Digestive System

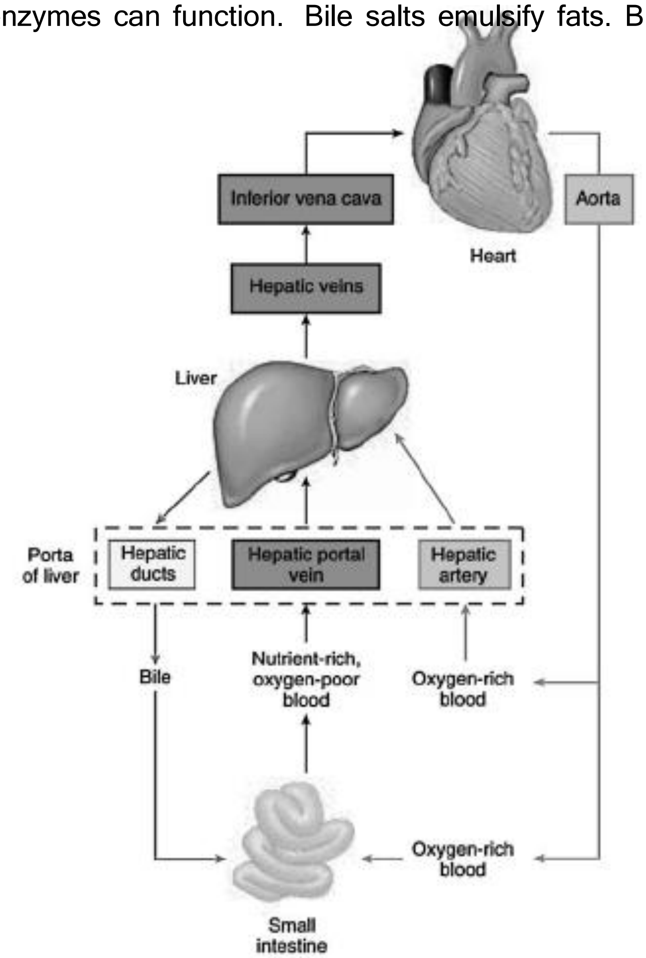
Liver

Functions of the Liver

The liver performs important digestive and excretory functions, stores and processes nutrients, synthesizes new molecules, and detoxifies harmful chemicals.

1- Bile Production

The liver produces and secretes about 600-1000 mL of bile each day. Bile contains no digestive enzymes, but it plays a role indigestion because it neutralizes and dilutes stomach acid and emulsifies fats. The pH of chyme as it leaves the stomach is too low for the normal function of pancreatic enzymes. Bile helps to neutralize the acidic chyme and to bring the pH up to a level at which pancreatic enzymes can function. Bile salts emulsify fats. Bile also contains excretory products like bile pigments. Bilirubin is a bile pigment that results from the breakdown of hemoglobin. Bile also contains cholesterol, fats, fat-soluble hormones, and lecithin.



Blood and Bile Flow Through the Liver

Secretin stimulates bile secretion, primarily by increasing the water and bicarbonate ion content of bile. Bile salts also increase bile secretion through a positive-feedback system. Most bile salts are reabsorbed in the ileum and carried in the blood back to the liver, where they contribute to further bile secretion. The loss of bile salts in the feces is reduced by this recycling process. Bile secretion into the duodenum continues until the duodenum empties.

2- Storage

Hepatocytes can remove sugar from the blood and store it in the form of glycogen. They can also store fat, vitamins (A, B_{12}, D, E, and K), copper, and iron. This storage function is usually short term, and the amount of stored material in the hepatocytes and, thus, the cell size fluctuate during a given day.

Hepatocytes help control blood sugar levels within very narrow limits. If a large amount of sugar enters the general circulation after a meal, it will increase the osmolality of the blood and produce hyperglycemia. This is prevented because the blood from the intestine passes through the hepatic portal vein to the liver, where glucose and other substances are removed from the blood by hepatocytes, stored, and secreted back into the circulation when needed.

3- Nutrient Interconversion

Interconversion of nutrients is another important function of the liver. Ingested nutrients are not always in the proportion needed by the tissues. If this is the case, the liver can convert some nutrients into others. If, for example, a person is on a diet that is excessively high in protein, an oversupply of amino acids and an undersupply of lipids and carbohydrates may be delivered to the liver. The hepatocytes break down the amino acids and cycle many of them through metabolic pathways so they can be used to produce adenosine triphosphate, lipids, and glucose.

Hepatocytes also transform substances that cannot be used by most cells into more readily usable substances. For example, ingested fats are combined with choline and phosphorus in the liver to produce phospholipids, which are essential components of plasma membranes. Vitamin D is hydroxylated in the liver. The hydroxylated form of vitamin D is the major circulating form of vitamin D, which is transported through the circulation to the kidney, where it's again hydroxylated. The double-hydroxylated vitamin D is the active form of the vitamin, which functions in calcium maintenance.

4- Detoxification

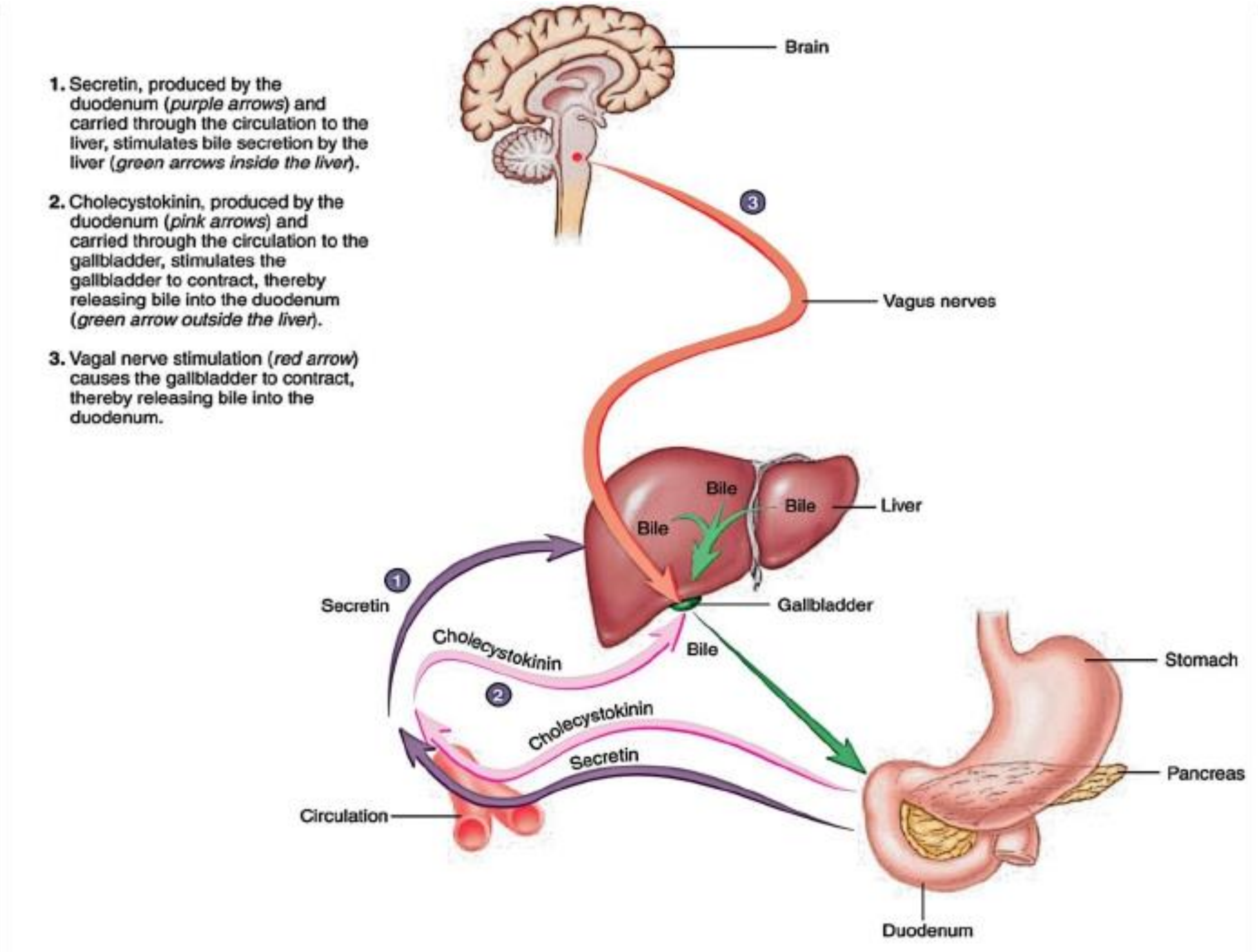
Many ingested substances are harmful to the cells of the body. In addition, the body itself produces many by-products of metabolism that, if accumulated, are toxic. The liver forms a major line of defense against many of these harmful substances. It detoxifies many substances by altering their structure to make them less toxic or make their elimination easier. Ammonia, for example, a by-product of amino acid metabolism, is toxic and is not readily removed from the circulation by the kidneys. Hepatocytes remove ammonia from the circulation and convert it to urea, which is less toxic than ammonia and is secreted into the circulation and then eliminated by the kidneys in the urine. Other substances are removed from the circulation and excreted by the hepatocytes into the bile.

5- Phagocytosis

Hepatic phagocytic cells (Kupffer cells), which lie along the sinusoid walls of the liver, phagocytize "worn-out" and dying red and white blood cells, some bacteria, and other debris that enters the liver through the circulation.

6- Synthesis

The liver can also produce its own unique new compounds. It produces many blood proteins, such as albumins, fibrinogen, globulins, heparin, and clotting factors, which are released into the circulation.



Control of Bile Secretion and Release

Pancreatic Secretions

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for the function of pancreatic enzymes. Bicarbonate ions are actively secreted by the duct epithelium, and water follows passively to make the pancreatic juice isotonic.

The enzymes of the pancreatic juice are produced by the acinar cells of the pancreas and are important for the digestion of all major classes of food. Without the enzymes produced by the pancreas, lipids, proteins, and carbohydrates are not adequately digested.

The proteolytic pancreatic enzymes, which digest proteins, are secreted in inactive forms, whereas many of the other enzymes are secreted in active form. The major proteolytic enzymes are trypsin, chymotrypsin, and carboxypeptidase. They are secreted in their inactive forms as trypsinogen, chymotrypsinogen, and procarboxypeptidase and are activated by the removal of certain peptides from the larger precursor proteins. If these were produced in their active forms, they would digest the tissues producing them. The proteolytic enzyme enterokinase (intestinal enzyme), which is an enzyme attached to the brush border of the small intestine, activates trypsinogen. Trypsin then activates more trypsinogen, as well as chymotrypsinogen and procarboxypeptidase.

Pancreatic juice also contains pancreatic amylase, which continues the polysaccharide digestion that was initiated in the oral cavity. In addition, pancreatic juice contains a group of lipid-digesting enzymes called pancreatic lipases, which break down lipids into free fatty acids, glycerides, cholesterol, and other components.

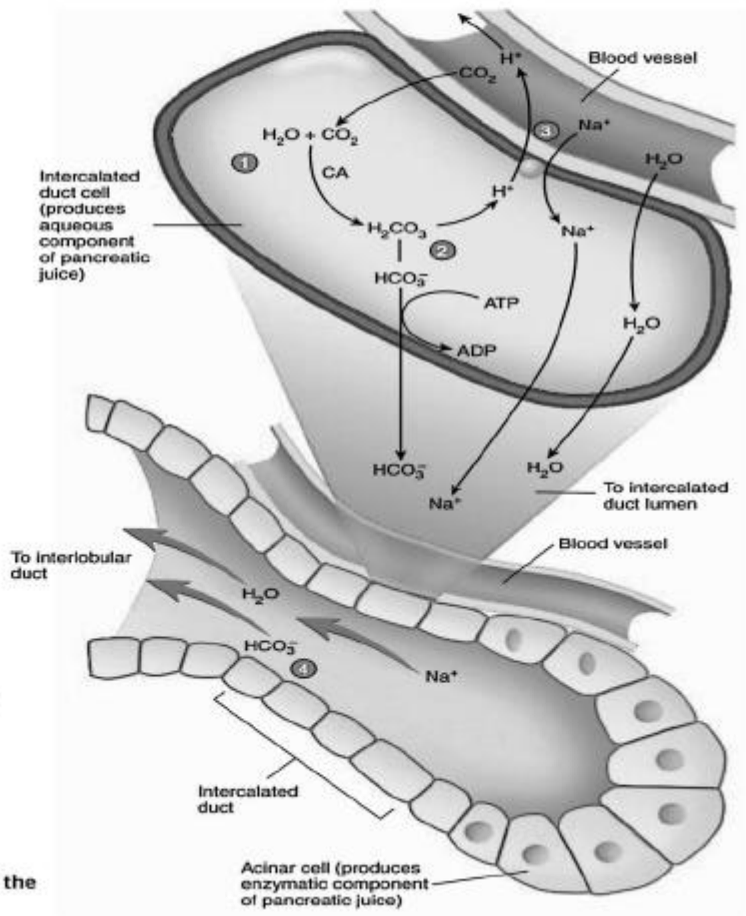
Enzymes that reduce DNA and ribonucleic acid to their component nucleotides, deoxyribonucleases and ribonucleases, respectively, are also present in pancreatic juice.

Regulation of Pancreatic Secretion

Both hormonal and neural mechanisms control the exocrine secretions of the pancreas. Secretin stimulates the secretion of a watery solution that contains a large amount of bicarbonate ions from the pancreas. The primary stimulus for secretin release is the presence of acidic chyme in the duodenum.

Cholecystokinin stimulates the release of bile from the gallbladder and the secretion of pancreatic juice rich in digestive enzymes. The major stimulus for the release of cholecystokinin is the presence of fatty acids and other lipids in the duodenum.

Parasympathetic stimulation through the vagus (X) nerves also stimulates the secretion of pancreatic juices rich in pancreatic enzymes, and sympathetic impulses inhibit secretion. The effect of vagal stimulation on pancreatic juice secretion is greatest during the cephalic and gastric phases of stomach secretion.

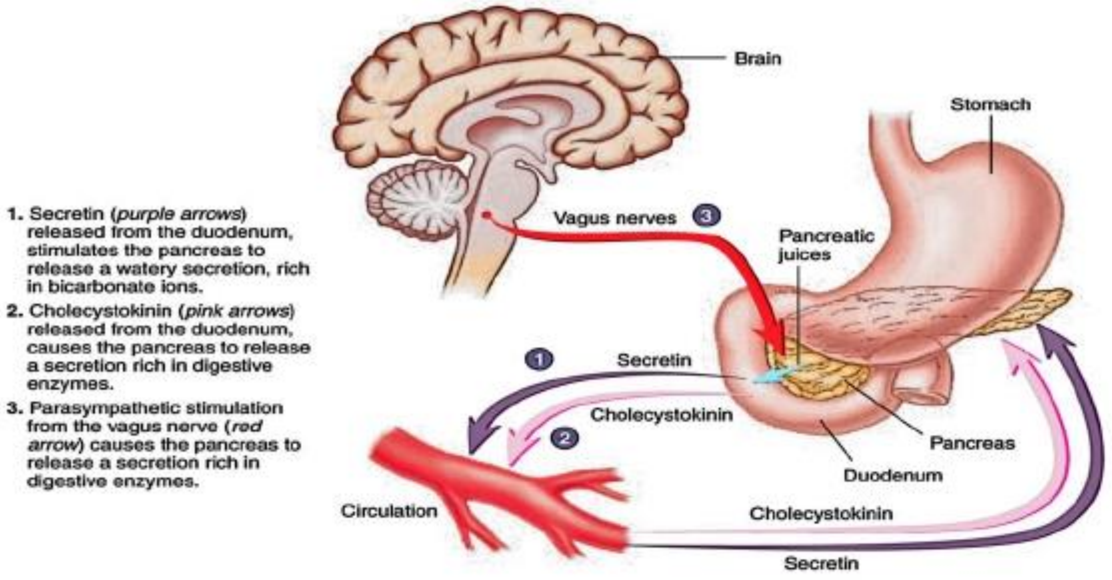


1. Water (H_2O) and carbon dioxide (CO_2) combine under the influence of carbon anhydrase (CA) to form carbonic acid.
2. Carbonic acid (H_2CO_3) dissociates to form hydrogen ions (H^+) and bicarbonate ions (HCO_3^-).
3. The H^+ are exchanged for sodium ions (Na^+) and are removed in the bloodstream.
4. The HCO_3^- are actively transported into the intercalated ducts. Na^+ and water follow the HCO_3^- ions into the ducts.

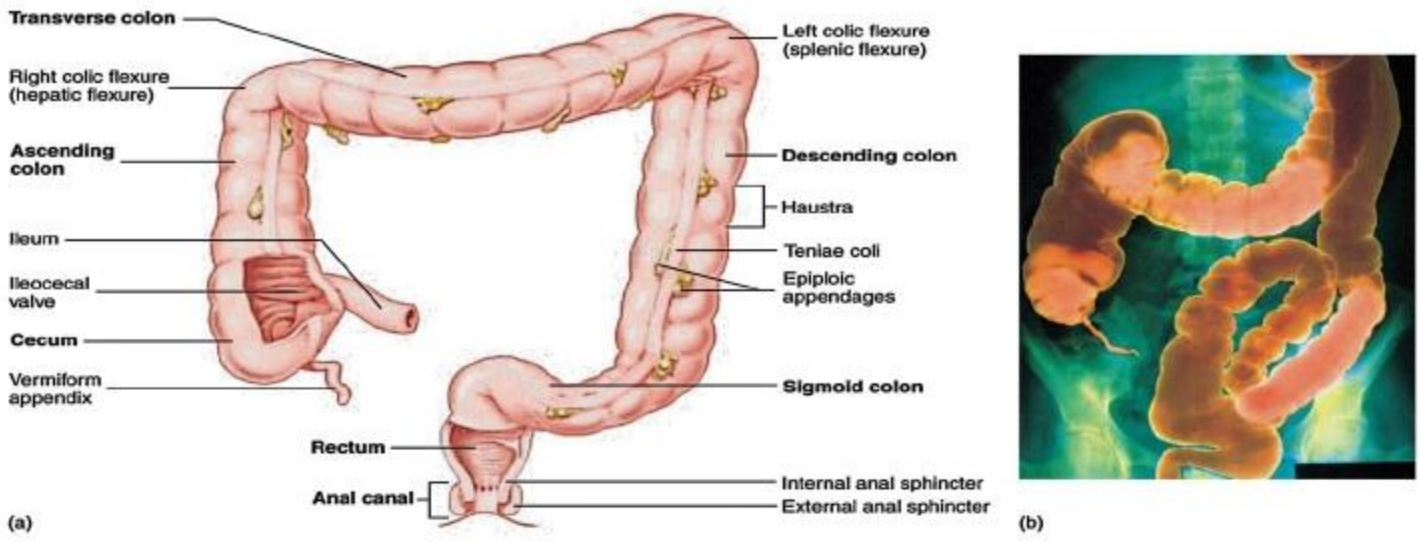
Bicarbonate Ion Production in the Pancreas

Large Intestine

The large intestine is the portion of the digestive tract extending from the ileocecal junction to the anus. It consists of the cecum, colon, rectum, and anal canal. Normally 18-24 hours are required for material to pass through the large intestine, in contrast to the 3-5 hours required for movement of chyme through the small intestine. Thus, the movements of the colon are more sluggish than those of the small intestine. While in the colon, chyme is converted to feces. Absorption of water and salts, the secretion of mucus, and extensive action of microorganisms are involved in the formation of feces, which the colon stores until the feces are eliminated by the process of defecation. About 1500mL of chyme enters the cecum each day, but more than 90% of the volume is reabsorbed so that only 80-150 mL of feces is normally eliminated by defecation.



Control of Pancreatic Secretion



Large Intestine

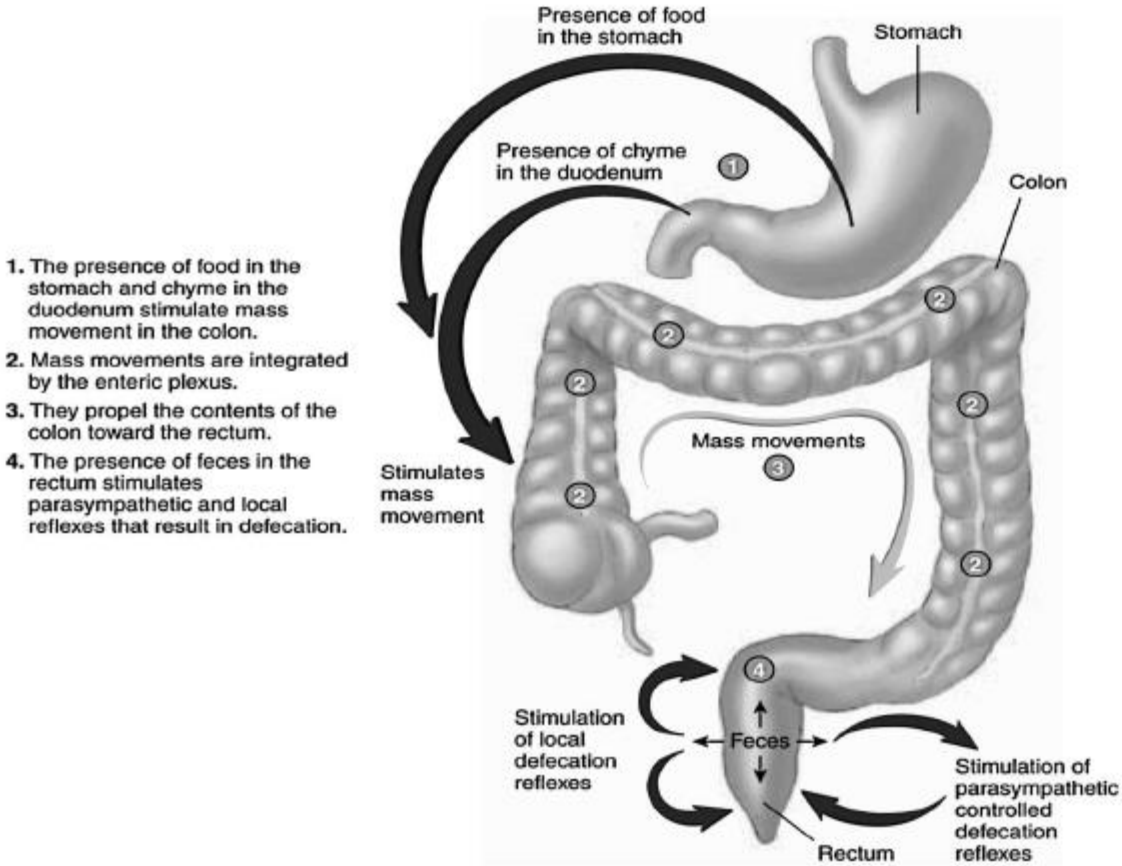
(*a*) Large intestine (i.e., cecum, colon, and rectum) and anal canal. The teniae coli and epiploic appendages are along the length of the colon. (*b*) A radiograph of the large intestine following a barium enema.

Movement in the Large Intestine

Segmental mixing movements occur in the colon much less often than in the small intestine. Peristaltic waves are largely responsible for moving chyme along the ascending colon. At widely spaced intervals (normally three or four times each day), large parts of the transverse and descending colon undergo several strong peristaltic contractions, called mass movements. Each mass movement contraction extends over a much longer part of the digestive tract (≥ 20 cm) than does a Peristaltic contraction and propels the colon contents a considerable distance toward the anus. Mass movements are very common after meals because the presence of food in the stomach or duodenum initiates them. Mass movements are most common about 15 minutes after breakfast. They usually persist for 10-30 minutes and then stop for perhaps half a day. Local reflexes in the enteric plexus, which are called gastrocolic reftexes if initiated by the stomach or duodenocolic reftexes if initiated by the duodenum, integrate mass movements.

Distention of the rectal wall by feces acts as a stimulus that initiates the defecation reftex. Local reflexes cause weak contractions of the rectum and relaxation of the internal anal sphincter. Parasympathetic reflexes cause strong contractions of the rectum and are normally responsible for most of the defecation reflex. Action potentials produced in response to the distention travel along afferent nerve fibers to the sacral region of the spinal cord, where efferent action potentials are initiated that reinforce peristaltic contractions in the lower colon and rectum. The defecation reflex reduces action potentials to the internal anal sphincter, causing it to relax. The external anal sphincter, which is composed of skeletal muscle and is under conscious cerebral control, prevents the movement of feces out of the rectum and through the anal opening. If this sphincter is relaxed voluntarily, feces are expelled. The defecation reflex persists for only a few minutes and quickly declines. Generally, the reflex is reinitiated after a period that may be as long as several hours. Mass movements in the colon are usually the reason for the reinitiation of the defecation reflex.

Defecation is usually accompanied by voluntary movements that support the expulsion of feces. These voluntary movements include large inspiration of air followed by closure of the larynx and forceful contraction of the abdominal muscles. As a consequence, the pressure in the abdominal cavity increases, thereby helping force the contents of the colon through the anal canal and out of the anus.



Reflexes in the Colon and Rectum

Digestion, Absorption, and Transport

Digestion is the breakdown of food to molecules that are small enough to be absorbed into the circulation. Mechanical digestion breaks large food particles down into smaller ones. Chemical digestion involves the breaking of covalent chemical bonds in organic molecules by digestive enzymes. Carbohydrates are broken down into monosaccharides, proteins are broken down into amino acids, and fats are broken down into fatty acids and glycerol. Absorption and transport are the means by which molecules are moved out of the digestive tract and into the circulation for distribution throughout the body. Not all molecules (e.g., vitamins, minerals, and water) are broken down before being absorbed. Digestion begins in the oral cavity and continues in the stomach, but most digestion occurs in the proximal end of the small intestine, especially in the duodenum.

Absorption of certain molecules can occur all along the digestive tract. A few chemicals, such as nitroglycerin, can be absorbed through the thin mucosa of the oral cavity below the tongue. Some small molecules (e.g., alcohol and aspirin) can diffuse through the stomach epithelium into the circulation. Most absorption, however, occurs in the duodenum and jejunum, although some absorption occurs in the ileum.

Once the digestive products have been absorbed, they are transported to other parts of the body by two different routes. Water, ions, and water-soluble digestion products, such as glucose and amino acids, enter the hepatic portal system and are transported to the liver. The products of lipid metabolism are coated with proteins and transported into lymphatic capillaries called lacteals. The lacteals are connected by lymphatic vessels to the thoracic duct, which empties into the left subclavian vein. The protein-coated lipid products then travel in the circulation to adipose tissue or to the liver.

Carbohydrates

Ingested carbohydrates consist primarily of polysaccharides, such as starches and glycogen; disaccharides, such as sucrose (table sugar) and lactose (milk sugar); and monosaccharides, such as glucose and fructose (found in many fruits). During the digestion process, polysaccharides are broken down into smaller chains and finally into disaccharides and monosaccharides. Disaccharides are broken down into monosaccharides. Carbohydrate digestion begins in the oral cavity with the partial digestion of starches by salivary amylase. A minor amount of digestion occurs in the stomach through the action of gastric amylase and gelatinase. Carbohydrate digestion is continued in the intestine by pancreatic amylase. A series of disaccharidases that are bound to the microvilli of the intestinal epithelium digest disaccharides into monosaccharides

Monosaccharides such as glucose and galactose are taken up into intestinal epithelial cells by cotransport, powered by a sodium ion gradient. Monosaccharides such as fructose are taken up by facilitated diffusion. The monosaccharides are transferred by facilitated diffusion to the capillaries of the intestinal villi and are carried by the hepatic portal system to the liver, where the nonglucose sugars are converted to glucose. Glucose enters the cells through facilitated diffusion. The rate of glucose transport into most types of cells is greatly influenced by insulin and may increase 10-fold in its presence.

Lipids

Lipids are molecules that are insoluble or only slightly soluble in water. They include triglycerides, phospholipids, cholesterol, steroids, and fat-soluble vitamins. Triglycerides, also called triacylglycerol, consist of three fatty acids and one glycerol molecule covalently bound together. The first step in lipid digestion is emulsification, which is the transformation of large lipid droplets into much smaller droplets. The enzymes that digest lipids are water-soluble and can digest the lipids only by acting at the surface of the droplets. The emulsification process increases the surface area of the lipid exposed to the digestive enzymes by decreasing the droplet size. Emulsification is accomplished by bile salts secreted by the liver and stored in the gallbladder.

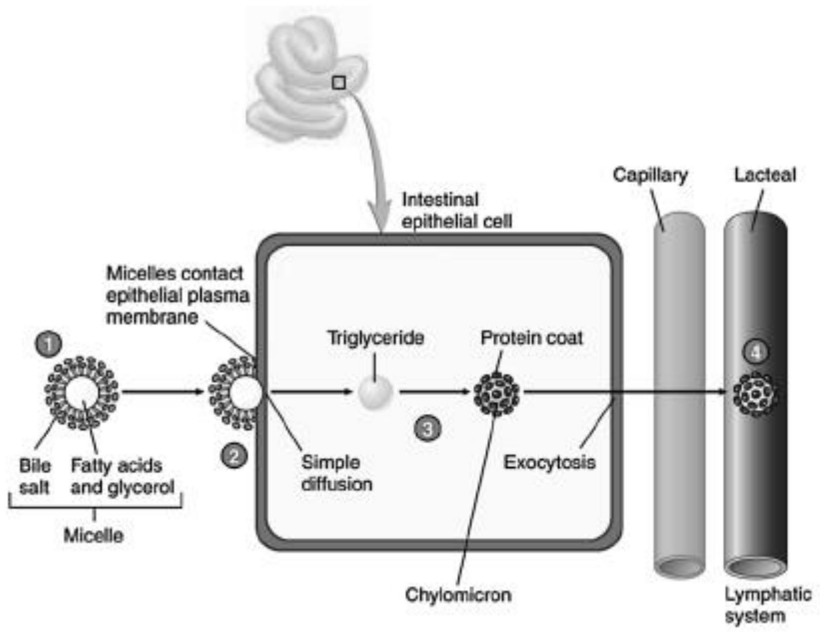
Lipase digests lipid molecules. The vast majority of lipase is secreted by the pancreas. A minor amount of lingual lipase is secreted in the oral cavity, is swallowed with the food, and digests a small amount (< 10%) of lipid in the stomach. The stomach also produces very small amounts of gastric lipase. The primary products of lipase digestion are free fatty acids and glycerol. Cholesterol and phospholipids also constitute part of the lipid digestion products.

Once lipids are digested in the intestine, bile salts aggregate around the small droplets to form micelles (small morsel). The hydrophobic ends of the bile salts are directed toward the free fatty acids, cholesterol, and glycerides at the center of the micelle; and the hydrophilic ends are directed outward toward the water environment. When a micelle comes into contact with the epithelial cells of the small intestine, the contents of the micelle pass by means of simple diffusion through the plasma membrane of the epithelial cells.

Digestion of the Three Major Food Types

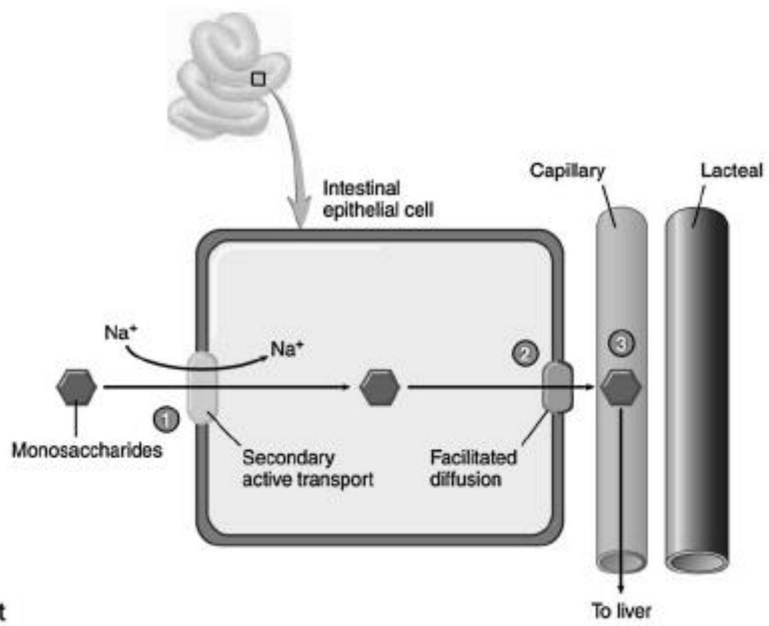
	Carbohydrates	Proteins	Lipids
Mouth (Salivary Glands)	Salivary amylase → Polysaccharides, Disaccharides		
Stomach	Gastric amylase and gelatinase →	Pepsin → Dipeptides, Polypeptides	Lingual lipase → Gastric lipase →
Duodenum (Pancreas)	Pancreatic amylase → Disaccharides	Trypsin, Chymotrypsin, Carboxypeptidase →	Lipase, Esterase →
Lining of Small Intestine	Lactase, Sucrase, Maltase, Isomaltase → Monosaccharides	Aminopeptidase, Peptidase → Amino acids, Dipeptides, Tripeptides	Lipase → Glycerol, Fatty acids

1. Bile salts surround fatty acids and glycerol to form micelles.
2. Micelles attach to the plasma membranes of intestinal epithelial cells, and the fatty acids and glycerol pass by simple diffusion into the intestinal epithelial cells.
3. Within the intestinal epithelial cell, the fatty acids and glycerol are converted to triglyceride; proteins coat the triglyceride to form chylomicrons, which move out of the intestinal epithelial cells by exocytosis.
4. The chylomicrons enter the lacteals of the intestinal villi and are carried through the lymphatic system to the general circulation.



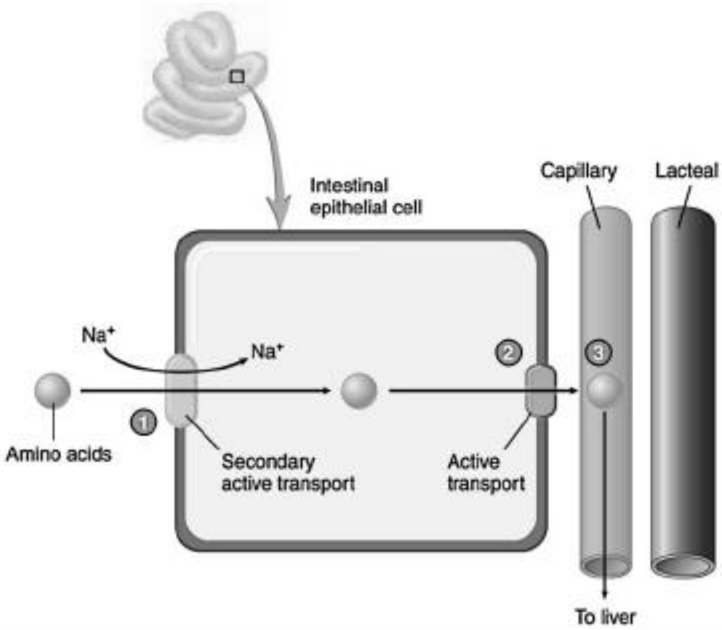
Lipid Transport

1. Monosaccharides are absorbed by secondary active transport into intestinal epithelial cells.
2. Monosaccharides move out of intestinal epithelial cells by facilitated diffusion.
3. They enter the capillaries of the intestinal villi and are carried through the hepatic portal vein to the liver.



Monosaccharide Transport

1. Amino acids are absorbed by secondary active transport into intestinal epithelial cells.
2. Amino acids move out of intestinal epithelial cells by active transport.
3. They enter the capillaries of the intestinal villi and are carried through the hepatic portal vein to the liver.



Amino Acid Transport