

DIGESTIVE SYSTEM -3

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LEARNING OBJECTIVES

1. Explain the mechanisms of digestion and absorption of nutrients and identify where these occur within the gastrointestinal tube.
2. Explain the mechanisms of absorption of water and identify where this occurs within the gastrointestinal tube.
3. Explain the underlying mechanism for diarrhea and its causes.

SMALL INTESTINE & NUTRIENT ABSORPTION

Muscle contractions cause a ripple like movement that carries the food down the small intestine –like a conveyor belt. This transit is normally slow occurring over several hours. As complex food moves within the lumen of the small intestine, it is digested into small molecules. Subsequently these small molecules such as amino acids and sugars are absorbed into the body. These functions are coordinated by hormones.

The small intestine is divided into three regions: **duodenum, jejunum and ileum**. The first, duodenum, is 10 inches long; the other two total 10 feet.

The initial segment, the duodenum, receives the acidic chyme. Here the epithelium contains **mucous glands and goblet cells** which secrete mucus to neutralize the pH of the chyme. The duodenal epithelium cells also secrete three hormones (Fig 1), **glucagon like peptide 1 (GLP-1), cholecystokinin (CCK) and secretin**, which signal the arrival of food to the pancreas, gall bladder, and stomach, respectively (Fig 1). Secretions from the pancreas and gall bladder are delivered directly to the lumen of the duodenum.

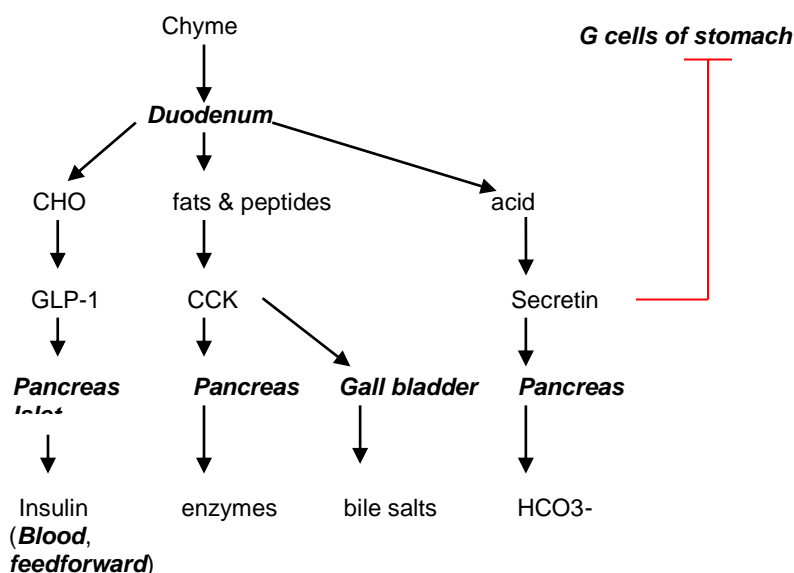


Figure 1. Digestive products signal the release of 3 hormones from the duodenum, glucagon like peptide 1 (GLP-1), CCK, and secretin.

The specific reflex loops include the following hormones:

- 1. Arrival of acidic chyme (low pH) stimulates the release of secretin** from the duodenal epithelial cells. Secretin in turn increases the secretion of HCO_3^- from the **pancreatic ducts**. Secretin also mediates the **negative feedback to the stomach G cells to inhibit gastrin secretion**.
- 2. Arrival of carbohydrates** increases glucagon like peptide-1 (GLP-1) secretion from the duodenal epithelial cells. GLP-1 acts in a **feed-forward manner to prime the pancreatic beta islet cells** to secrete insulin.
- 3. Arrival of amino acids and fat increases the secretion of cholecystokinin (CCK)** from the duodenal epithelial cells. CCK acts in the pancreas to increase the **secretion of zymogens** (inactive enzymes). It also acts on the smooth muscle of the gall bladder to expel **bile**. Bile is a detergent like molecule that plays an important role in the absorption of lipid. It is synthesized continuously by the **liver** and is stored within the **gall bladder** until needed.

PHYSIOLOGIC ROLES OF THE PANCREAS

The **pancreas** consists of two separate glands: endocrine and exocrine. The **endocrine pancreas secretes insulin and glucagon**. The **exocrine pancreas secretes digestive enzymes** (proteases, lipases, nucleases, etc.) as inactive **zymogens** into a duct which delivers these products to the duodenum (Fig. 2). Within the lumen of the duodenum, the zymogens are activated by the protease **trypsin** which is secreted by the epithelium of the duodenum. Digestion of complex foods into simple molecules by these enzymes occurs within the lumen of the duodenum, jejunum and ileum.

In addition to the secretion of zymogens from the pancreatic exocrine cells, **pancreatic duct cells secrete HCO_3^-** to neutralize the acidic chyme. Neutralization of the chyme protects the epithelial cells of the small intestine and provides an optimal pH for the activity of the pancreatic enzymes.

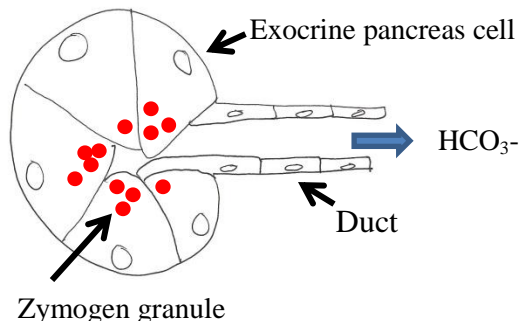


Figure 2. Exocrine pancreas cells contain stored zymogens (inactive enzymes) in membrane bound vesicles called granules (red dots) which are secreted into ducts and delivered to the duodenum in response to CCK. The duct cells secrete HCO_3^- which is delivered to the duodenum in response to secretin.

JEJUNUM, ILEUM & NUTRIENT ABSORPTION

Movement through the small intestine is usually slow (several hours). This slow movement permits maximal absorption of nutrients. The epithelial cells that line the wall of the small intestine are covered with small folds called microvilli which increase the surface area. Without the microvilli, the intestinal epithelium would cover about 6 square feet of absorptive surface. The microvilli increase the absorptive area to 4,000 square feet (~ the surface of a doubles tennis court!).

Absorption is the movement of a substance from the lumen across the epithelial cell and into the interstitial fluid compartment (IS). This is transcellular transport of materials. Absorption begins with the

entry of a given substance at the luminal surface of the epithelial cell. The transport mechanism varies with the type of molecule as described below (Fig 3).

Simple sugars and amino acids are absorbed by secondary active transport. These molecules enter the intestinal cells via **symporters** usually **coupled to Na⁺** entry (Fig 3). The simple sugars leave the cells by facilitated diffusion at the basal surface to enter the blood.

Di/tri-peptides enter by a symporter (called the PepT). The **PepT** is a symporter which is **coupled to H⁺** entry (Fig. 3). The dipeptides and tripeptides are degraded to simple amino acids by the epithelial cells. The simple amino acids transverse the cell, exit at the basal surface and **enter the blood**. They are transported to the liver.

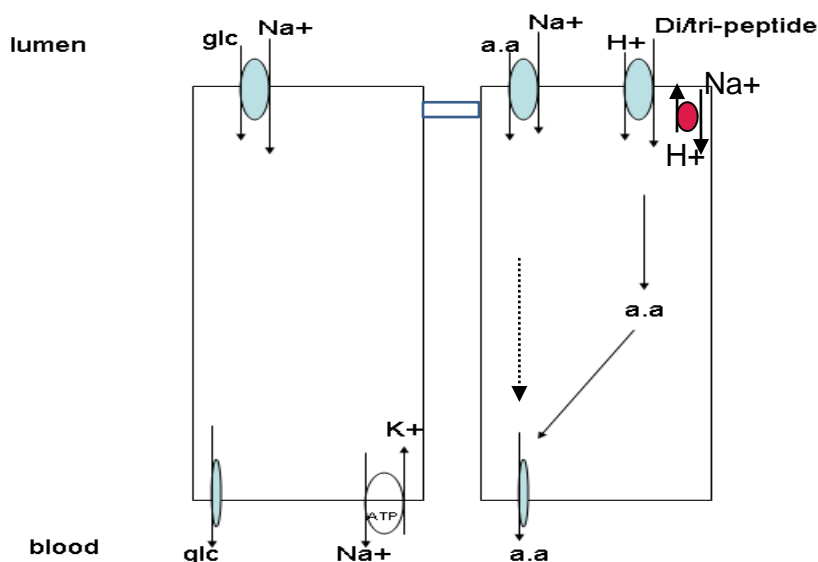


Figure 3. Co-transporters of the jejunum and ileum. Na⁺ moves with glucose (SGLT1) or with amino acids while protons move with peptides (PEPT) to enter the intestinal epithelial cells. Simple sugars and amino acids exit the cells at the basal surface by facilitated diffusion.

Fats (lipids) are digested to free fatty acids and cholesterol within the intestinal lumen (Fig. 4) by lipases. These substances enter the epithelial cell primarily by **simple diffusion**. Once inside the epithelial cell, they are assembled with proteins into particles called **chylomicrons**, which leave the cell at the basal surface by exocytosis. The chylomicrons are too big to cross the capillary epithelium and instead they enter the **lymphatic circulation** and are transported to the liver.

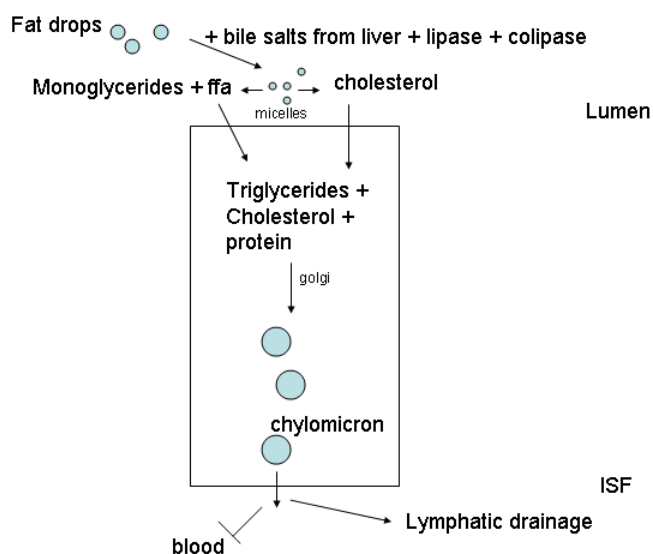


Figure 4. Digestion of lipids to free fatty acids and glycerol occurs in the lumen of the intestine by lipase. These lipid products enter the epithelial cells by simple diffusion. They are packaged with proteins to form chylomicrons and then secreted from the basal surface to enter into lymphatic circulation.

SMALL & LARGE INTESTINE ABSORB WATER

The lumen of the small and large intestine is freely permeable to water. **Water moves across the intestinal epithelium to maintain the luminal content isotonic at all times!**

The **ileum is the dominant site for absorption of water (~7L/day)**. The ileum is also the site for the **absorption of intrinsic factor-vitamin B12 complex** and for **bile**.

The **large intestine (colon)** receives about 2.0 L of chyme per day. Here, watery chyme is converted into semisolid feces by the absorption of water and electrolytes. Eventually, the feces (~0.1-0.5 L/day) are expelled from the body through the anal sphincter that is under voluntary control.

DISORDERS OF THE GI TRACT are due to abnormal emptying and include:

Delayed emptying- nausea, vomiting, bloating, heartburn

Rapid emptying- anxiety, weakness, dizziness, sweating, diarrhea

Diarrhea is the loss of HCO_3^- and watery feces from the body ($> 0.5\text{L/day}$ in the adult). Death may occur due to dehydration leading to cardiovascular collapse and metabolic acidosis. Diarrhea is classified by its underlying cause: secretory or osmotic. In both types of diarrhea, the feces will be isotonic (300 mOsm) always!

Secretory diarrhea is caused by an infection (such as *cholera vibrio*). In cholera, the infection results in increased secretion of chloride into the lumen of the ileum. Sodium follows chloride and water follows sodium to maintain isotonicity. The amount of fluid delivered to the colon exceeds the absorptive capacity of the colon and diarrhea results. Note that the concentration of Na^+ and Cl^- in the feces will equal ~300 mOsm (isotonic to the body).

In **osmotic diarrhea**, undigested material (lactose) or poorly absorbed solute (such as Epsom salts) is delivered to the colon. Water from the body enters the lumen to maintain isotonicity. The feces will be isotonic but the sum of the Na^+ and Cl^- concentrations in the feces will be less than 250 mOsM due to the presence of the osmotically active solute (such as Epsom salts).

When the digestive system is working normally, you should not be aware of its functions.

GENERAL CONCEPTS

1. Gastric emptying into the duodenum occurs over several hours to allow for neutralization of the acidic chyme.
2. Hormonal pathways coordinate the secretion of bicarbonate, digestive enzymes, and insulin from the pancreas and bile salts from the gall bladder.
3. Digestion of complex food to small molecules occurs within the lumen of the small intestine.
4. The small intestine is the major site for the absorption of nutrients, solutes, and water.
5. The luminal content of the small and large intestine is isotonic at all times.

QUESTIONS

1. Jane had severe diarrhea (isotonic fluid loss) for 2 days. What would be the best way to rehydrate her body?
 - A. Drink water.
 - B. Drink hypertonic coke.
 - C. Drink isotonic salt (NaCl) solution containing glucose.
 - D. Drink isotonic salt (NaCl) solution containing rice (i.e., polymers of glucose).
2. In individuals who are “lactose intolerant”, the lumen of the colon contains osmotically active material that is _____ leading to an influx of water from the body (diarrhea).
 - A. hypertonic to the intestinal cells.
 - B. hypotonic to the intestinal cells.
 - C. isotonic to the intestinal cells.

ANSWERS

1. D. This solution will rehydrate the body faster. The rice will be digested into many molecules of glucose. This glucose plus the Na^+ will drive the Na^+ -Glucose (SGLT) transporter in the small intestine. Water will follow the Na^+ into the body.
2. These individuals do not have lactase, an enzyme that digests lactose. The undigested lactose is delivered to the colon where bacteria degrade the lactose into many osmotically active molecules within the lumen of the colon (leading to a hypertonic state). Water enters the colon to maintain isotonicity resulting to diarrhea.