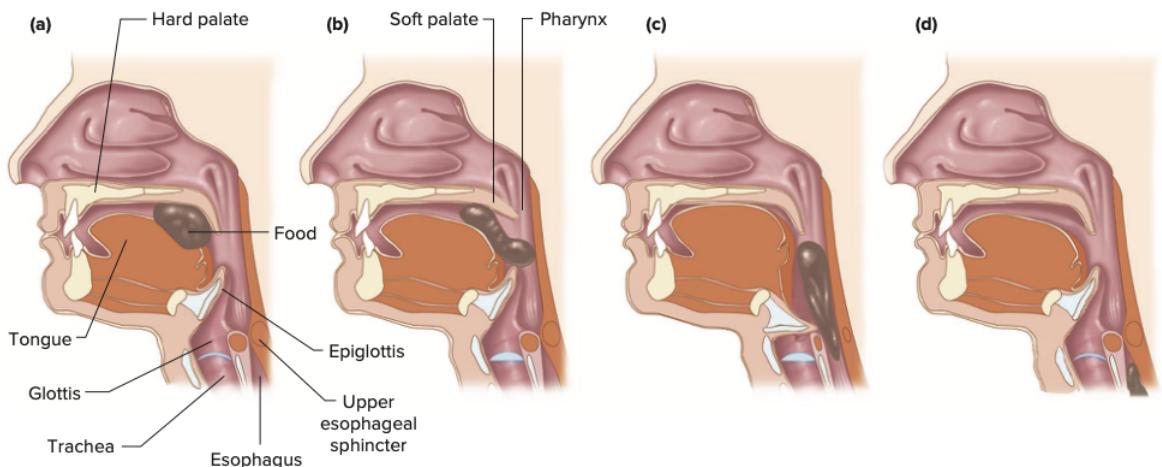


Figure 4: Stages of Swallowing. (Source: Vander's Human Physiology)

5. Breathing resumes, and the epiglottis and glottis relax following the passage of the food through the upper esophageal sphincter.
6. **Peristaltic waves** are muscular contractions in the smooth muscle of the esophagus that push food down to the stomach. This allows for people to swallow food even while upside down.

7. If the bolus does not reach the stomach, **secondary peristalsis** occurs. This is possible because the esophagus and stomach communicate via plexi.

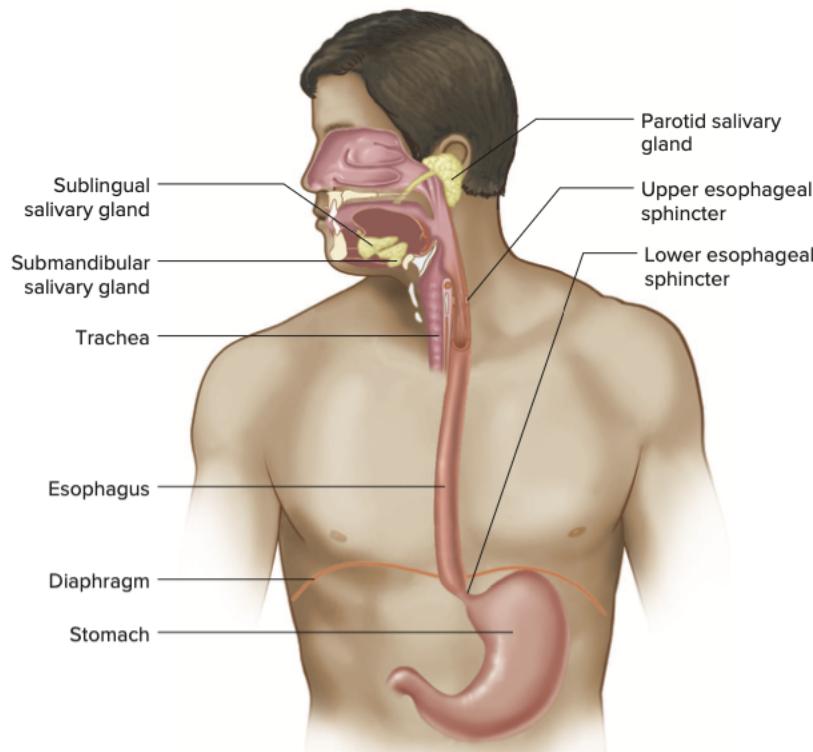


Figure 5: Upper Digestive Anatomy. (Source: Vander's Human Physiology)

Example 4.1 (Campbell Biology) The mammalian trachea and esophagus both connect to

- A. pharynx.
- B. stomach
- C. large intestine.
- D. rectum.

Solution: The trachea leads to the lungs, while the esophagus leads to the stomach. Therefore, the only connection between them is in the pharynx above (A).

5 Stomach

The stomach plays two important roles in digestion: the storage of food and the secretion of digestive fluid (i.e., gastric juice) with concurrent mixing to create a food paste called **chyme**. However, it is important to note that very little food absorption occurs in the stomach.

The phases of digestion are as follows:

1. The **cephalic** phase occurs when sensory receptors in the head respond to the sight or smell of food and modulate the secretory and contractile activity of the GI tract.

2. The **gastric**, or stomach, phase is modulated by distension, acidity, amino acids, and peptides.
3. The **intestinal** phase is simply the digestion that occurs in the intestine.

The top, middle, and bottom sections of the stomach are known as the **fundus**, **body**, and **antrum**, respectively.

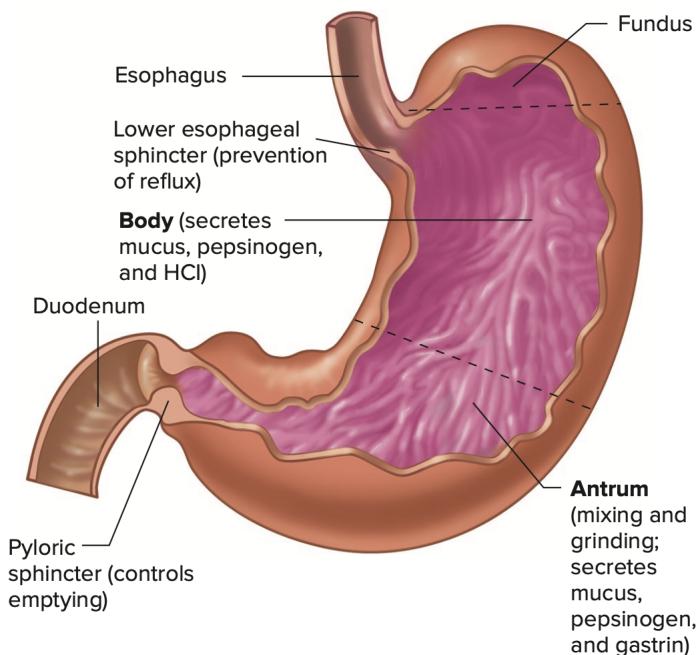


Figure 6: Upper Digestive Anatomy. (Source: Vander's Human Physiology)

- **Parietal cells** secrete hydrochloric acid (HCl) and intrinsic factor. They contain invaginations called canaliculi, which increase surface area.
 - Intrinsic factor is a protein responsible for the absorption of vitamin B12, which is required for red blood cell (RBC) function. The lack of intrinsic factor is known as *pernicious anemia* and results in low red blood cell count.
 - Within the parietal cells, an enzyme called **carbonic anhydrase** produces HCO_3^- and H^+ from CO_2 and O_2 . Removing the products of carbonic anhydrase from the cell allows for continuous H^+ secretion by influencing the equilibrium of the reaction.
- **Gastrin**, **acetylcholine**, and **histamine** bind to parietal cells in order to increase acid secretion via increased H^+/K^+ ATPase expression.
- Neurons also synapse directly upon parietal cells following thoughts of food to increase secretion.
- During the cephalic phase, neurons synapse on plexi to increase the secretion of acid from parietal cells.

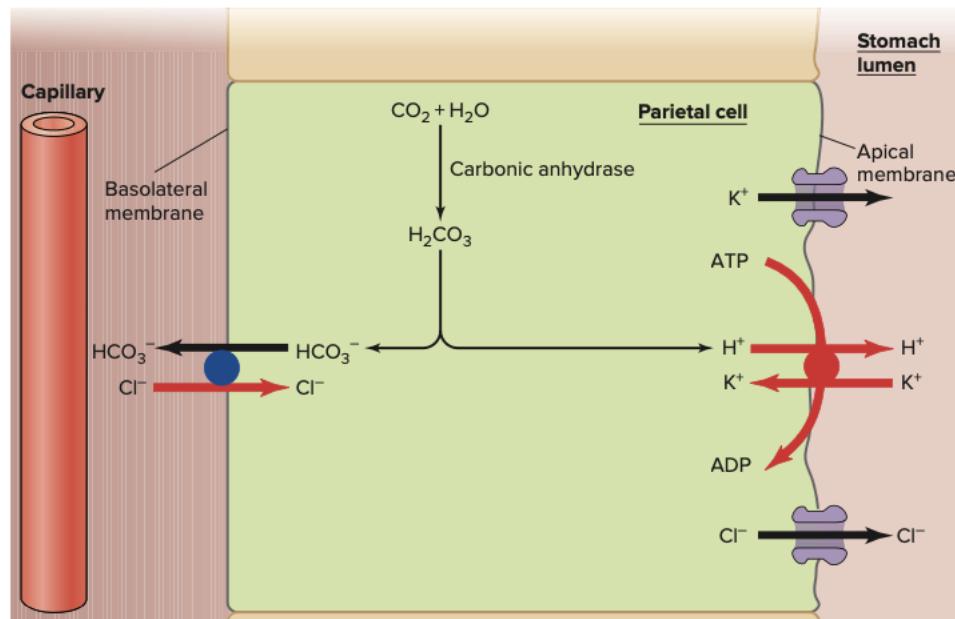
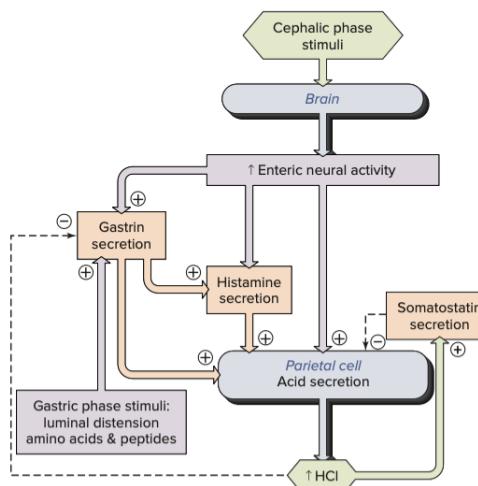


Figure 7: Parietal Cell Secretions. (Source: Vander's Human Physiology)

- **D cells** secrete somatostatin, which binds to parietal cells to inhibit acid release.
- **G cells** secrete gastrin.
- **Enterochromaffin-like cells (ELC)** secrete histamine.
- **Chief cells** secrete pepsinogen, a zymogen. A *zymogen* is an inactive substance that is activated by another substance. In this case, HCl activates pepsinogen into pepsin in the stomach. Thus pepsin is only activated at low pH. This prevents self-digestion of the cell that secretes it.
- When food reaches the stomach, increased stretch, or distension, along with the appearance of amino acids, results in the increased secretion of these hormones via plexi. Amino acids can bind directly to G cells and stimulate secretion.



Flowchart of HCL Secretion. Source: Vander's Human Physiology

- As peptides enter the stomach, they increase acidity by buffering pre-existing acid. This decreases the inhibition of G cells via decreased somatostatin and acid, since acid stimulates somatostatin and inhibits G cells.
- Efferent input from the swallowing center in the medulla results in receptive relaxation of the stomach, thus increasing the volume of the stomach before food enters. Afferent vagus nerve feedback to the CNS aids in this process.
- **Stomach contractions** begin in the fundus and move their way down relatively weakly. However, once they hit the muscular antrum, contractions strengthen.
- To prevent food from reaching the small intestine during contractions, the **pyloric sphincter**, located at the entrance of the small intestine, prevents chyme from escaping. Thus, it closes reflexively during contraction, preventing too much chyme from reaching the small intestine at a time.
- Once the chyme hits the antrum, it is forced backward by the closed sphincter, causing shear stress to break food particles down using mechanical digestion.
- The creation of such contractions is the result of a basal electrical rhythm in the stomach that can be increased by gastrin, parasympathetic stimulation, and other stimuli.

6 Small Intestine

Although chemical digestion begins in the stomach and mouth, the small intestine is responsible for most of the breakdown of macromolecules.

- High osmolarity, high acidity, high amino acids, and high fats slow down stomach motility via enterogastrones, which are hormones that lower acidity and thus inhibit gastrin. This allows the small intestine to control the rate of digestion and ensure that enzymatic and absorptive capabilities are maximized.
- The small intestine has **three sections**: the **duodenum**, the **ileum**, and the **jejunum**.
 - Most of the nutrients are absorbed in the jejunum and the first part of the ileum. However, the duodenum is the source of intestinal digestive enzymes, which combine with pancreatic and liver secretions to carry out most non-absorptive digestion.
 - B12 is absorbed in the ileum.
- Between and on the villi of the small intestine, which are composed of simple columnar epithelium, are goblet cells that secrete mucus to protect from self-digestion and acidity.

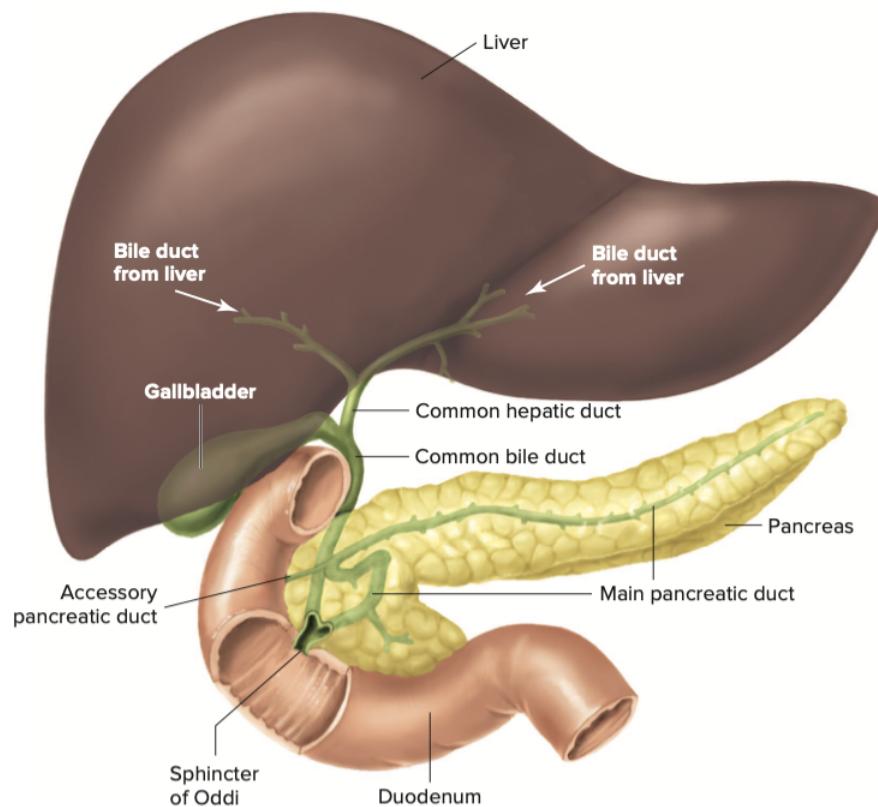


Figure 9: Pancreatic and Liver Secretions. (Source: Vander's Human Physiology)

• Pancreatic Secretions

- The pancreas has an exocrine and endocrine function, the exocrine function is what we will focus on in this section. Please see the endocrine system handout to read more on the endocrine section.
- Pancreatic **acinar cells** are involved in the secretion of enzymes. Meanwhile, **ductal cells**, through which the enzymes flow into the small intestine, are responsible for the secretion of bicarbonate ions. The bicarbonate neutralizes stomach acidity.

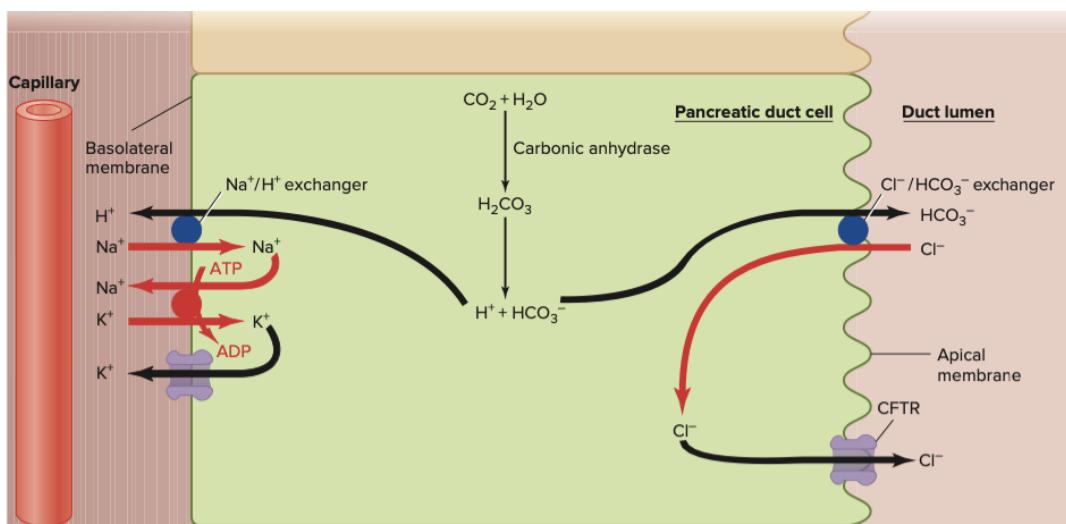


Figure 10: Pancreatic Duct Cell Secretion. (Source: Vander's Human Physiology)

- In a disease known as **cystic fibrosis**, the CFTR protein is dysfunctional, resulting in toughened pancreatic secretions. This causes lowered digestion and scarring, or fibrosis, of the pancreas.
- H^+ diffuses into blood vessels via H^+/Na^+ counter-transporters, where it combines with HCO_3^- , produced by parietal cells in the liver, to form H_2CO_3 and thus maintain the proper pH of blood.
- **Trypsinogen** is a zymogen released by the pancreas that is cleaved by enterokinase in the small intestine to form trypsin. Trypsin activates other proteolytic enzymes. Non-proteolytic enzymes are released in active form.
- **Trypsin, chymotrypsin, and elastase** begin by cleaving polypeptides into smaller peptide fragments. Trypsin cleaves at the C-terminus of lysine and arginine. Chymotrypsin cleaves at the C-terminus of phenylalanine, tryptophan, and tyrosine. Elastase cleaves at the C-terminus of small hydrophobic amino acids.
- **Carboxypeptidase** the terminal amino acid on the C-terminus of the polypeptide.
- **Amylase** cleaves polysaccharides into maltose or small branched chains of glucose.
- **Ribonuclease** and **deoxyribonuclease** break nucleic acids down into nucleotides.
- **Lipase** breaks triglycerides down into 2 free fatty acids and a monoglyceride.
- Bile is secreted by the liver and carried to the small intestine. It functions to break down fats and is involved with the homeostasis of many molecules. Bile contains phospholipids, cholesterol, bile salts, metabolic waste products, bile pigments, and trace metals.
 - There are certain pigments found in bile formed from broken-down heme, the pigment in hemoglobin. These pigments may escape to the blood and are responsible for yellow urine, while others are modified by bacterial enzymes to make fecal matter brown.
 - Bile is reabsorbed in the ileum via Na^+ cotransport, then recycled back into the liver via Na^+ -coupled active transport. This is known as enterohepatic circulation
 - Dietary fiber sequesters bile salts and prevents them from being reabsorbed into the ileum.
 - Bile is stored in the gallbladder where it becomes concentrated as Na^+ and water leave.

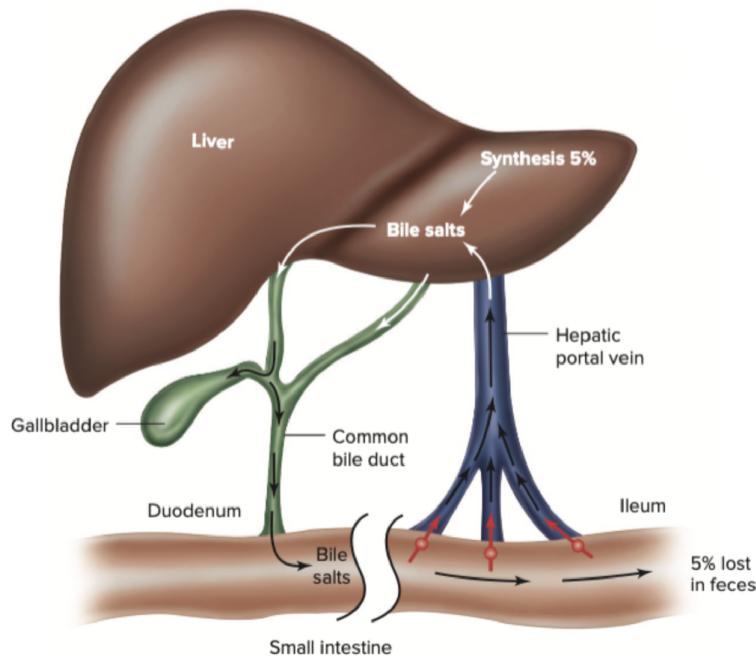


Figure 11: Enterohepatic Circulation. (Source: Vander's Human Physiology)

- Disaccharides like maltose are broken down by *brush border enzymes*, which are found on the epithelium of the small intestine, into fructose, glucose, and galactose. Fructose is absorbed by GLUT5 transporters found in the apical, or lumen-facing, membrane of the epithelium. Glucose and galactose are absorbed by transporters known as **SGLT** with Na^+ -coupled transport.
 - In diarrhea, sugars are unable to be absorbed as food passes through the tract far too quickly. Doctors exploit Na^+ -coupled transport in the small intestine by making those affected drink sodium glucose solutions to increase glucose secretion.
- Carbohydrates are then absorbed into the blood via GLUT transporters located in the basolateral, or blood-facing, membrane.
- After digestion by proteases like trypsin and chymotrypsin, small peptides can be absorbed through $\text{H}^+/\text{Peptide}$ transporter. Alternatively, they can be further digested by an carboxypeptidase or aminopeptidase.
- Amino acids are transported into the cell via diffusion and then into the bloodstream via specific amino acid transporters.
- Sometimes we can absorb proteins without digestion, but the ability only exists in fetuses for immunoglobulin absorption and declines as we grow older.

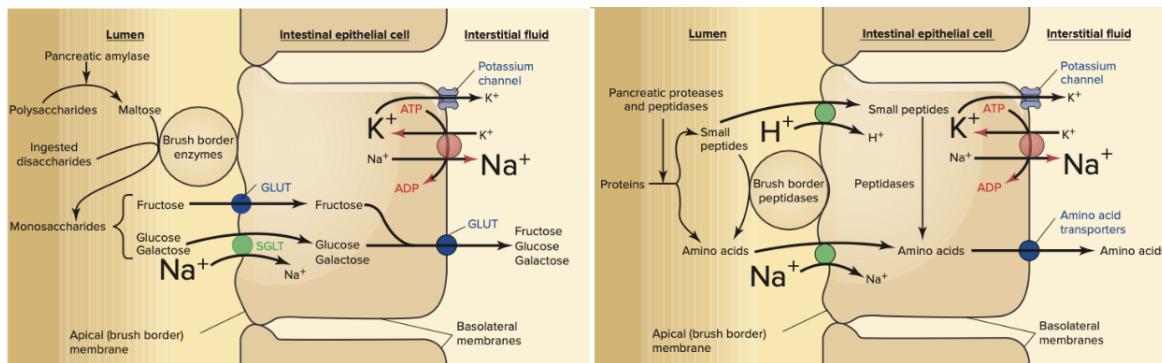


Figure 12: Protein and Carbohydrate Digestion. (Source: Vander's Human Physiology)

- Fats are digested by **pancreatic lipase**. However, pancreatic lipase is water soluble and therefore cannot digest from within the fat globule. Thus, fats are emulsified into smaller drops and stabilized by phospholipids derived from food and bile salts derived from bile, which are **amphipathic**, meaning they have both polar and nonpolar portions.
- These bile salts, however, block the ability of lipase to bind. Therefore, a protein called **colipase** holds pancreatic lipase on the emulsion drops, allowing space for digestion into free fatty acid tails and monoglycerides.
- These components are then held in micelles, which are essentially holding stations for fat. Digestion products found in the micelles are slowly released and diffuse across the apical surface, where they are transformed back into triglycerides in the smooth ER of the epithelial cell.
- The triglycerides, along with other fat-soluble substances such as certain vitamins and cholesterol, are sent to the Golgi from the ER and exocytosed out of the cell as **chylomicrons**. Chylomicrons are lipoproteins composed of lipid digestive products in the small intestine. They are too large to diffuse into the blood and therefore enter through holes into **lacteals**, lymphatic vessels that drain back into the heart to join the general circulation.

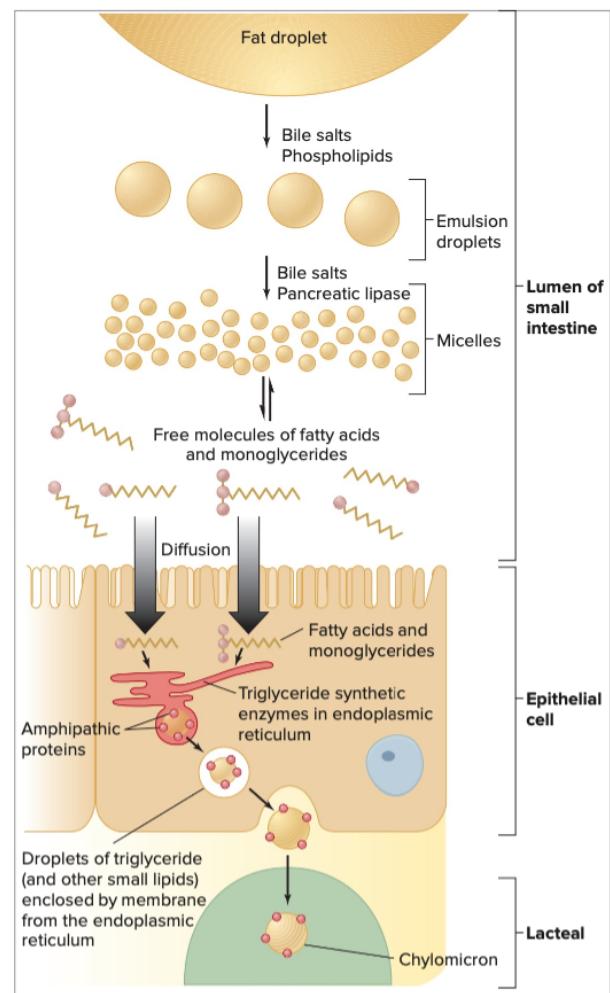


Figure 13: Fat Digestion and Absorption. (Source: Vander's Human Physiology)

- Vitamin K requires bile salts in order to be absorbed, and thus liver diseases are often associated with vitamin K deficiency.
- Celiac disease, or nontropical sprue, results from loss of the apical surface of epithelium due to autoimmune reaction to gluten and thus the lack of proper vitamin diffusion, such as with vitamin D.
- Water-soluble vitamins usually diffuse into epithelium cells.

Table 41.1 Vitamin Requirements of Humans			
Vitamin	Major Dietary Sources	Major Functions in the Body	Symptoms of Deficiency
Water-Soluble Vitamins			
B ₁ (thiamine)	Pork, legumes, peanuts, whole grains	Coenzyme used in removing CO ₂ from organic compounds	Beriberi (tingling, poor coordination, reduced heart function)
B ₂ (riboflavin)	Dairy products, meats, enriched grains, vegetables	Component of coenzymes FAD and FMN	Skin lesions, such as cracks at corners of mouth
B ₃ (niacin)	Nuts, meats, grains	Component of coenzymes NAD ⁺ and NADP ⁺	Skin and gastrointestinal lesions, delusions, confusion
B ₅ (pantothenic acid)	Meats, dairy products, whole grains, fruits, vegetables	Component of coenzyme A	Fatigue, numbness, tingling of hands and feet
B ₆ (pyridoxine)	Meats, vegetables, whole grains	Coenzyme used in amino acid metabolism	Irritability, convulsions, muscular twitching, anemia
B ₇ (biotin)	Legumes, other vegetables, meats	Coenzyme in synthesis of fat, glycogen, and amino acids	Scaly skin inflammation, neuromuscular disorders
B ₉ (folic acid)	Green vegetables, oranges, nuts, legumes, whole grains	Coenzyme in nucleic acid and amino acid metabolism	Anemia, birth defects
B ₁₂ (cobalamin)	Meats, eggs, dairy products	Production of nucleic acids and red blood cells	Anemia, numbness, loss of balance
C (ascorbic acid)	Citrus fruits, broccoli, tomatoes	Used in collagen synthesis; antioxidant	Scurvy (degeneration of skin and teeth), delayed wound healing
Fat-Soluble Vitamins			
A (retinol)	Dark green and orange vegetables and fruits, dairy products	Component of visual pigments; maintenance of epithelial tissues	Blindness, skin disorders, impaired immunity
D	Dairy products, egg yolk	Aids in absorption and use of calcium and phosphorus	Rickets (bone deformities) in children, bone softening in adults
E (tocopherol)	Vegetable oils, nuts, seeds	Antioxidant; helps prevent damage to cell membranes	Nervous system degeneration
K (phylloquinone)	Green vegetables, tea; also made by colon bacteria	Important in blood clotting	Defective blood clotting

Figure 14: Human vitamins; shows up often on USABO, so I would recommend memorizing. You should definitely know the names of every vitamin. (Source: Campbell Biology)

Example 6.1: (Campbell Biology) If you put the following events in the order they occur in the human digestive system, the third event in the series would be

- Cells in gastric pits secrete protons.
- Pepsin activates pepsinogen.
- HCl activates pepsinogen.
- Partially digested food enters the small intestine.

Solution: Parietal cells secrete H⁺ first. H⁺ joins with Cl⁻, also secreted by the parietal cells. The newly formed HCl activates pepsinogen into pepsin, which activates other pepsinogens. This

leads to the digestion of food and then the entry of the food into the small intestine. The third event in this sequence is pepsin activating other pepsinogens (**B**).

Example 6.2: (Campbell Biology) After surgical removal of the gallbladder, a person might need to limit his or her dietary intake of

- A. starch.
- B. protein.
- C. sugar.
- D. fat.

Solution: Surgical removal of the gallbladder would result in loss of a significant amount of bile secretion and thus lowered digestion of fats (**D**).

7 Control of Hunger and Diabetes

As you will learn in the endocrine handout, the pancreas has both an endocrine and exocrine function. The exocrine component secretes the digestive enzymes covered prior in this handout while the endocrine component secretes insulin and glucagon into the bloodstream. Insulin acts to increase uptake of glucose into cell and lowers the blood levels of glucose while glucagon acts to increase levels of blood glucose by making the liver synthesize more.

7.1 Diabetes Mellitus

- In diabetes mellitus, lack of insulin or lack of receptors for insulin leads to high glucose levels but lack of uptake of this glucose. Individuals with this condition must undergo large amounts of **lipolysis**, break down of adipose (fat) tissue as an alternative energy source.
 - This process results in a large amount of acidic metabolites that can lead to loss of life by lowered pH.
- **Type 1 Diabetes** occurs when the immune system attacks and destroys the insulin secreting cells of the pancreas. This autoimmune disease can be treated with insulin secretion.
- **Type 2 Diabetes**, the most common form of diabetes, is thought to be caused by obesity and inactivity, although, heredity plays a role. This disease occurs when insulin's target cells do not respond normally to insulin, thought to be as a result of innate inflammation.

7.2 Control of Hunger

- Overnourishment is defined as eating more calories than your body can normally metabolise.
 - This can lead to obesity which leads to 300k deaths in the US.
- **Ghrelin** is released by the stomach wall signals the body to be more hungry as mealtime approaches.

- **Insulin** released by rise in blood sugar signals the body to be less hungry.
- **Leptin** is secreted by adipose tissue and suppresses appetite.
 - When you have more adipose tissue your appetite decreases and vice versa.
 - It acts by inhibiting neuropeptide Y, a hypothalamic neurotransmitter that stimulates appetite.
- **PYY** is secreted by the small intestine after meal to counter ghrelin secretion.

8 Non-Human Digestion

- **Gastrovascular cavities** consist of a single digestive compartment with a single opening. The hydra, for example, has a single pouch with cells that both absorb and digest food molecules in the gastrovascular cavity.
- **Alimentary canals** have two openings. Organisms with two entry points can have specialized compartments involved in specific digestive processes (e.g., humans). These organisms can also eat new meals while the previous meal is being digested.
- A larger alimentary canal allows for better absorption of the cell wall-heavy food that herbivores consume.
- A large expandable stomach allows carnivores to eat as much as they can in one go and wait for their next meal. Their alimentary canals are not as long as those of herbivores.

► **Figure 41.19 Ruminant digestion.** The stomach of a cow, a ruminant, has four chambers. ① Chewed food first enters the rumen and reticulum, where mutualistic microorganisms digest cellulose in the plant material. ② Periodically, the cow regurgitates and rechews "cud" from the reticulum, further breaking down fibers and thereby enhancing microbial action. ③ The reswallowed cud passes to the omasum, where some water is removed. ④ It then passes to the abomasum for digestion by the cow's enzymes. In this way, the cow obtains significant nutrients from both the grass and the mutualistic microorganisms, which maintain a stable population in the rumen.

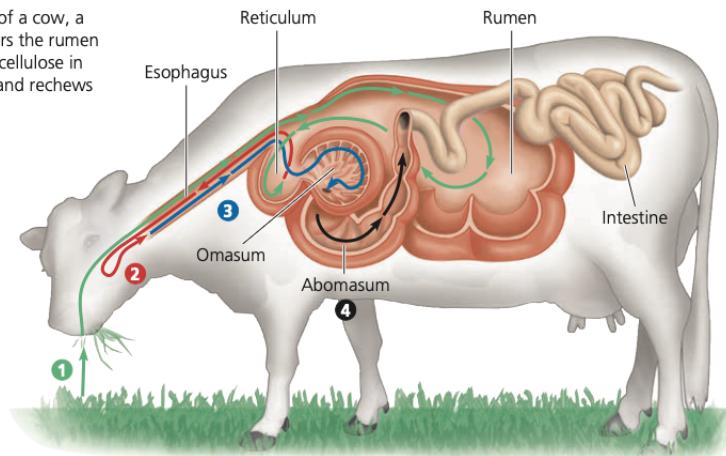


Figure 15: The ruminant digestive system. (Source: Campbell Biology)

9 Mutualistic Interactions, Large Intestine, and the Hepatic Portal Vein

- The large intestine mainly functions to reabsorb sodium and digest bacteria. It is involved in very little digestion or absorption. However, bacteria within the large intestine form

important short-chain fatty acids.

- **The Hepatic portal vein** carries capillary absorption from the GI tract to the capillaries of the liver. This allows the liver to remove toxic elements and ensure the health of the body.
- The intestine and stomach are filled with **mutualistic bacteria** that aid in digestion and the production of vitamins and other products.
- *H. pylori* is a bacteria that, along with acidity, causes **gastric ulcers** in the stomach. In *H. pylori* infections, the levels of other bacteria are greatly lowered, revealing the importance of mutualistic bacteria in GI health. Gastric ulcers are also caused by reduced mucus, allowing for acidity to destroy the epithelium faster.

10 Problems and Solutions

Example 1: (USABO Open Exam 2017) During your rounds as a medical student, your mentor asks you to identify potential causes for the pernicious anemia of the patient that you are visiting. Having recently studied your GI physiology, you correctly answer that it could have been caused by (Select ALL that apply):

- A. Faulty iron absorption.
- B. Damage to the absorptive cells of the duodenum.
- C. Damage to chief cells.
- D. Damage to parietal cells.
- E. Damage to the absorptive cells of the ileum.

Solution: As discussed before, pernicious anemia is the result of a lack of B12. If you remember from our previous discussion, parietal cells secrete intrinsic factor, which allows for B12 absorption in the upper ileum. Thus, the **answer is D and E**.

Example 2: (USABO Semifinal Exam 2019) Which of the following is not a function of the liver?

- A. Gluconeogenesis.
- B. Synthesizing essential amino acids.
- C. Fatty acid oxidation.
- D. Maintaining glucose homeostasis.
- E. Synthesizing cholesterol.

Solution: The liver is involved with the processing of all the nutrients from the digestive system, as well as the production of bile, which contains cholesterol. Therefore, it makes sense for the production of glucose (i.e., gluconeogenesis) to be under the control of the liver, as well as glucose homeostasis. Fatty acid oxidation cannot be ruled out. However, synthesizing essential amino acids are so-called because they cannot be synthesized within the body. Rather, they must be obtained from food. Therefore, the **answer is B**.

Example 3: (USABO Semifinal Exam 2020) You discover a new drug affecting the digestive system. Upon characterization, you discover that it inhibits H⁺/K⁺ ATPase and increases mucin secretion in the stomach. Its half-life is 75 minutes and is easily absorbed by the body. Which of the following is true after taking the drug? Select ONE.

- A. The blood after passing through the stomach will have a higher pH than before.
- B. The change in K⁺ concentration will cause increased stomach muscle contractions.
- C. The stomach will become more vulnerable to enzymatic damage.
- D. The drug will be ineffective against gastric ulcers.
- E. The drug will be ineffective for nighttime use.

Solution: H⁺/K⁺ ATPase on the luminal side of the parietal cells is responsible for acid secretion. Thus, this drug would reduce acidity and increase mucus. Therefore, it is likely that this drug would be used to treat gastric ulcers. We can now cross out choices C and D. As for choice A, H⁺ would stay in the cell, thus not interacting with the capillaries of the GI tract. Although increased potassium concentrations can lead to muscle contractions, the smooth muscle layer is located away from the lumen and therefore would not affect it significantly. **E, however, is correct.** The half-life of the drug is only 75 minutes, so it would quickly wear off as you sleep and be ineffective for long amounts of time (e.g., nighttime use).

11 Conclusion

As we bring our exploration of the digestive system to a close, we stand in awe of the incredible complexity and efficiency that underlie the simple act of nourishing our bodies. Throughout this journey, we've traced the path of food from the first bite to the final absorption of nutrients, unraveling the intricate mechanisms that sustain our lives. I hope this handout has been helpful, and I hope it aids you on your USABO endeavors.

Peace Out - Zelmay Jan