23

The Digestive System

Children are fascinated by the workings of the digestive system. They relish crunching a potato chip, delight in making "mustaches" with milk, and giggle when their stomach "growls." As adults, we know that a healthy digestive system is essential to maintaining life, because it converts foods into the raw materials that build and fuel our body's cells. Specifically, the **digestive system** takes in food, breaks it down into nutrient molecules, absorbs these molecules into the bloodstream, and then rids the body of the indigestible remains.

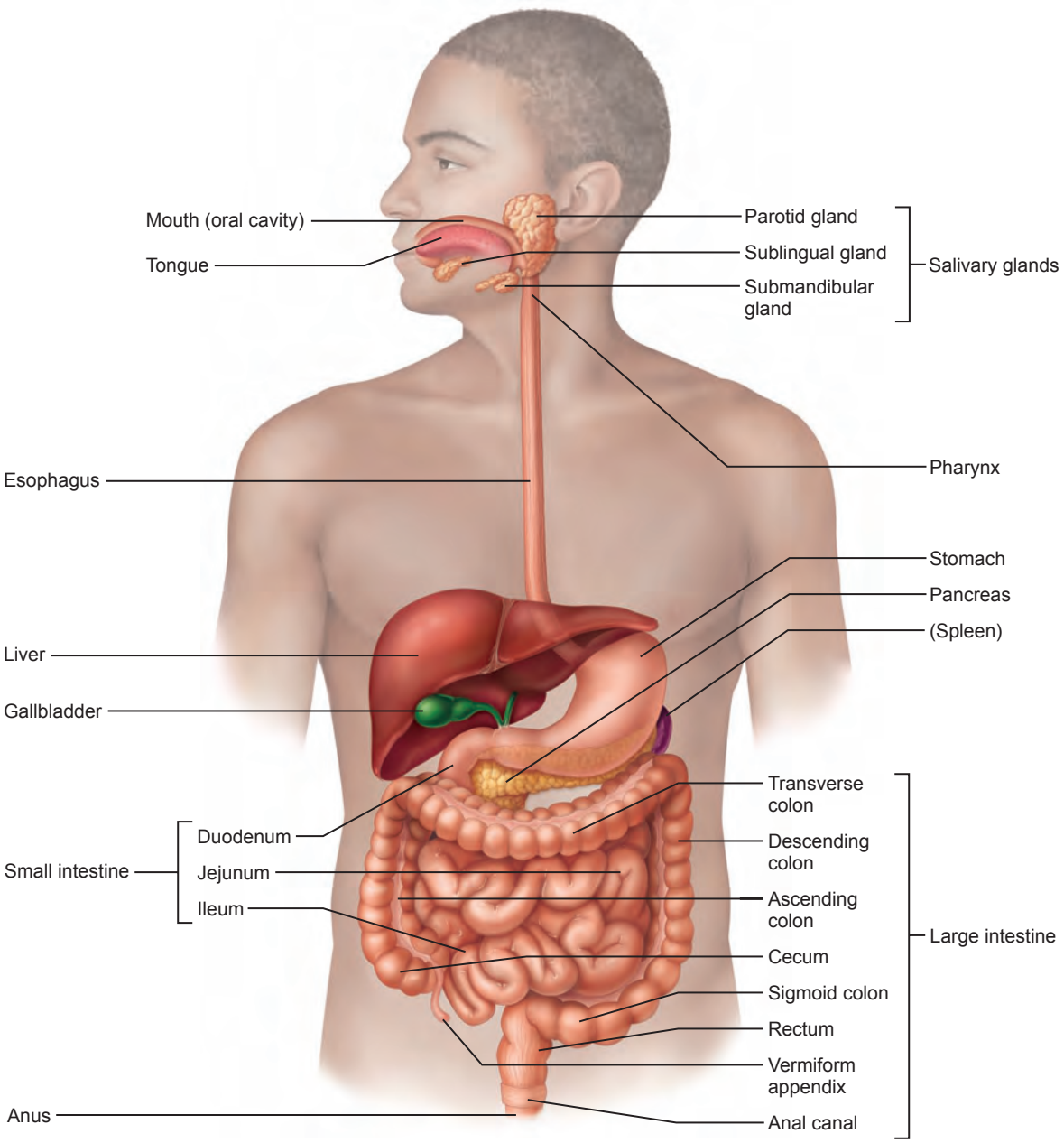


Figure 23.1 Alimentary canal and related accessory digestive organs. (See *A Brief Atlas of the Human Body*, Figure 64a.)

PART 1

OVERVIEW OF THE DIGESTIVE SYSTEM

- Describe the function of the digestive system, and differentiate between organs of the alimentary canal and accessory digestive organs.

The organs of the digestive system fall into two main groups: (1) those of the *alimentary canal* (al″ĭ-men′tar-e; *aliment* = nourish) and (2) *accessory digestive organs* (Figure 23.1).

The **alimentary canal**, also called the **gastrointestinal (GI) tract** or **gut**, is the continuous, muscular digestive tube that winds through the body. It **digests** food—breaks it down into smaller fragments (*digest* = dissolved)—and **absorbs** the digested fragments through its lining into the blood. The organs of the alimentary canal are the *mouth*, *pharynx*, *esophagus*, *stomach*, *small intestine*, and *large intestine*. The large intestine leads to the terminal opening, or *anus*. In a cadaver, the alimentary canal is approximately 9 m (about 30 ft) long, but in a living person, it is considerably shorter because of its muscle tone. Food material in this tube is technically outside the body because the canal is open to the external environment at both ends.

The **accessory digestive organs** are the *teeth*, *tongue*, *gallbladder*, and a number of large digestive glands—the *salivary*

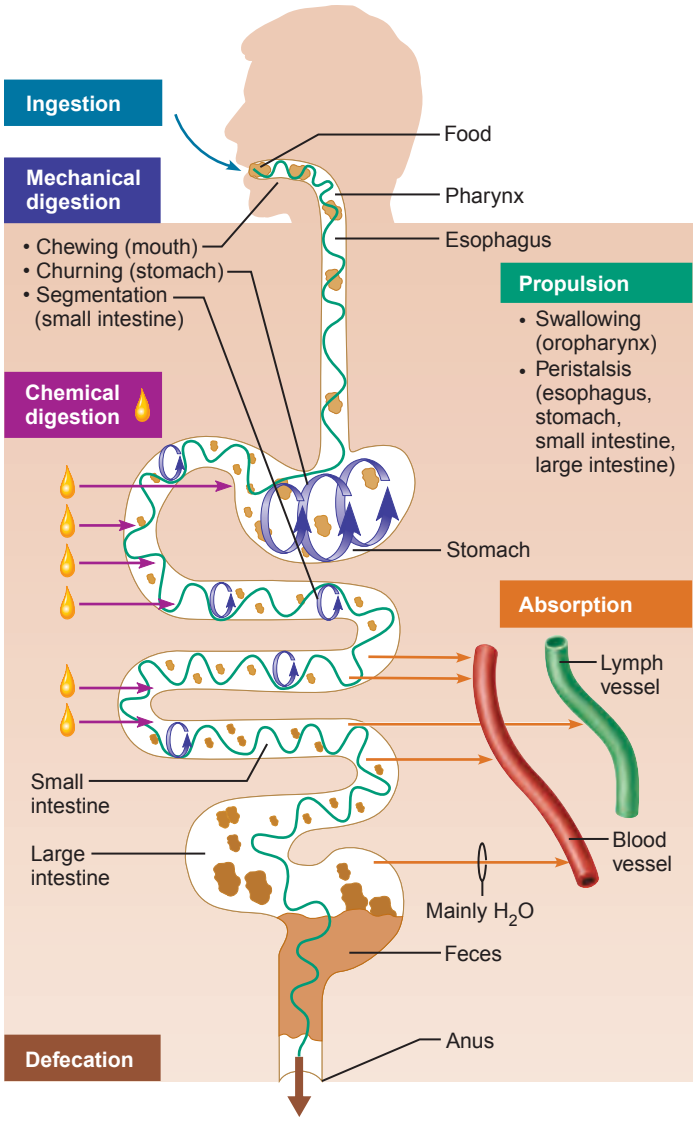
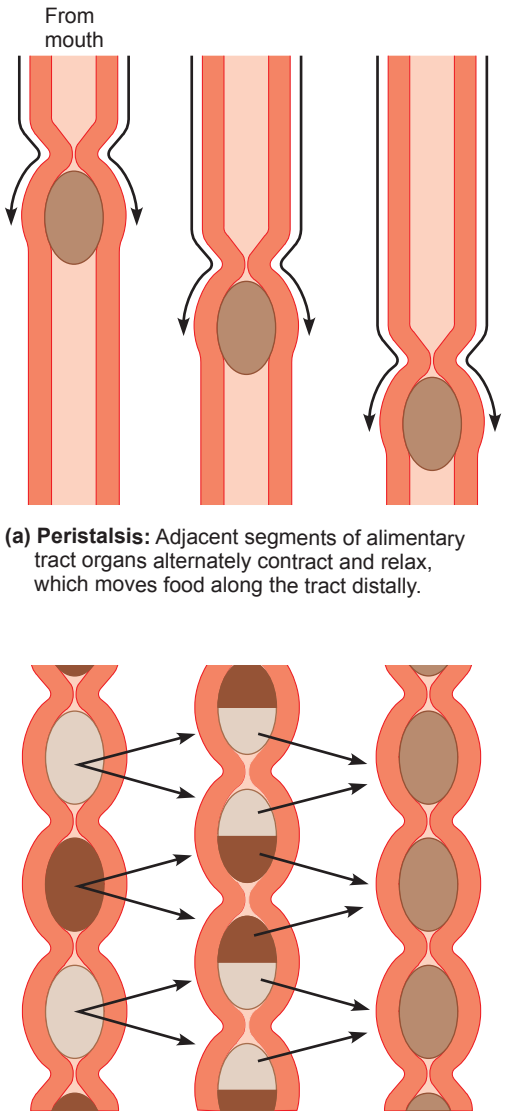


Figure 23.2 Gastrointestinal tract activities. Note that sites of chemical digestion produce enzymes or receive enzymes or other secretions made by accessory organs outside the alimentary canal.



(a) Peristalsis: Adjacent segments of alimentary tract organs alternately contract and relax, which moves food along the tract distally.

(b) Segmentation: Nonadjacent segments of alimentary tract organs alternately contract and relax, moving the food forward then backward. Food mixing and slow food propulsion occurs.

Figure 23.3 Peristalsis and segmentation.

glands, *liver*, and *pancreas*. The teeth and tongue are in the mouth, or oral cavity, while the digestive glands and gallbladder lie outside the GI tract and connect to it by ducts. The accessory digestive glands produce a variety of secretions that contribute to the breakdown of foodstuffs.

Digestive Processes

▶ List and define the major processes occurring during digestive system activity.

We can view the digestive tract as a "disassembly line" in which food becomes less complex at each step of processing and its nutrients become available to the body. The processing of food by the digestive system involves six essential activities: ingestion, propulsion, mechanical digestion, chemical digestion, absorption, and defecation (Figure 23.2).

1. **Ingestion** is simply taking food into the digestive tract, usually via the mouth.
2. **Propulsion**, which moves food through the alimentary canal, includes *swallowing*, which is initiated voluntarily, and *peristalsis* (per″ĭ-stal′sis), an involuntary process. **Peristalsis** (*peri* = around; *stalsis* = constriction), the major means of propulsion, involves alternate waves of contraction and relaxation of muscles in the organ walls (Figure 23.3a). Its main effect is to squeeze food along the tract, but some mixing occurs as well. In fact, peristaltic waves are so powerful that, once swallowed, food and fluids will reach your stomach even if you stand on your head.
3. **Mechanical digestion** physically prepares food for chemical digestion by enzymes. Mechanical processes include chewing, mixing of food with saliva by the tongue, churning food in the stomach, and **segmentation**, or rhythmic

local constrictions of the small intestine (Figure 23.3b). Segmentation mixes food with digestive juices and increases the efficiency of absorption by repeatedly moving different parts of the food mass over the intestinal wall.

4. **Chemical digestion** is a series of catabolic steps in which complex food molecules are broken down to their chemical building blocks by enzymes secreted into the lumen of the alimentary canal. Chemical digestion of foodstuffs begins in the mouth and is essentially complete in the small intestine.
5. **Absorption** is the passage of digested end products (plus vitamins, minerals, and water) from the lumen of the GI tract through the mucosal cells by active or passive transport into the blood or lymph. The small intestine is the major absorptive site.
6. **Defecation** eliminates indigestible substances from the body via the anus in the form of feces.

Some of these processes are the job of a single organ. For example, only the mouth ingests and only the large intestine defecates. But most digestive system activities require the cooperation of several organs and occur bit by bit as food moves along the tract. Later, we will consider which of these specific processes each GI tract organ performs and the neural or hormonal factors that regulate these processes.

CHECK YOUR UNDERSTANDING

1. Name one organ of the alimentary canal found in the thorax. Name three organs located in the abdominal cavity.
2. What is the usual site of ingestion?
3. Which essential digestive activity actually moves nutrients from the outside to the inside of the body?

For answers, see Appendix G.

Basic Functional Concepts

23

▶ Describe stimuli and controls of digestive activity.

A theme we have stressed in this book is the body's efforts to maintain the constancy of its internal environment. Most organ systems respond to changes in that environment either by attempting to restore some plasma variable to its former levels or by changing their own function. The digestive system, however, creates an optimal environment for its functioning in the lumen (cavity) of the GI tract, an area that is actually *outside* the body, and essentially all digestive tract regulatory mechanisms act to control luminal conditions so that digestion and absorption can occur there as effectively as possible.

Two facts apply to these regulatory mechanisms:

1. **Digestive activity is provoked by a range of mechanical and chemical stimuli.** Sensors (mechanoreceptors and chemoreceptors) involved in controls of GI tract activity are located in the walls of the tract organs. These sensors respond to several stimuli. The most important are stretching of the organ by food in the lumen, osmolarity (solute concentration) and pH of the contents, and the presence of substrates and end products of digestion. When stimulated, these receptors initiate reflexes that (1) activate or inhibit glands that secrete digestive juices into the lumen or hormones into the blood or (2) stimulate smooth muscle of the GI tract walls to mix lumen contents and move them along the tract.
2. **Controls of digestive activity are both intrinsic and extrinsic.** Many of the controlling systems of the digestive tract are *intrinsic*—a product of "in-house" nerve plexuses or hormone-producing cells. Between the muscle layers in the wall of the alimentary canal is the so-called **gut brain** consisting of enteric nerve plexuses which spread like chicken wire along the entire length of the GI tract and influence each other both in the same and in different digestive organs.

   As a result, two kinds of reflex activity occur, short and long. *Short reflexes* are mediated entirely by the local *enteric* or "gut" plexuses in response to stimuli arising in the GI tract. *Long reflexes* are initiated by stimuli arising inside or outside the GI tract and involve CNS centers and extrinsic autonomic nerves **(Figure 23.4)**. Generally speaking, nerve fibers that excite smooth muscle secrete acetylcholine or substance P, and those that inhibit smooth muscle release vasoactive intestinal peptide (VIP) or nitric oxide.

   The stomach and small intestine also contain hormone-producing cells. When appropriately stimulated, these cells release their products to the interstitial fluid in the extracellular space. Their hormones are distributed via blood and interstitial fluid to their target cells in the same or different digestive tract organs, which they prod to secrete or contract.

CHECK YOUR UNDERSTANDING

4. When sensors in the GI tract are stimulated, they respond via reflexes. What types of digestive activity may be put into motion via those reflexes?
5. The term "gut brain" does not really mean there is a brain in the digestive system. What does it refer to?

For answers, see Appendix G.

Digestive System Organs: Relationships

Relationship of the Digestive Organs to the Peritoneum

▶ Describe the location and function of the peritoneum.

▶ Define retroperitoneal and name the retroperitoneal organs.

Most digestive system organs reside in the abdominopelvic cavity. Recall from Chapter 1 that all ventral body cavities contain

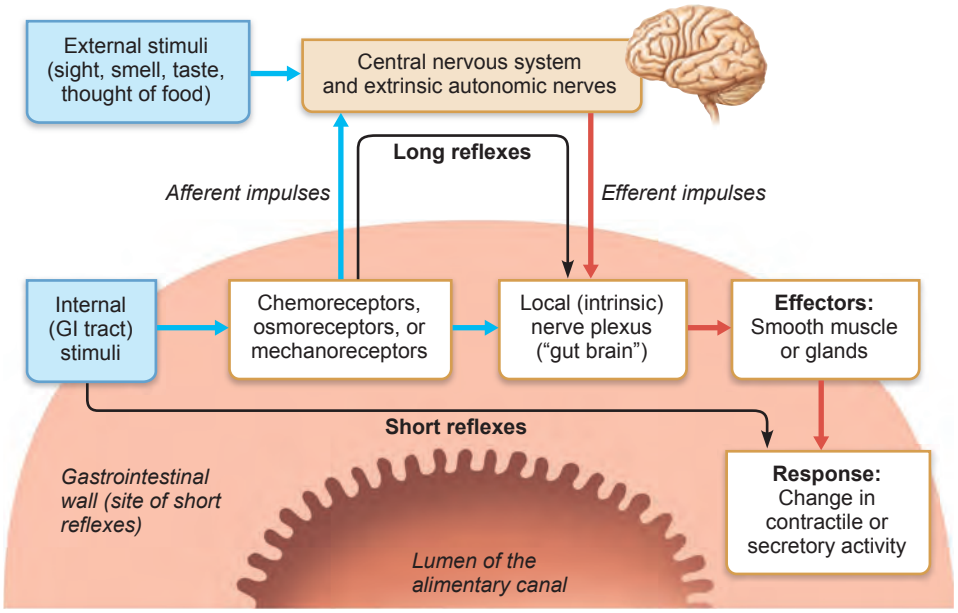
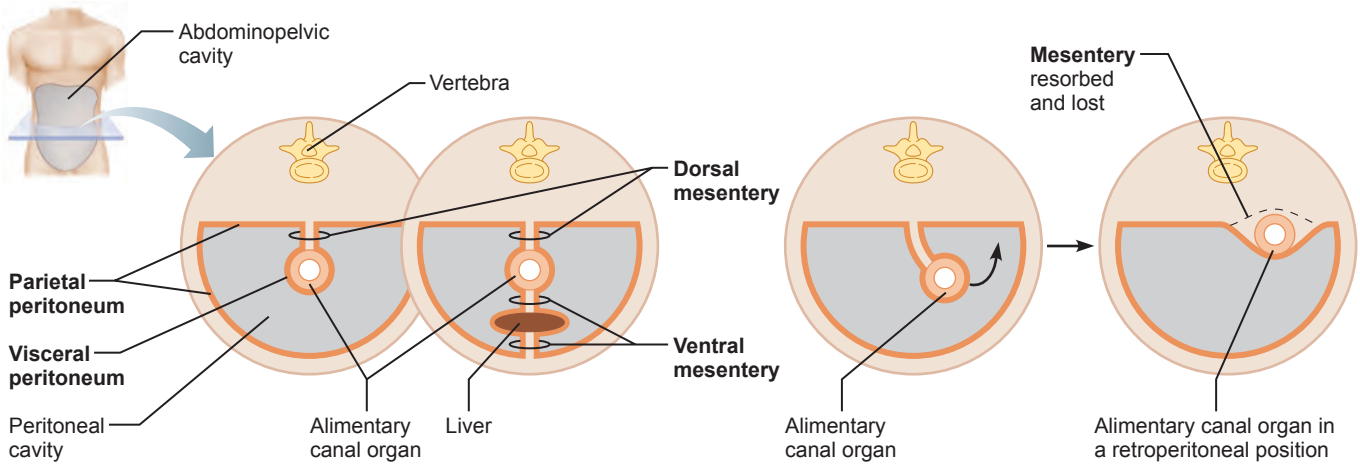


Figure 23.4 Neural reflex pathways initiated by stimuli inside or outside the gastrointestinal tract.

slippery *serous membranes*. The **peritoneum** of the abdominopelvic cavity is the most extensive of these membranes (Figure 23.5a). The **visceral peritoneum** covers the external surfaces of most digestive organs and is continuous with the **parietal peritoneum** that lines the body wall. Between the two peritoneums is the **peritoneal cavity**, a slitlike potential space containing a slippery fluid secreted by the serous membranes. The serous fluid lubricates the mobile digestive organs, allowing them to glide easily across one another and along the body wall as they carry out their digestive activities.

A **mesentery** (mes′en-ter″e) is a double layer of peritoneum—a sheet of two serous membranes fused back to back—that extends to the digestive organs from the body wall. Mesenteries provide routes for blood vessels, lymphatics, and nerves to reach the digestive viscera; hold organs in place; and store fat. In most places the mesentery is *dorsal* and attaches to the posterior abdominal wall, but there are *ventral* mesenteries as well, such as the one that extends from the liver to the anterior abdominal wall (Figure 23.5a). As you read about the digestive organ mesenteries, you will see that some of them are given specific names (such as the *omenta*), or are called "ligaments" (even though these peritoneal folds are nothing like the fibrous ligaments that connect bones).

Not all alimentary canal organs are suspended by a mesentery. For example, during development, some parts of the small



(a) Schematic cross sections of abdominal cavity illustrate the peritoneums and mesenteries.

(b) Some organs lose their mesentery and become retroperitoneal during development.

Figure 23.5 The peritoneum and the peritoneal cavity. Note that the peritoneal cavity is much smaller than depicted here.

intestine adhere to the dorsal abdominal wall (Figure 23.5b). In so doing, they lose their mesentery and come to lie posterior to the peritoneum. These organs, which include most of the pancreas and parts of the large intestine, are called **retroperitoneal organs** (*retro* = behind). By contrast, digestive organs (like the stomach) that keep their mesentery and remain in the peritoneal cavity are called **intraperitoneal** or **peritoneal organs**.

HOMEOSTATIC IMBALANCE

Peritonitis is inflammation of the peritoneum. It can arise from a piercing abdominal wound, from a perforating ulcer that leaks stomach juices into the peritoneal cavity, or from poor sterile technique during abdominal surgery, but most commonly it results from a burst appendix (that sprays bacteria-containing feces all over the peritoneum). In peritonitis, the peritoneal coverings tend to stick together around the infection site. This localizes the infection, providing time for macrophages to attack to prevent the inflammation from spreading. If peritonitis becomes widespread within the peritoneal cavity, it is dangerous and often lethal. Treatment includes removing as much infectious debris as possible from the peritoneal cavity and administering megadoses of antibiotics. ■

Blood Supply: The Splanchnic Circulation

- Define splanchnic circulation.
- Indicate the importance of the hepatic portal system.

The **splanchnic circulation** includes those arteries that branch off the abdominal aorta to serve the digestive organs and the *hepatic portal circulation.* The arterial supply—the hepatic, splenic, and left gastric branches of the celiac trunk that serve the spleen, liver, and stomach, and the mesenteric arteries (superior and inferior) that serve the small and large intestines (see pp. 730 and 731)—normally receives one-quarter of the cardiac output. This blood volume percentage increases after a meal has been eaten. The hepatic portal circulation (described on pp. 742–743) collects nutrient-rich venous blood draining from the digestive viscera and delivers it to the liver. The liver collects the absorbed nutrients for metabolic processing or for storage before releasing them back to the bloodstream for general cellular use.

CHECK YOUR UNDERSTANDING

6. How does the location of the visceral peritoneum differ from that of the parietal peritoneum?
7. Of the following organs, which is/are retroperitoneal? Stomach, pancreas, liver.
8. What name is given to the venous portion of the splanchnic circulation?

For answers, see Appendix G.

Histology of the Alimentary Canal

- Describe the tissue composition and the general function of each of the four layers of the alimentary canal.

Each digestive organ has only a share of the work of digestion. Consequently, it helps to consider structural characteristics that promote similar functions in all parts of the alimentary canal before we consider the functional anatomy of the digestive system.

From the esophagus to the anal canal, the walls of the alimentary canal have the same four basic layers, or *tunics*—*mucosa*, *submucosa*, *muscularis externa*, and *serosa* (Figure 23.6). Each layer contains a predominant tissue type that plays a specific role in food breakdown.

The Mucosa

The **mucosa**, or **mucous membrane**—the innermost layer—is a moist epithelial membrane that lines the alimentary canal lumen from mouth to anus. Its major functions are (1) to *secrete* mucus, digestive enzymes, and hormones, (2) to *absorb* the end products of digestion into the blood, and (3) to *protect* against infectious disease. The mucosa in a particular region of the GI tract may express one or all three of these capabilities.

More complex than most other mucosae in the body, the typical digestive mucosa consists of three sublayers: (1) a lining epithelium, (2) a lamina propria, and (3) a muscularis mucosae. Typically, the **epithelium** of the mucosa is a *simple columnar epithelium* rich in mucus-secreting cells. The slippery mucus it produces protects certain digestive organs from being digested themselves by enzymes working within their cavities and eases food passage along the tract. In the stomach and small intestine, the mucosa also contains both enzyme-synthesizing and hormone-secreting cells. For this reason, in such sites, the mucosa is a diffuse kind of endocrine organ as well as part of the digestive organ.

The **lamina propria** (*proprius* = one's own), which underlies the epithelium, is loose areolar connective tissue. Its capillaries nourish the epithelium and absorb digested nutrients. Its isolated lymphoid follicles, part of **MALT**, the mucosa-associated lymphatic tissue described on p. 761, help defend us against bacteria and other pathogens, which have rather free access to our digestive tract. Particularly large collections of lymphoid follicles occur within the pharynx (as the tonsils) and in the appendix.

External to the lamina propria is the **muscularis mucosae**, a scant layer of smooth muscle cells that produces local movements of the mucosa. For example, twitching of this muscle layer dislodges food particles that have adhered to the mucosa. In the small intestine, this muscle layer's tone throws the mucosa into a series of small folds that immensely increase its surface area.

The Submucosa

The **submucosa**, just external to the mucosa, is areolar connective tissue containing a rich supply of blood and lymphatic vessels, lymphoid follicles, and nerve fibers. Its abundant elastic

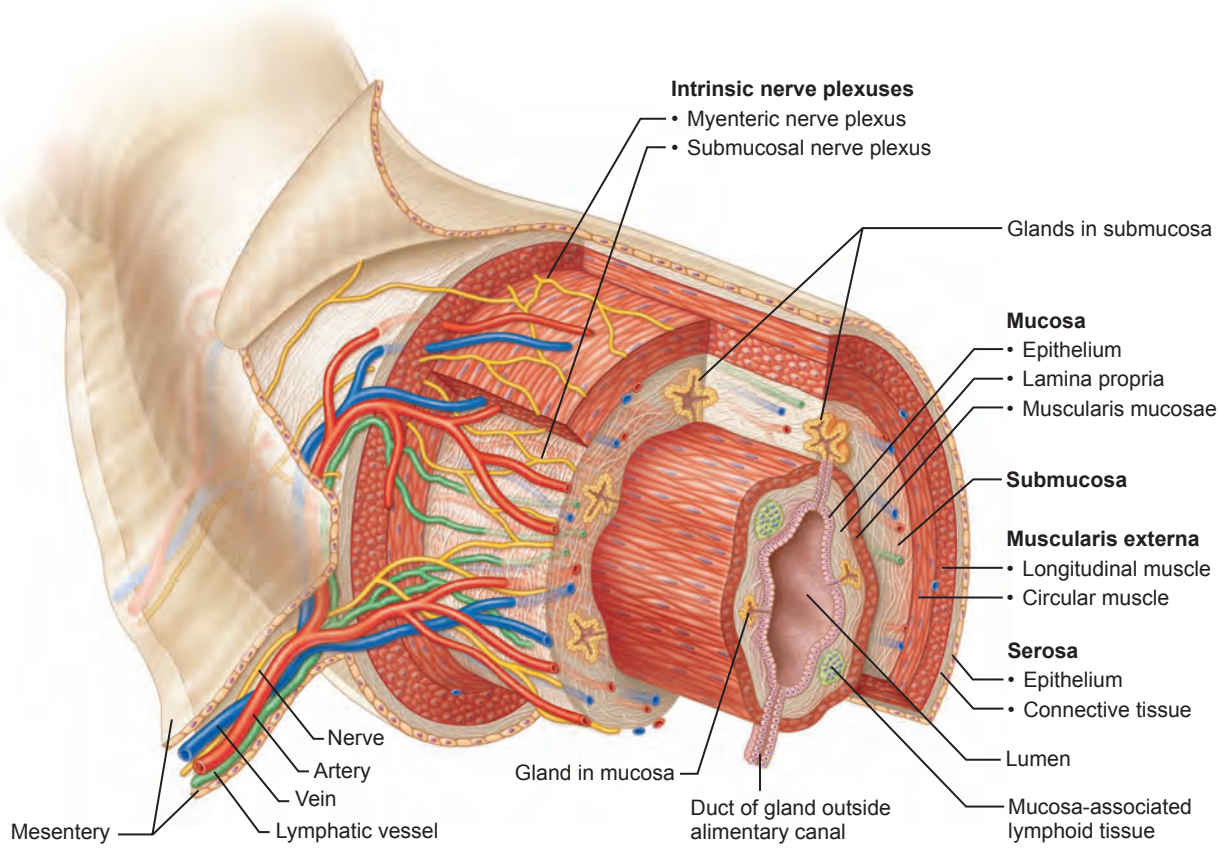


Figure 23.6 Basic structure of the alimentary canal. Its four basic layers are the mucosa, submucosa, muscularis externa, and serosa.

fibers enable the stomach to regain its normal shape after temporarily storing a large meal. Its extensive vascular network supplies surrounding tissues of the GI tract wall.

The Muscularis Externa

Surrounding the submucosa is the **muscularis externa**, also simply called the **muscularis**. This layer is responsible for segmentation and peristalsis. It typically has an inner *circular layer* and an outer *longitudinal layer* of smooth muscle cells (see Figures 4.10c and 23.6). In several places along the tract, the circular layer thickens, forming *sphincters* that act as valves to prevent backflow and control food passage from one organ to the next.

The Serosa

The **serosa**, the protective outermost layer of the intraperitoneal organs, is the *visceral peritoneum*. It is formed of areolar connective tissue covered with *mesothelium*, a single layer of squamous epithelial cells (see Figures 4.8a and 4.3a, respectively).

In the esophagus, which is located in the thoracic instead of the abdominopelvic cavity, the serosa is replaced by an **adventitia** (ad″ven-tish′e-ah). The adventitia is ordinary fibrous connective tissue that binds the esophagus to surrounding structures. Retroperitoneal organs have *both* a serosa (on the side facing the peritoneal cavity) and an adventitia (on the side abutting the dorsal body wall).

Enteric Nervous System of the Alimentary Canal

As we noted earlier, the alimentary canal has its own in-house nerve supply, staffed by the so-called **enteric neurons** (*enter* = gut), which communicate widely with one another to regulate digestive system activity. These semiautonomous enteric neurons constitute the bulk of the two major *intrinsic nerve plexuses* (ganglia interconnected by unmyelinated fiber tracts) found in the walls of the alimentary canal: the submucosal and myenteric nerve plexuses (Figure 23.6).

The **submucosal nerve plexus** occupies the submucosa. It includes sensory as well as motor neurons, and it chiefly regulates the activity of glands and smooth muscle in the mucosa.

The large **myenteric nerve plexus** (mi-en′ter-ik; "intestinal muscle") lies between the circular and longitudinal muscle layers of the muscularis externa. Enteric neurons of this plexus provide the major nerve supply to the GI tract wall and control GI tract motility. Control of the patterns of segmentation and peristalsis is largely automatic, involving pacemaker cells and local reflex arcs between enteric neurons in the same or different plexuses or (even) organs.

The enteric nervous system is also linked to the central nervous system by afferent visceral fibers and by sympathetic and parasympathetic branches (motor fibers) of the autonomic nervous system that enter the intestinal wall and synapse with

neurons in the intrinsic plexuses. Hence, digestive activity is also subject to extrinsic controls exerted by autonomic fibers via long reflex arcs (see Figure 23.4). Generally speaking, parasympathetic inputs enhance secretory activity and motility, whereas sympathetic impulses inhibit digestive activities.

But the largely independent enteric ganglia are much more than just way stations for the autonomic nervous system as is the case in other organ systems. Indeed, the enteric nervous system contains over 100 million neurons, more than the entire spinal cord.

CHECK YOUR UNDERSTANDING

9. Name the layers of the alimentary canal from the inside out.
10. Jerry has been given a drug that inhibits parasympathetic stimulation of his digestive tract. Should he "eat hearty" or temporarily refrain from eating, and why?

For answers, see Appendix G.

PART 2

FUNCTIONAL ANATOMY OF THE DIGESTIVE SYSTEM

Now that we have summarized some points that unify the digestive system organs, let's consider the special structural and functional capabilities of each organ of this system. Most of the digestive organs are shown in their normal body positions in Figure 23.1, so you may find it helpful to refer back to that illustration from time to time as you read the following sections.

The Mouth and Associated Organs

- Describe the gross and microscopic anatomy and the basic functions of the mouth, pharynx, and esophagus.
- Describe the composition and functions of saliva, and explain how salivation is regulated.
- Explain the dental formula and differentiate clearly between deciduous and permanent teeth.

The mouth is the only part of the alimentary canal involved in ingestion. However, most digestive functions associated with the mouth reflect the activity of the related accessory organs, such as the teeth, salivary glands, and tongue, because in the mouth food is chewed and mixed with saliva containing enzymes that begin the process of chemical digestion. The mouth also begins the propulsive process of swallowing, which carries food through the pharynx and esophagus to the stomach.

The Mouth

The **mouth**, a mucosa-lined cavity, is also called the **oral cavity**, or *buccal cavity* (buk′al). Its boundaries are the lips anteriorly, cheeks laterally, palate superiorly, and tongue inferiorly (Figure 23.7). Its anterior opening is the **oral orifice**. Posteriorly, the oral cavity is continuous with the *oropharynx*.

The walls of the mouth are lined with a thick stratified squamous epithelium (see Figure 4.3e) which can withstand considerable friction. The epithelium on the gums, hard palate, and dorsum of the tongue is slightly keratinized for extra protection against abrasion during eating. Like all moist surface linings, the oral mucosa responds to injury by producing antimicrobial peptides called *defensins*, which helps to explain how the mouth, a site teeming with disease-causing microbes, remains so remarkably healthy.

The Lips and Cheeks

The **lips** (**labia**) and the **cheeks**, which help keep food between the teeth when we chew, are composed of a core of skeletal muscle covered externally by skin. The *orbicularis oris muscle* forms the fleshy lips; the cheeks are formed largely by the *buccinators*. The recess bounded externally by the lips and cheeks and internally by the gums and teeth is called the **vestibule** ("porch"). The area that lies within the teeth and gums is the **oral cavity proper**.

The lips are much larger than most people think. Anatomically they extend from the inferior margin of the nose to the superior boundary of the chin. The reddened area where a person applies lipstick or lands a kiss is called the **red margin**. This transitional zone, where keratinized skin meets the oral mucosa, is poorly keratinized and translucent, allowing the red color of blood in the underlying capillaries to show through. Because the red margin lacks sweat or sebaceous glands, it must be moistened with saliva periodically to prevent it from becoming dry and cracked (chapped lips). The **labial frenulum** (fren′u-lum) is a median fold that joins the internal aspect of each lip to the gum (Figure 23.7b).

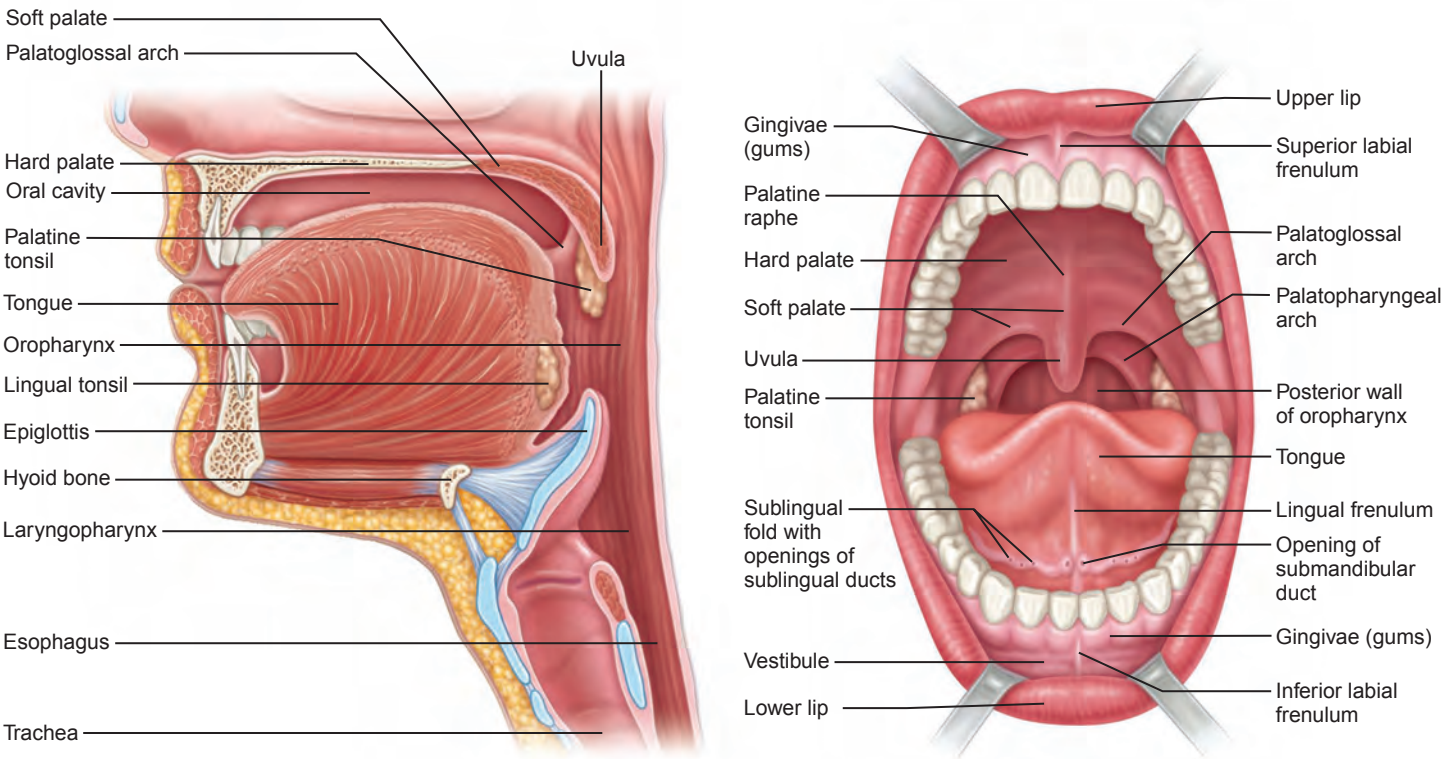
The Palate

The **palate**, forming the roof of the mouth, has two distinct parts: the hard palate anteriorly and the soft palate posteriorly (Figure 23.7). The **hard palate** is underlain by the palatine bones and the palatine processes of the maxillae, and it forms a rigid surface against which the tongue forces food during chewing. The mucosa on either side of its *raphe* (ra′fe), a midline ridge, is slightly corrugated, which helps to create friction.

The **soft palate** is a mobile fold formed mostly of skeletal muscle that rises reflexively to close off the nasopharynx when we swallow.

- To demonstrate this action, try to breathe and swallow at the same time.

Laterally, the soft palate is anchored to the tongue by the **palatoglossal arches** and to the wall of the oropharynx by the more posterior **palatopharyngeal arches**. These two paired folds form the boundaries of the **fauces** (faw′sēz; *fauc* = throat), the arched area of the oropharynx that contains the palatine tonsils. Projecting downward from the free edge of the soft palate is the fingerlike **uvula** (u′vu-lah).



(a) Sagittal section of the oral cavity and pharynx

(b) Anterior view

Figure 23.7 Anatomy of the oral cavity (mouth).

The Tongue

The **tongue** occupies the floor of the mouth and fills most of the oral cavity when the mouth is closed (Figure 23.7). The tongue is composed of interlacing bundles of skeletal muscle fibers, and during chewing, it grips the food and constantly repositions it between the teeth. The tongue also mixes food with saliva forming it into a compact mass called a **bolus** (bo′lus; "a lump"), and then initiates swallowing by pushing the bolus posteriorly into the pharynx. The versatile tongue also helps us form consonants (k, d, t, and so on) when we speak.

The tongue has both intrinsic and extrinsic skeletal muscle fibers. The **intrinsic muscles** are confined in the tongue and are not attached to bone. Their muscle fibers, which run in several different planes, allow the tongue to change its shape (but not its position), becoming thicker, thinner, longer, or shorter as needed for speech and swallowing.

The **extrinsic muscles** extend to the tongue from their points of origin on bones of the skull or the soft palate, as described in Chapter 10 (see Table 10.2 and Figure 10.7). The extrinsic muscles alter the tongue's position. They protrude it, retract it, and move it from side to side. The tongue has a median septum of connective tissue, and each half contains identical muscle groups. A fold of mucosa called the **lingual frenulum** secures the tongue to the floor of the mouth and limits its posterior movements of the tongue.

HOMEOSTATIC IMBALANCE

Children born with an extremely short lingual frenulum are often referred to as "tongue-tied" because when tongue movement is restricted, speech is distorted. This congenital condition, called *ankyloglossia* ("fused tongue"), is corrected surgically by snipping the frenulum. ■

The superior tongue surface bears papillae, peglike projections of the underlying mucosa (Figure 23.8). The conical **filiform papillae** give the tongue surface a roughness that aids in licking semisolid foods (such as ice cream) and provide friction for manipulating foods in the mouth. These papillae, the smallest and most numerous type, align in parallel rows on the tongue dorsum. They contain keratin, which stiffens them and gives the tongue its whitish appearance.

The mushroom-shaped **fungiform papillae** are scattered widely over the tongue surface. Each has a vascular core that gives it a reddish hue. Ten to twelve large **circumvallate**, or **vallate**, **papillae** are located in a V-shaped row at the back of the tongue. They resemble the fungiform papillae but have an additional surrounding furrow. Pleatlike **foliate papillae** are located on the lateral aspects of the posterior tongue. The fungiform, circumvallate, and foliate papillae house taste buds, but those on the foliate papillae function in taste primarily in infancy and early childhood.

Immediately posterior to the circumvallate papillae is the **terminal sulcus**, a groove that distinguishes the portion of the

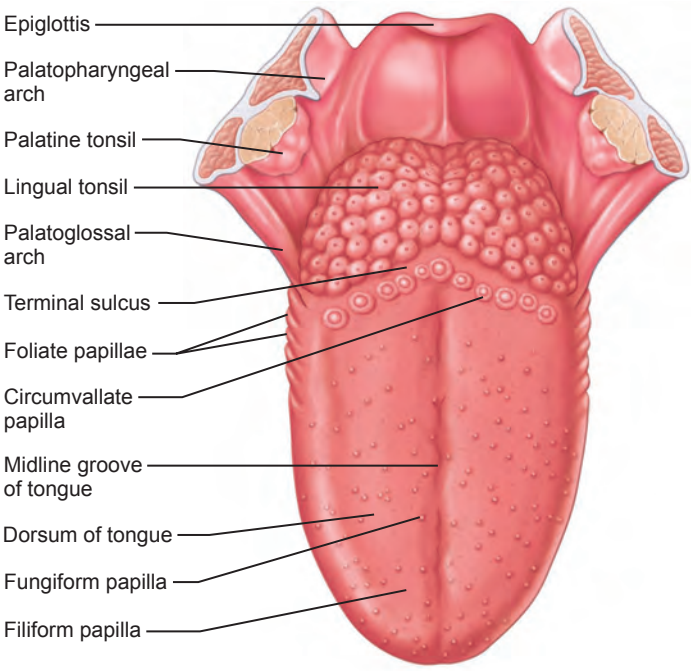


Figure 23.8 Dorsal surface of the tongue, and the tonsils.

tongue that lies in the oral cavity (its *body*) from its posterior portion in the oropharynx (its *root*). The mucosa covering the root of the tongue lacks papillae, but it is still bumpy because of the nodular *lingual tonsil*, which lies just deep to its mucosa (Figure 23.8).

CHECK YOUR UNDERSTANDING

11. How does the vestibule of the mouth differ from the oral cavity proper?
12. What structure forms the roof of the mouth?
13. Besides preparing food for swallowing, the tongue has another role. What is it?

For answers, see Appendix G.

The Salivary Glands

A number of glands associated with the oral cavity secrete **saliva**. Saliva (1) cleanses the mouth, (2) dissolves food chemicals so that they can be tasted, (3) moistens food and aids in compacting it into a bolus, and (4) contains enzymes that begin the chemical breakdown of starchy foods.

Most saliva is produced by **extrinsic salivary glands** that lie outside the oral cavity and empty their secretions into it. Their output is augmented slightly by small **intrinsic salivary glands**, also called **buccal glands**, scattered throughout the oral cavity mucosa.

The extrinsic salivary glands are paired compound tubuloalveolar glands that develop from the oral mucosa and remain connected to it by ducts (Figure 23.9a). The large **parotid gland** (pah-rot′id; *par* = near, *otid* = the ear) lies anterior to the ear between the masseter muscle and the skin. The prominent parotid duct parallels the zygomatic arch, pierces the buccinator muscle, and opens into the vestibule next to the second upper molar. Branches of the facial nerve run through the parotid gland on their way to the muscles of facial expression. For this reason, surgery on this gland can result in facial paralysis.

HOMEOSTATIC IMBALANCE

Mumps, a common children's disease, is an inflammation of the parotid glands caused by the mumps virus (*myxovirus*), which spreads from person to person in saliva. If you check the location of the parotid glands in Figure 23.9a, you can understand why people with mumps complain that it hurts to open their mouth or chew. Besides that discomfort, other signs and symptoms of mumps include moderate fever and pain when swallowing acid foods (sour pickles, grapefruit juice, etc.). Mumps viral infections in adult males carry a 25% risk that the testes may become infected as well, leading to sterility. ■

About the size of a walnut, the **submandibular gland** lies along the medial aspect of the mandibular body. Its duct runs beneath the mucosa of the oral cavity floor and opens at the base of the lingual frenulum (see Figure 23.7b). The small **sublingual gland** lies anterior to the submandibular gland under the tongue and opens via 10–12 ducts into the floor of the mouth (Figure 23.9a).

To a greater or lesser degree, the salivary glands are composed of two types of secretory cells: mucous and serous (Figure 23.9b). **Serous cells** produce a watery secretion containing enzymes, ions, and a tiny bit of mucin, whereas the **mucous cells** produce **mucus**, a stringy, viscous solution. The parotid glands contain only serous cells. Submandibular and buccal glands have approximately equal numbers of serous and mucous cells. The sublingual glands contain mostly mucous cells.

Composition of Saliva

Saliva is largely water—97 to 99.5%—and therefore is hypoosmotic. Its osmolarity depends on the precise glands that are active and the nature of the stimulus for salivation. As a rule, saliva is slightly acidic (pH 6.75 to 7.00), but its pH may vary. Its solutes include electrolytes (Na^+, K^+, Cl^-, PO_4^{3-}, and HCO_3^-); the digestive enzymes salivary amylase and lingual lipase (both optimally active at an acid pH); the proteins mucin (mu′sin), lysozyme, and IgA; and metabolic wastes (urea and uric acid). When dissolved in water, the glycoprotein *mucin* forms thick mucus that lubricates the oral cavity and hydrates foodstuffs.

Protection against microorganisms is provided by (1) *IgA antibodies*; (2) *lysozyme*, a bactericidal enzyme that inhibits bacterial growth in the mouth and may help to prevent tooth decay; (3) a cyanide compound; and (4) *defensins* (see p. 644). Besides acting as a local antibiotic, defensins function as cytokines to call defensive cells (lymphocytes, neutrophils, etc.) into the mouth for battle.

In addition to these four protectors, the friendly bacteria that live on the back of the tongue convert food-derived nitrates in saliva into nitrites which, in turn, are converted into *nitric oxide* in an acid environment. This transformation occurs around the

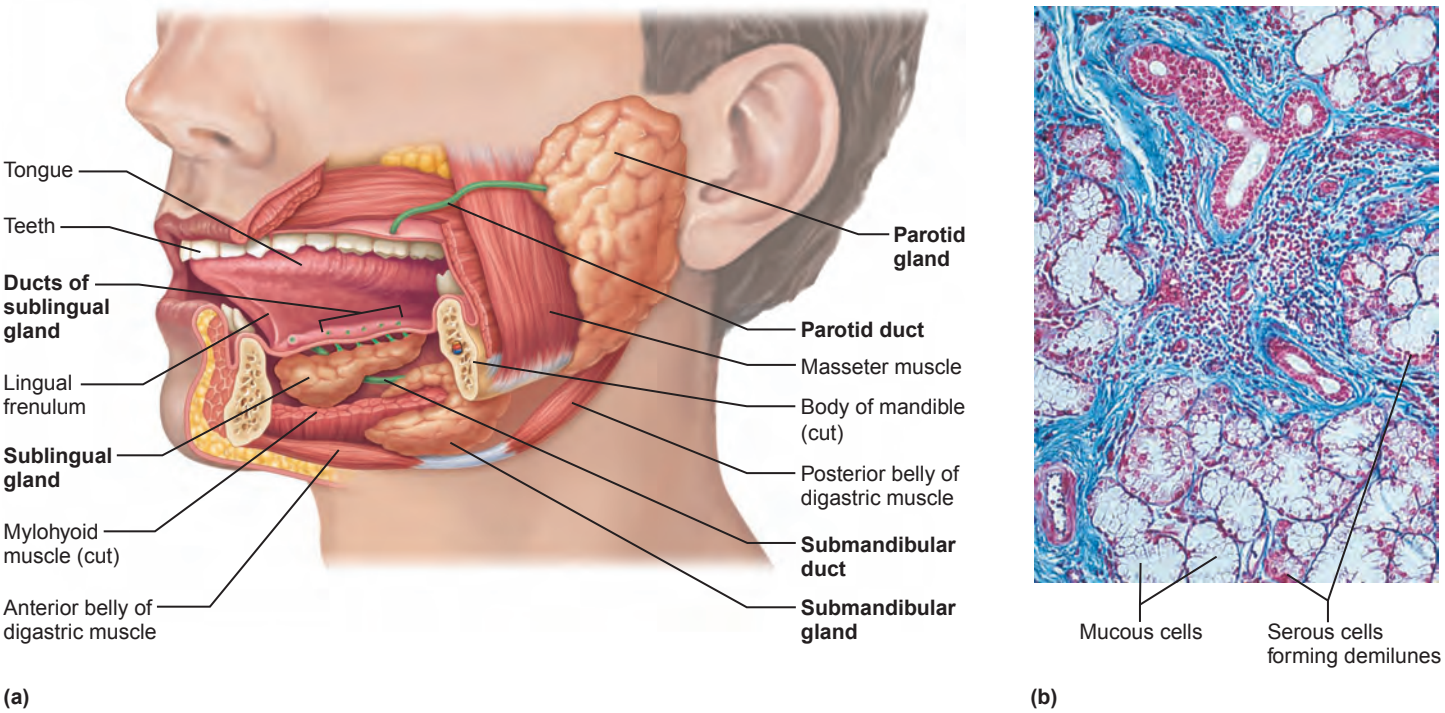


Figure 23.9 The salivary glands. (a) The parotid, submandibular, and sublingual glands associated with the left aspect of the oral cavity. **(b)** Photomicrograph of the sublingual gland (150×), which is a mixed salivary gland. Mucus-producing cells stain light blue and serous-secreting units stain purple. The serous cells sometimes form demilunes (caps) around the bases of the mucous cells.

gums, where acid-producing bacteria tend to cluster, and in the hydrochloric acid–rich secretions of the stomach. The highly toxic nitric oxide is believed to act as a bactericidal agent in these locations.

Saliva also serves as a clinical medium that can be used to detect and monitor certain diseases. For example, saliva tests for HIV antibodies, oral cancer, and diabetes are available. Additionally, quick assessments of body hormone levels may be done using saliva.

Control of Salivation

The intrinsic salivary glands secrete saliva continuously in amounts just sufficient to keep the mouth moist. But when food enters the mouth, the extrinsic glands are activated and copious amounts of saliva pour out. The average output of saliva is 1000–1500 ml per day.

Salivation is controlled primarily by the parasympathetic division of the autonomic nervous system. When we ingest food, chemoreceptors and mechanoreceptors in the mouth send signals to the **salivatory nuclei** in the brain stem (pons and medulla). As a result, parasympathetic nervous system activity increases and impulses sent via motor fibers in the *facial* (*VII*) and *glossopharyngeal* (*IX*) *nerves* trigger a dramatically increased output of watery (serous), enzyme-rich saliva. The chemoreceptors are activated most strongly by acidic substances such as vinegar and citrus juice. The mechanoreceptors are activated by virtually any mechanical stimulus in the mouth—even rubber bands.

Sometimes just the sight or smell of food is enough to get the juices flowing. The mere thought of hot fudge sauce on peppermint stick ice cream will make many a mouth water! Irritation of the lower regions of the GI tract by bacterial toxins, spicy foods, or hyperacidity—particularly when accompanied by a feeling of nausea—also increases salivation. This response may help wash away or neutralize the irritants.

In contrast to parasympathetic controls, the sympathetic division (specifically fibers in T_1–T_3) causes release of a thick, mucin-rich saliva. Extremely strong activation of the sympathetic division constricts blood vessels serving the salivary glands and almost completely inhibits saliva release, causing a dry mouth (*xerostomia*). Dehydration also inhibits salivation because low blood volume results in reduced filtration pressure at capillary beds.

HOMEOSTATIC IMBALANCE

Any disease process that inhibits saliva secretion causes a marked increase in dental caries (cavities) and difficulty in talking, swallowing, and eating. Because decomposing food particles are allowed to accumulate and bacteria flourish, *halitosis* (hal″ĭ-to′sis; "bad breath") can result. The odor is caused mainly by the metabolic activity of anaerobic protein-digesting bacteria at the back of the tongue that yields hydrogen sulfide (rotten egg smell), and methyl mercaptan (also in feces), cadaverine (associated with rotting corpses), and others. ■

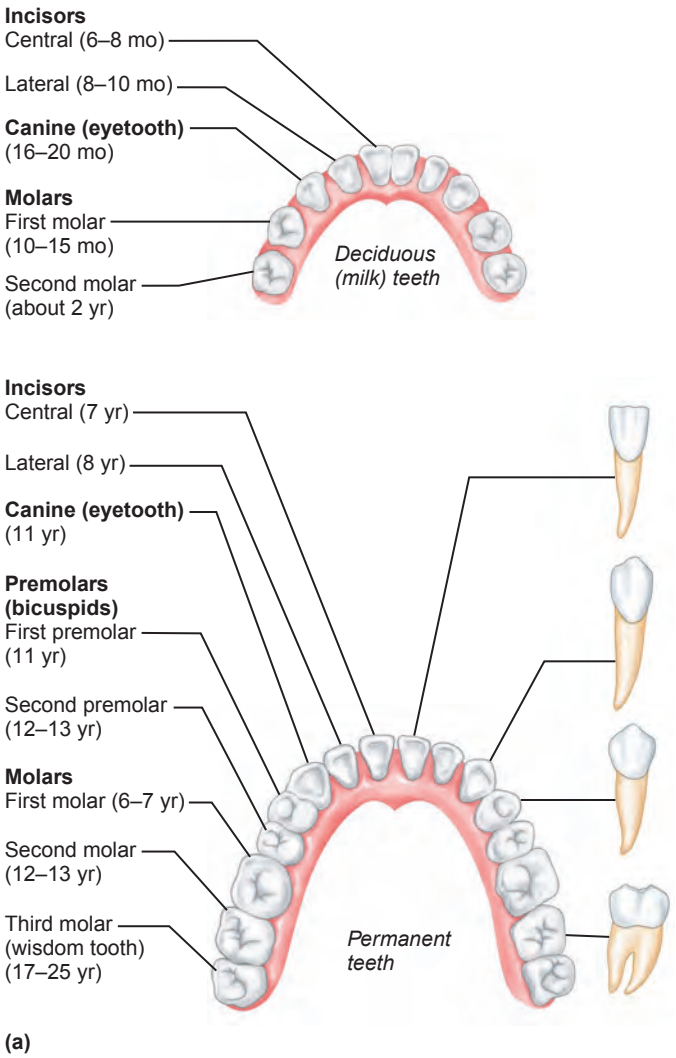


Figure 23.10 Human dentition. (a) Teeth of the lower jaw: the deciduous and permanent sets. Approximate age at which tooth erupts is shown in parentheses. The shapes of individual teeth are shown on the right. **(b)** X ray of the mouth of a child of 7 years showing permanent teeth forming deep to the deciduous teeth.

CHECK YOUR UNDERSTANDING

14. What is the importance of the serous portion of saliva?
15. Name four antimicrobial substances found in saliva.

For answers, see Appendix G.

The Teeth

The **teeth** lie in sockets (alveoli) in the gum-covered margins of the mandible and maxilla. The role of the teeth in food processing needs little introduction. We *masticate*, or chew, by opening and closing our jaws and moving them from side to side while continually using our tongue to move the food between our teeth. In the process, the teeth tear and grind the food, breaking it down into smaller fragments.

Dentition and the Dental Formula

Ordinarily by age 21, two sets of teeth, the **primary** and **permanent dentitions**, have formed (Figure 23.10a). The primary dentition consists of the **deciduous teeth** (de-sid′u-us; *decid* = falling off), also called **milk** or **baby teeth**. The first teeth to appear, at about age 6 months, are the lower central incisors. Additional pairs of teeth erupt at one- to two-month intervals until about 24 months, when all 20 milk teeth have emerged.

As the deep-lying **permanent teeth** enlarge and develop, the roots of the milk teeth are resorbed from below (Figure 23.10b), causing them to loosen and fall out between the ages of 6 and 12 years. Generally, all the teeth of the permanent dentition but the third molars have erupted by the end of adolescence. The third molars, also called *wisdom teeth*, emerge between the ages of 17 and 25 years. There are usually 32 permanent teeth in a full set, but sometimes the wisdom teeth never erupt or are completely absent.

HOMEOSTATIC IMBALANCE

When a tooth remains embedded in the jawbone, it is said to be *impacted*. Impacted teeth can cause a good deal of pressure and pain and must be removed surgically. Wisdom teeth are most commonly impacted. ■

Teeth are classified according to their shape and function as incisors, canines, premolars, and molars (Figure 23.10a). The chisel-shaped **incisors** are adapted for cutting or nipping off pieces of food. The conical or fanglike **canines** (cuspids or eyeteeth) tear and pierce. The **premolars** (bicuspids) and **molars** have broad crowns with rounded cusps (tips) and are best suited for grinding or crushing. The molars (literally, "millstones"), with four or five cusps, are the best grinders. During chewing, the upper and lower molars repeatedly lock together, an action that generates tremendous crushing forces.

The **dental formula** is a shorthand way of indicating the numbers and relative positions of the different types of teeth in the mouth. This formula is written as a ratio, uppers over lowers, for *one-half* of the mouth. Since the other side is a mirror image, the total dentition is obtained by multiplying the dental

formula by 2. The primary dentition consists of two incisors (I), one canine (C), and two molars (M) on each side of each jaw, and its dental formula is written as

$$\frac{\text{2I, 1C, 2M (upper jaw)}}{\text{2I, 1C, 2M (lower jaw)}} \times 2 \text{ (20 teeth)}$$

Similarly, the permanent dentition [two incisors, one canine, two premolars (PM), and three molars] is

$$\frac{\text{2I, 1C, 2PM, 3M}}{\text{2I, 1C, 2PM, 3M}} \times 2 \text{ (32 teeth)}$$

Tooth Structure

Each tooth has two major regions: the crown and the root (Figure 23.11). The enamel-covered **crown** is the exposed part of the tooth above the **gingiva** (jin′jĭ-vah), or **gum**, which surrounds the tooth like a tight collar. **Enamel**, a brittle ceramic-like material thick as a dime, directly bears the force of chewing. The hardest substance in the body, it is heavily mineralized with calcium salts, and its densely packed hydroxyapatite (mineral) crystals are oriented in force-resisting columns perpendicular to the tooth's surface. The cells that produce enamel degenerate when the tooth erupts; consequently, any decayed or cracked areas of the enamel will not heal and must be artificially filled.

The portion of the tooth embedded in the jawbone is the **root**. Canine teeth, incisors, and premolars have one root, although the first upper premolars commonly have two. The first two upper molars have three roots, while the corresponding lower molars have two. The root pattern of the third molar varies, but a fused single root is most common.

The crown and root are connected by a constricted tooth region called the **neck**. The outer surface of the root is covered by **cementum**, a calcified connective tissue, which attaches the tooth to the thin **periodontal ligament** (per″e-o-don′tal; "around the tooth"). This ligament anchors the tooth in the bony alveolus of the jaw, forming a fibrous joint called a *gomphosis*. Where the gingiva borders on a tooth, it dips downward to form a shallow groove called the *gingival sulcus*.

In youth, the gingiva adheres tenaciously to the enamel covering the crown. But as the gums begin to recede with age, the gingiva adheres to the more sensitive cementum covering the superior region of the root. As a result, the teeth *appear* to get longer in old age—hence the expression "long in the tooth" sometimes applied to elderly people.

Dentin, a protein-rich bonelike material, underlies the enamel cap and forms the bulk of a tooth. More resilient than enamel, dentin acts as a shock absorber for forces acting on the enamel during biting and chewing. Dentin surrounds a central **pulp cavity** containing a number of soft tissue structures (connective tissue, blood vessels, and nerve fibers) collectively called **pulp**. Pulp supplies nutrients to the tooth tissues and provides for tooth sensation. Where the pulp cavity extends into the root, it becomes the **root canal**. At the proximal end of each root canal is an **apical foramen** that allows blood vessels, nerves, and other structures to enter the pulp cavity.

The teeth are served by the superior and inferior alveolar nerves, branches of the trigeminal nerve (see Table 13.2, p. 497).

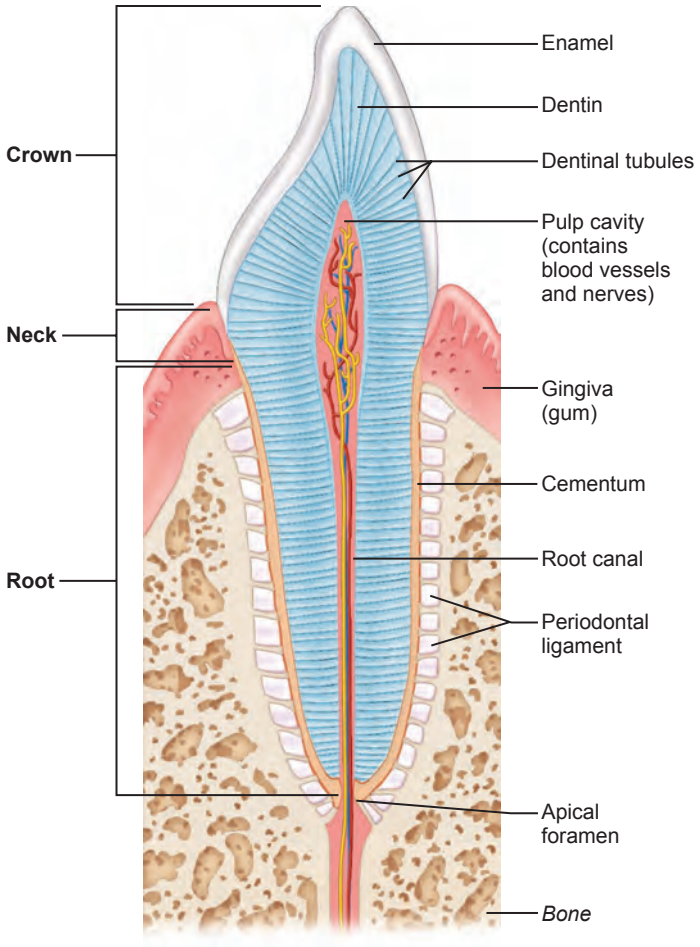


Figure 23.11 Longitudinal section of a canine tooth within its bony alveolus.

Blood is supplied by the superior and inferior alveolar arteries, branches of the maxillary artery (see Figure 19.22b, p. 727).

Dentin contains unique radial striations called *dentinal tubules* (Figure 23.11). Each tubule contains an elongated process of an **odontoblast** (o-don′to-blast; "tooth former"), the cell type that secretes and maintains the dentin. The cell bodies of odontoblasts line the pulp cavity just deep to the dentin. Dentin is formed throughout adult life and gradually encroaches on the pulp cavity. New dentin can also be laid down fairly rapidly to compensate for tooth damage or decay.

Enamel, dentin, and cementum are all calcified and resemble bone (to differing extents), but they differ from bone in that they are avascular. Enamel also differs from cementum and dentin because it lacks collagen as its main organic component and it is almost entirely mineral.

HOMEOSTATIC IMBALANCE

Death of a tooth's nerve and consequent darkening of the tooth is commonly caused by a blow to the jaw. Local swelling pinches off the blood supply to the tooth and the nerve dies. Typically the pulp becomes infected by bacteria sometime later and must be removed by *root canal therapy*. After the cavity is sterilized

and filled with an inert material, the tooth is capped (covered with an artificial crown). ■

Tooth and Gum Disease

Dental caries (kār′ēz; "rottenness"), or **cavities**, result from gradual demineralization of enamel and underlying dentin by bacterial action. Decay begins when **dental plaque** (a film of sugar, bacteria, and other mouth debris) adheres to the teeth. Bacterial metabolism of the trapped sugars produces acids, which can dissolve the calcium salts of the teeth. Once the salts are leached out, the remaining organic matrix of the tooth is readily digested by protein-digesting enzymes released by the bacteria. Frequent brushing and flossing daily help prevent damage by removing forming plaque.

More serious than tooth decay is the effect of unremoved plaque on the gums. As dental plaque accumulates, it calcifies, forming **calculus** (kal′ku-lus; "stone") or tartar. These stony-hard deposits disrupt the seals between the gingivae and the teeth, deepening the sulcus and putting the gums at risk for infection by pathogenic anaerobic bacteria. In the early stages of such an infection, called **gingivitis** (jin″jĭ-vi′tis), the gums are red, sore, swollen, and may bleed.

Gingivitis is reversible if the calculus is removed, but if it is neglected the bacteria eventually form pockets of infection which become inflamed. Neutrophils and immune system cells (lymphocytes and macrophages) attack not only the intruders but also body tissues, carving deep pockets around the teeth, destroying the periodontal ligament, and activating osteoclasts which dissolve the bone away. This more serious condition, called **periodontal disease**, or **periodontitis**, affects up to 95% of all people over the age of 35 and accounts for 80–90% of tooth loss in adults. While periodontitis is widely thought to be a bacterial disease, a 14-year study of young adults indicates that those who regularly smoke marijuana are three to five times as likely as nonusers to have areas of severe gum detachment.

Regardless of its cause, tooth loss from periodontitis is not inevitable. Even advanced periodontitis can be treated by scraping the teeth, cleaning the infected pockets, then cutting the gums to shrink the pockets, and following up with anti-inflammatory and antibiotic therapy. Together, these treatments alleviate the bacterial infestations and encourage reattachment of the surrounding tissues to the teeth and bone.

Much less painful are (1) a new laser approach for destroying the diseased tissues and (2) a nonsurgical therapy now in clinical trials in which an antibiotic-impregnated film is temporarily glued to the exposed root surface. Clinical treatment is followed up by a home regimen to remove plaque by consistent frequent brushing and flossing and hydrogen peroxide rinses.

There may be more at risk than teeth in people with periodontal disease. Some contend that it increases the risk of heart disease and stroke in at least two ways: (1) the chronic inflammation promotes atherosclerotic plaque formation, and (2) bacteria entering the blood from infected gums stimulate clot formation that helps to clog coronary and cerebral arteries. Risk factors for periodontal disease include smoking, diabetes mellitus, and oral (tongue or lip) piercing.

CHECK YOUR UNDERSTANDING

16. Seven-year-old Tina ran to her daddy to show him her lower central incisor which she had wiggled until it "fell out." Is this a primary or secondary tooth? What name is given to teeth that (according to Tina) fall out?
17. What tooth substance is harder than bone? Which tooth part includes nervous tissue and blood vessels?
18. Which teeth are the "grinders"?

For answers, see Appendix G.

The Pharynx

From the mouth, food passes posteriorly into the **oropharynx** and then the **laryngopharynx** (see Figure 23.7a), both common passageways for food, fluids, and air. (The nasopharynx has no digestive role.)

The histology of the pharyngeal wall resembles that of the oral cavity. The mucosa contains a friction-resistant stratified squamous epithelium well supplied with mucus-producing glands. The external muscle layer consists of two *skeletal muscle* layers. The cells of the inner layer run longitudinally. Those of the outer layer, the *pharyngeal constrictor* muscles, encircle the wall like three stacked fists (see Figure 10.8b). Contractions of these muscles propel food into the esophagus below.

The Esophagus

The **esophagus** (ĕ-sof′ah-gus; "carry food"), a muscular tube about 25 cm (10 inches) long, is collapsed when not involved in food propulsion **(Figure 23.12)**. After food moves through the laryngopharynx, it is routed into the esophagus posteriorly as the epiglottis closes off the larynx to food entry.

As shown in Figure 23.1, the esophagus takes a fairly straight course through the mediastinum of the thorax. It pierces the diaphragm at the **esophageal hiatus** (hi-a′tus; "gap") to enter the abdomen. It joins the stomach at the **cardiac orifice** within the abdominal cavity. The cardiac orifice is surrounded by the **gastroesophageal** or **cardiac sphincter** (gas″tro-ĕ-sof″ah-je′al), which is a *physiological* sphincter (see Figure 23.13). That is, it acts as a valve, but the only structural evidence of this sphincter is a slight thickening of the circular smooth muscle at that point. The muscular diaphragm, which surrounds this sphincter, helps keep it closed when food is not being swallowed.

HOMEOSTATIC IMBALANCE

Heartburn, the first symptom of *gastroesophageal reflux disease* (*GERD*), is the burning, radiating substernal pain that occurs when the acidic gastric juice regurgitates into the esophagus. Symptoms are so similar to those of a heart attack that many first-time sufferers of heartburn are rushed to the hospital emergency room. Heartburn is most likely to happen when a person has eaten or drunk to excess, and in conditions that force abdominal contents superiorly, such as extreme obesity,

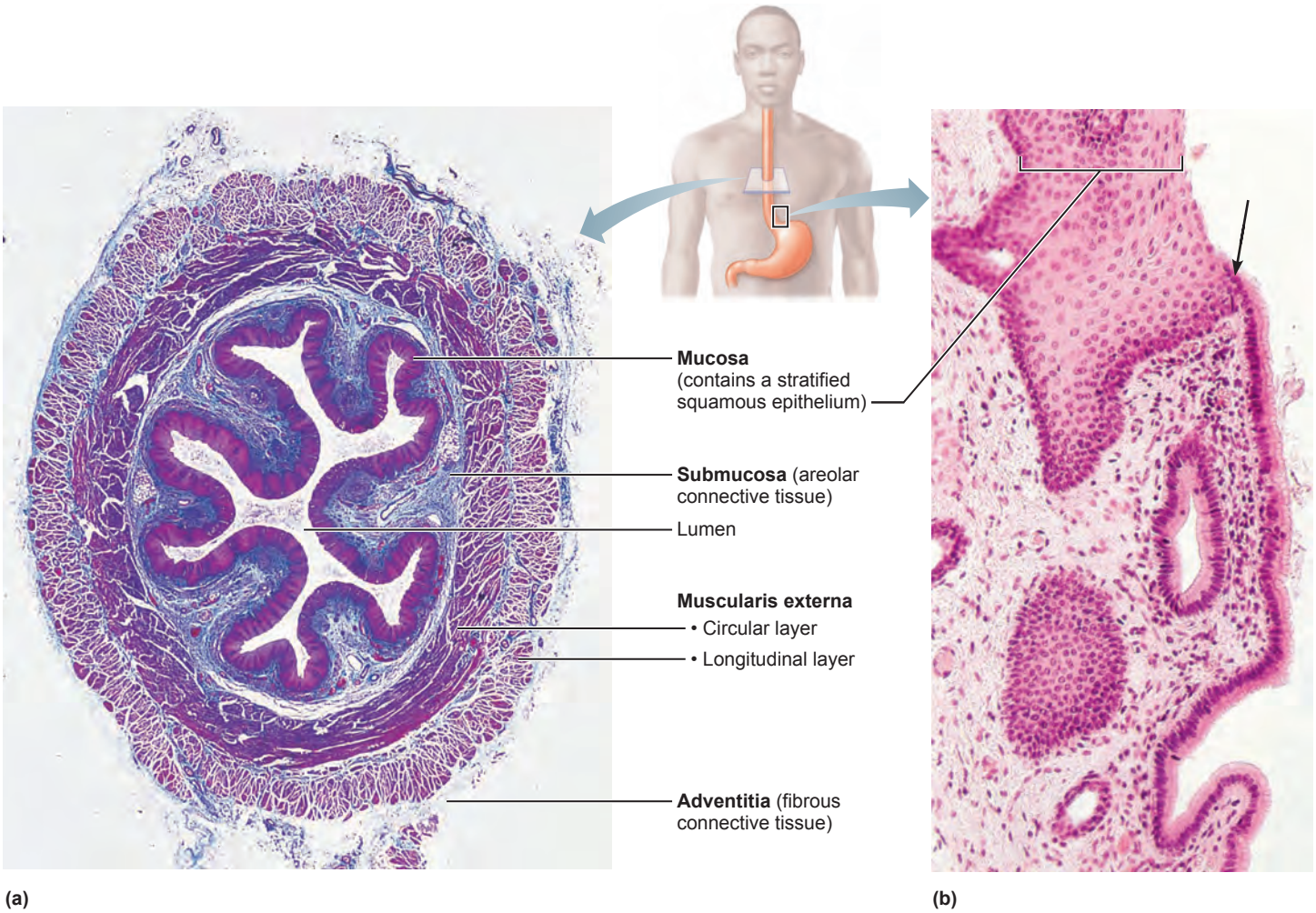


Figure 23.12 Microscopic structure of the esophagus. (a) Cross-sectional view of the esophagus taken from the region close to the stomach junction (10×). The muscularis is composed of smooth muscle. **(b)** Longitudinal section through the esophagus-stomach junction (120×). Arrow shows the point of abrupt transition from the stratified squamous epithelium of the esophagus (top) to the simple columnar epithelium of the stomach (bottom).

pregnancy, and running, which causes stomach contents to splash upward with each step (runner's reflux).

Heartburn is also common in those with a **hiatal hernia**, a structural abnormality (most often due to an abnormal relaxation or weakening of the gastroesophageal sphincter) in which the superior part of the stomach protrudes slightly above the diaphragm. Since the diaphragm no longer reinforces the sphincter, gastric juice may enter the esophagus, particularly when lying down. If the episodes are frequent and prolonged, *esophagitis* (inflammation of the esophagus) and *esophageal ulcers* may result. An even more threatening sequel is esophageal cancer. These consequences can usually be prevented or managed by avoiding late-night snacks and by using antacid preparations. ■

Unlike the mouth and pharynx, the esophagus wall has all four of the basic alimentary canal layers described earlier. Some features of interest:

1. The esophageal mucosa contains a nonkeratinized stratified squamous epithelium. At the esophagus-stomach junction, that abrasion-resistant epithelium changes abruptly to the simple columnar epithelium of the stomach, which is specialized for secretion (Figure 23.12b).
2. When the esophagus is empty, its mucosa and submucosa are thrown into longitudinal folds (Figure 23.12a). When food is in transit in the esophagus, these folds flatten out.
3. The submucosa contains mucus-secreting *esophageal glands*. As a bolus moves through the esophagus, it compresses these glands, causing them to secrete mucus that "greases" the esophageal walls and aids food passage.
4. The muscularis externa is skeletal muscle in its superior third, a mixture of skeletal and smooth muscle in its middle third, and entirely smooth muscle in its inferior third.
5. Instead of a serosa, the esophagus has a fibrous adventitia composed entirely of connective tissue, which blends with surrounding structures along its route.

CHECK YOUR UNDERSTANDING

19. To what two organ systems does the pharynx belong?
20. How is the muscularis externa of the esophagus unique in the body?
21. What is the functional significance of the epithelial change seen at the esophagus-stomach junction?

For answers, see Appendix G.

Digestive Processes: Mouth to Esophagus

▶ Describe the mechanisms of chewing and swallowing.

The mouth and its accessory digestive organs are involved in most digestive processes. The mouth (1) ingests, (2) begins mechanical digestion by chewing, (3) initiates propulsion by swallowing, and (4) starts the chemical breakdown of polysaccharides. Salivary amylase, the main enzyme in saliva, digests starch and glycogen, liberating smaller fragments of linked glucose molecules. (If you chew a piece of bread for a few minutes, it will begin to taste sweet as sugars are released.) Lingual lipase, a fat-digesting enzyme in saliva, also acts in the acidic environment of the stomach. Except for a few drugs that are absorbed through the oral mucosa (for example, nitroglycerine used to alleviate the pain of angina), essentially no absorption occurs in the mouth.

In contrast to the multifunctional mouth, the pharynx and esophagus merely serve as conduits to pass food from the mouth to the stomach. Their single digestive function is food propulsion, accomplished by the role they play in swallowing.

Since we will cover chemical digestion in a special physiology section later in the chapter, only the mechanical processes of chewing and swallowing are discussed here.

Mastication (Chewing)

As food enters the mouth, its mechanical breakdown begins with **mastication**, or chewing. The cheeks and closed lips hold food between the teeth, the tongue mixes food with saliva to soften it, and the teeth cut and grind solid foods into smaller morsels. Mastication is partly voluntary and partly reflexive. We voluntarily put food into our mouths and contract the muscles that close our jaws. The pattern and rhythm of continued jaw movements are controlled mainly by stretch reflexes and in response to pressure inputs from receptors in the cheeks, gums, and tongue, but they can also be voluntary if desired.

Deglutition (Swallowing)

To send food on its way from the mouth, it is first compacted by the tongue into a bolus and then swallowed. **Deglutition** (deg″loo-tish′un), or swallowing, is a complicated process that involves coordinated activity of over 22 separate muscle groups. It has two major phases, the buccal and the pharyngeal-esophageal.

The **buccal phase** occurs in the mouth and is voluntary. In the buccal phase, we place the tip of the tongue against the hard palate, and then contract the tongue to force the bolus into the oropharynx (Figure 23.13, 1). As food enters the pharynx and stimulates tactile receptors there, it passes out of our control and into the realm of involuntary reflex activity.

Triggered by that "bit of saliva" or food reaching receptors in the posterior pharynx, the involuntary **pharyngeal-esophageal phase** of swallowing is controlled by the swallowing center located in the brain stem (medulla and lower pons). Motor impulses from that center are transmitted via various cranial nerves, most importantly the vagus nerves, to the muscles of the pharynx and esophagus. Once food enters the pharynx, respiration is momentarily inhibited and as illustrated in Figure 23.13, 2, all routes except the desired one into the digestive tract are blocked off: The tongue blocks off the mouth. The soft palate rises to close off the nasopharynx. The larynx rises so that the epiglottis covers its opening into the respiratory passageways, and the upper esophageal sphincter relaxes.

Food is moved along through the pharynx and into the esophagus by pressure gradients created by wavelike peristaltic contractions (Figure 23.13, 3–5). Solid foods pass from the oropharynx to the stomach in about 8 seconds, and fluids, aided by gravity, pass in 1 to 2 seconds. Just before the peristaltic wave (and food) reaches the end of the esophagus, the gastroesophageal sphincter relaxes reflexively to allow food to enter the stomach. After food entry, that sphincter closes, preventing regurgitation.

If we try to talk or inhale while swallowing, the various protective mechanisms may be short-circuited and food may enter the respiratory passageways instead. This event typically triggers the cough reflex in an attempt to expel the food.

CHECK YOUR UNDERSTANDING

22. What role does the tongue play in swallowing?
23. How are the respiratory passages blocked during swallowing?

For answers, see Appendix G.

The Stomach

▶ Identify structural modifications of the wall of the stomach that enhance the digestive process.

▶ Name the cell types responsible for secreting the various components of gastric juice and indicate the importance of each component in stomach activity.

▶ Describe stomach structure and indicate changes in the basic alimentary canal structure that aid its digestive function.

Below the esophagus, the GI tract expands to form the **stomach** (see Figure 23.1), a temporary "storage tank" where chemical breakdown of proteins begins and food is converted to a creamy paste called **chyme** (kīm; "juice"). The stomach lies in the upper left quadrant of the peritoneal cavity, nearly hidden by the liver

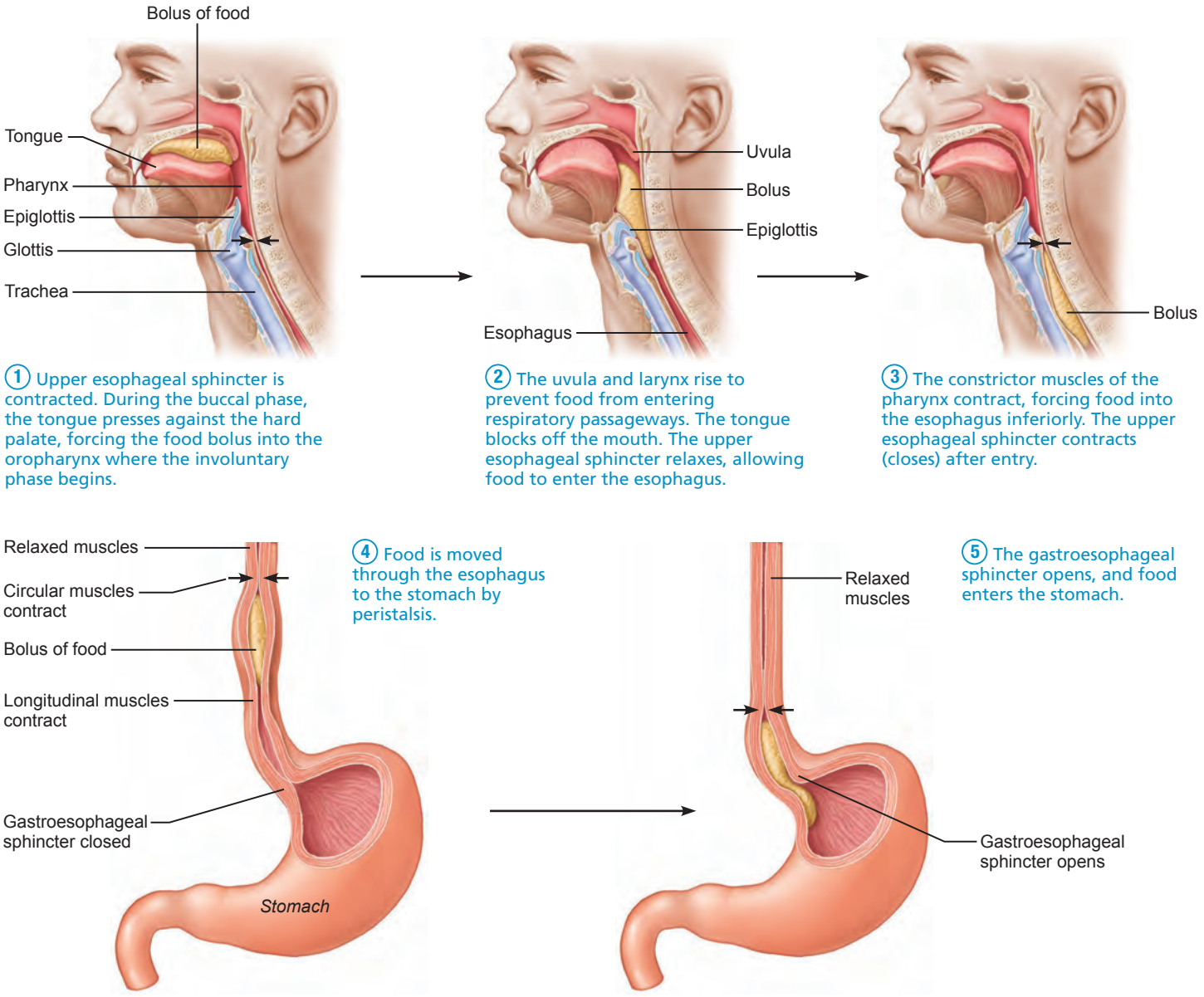


Figure 23.13 Deglutition (swallowing). The process of swallowing consists of a voluntary (buccal) phase (step 1) and an involuntary (pharyngeal-esophageal) phase (steps 2–5).

and diaphragm. Specifically, it lies in the left hypochondriac, epigastric, and umbilical regions of the abdomen. Though relatively fixed at both ends, the stomach is quite movable in between. It tends to lie high and run horizontally in short, stout people (a steer-horn stomach) and is often elongated vertically in tall, thin people (a J-shaped stomach).

Gross Anatomy

The adult stomach varies from 15 to 25 cm (6 to 10 inches) long, but its diameter and volume depend on how much food it contains. An empty stomach has a volume of about 50 ml and a cross-sectional diameter only slightly larger than the large intestine, but when it is really distended it can hold about 4 L (1 gallon) of food and may extend nearly all the way to the pelvis! When empty, the stomach collapses inward, throwing its mucosa (and submucosa) into large, longitudinal folds called **rugae** (roo′ge; *ruga* = wrinkle, fold).

The major regions of the stomach are shown in Figure 23.14a. The small **cardiac region**, or **cardia** ("near the heart"), surrounds the cardiac orifice through which food enters the stomach from the esophagus. The **fundus** is its dome-shaped part, tucked beneath the diaphragm, that bulges superolaterally to the cardia. The **body**, the midportion of the stomach, is continuous inferiorly with the funnel-shaped **pyloric region**. The wider and more superior part of the pyloric region, the **pyloric antrum** (*antrum* = cave) narrows to form the **pyloric canal**, which terminates at the **pylorus**. The pylorus is continuous with the duodenum (the first part of the small intestine) through the **pyloric valve** or **sphincter**, which controls stomach emptying (*pylorus* = gatekeeper).

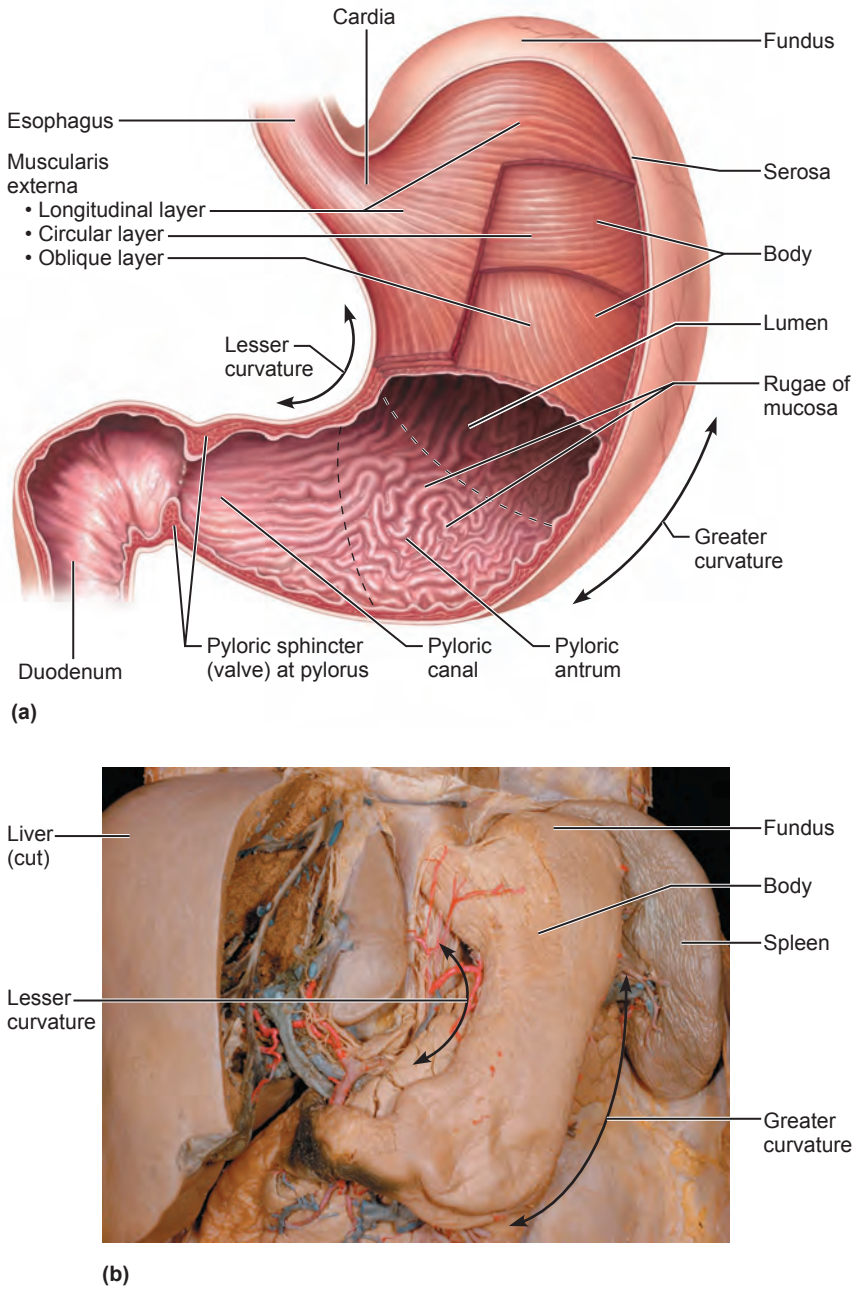


Figure 23.14 Anatomy of the stomach. (a) Gross internal anatomy (frontal section). **(b)** Photograph of external aspect of stomach. (See *A Brief Atlas of the Human Body*, Figure 69a.)

The convex lateral surface of the stomach is its **greater curvature**, and its concave medial surface is the **lesser curvature**. Extending from these curvatures are two mesenteries, called *omenta* (o-men′tah), that help tether the stomach to other digestive organs and the body wall (see Figure 23.30, p. 892). The **lesser omentum** runs from the liver to the lesser curvature of the stomach, where it becomes continuous with the visceral peritoneum covering the stomach. The **greater omentum** drapes inferiorly from the greater curvature of the stomach to cover the coils of the small intestine. It then runs dorsally and superiorly, wrapping the spleen and the transverse portion of the large intestine before blending with the *mesocolon*, a dorsal mesentery that secures the large intestine to the parietal peritoneum of the posterior abdominal wall. The greater omentum is riddled with fat deposits (*oment* = fatty skin) that give it the appearance of a lacy apron. It also contains large collections of lymph nodes. The immune cells and macrophages in these nodes "police" the peritoneal cavity and intraperitoneal organs.

The stomach is served by the autonomic nervous system. Sympathetic fibers from thoracic splanchnic nerves are relayed through the celiac plexus. Parasympathetic fibers are supplied

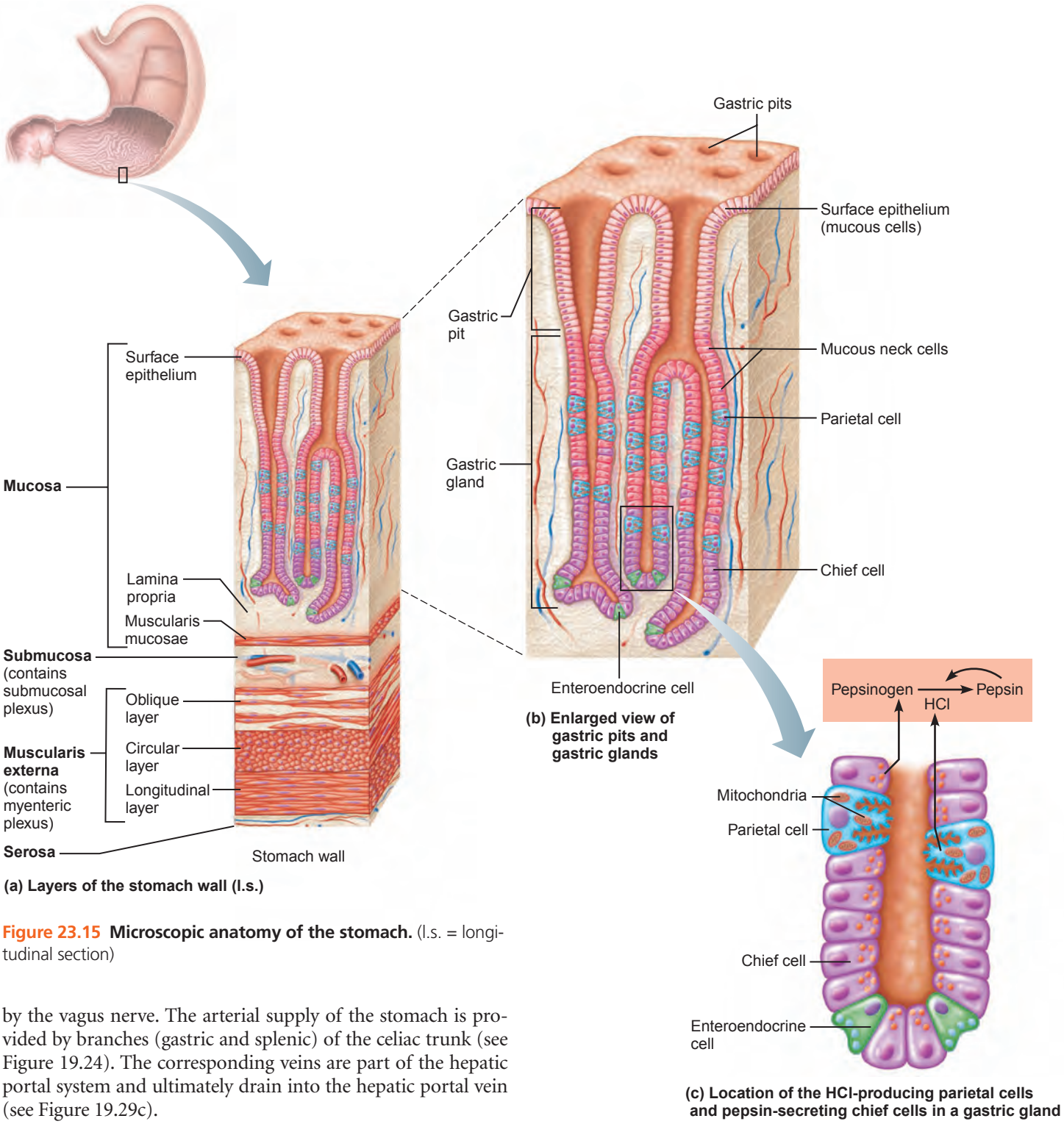


Figure 23.15 Microscopic anatomy of the stomach. (l.s. = longitudinal section)

by the vagus nerve. The arterial supply of the stomach is provided by branches (gastric and splenic) of the celiac trunk (see Figure 19.24). The corresponding veins are part of the hepatic portal system and ultimately drain into the hepatic portal vein (see Figure 19.29c).

Microscopic Anatomy

The stomach wall contains the four tunics typical of most of the alimentary canal, but its muscularis and mucosa are modified for the special roles of the stomach. Besides the usual circular and longitudinal layers of smooth muscle, the muscularis externa has an innermost layer of smooth muscle fibers that runs *obliquely* (Figure 23.14a and **Figure 23.15a**). This arrangement allows the stomach not only to mix, churn, and move food along the tract (the job of the circular and longitudinal muscle layers), but also to pummel the food, physically breaking it down into smaller fragments, and to ram the food into the small intestine. (The oblique fibers accomplish the ramming by jackknifing the stomach into a V shape, which provides a propulsive action at the stomach terminus.)

The lining epithelium of the stomach mucosa is a simple columnar epithelium composed entirely of mucous cells. They produce a cloudy, protective two-layer coat of alkaline mucus in which the surface layer consists of viscous, insoluble mucus that traps a layer of bicarbonate-rich fluid beneath it. This otherwise smooth lining is dotted with millions of deep **gastric pits**, which lead into the tubular **gastric glands** that produce the stomach secretion called **gastric juice** (Figure 23.15).

The cells forming the walls of the gastric pits are primarily mucous cells, but those composing the gastric glands vary in different stomach regions. For example, the cells in the glands of the cardia and pylorus are primarily mucus secreting, whereas cells of the pyloric antrum produce mucus and several hormones including most of the stimulatory hormone called gastrin. Glands of the stomach fundus and body, where most chemical digestion occurs, are substantially larger and produce the majority of the stomach secretions. The glands in these regions contain a variety of secretory cells, including these four types:

1. **Mucous neck cells**, found in the upper, or "neck," regions of the glands, produce a thin, soluble mucus quite different from that secreted by the mucous cells of the surface epithelium (Figure 23.15b). It is not yet understood what special function this *acidic* mucus performs.
2. **Parietal cells**, found mainly in the middle region of the glands scattered among the chief cells (described next), simultaneously secrete *hydrochloric acid* (*HCl*) and *intrinsic factor* (Figure 23.15b, c). Although the parietal cells appear spherical when viewed with a light microscope, they actually have three prongs that bear dense microvilli (they look like fuzzy pitchforks!). This structure provides a huge surface area for secreting H^+ and Cl^- into the stomach lumen. HCl makes the stomach contents extremely acidic (pH 1.5–3.5), a condition necessary for activation and optimal activity of pepsin. The acidity also helps in food digestion by denaturing proteins and breaking down cell walls of plant foods, and is harsh enough to kill many of the bacteria ingested with foods. Intrinsic factor is a glycoprotein required for vitamin B_{12} absorption in the small intestine.
3. **Chief cells** occur mainly in the basal regions of the gastric glands. The chief cells produce *pepsinogen* (pep-sin′o-jen), the inactive form of the protein-digesting enzyme **pepsin**. When these cells are stimulated, the first pepsinogen molecules they release are activated by HCl encountered in the apical region of the gland (Figure 23.15c). But once pepsin is present, it also catalyzes the conversion of pepsinogen to pepsin. The activation process involves removal of a small peptide fragment from the pepsinogen molecule, causing it to change shape and expose its active site. This positive feedback process is limited only by the amount of pepsinogen present. Chief cells also secrete insignificant amounts of lipases (fat-digesting enzymes).
4. **Enteroendocrine cells** (en″ter-o-en′do-krin; "gut endocrine"), typically located deep in the gastric glands (Figure 23.15b, c), release a variety of chemical messengers directly into the interstitial fluid of the lamina propria. Some of these, for example **histamine** and **serotonin**, act locally as paracrines. Others, such as **somatostatin**, act both locally and as hormones, diffusing into the blood capillaries to influence several digestive system target organs (**Table 23.1**, p. 875). **Gastrin**, a hormone, plays essential roles in regulating stomach secretion and motility, as we will describe shortly.

The stomach mucosa is exposed to some of the harshest conditions in the entire digestive tract. Gastric juice is corrosively acidic (the H^+ concentration in the stomach can be 100,000 times that found in blood), and its protein-digesting enzymes can digest the stomach itself.

However, the stomach is not a passive victim of its formidable environment. It mounts an aggressive counterattack to protect itself, producing what is called the **mucosal barrier**. Three factors create this barrier:

1. *A thick coating of bicarbonate-rich mucus* is built up on the stomach wall.
2. *The epithelial cells of the mucosa are joined together by tight junctions* that prevent gastric juice from leaking into the underlying tissue layers.
3. *Damaged epithelial mucosal cells are shed and quickly replaced* by division of *undifferentiated stem cells* that reside where the gastric pits join the gastric glands. The stomach surface epithelium of mucous cells is completely renewed every three to six days, because these cells can survive only a few days in the stomach's harsh environment. (However, the more sheltered glandular cells deep within the gastric glands have a much longer life span.)

HOMEOSTATIC IMBALANCE

Anything that breaches the gel-like mucosal barrier causes inflammation of the stomach wall, a condition called *gastritis*. Persistent damage to the underlying tissues can promote **peptic ulcers**, specifically called **gastric ulcers** when they are erosions of the stomach wall **(Figure 23.16a)**. The most distressing symptom of gastric ulcers is gnawing epigastric pain that seems to bore through to your back. The pain typically occurs 1–3 hours after eating and is often relieved by eating again. The danger posed by ulcers is perforation of the stomach wall followed by peritonitis and, perhaps, massive hemorrhage.

For years, the blame for causing ulcers was put on factors that favor high HCl production or low mucus secretion such as aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs such as ibuprofen), smoking, spicy food, alcohol, coffee, and stress. Although acid conditions *are* necessary for ulcer formation, acidity in and of itself is not sufficient to cause ulcer formation. Most recurrent ulcers (90%) are the work of a certain strain of acid-resistant, corkscrew-shaped *Helicobacter pylori* bacteria (Figure 23.16b), which burrow much like a drill bit through the mucus and destroy the protective mucosal layer, leaving denuded areas.

These pathological effects occur in 10–20% of infected individuals. The antimicrobial activity of gastric mucin appears to

play a major role in protecting the remaining 80–90% from *H. pylori*'s invasive attacks. The bacterial causal theory has been difficult to prove because the bacterium is also found in more than 50% of healthy people. Even more troubling are studies that link this bacterium to some stomach cancers.

These bacteria release several chemicals that help them do their "dirty work," including (1) some that curb HCl production and release ammonia (which then acts as a base to neutralize some of the stomach acid in their locale), (2) a *cytotoxin* that damages the stomach epithelium, (3) proteins that disrupt adhesion molecules and so cause the epithelial cells to detach from each other, and (4) proteins that act as chemotactic agents to attract macrophages and other defensive cells into the area, thus promoting a chronic inflammatory response.

The presence or absence of *H. pylori* is easily detected by a breath test. In ulcers colonized by it, the goal is to kill the embedded bacteria. A simple two-week-long course of antibiotics promotes healing and prevents recurrence. For active ulcers, a blocker for H_2- (histamine) receptors may also help because it inhibits HCl secretion by blocking histamine's effects. The relatively few peptic ulcers not caused by *H. pylori* generally result from the long-term use of NSAIDs. In such noninfectious cases, H_2-receptor blocker drugs such as cimetidine (Tagamet) and ranitidine (Zantac) are the therapy of choice. ■

CHECK YOUR UNDERSTANDING

24. What structural modification of the stomach wall underlies the stomach's ability to mechanically digest food?

25. Two substances secreted by cells of the gastric glands are needed to produce the active protein-digesting enzyme pepsin. What are these substances and what cells secrete them?

26. What protective substances or activities make up the so-called mucosal barrier?

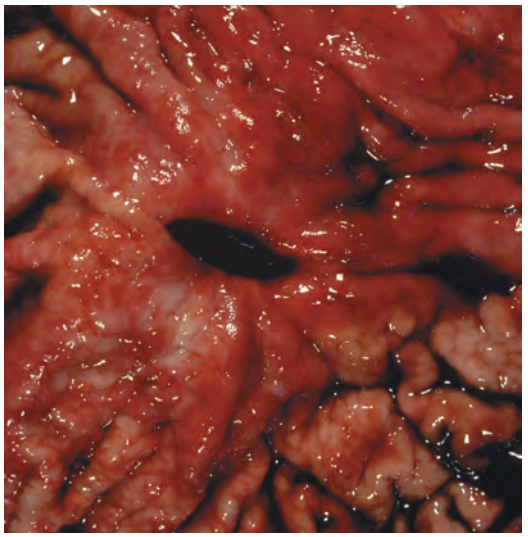
For answers, see Appendix G.

Digestive Processes Occurring in the Stomach

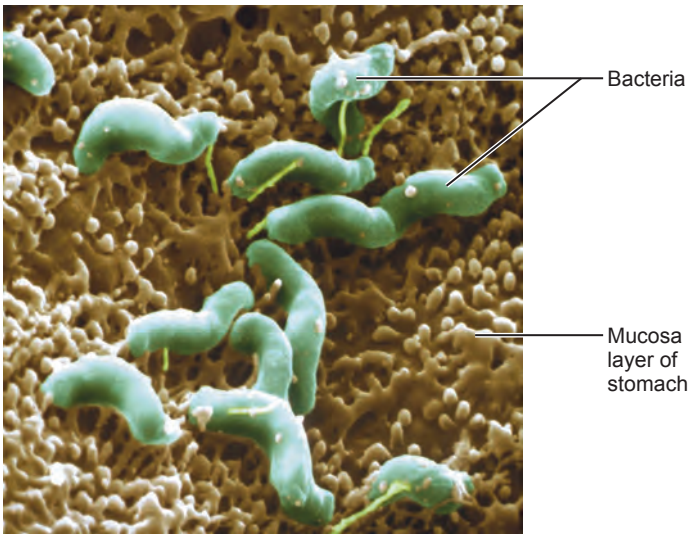
- Explain how gastric secretion and stomach motility are regulated.
- Define and account for the alkaline tide.

Except for ingestion and defecation, the stomach is involved in the whole "menu" of digestive activities. Besides serving as a holding area for ingested food, the stomach continues the demolition job begun in the oral cavity by further degrading food both physically and chemically. It then delivers chyme, the product of its activity, into the small intestine.

Protein digestion begins in the stomach and is the only significant type of enzymatic digestion that occurs there. Dietary proteins are denatured by HCl produced by stomach glands in preparation for enzymatic digestion. (The unfolded amino acid chain is more accessible to the enzymes.) The most important protein-digesting enzyme produced by the gastric mucosa is pepsin. In infants, however, the stomach glands also secrete **rennin**, an enzyme that acts on milk protein (casein), converting it to a curdy substance that looks like soured milk. Additionally, lingual lipase released by the intrinsic salivary glands may digest some triglycerides in the stomach.



(a) A gastric ulcer lesion



(b) *H. pylori* bacteria

Figure 23.16 Photographs of a gastric ulcer lesion and of the bacteria that most commonly cause it.

Two common lipid-soluble substances—alcohol and aspirin—pass easily through the stomach mucosa into the blood. Alcohol and aspirin may cause gastric bleeding, so these substances should be avoided by people with gastric ulcers.

Despite the obvious benefits of preparing food to enter the intestine, the only stomach function essential to life is secretion of intrinsic factor. **Intrinsic factor** is required for intestinal absorption of vitamin B_{12}, needed to produce mature erythrocytes. In its absence, *pernicious anemia* results. However, if

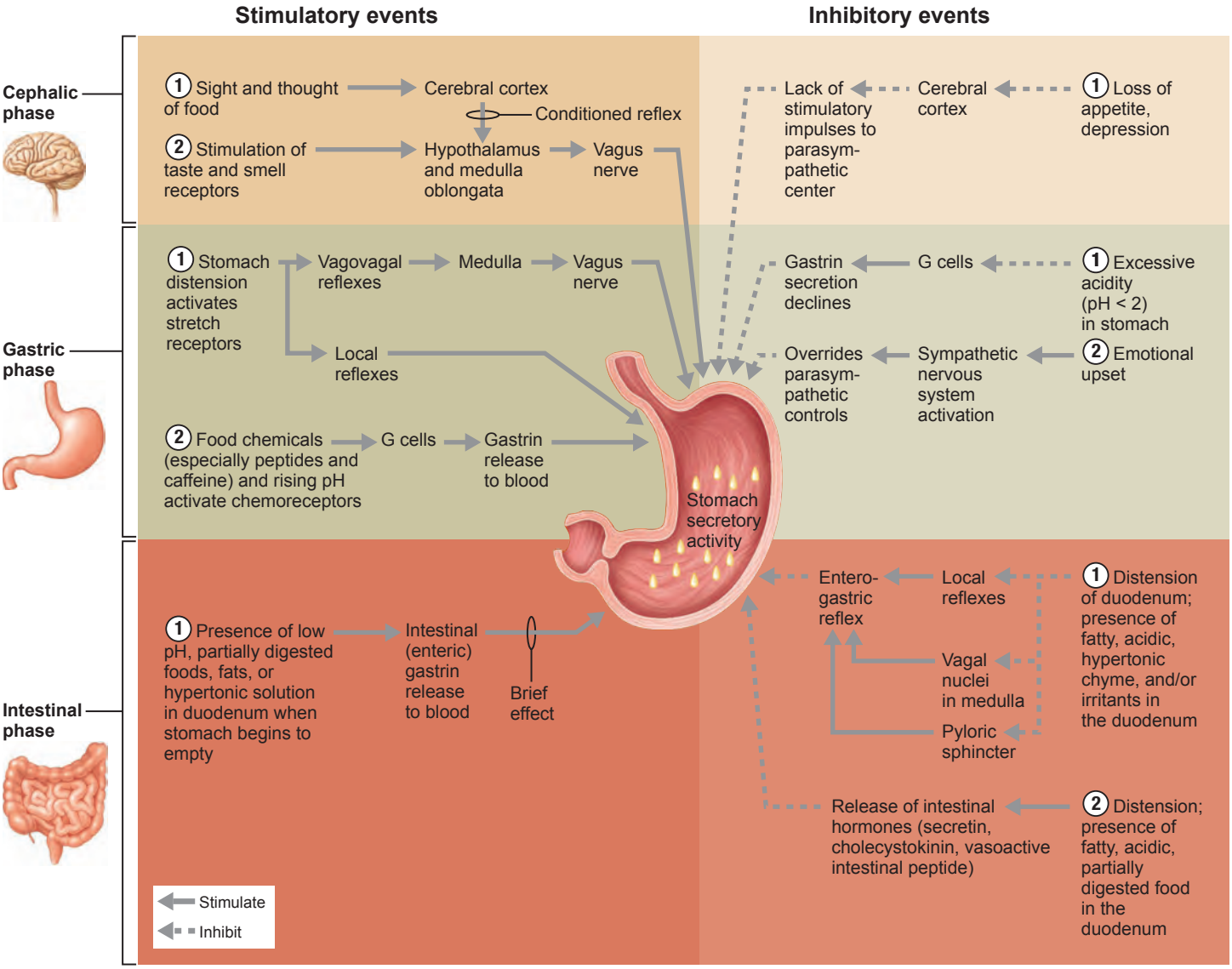


Figure 23.17 Neural and hormonal mechanisms that regulate release of gastric juice.
Stimulatory factors are shown on the left; inhibitory factors are shown on the right.

vitamin B_{12} is administered by injection, individuals can survive with minimal digestive problems even after total gastrectomy (stomach removal). (The stomach's activities are summarized in Table 23.2, p. 888).

Since we describe chemical digestion and absorption later, here we will focus on events that (1) control secretory activity of the gastric glands and (2) regulate stomach motility and emptying.

Regulation of Gastric Secretion

Both neural and hormonal mechanisms control gastric secretion. Under normal conditions the gastric mucosa pours out as much as 3 L of gastric juice—an acid brew so potent it can dissolve nails—every day. Nervous control is provided both by long (vagus nerve–mediated) and short (local enteric) nerve reflexes. When the vagus nerves stimulate the stomach, secretory activity of virtually all of its glands increases. (By contrast, activation of sympathetic nerves depresses secretory activity.) Hormonal control of gastric secretion is largely the province of gastrin, which stimulates secretion of enzymes and HCl, and of hormones produced by the small intestine, which are mostly gastrin antagonists.

Stimuli acting at three distinct sites—the head, stomach, and small intestine—provoke or inhibit gastric secretory activity. Accordingly, the three phases of gastric secretion are called the *cephalic*, *gastric*, and *intestinal phases* (Figure 23.17). The effector site is the stomach in all cases and, once initiated, one or all three phases may be occurring at the same time.

Phase 1: Cephalic (Reflex) The **cephalic**, or **reflex**, **phase** of gastric secretion occurs *before* food enters the stomach (Figure 23.17). Only a few minutes long, this phase is triggered by the

aroma, taste, sight, or thought of food, and it gets the stomach ready for its upcoming digestive chore. Inputs from activated olfactory receptors and taste buds are relayed to the hypothalamus. The hypothalamus, in turn, stimulates the vagal nuclei of the medulla oblongata, causing motor impulses to be transmitted via the vagus nerves to parasympathetic enteric ganglia. Enteric ganglionic neurons then stimulate the stomach glands.

The enhanced secretory activity that results when we see or think of food is a *conditioned reflex* and occurs only when we like or want the food. If we are depressed or have no appetite, this part of the cephalic reflex is suppressed.

Phase 2: Gastric Once food reaches the stomach, local neural and hormonal mechanisms initiate the **gastric phase** (Figure 23.17). This phase lasts three to four hours and provides about two-thirds of the gastric juice released. The most important stimuli are distension, peptides, and low acidity. Stomach distension activates stretch receptors and initiates both local (myenteric) reflexes and the long vagovagal reflexes. In the long type of reflex, impulses travel to the medulla and then back to the stomach via vagal fibers. Both types of reflexes lead to acetylcholine (ACh) release, which in turn stimulates the output of more gastric juice.

Though neural influences initiated by stomach distension are important, the hormone gastrin probably plays a greater role in stimulating stomach gland secretion during the gastric phase. Chemical stimuli provided by partially digested proteins, caffeine, and rising pH directly activate gastrin-secreting enteroendocrine cells called **G cells** in the stomach antrum. Gastrin stimulates the release of enzymes, but its main target is the HCl-secreting parietal cells, which it prods to spew out even more HCl. Highly acidic (pH below 2) gastric contents *inhibit* gastrin secretion.

When protein foods are in the stomach, the pH of the gastric contents generally rises because proteins act as buffers to tie up H^+. The rise in pH stimulates gastrin secretion and subsequently HCl release, which in turn provides the acidic conditions needed for protein digestion. The more protein in the meal, the greater the amount of gastrin and HCl released. As proteins are digested, the gastric contents gradually become more acidic, which again inhibits the gastrin-secreting cells. This negative feedback mechanism helps maintain optimal pH and working conditions for the gastric enzymes.

G cells are also activated by the neural reflexes already described. Emotional upset, fear, anxiety, or anything that triggers the fight-or-flight response inhibits gastric secretion because during such times the sympathetic division overrides parasympathetic controls of digestion (Figure 23.17).

The control of the HCl-secreting parietal cells is multifaceted. HCl secretion is stimulated by three chemicals, all of which work through second-messenger systems. Both *ACh* released by parasympathetic nerve fibers and *gastrin* secreted by G cells bring about their effects by increasing intracellular Ca^{2+} levels. *Histamine*, released by the so-called *enterochromaffin-like* (ECL) cells in response to gastrin (and to a lesser extent in response to ACh) acts through cyclic AMP (cAMP). When only one of the three chemicals binds to the parietal cells, HCl secretion is scanty, but when all three bind, HCl pours forth as if shot out by a high-pressure hose. [As we noted earlier, antihistamines, such as cimetidine, which bind to and block the H_2 (histamine) receptors of parietal cells, are used to treat gastric ulcers due to hyperacidity.]

The process of HCl formation within the parietal cells is complicated, but it appears to go something like this **(Figure 23.18)**: When parietal cells are appropriately stimulated, H^+ is actively pumped into the stomach lumen against a tremendous concentration gradient by H^+-K^+ ATPases in exchange for K^+ ions that move into the cell. K^+ then cycles back into the lumen via K^+ channels. Chloride ions (Cl^-) follow H^+ into the lumen to maintain an electrical balance in the stomach, completing the process of HCl secretion. The Cl^- is obtained from blood plasma, while H^+ comes from the breakdown of carbonic acid (formed by the combination of carbon dioxide and water) within the parietal cell:

$$CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^-$$

As H^+ is pumped from the cell and HCO_3^- (bicarbonate ion) accumulates within the cell, HCO_3^- is ejected through the basal cell membrane into the capillary blood. As a result, blood draining from the stomach is more alkaline than the blood serving it. This phenomenon is called the **alkaline tide**. Notice that HCO_3^- and Cl^- are moved in opposite directions by a HCO_3^--Cl^- antiporter in the basolateral membrane, and this is the means of entry of the Cl^- that moves into the lumen as the chloride part of the HCl product. K^+ and Cl^- move into the stomach lumen by diffusing through membrane channels.

Phase 3: Intestinal The **intestinal phase** of gastric secretion has two components—one excitatory and the other inhibitory (see Figure 23.17). The *excitatory* aspect is set into motion as partially digested food fills the initial part (duodenum) of the small intestine. This stimulates intestinal mucosal cells to release **intestinal (enteric) gastrin**, a hormone that encourages the gastric glands to continue their secretory activity. This stimulatory effect is brief because as the intestine distends with chyme containing large amounts of H^+, fats, partially digested proteins, and various irritating substances, the *inhibitory* component is triggered in the form of the **enterogastric reflex**.

The enterogastric reflex is actually a trio of reflexes that (1) inhibit the vagal nuclei in the medulla, (2) inhibit local reflexes, and (3) activate sympathetic fibers that cause the pyloric sphincter to tighten and prevent further food entry into the small intestine. As a result, gastric secretory activity declines. These "brakes" on gastric activity protect the small intestine from excessive acidity and match the small intestine's processing abilities to the amount of chyme entering it at a given time.

In addition, the factors we just named trigger the release of several intestinal hormones, collectively called **enterogastrones**. They include **secretin** (se-kre′tin), **cholecystokinin (CCK)** (ko″le-sis″to-ki′nin), and **vasoactive intestinal peptide (VIP)**. All of these hormones inhibit gastric secretion when the stomach is very active and also play other roles, which are summarized in Table 23.1.

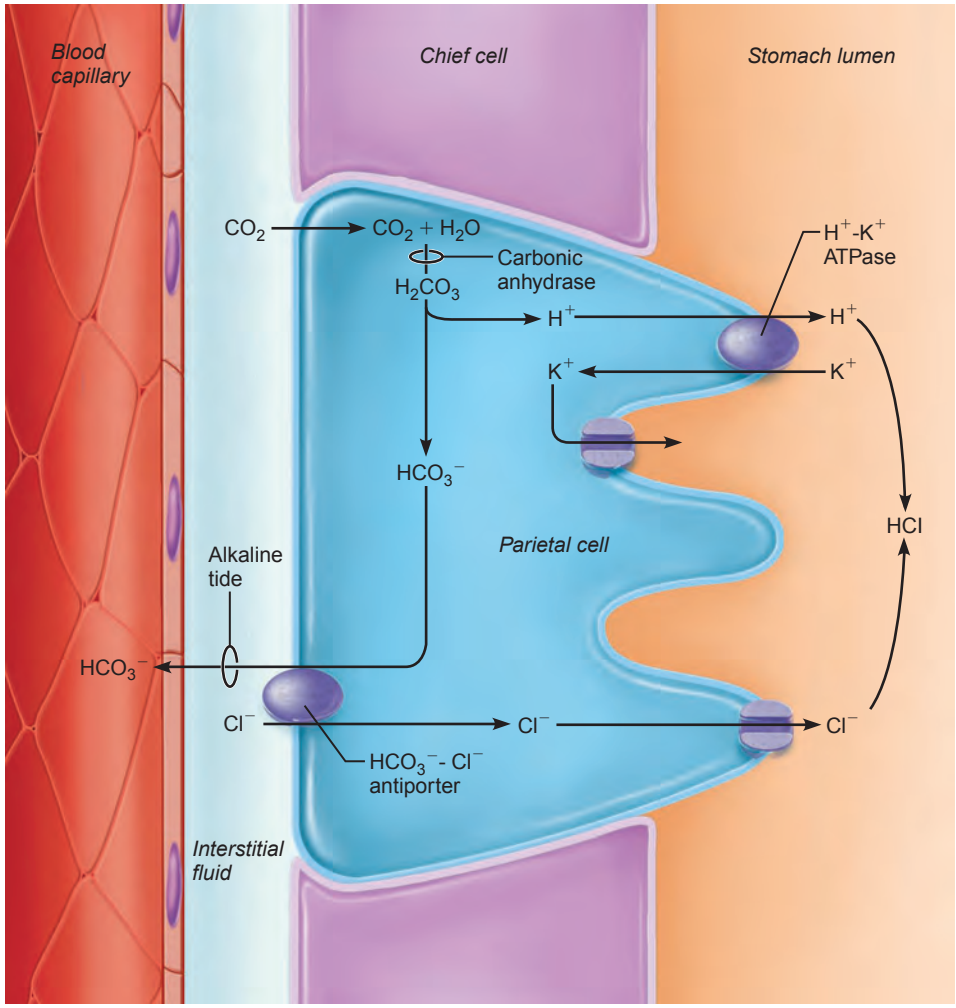


Figure 23.18 Mechanism of HCl secretion by parietal cells. H^+ and HCO_3^- (bicarbonate ions) are generated from the dissociation of carbonic acid (H_2CO_3) within the parietal cell. As H^+-K^+ ATPase pumps H^+ into the lumen, K^+ enters the cell. Meanwhile, the HCO_3^--Cl^- antiporter transports HCO_3^- into the interstitial space in exchange for chloride ions (Cl^-), establishing the alkaline tide. Cl^- and K^+ then diffuse into the lumen through membrane channels.

23

Gastric Motility and Emptying

Stomach contractions not only accommodate its filling and cause its emptying, but they also compress, knead, and continually mix the food with gastric juice to produce chyme. The processes of mechanical digestion and propulsion are inseparable in the stomach because the mixing movements are accomplished by a unique type of peristalsis. For example, in the pylorus, peristalsis is bidirectional rather than unidirectional.

Response of the Stomach to Filling The stomach stretches to accommodate incoming food, but internal stomach pressure remains constant until about 1.5 L of food has been ingested. Thereafter, the pressure rises. The relatively unchanging pressure in a filling stomach is due to (1) the reflex-mediated receptive relaxation of the stomach muscle and (2) the plasticity of visceral smooth muscle.

Receptive relaxation of smooth muscle in the stomach fundus and body occurs both in anticipation of and in response to food movement through the esophagus and into the stomach. This process is coordinated by the swallowing center of the brain stem and mediated by the vagus nerves acting on serotonin and NO-releasing enteric neurons.

Gastric accommodation, an example of smooth muscle *plasticity*, is the intrinsic ability of visceral smooth muscle to exhibit the *stress-relaxation response*, in other words, to be stretched without greatly increasing its tension and contracting expulsively. As we described in Chapter 9, this capability is very important in hollow organs, like the stomach, that must serve as temporary reservoirs.

Gastric Contractile Activity As in the esophagus, the stomach exhibits peristalsis. After a meal, peristalsis begins near the gastroesophageal sphincter, where it produces gentle rippling movements of the thin stomach wall. But as the contractions approach the pylorus, where the stomach musculature is thicker, they become much more powerful. Consequently, the

TABLE 23.1 Hormones and Paracrines That Act in Digestion*

HORMONE	SITE OF PRODUCTION	STIMULUS FOR PRODUCTION	TARGET ORGAN	ACTIVITY
Cholecystokinin (CCK)	Duodenal mucosa	Fatty chyme, in particular, but also partially digested proteins	Liver/pancreas	▪ Potentiates secretin's actions on these organs
			Pancreas	▪ Increases output of enzyme-rich pancreatic juice
			Gallbladder	▪ Stimulates organ to contract and expel stored bile
			Hepatopancreatic sphincter	▪ Relaxes sphincter to allow entry of bile and pancreatic juice into duodenum
Gastric inhibitory peptide (GIP) (or glucose-dependent insulinotropic peptide)	Duodenal mucosa	Glucose, fatty acids, and amino acids in small intestine	Stomach	▪ Inhibits HCl production (minor effect)
			Pancreas (beta cells)	▪ Stimulates insulin release
Gastrin	Stomach mucosa (G cells)	Food (particularly partially digested proteins) in stomach (chemical stimulation); acetylcholine released by nerve fibers	Stomach (parietal cells)	▪ Increases HCl secretion
				▪ Stimulates gastric emptying (minor effect)
			Small intestine	▪ Stimulates contraction of intestinal muscle
			Ileocecal valve	▪ Relaxes ileocecal valve
			Large intestine	▪ Stimulates mass movements
Histamine	Stomach mucosa	Food in stomach	Stomach	▪ Activates parietal cells to release HCl
Intestinal gastrin	Duodenal mucosa	Acidic and partially digested foods in duodenum	Stomach	▪ Stimulates gastric glands and motility
Motilin	Duodenal mucosa	Fasting; periodic release every 1½–2 hours by neural stimuli	Proximal duodenum	▪ Stimulates migrating motility complex
Secretin	Duodenal mucosa	Acidic chyme (also partially digested proteins, fats, hypertonic or hypotonic fluids, or irritants in chyme)	Stomach	▪ Inhibits gastric gland secretion and gastric motility during gastric phase of secretion
			Pancreas	▪ Increases output of pancreatic juice rich in bicarbonate ions; potentiates CCK's action
			Liver	▪ Increases bile output
Serotonin	Stomach mucosa	Food in stomach	Stomach	▪ Causes contraction of stomach muscle
Somatostatin	Stomach mucosa; duodenal mucosa	Food in stomach; stimulation by sympathetic nerve fibers	Stomach	▪ Inhibits gastric secretion of all products
			Pancreas	▪ Inhibits secretion
			Small intestine	▪ Inhibits GI blood flow; thus inhibits intestinal absorption
			Gallbladder and liver	▪ Inhibits contraction and bile release
Vasoactive intestinal peptide (VIP)	Enteric neurons	Chyme containing partially digested foods	Small intestine	▪ Stimulates buffer secretion; dilates intestinal capillaries
				▪ Relaxes intestinal smooth muscle
			Pancreas	▪ Increases secretion
			Stomach	▪ Inhibits acid secretion

* Except for somatostatin, all of these polypeptides also stimulate the growth (particularly of the mucosa) of the organs they affect.

contents of the fundus and body (food storage area) remain relatively undisturbed, while foodstuffs in and around the pyloric antrum receive a truly lively pummeling and mixing.

The pyloric region of the stomach, which holds about 30 ml of chyme, acts as a "dynamic filter" that allows only liquids and small particles to pass through the barely open pyloric valve during the digestive period. Normally, each peristaltic wave reaching the pyloric muscle "spits" or squirts 3 ml or less of chyme into the small intestine. Because the contraction also *closes* the valve, which is normally partially relaxed, the rest (about 27 ml) is

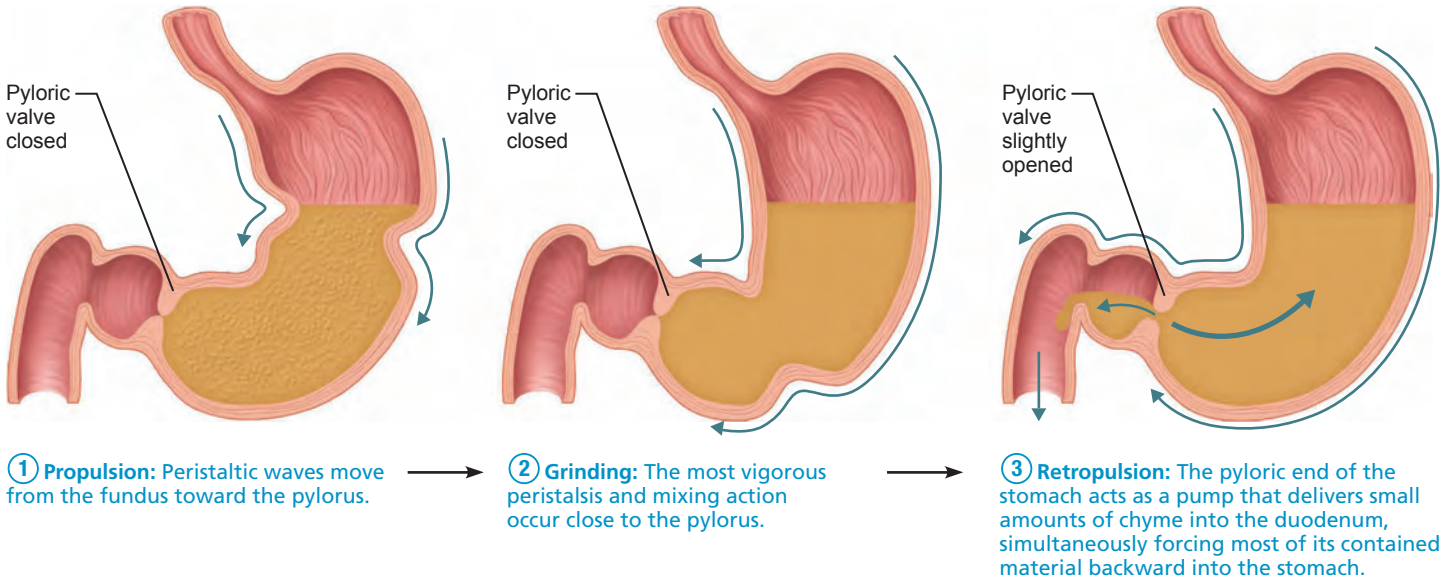


Figure 23.19 Peristaltic waves in the stomach.

propelled backward into the stomach, where it is mixed further (Figure 23.19). This back-and-forth pumping action (retropulsion) effectively breaks up solids in the gastric contents.

Although the intensity of the stomach's peristaltic waves can be modified, their rate is constant—always around three per minute. This contractile rhythm is set by the spontaneous activity of *pacemaker cells* located in the longitudinal smooth muscle layer. The pacemaker cells, muscle-like noncontractile cells called *interstitial cells of Cajal* (ka-hal′), depolarize and repolarize spontaneously three times each minute, establishing the so-called *cyclic slow waves* of the stomach, or its **basic electrical rhythm (BER)**. Since the pacemakers are electrically coupled to the rest of the smooth muscle sheet by gap junctions, their "beat" is transmitted efficiently and quickly to the entire muscularis.

The pacemakers set the maximum rate of contraction, but they do not initiate the contractions or regulate their force. Instead, they generate subthreshold depolarization waves, which are then "ignited" (enhanced by further depolarization and brought to threshold) by neural and hormonal factors.

Factors that increase the strength of stomach contractions are the same factors that enhance gastric secretory activity. Distension of the stomach wall by food activates stretch receptors and gastrin-secreting cells, both of which ultimately stimulate gastric smooth muscle and so increase gastric motility. For this reason, the more food there is in the stomach, the more vigorous the stomach mixing and emptying movements will be—within certain limits—as we describe next.

Regulation of Gastric Emptying The stomach usually empties completely within four hours after a meal. However, the larger the meal (the greater the stomach distension) and the more liquid its contents, the faster the stomach empties. Fluids pass quickly through the stomach. Solids linger, remaining until they are well mixed with gastric juice and converted to the liquid state.

The rate of gastric emptying depends as much—and perhaps more—on the contents of the duodenum as on what is happening in the stomach. The stomach and duodenum act in tandem like a "coupled meter" that functions at less than full capacity. As chyme enters the duodenum, receptors in its wall respond to chemical signals and to stretch, initiating the enterogastric reflex and the hormonal (enterogastrone) mechanisms that inhibit acid and pepsin secretion as we described earlier. These mechanisms inhibit gastric secretory activity and prevent further duodenal filling by reducing the force of pyloric contractions (Figure 23.20).

A carbohydrate-rich meal moves through the duodenum rapidly, but fats form an oily layer at the top of the chyme and are digested more slowly by enzymes acting in the small intestine. For this reason, when chyme entering the duodenum is fatty, food may remain in the stomach six hours or more.

HOMEOSTATIC IMBALANCE

Vomiting, or **emesis**, is an unpleasant experience that causes stomach emptying by a different route. Many factors signal the stomach to "launch lunch," but the most common are extreme stretching of the stomach or small intestine or the presence of irritants such as bacterial toxins, excessive alcohol, spicy foods, and certain drugs in those organs. Both bloodborne molecules and sensory impulses streaming from the irritated sites to the **emetic center** (e-met′ik) of the medulla initiate a number of motor responses. The diaphragm and abdominal wall muscles contract, increasing intra-abdominal pressure, the gastroesophageal sphincter relaxes, and the soft palate rises to close off the nasal passages. As a result, the stomach (and perhaps duodenal) contents are forced upward through the esophagus and pharynx and out the mouth.

Before vomiting, an individual typically is pale, feels nauseated, and salivates. Excessive vomiting can cause dehydration and may lead to severe disturbances in the electrolyte and acid-base balance of the body. Since large amounts of HCl are lost in vomitus, the blood becomes alkaline as the stomach attempts to replace its lost acid. ■

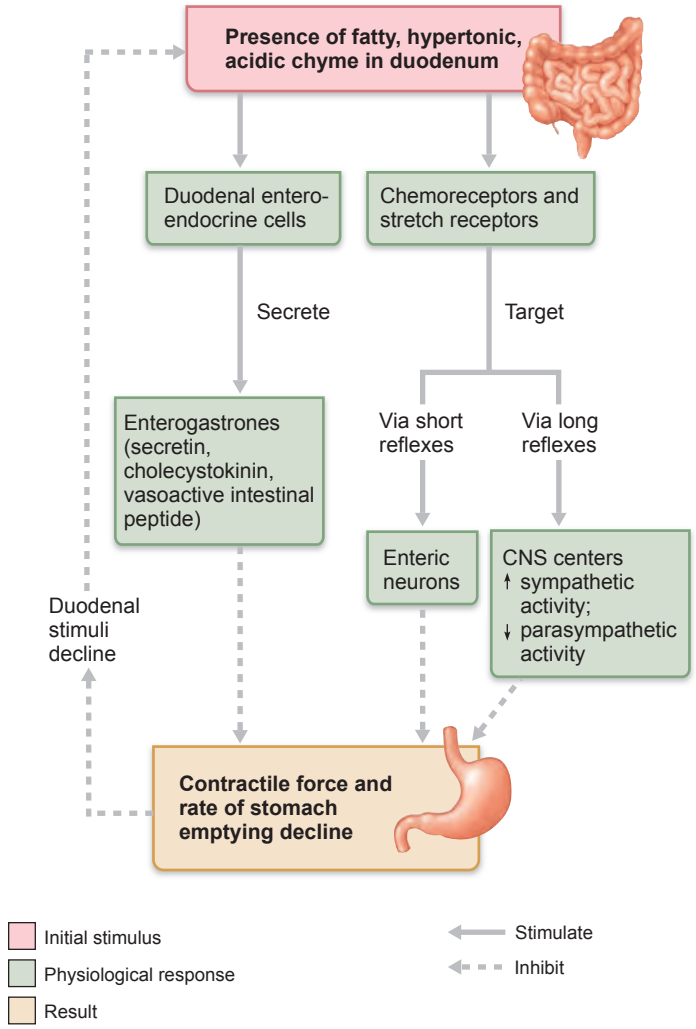


Figure 23.20 Neural and hormonal factors inhibiting gastric emptying. These controls ensure that the food will be well liquefied in the stomach and prevent the small intestine from being overwhelmed.

CHECK YOUR UNDERSTANDING

27. Name the three phases of gastric secretion.
28. How does the presence of food in the small intestine inhibit gastric secretion and motility?
29. How does the pH of venous blood leaving the stomach change during a meal?

For answers, see Appendix G.

The Small Intestine and Associated Structures

- Identify and describe structural modifications of the wall of the small intestine that enhance the digestive process.
- Differentiate between the roles of the various cell types of the intestinal mucosa.
- Describe the function of intestinal hormones and paracrines.

In the small intestine, usable food is finally prepared for its journey into the cells of the body. However, this vital function cannot be accomplished without the aid of secretions from the liver (bile) and pancreas (digestive enzymes). We will also consider these accessory organs in this section.

The Small Intestine

The **small intestine** is the body's major digestive organ. Within its twisted passageways, digestion is completed and virtually all absorption occurs.

Gross Anatomy

The small intestine is a convoluted tube extending from the pyloric sphincter in the epigastric region to the **ileocecal valve (sphincter)** (il″e-o-se′kal) in the right iliac region where it joins the large intestine. It is the longest part of the alimentary canal, but is only about half the diameter of the large intestine, ranging from 2.5 to 4 cm (1–1.6 inches). Although it is 6–7 m long (approximately 20 ft, or as tall as a two-story building) in a cadaver, the small intestine is only about 2–4 m (7–13 ft) long during life because of muscle tone.

The small intestine has three subdivisions: the duodenum, which is mostly retroperitoneal, and the jejunum and ileum, both intraperitoneal organs (see Figure 23.1). The relatively immovable **duodenum** (du″o-de′num; "twelve finger widths long"), which curves around the head of the pancreas, is about 25 cm (10 inches) long **(Figure 23.21)**. Although it is the shortest intestinal subdivision, the duodenum has the most features of interest.

The bile duct, delivering bile from the liver, and the main pancreatic duct, carrying pancreatic juice from the pancreas, unite at the wall of the duodenum in a bulblike point called the **hepatopancreatic ampulla** (hep″ah-to-pan″kre-at′ik ampul′ah; *ampulla* = flask). The ampulla opens into the duodenum via the volcano-shaped **major duodenal papilla**. The entry of bile and pancreatic juice is controlled by a smooth muscle valve called the **hepatopancreatic sphincter**.

The **jejunum** (jĕ-joo′num; "empty"), about 2.5 m (8 ft) long, extends from the duodenum to the ileum. The **ileum** (il′e-um; "twisted"), approximately 3.6 m (12 ft) in length, joins the large intestine at the ileocecal valve. The jejunum and ileum hang in sausagelike coils in the central and lower part of the abdominal cavity, suspended from the posterior abdominal wall by the fan-shaped *mesentery* (see Figure 23.30). These more distal parts of the small intestine are encircled and framed by the large intestine.

Nerve fibers serving the small intestine include parasympathetics from the vagus and sympathetics from the thoracic splanchnic nerves, both relayed through the superior mesenteric (and celiac) plexus.

The arterial supply is primarily from the superior mesenteric artery (pp. 732–733). The veins parallel the arteries and typically drain into the superior mesenteric vein. From there, the

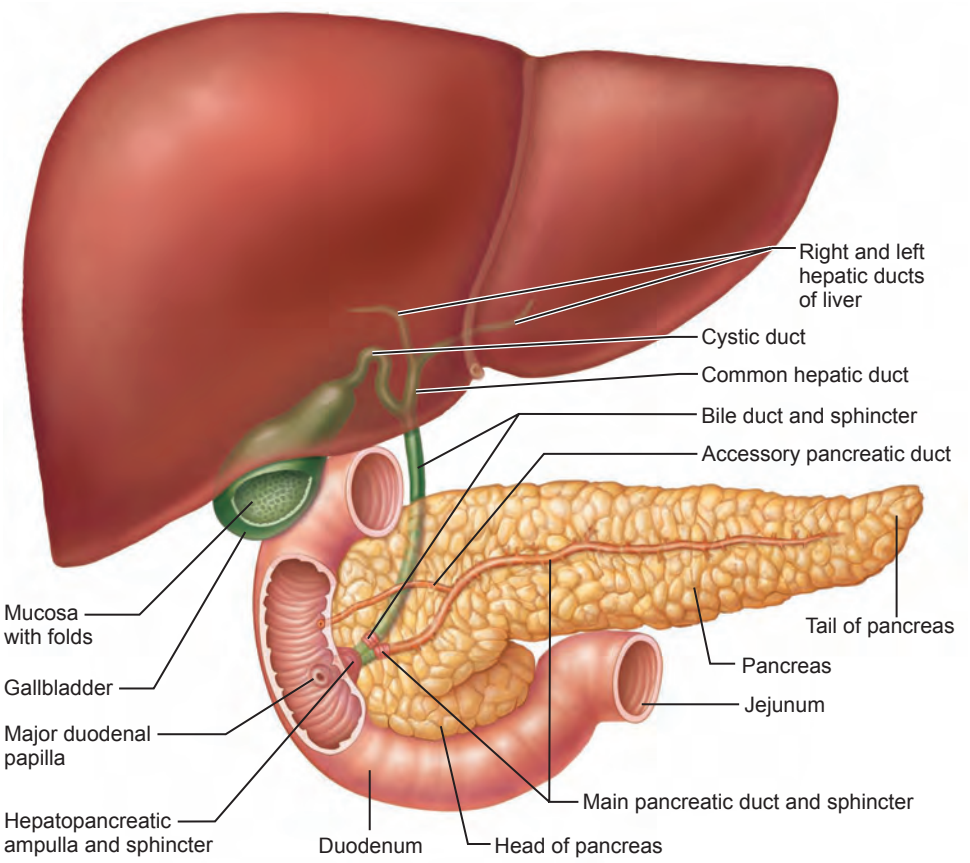


Figure 23.21 The duodenum of the small intestine, and related organs. Emptying into the duodenum are ducts from the pancreas, gallbladder, and liver.

nutrient-rich venous blood from the small intestine drains into the hepatic portal vein, which carries it to the liver.

Microscopic Anatomy

Modifications for Absorption The small intestine is highly adapted for nutrient absorption. Its length alone provides a huge surface area, and its wall has three structural modifications—circular folds, villi, and microvilli—that amplify its absorptive surface enormously (by a factor of more than 600 times). One estimate is that the intestinal surface area is about equal to 200 square meters or the surface area of a doubles tennis court. Most absorption occurs in the proximal part of the small intestine, so these specializations decrease in number toward its distal end.

The **circular folds**, or **plicae circulares** (pli′ke ser″ku-lar′ēs), are deep, permanent folds of the mucosa and submucosa (Figure 23.22a). Nearly 1 cm tall, these folds force chyme to spiral through the lumen, slowing its movement and allowing time for full nutrient absorption.

Villi (vil′i; "tufts of hair") are fingerlike projections of the mucosa, over 1 mm high, that give it a velvety texture, much like the soft nap of a towel (Figures 23.22 and Figure 23.23a). The epithelial cells of the villi (called *enterocytes*) are chiefly absorptive columnar cells. In the core of each villus is a dense capillary bed and a wide lymph capillary called a **lacteal** (lak′te-al). Digested foodstuffs are absorbed through the epithelial cells into both the capillary blood and the lacteal.

The villi are large and leaflike in the duodenum (the intestinal site of most active absorption) and gradually narrow and shorten along the length of the small intestine. A "slip" of smooth muscle in the villus core allows it to alternately shorten and lengthen. These pulsations (1) increase the contact between the villus and the contents of the intestinal lumen, making absorption more efficient, and (2) "milk" lymph along through the lacteals.

The exceptionally long, densely packed **microvilli** of the absorptive cells of the mucosa give the mucosal surface a fuzzy appearance called the **brush border** (Figure 23.22b enlargment and Figure 23.23b). The plasma membranes of the microvilli bear enzymes referred to as **brush border enzymes**, which complete the digestion of carbohydrates and proteins in the small intestine.

Histology of the Wall Externally the subdivisions of the small intestine appear to be nearly identical, but their internal and microscopic anatomies reveal some important differences. The four tunics typical of the GI tract are also seen here, but the mucosa and submucosa are modified to reflect the intestine's functions in the digestive pathway.

The epithelium of the villus mucosa is largely simple columnar *absorptive cells* bound by tight junctions and richly endowed with microvilli. These cells bear the primary responsibility for nutrient and electrolyte absorption. The epithelium also has many mucus-secreting *goblet cells*. Between the villi, the mucosa is studded with *pits* that lead into tubular glands called

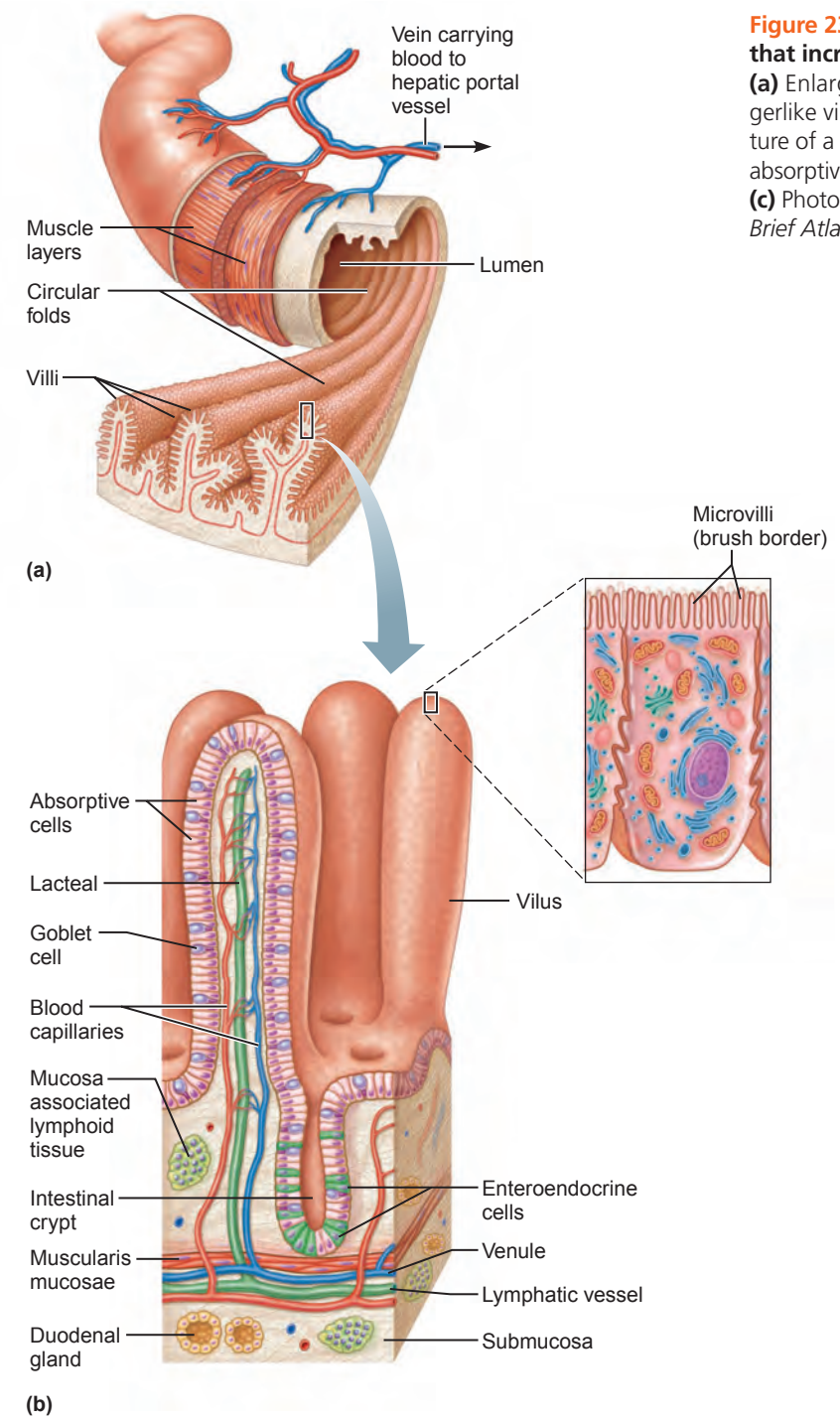


Figure 23.22 Structural modifications of the small intestine that increase its surface area for digestion and absorption. **(a)** Enlargement of a few circular folds, showing associated fingerlike villi (muscularis and serosa layers not indicated). **(b)** Structure of a villus. Enlargment shows one and part of two other absorptive cells that exhibit microvilli on their free (luminal) surface. **(c)** Photomicrograph of the mucosa, showing villi (250×). (See *A Brief Atlas of the Human Body*, Figure 69b.)

intestinal crypts, or **crypts of Lieberkühn** (le′ber-kun) (see Figure 23.22b, c). Crypt epithelial cells are primarily secretory cells that secrete *intestinal juice*, a watery mixture containing mucus that serves as a carrier fluid for absorbing nutrients from chyme. Scattered through the crypt epithelium are *enteroendocrine cells*, the source of the enterogastrones—secretin and cholecystokinin to name two—and T cells called *intraepithelial lymphocytes* (*IELs*), which represent an important immunological component. Unlike other T cells, IELs do *not* need "priming." Upon encountering antigens, they immediately release cytokines that cause killing of infected target cells.

Deep in the crypts are specialized secretory cells called *Paneth cells*, which fortify the small intestine's defenses by releasing antimicrobial agents such as defensins and *lysozyme*, an antibacterial enzyme. These secretions destroy certain bacteria and help to determine which bacteria may colonize the intestinal lumen. The crypts decrease in number along the length of the small intestine, but the goblet cells become more abundant.

The various epithelial cells arise from continuously dividing stem cells at the base of the crypts. As the daughter cells gradually migrate up the villi, they differentiate, becoming specialized cell

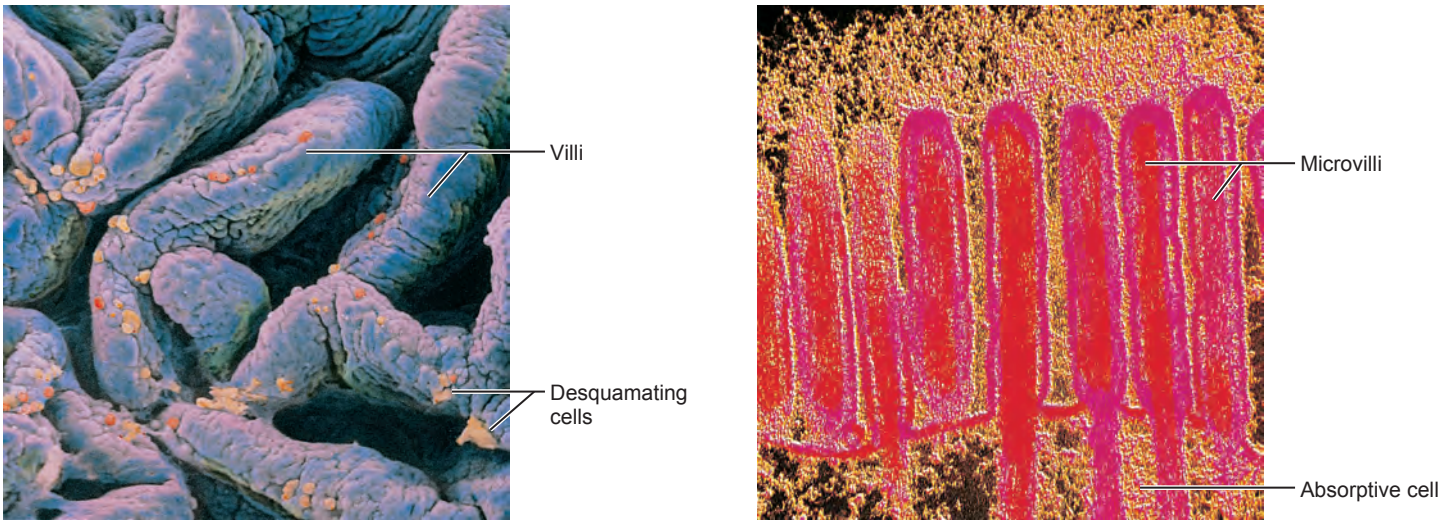


Figure 23.23 Villi and microvilli of the small intestine. False-color electron micrographs. **(a)** Villi (125×). Dead desquamating cells seen on the ridges of the villi are colored yellow and orange. **(b)** Microvilli (28,000×) of absorptive cells appear as red projections from the surface of the absorptive cell. Yellow granules are mucus granules.

types—absorptive cells, goblet cells, and enteroendocrine cells. The fourth differentiated cell type is the Paneth cells, which remain at the base of the crypts. The other three types undergo apoptosis and are shed from the villus tips, renewing the villus epithelium every two to four days.

The rapid replacement of intestinal (and gastric) epithelial cells has clinical as well as physiological significance. Treatments for cancer, such as radiation therapy and chemotherapy, preferentially target rapidly dividing cells. This kills cancer cells, but it also nearly obliterates the GI tract epithelium, causing nausea, vomiting, and diarrhea after each treatment.

The submucosa is typical areolar connective tissue. It contains both individual and *aggregated lymphoid follicles*, the latter called **Peyer's patches** (pi′erz). Peyer's patches increase in abundance toward the end of the small intestine. Their increasing abundance reflects the fact that this region of the small intestine contains huge numbers of bacteria that must be prevented from entering the bloodstream. The lymphoid tissue of the submucosa also contains proliferating lymphocytes that leave the intestine, enter the blood, and then home in on the intestinal lamina propria. There, in their new home, they release immunoglobin A (IgA), which helps provide protection against intestinal pathogens (see p. 784).

Elaborate mucus-secreting **duodenal glands** (also called *Brunner's glands*) are found in the submucosa of the duodenum only. These glands produce an alkaline (bicarbonate-rich) mucus that helps neutralize the acidic chyme moving in from the stomach. When this protective mucus barrier is inadequate, the intestinal wall erodes and *duodenal ulcers* result.

The muscularis is typical and bilayered. Except for the bulk of the duodenum, which is retroperitoneal and has an adventitia, the external intestinal surface is covered by visceral peritoneum (serosa).

Intestinal Juice: Composition and Control

The intestinal crypts normally secrete 1 to 2 L of **intestinal juice** daily. The major stimulus for its production is distension or irritation of the intestinal mucosa by hypertonic or acidic chyme. Normally, intestinal juice is slightly alkaline (7.4–7.8), and isotonic with blood plasma. Intestinal juice is largely water but it also contains some mucus, which is secreted both by the duodenal glands and by goblet cells of the mucosa. Intestinal juice is enzyme-poor because intestinal enzymes are limited to the bound enzymes of the brush border.

CHECK YOUR UNDERSTANDING

30. What common advantage do circular folds, villi, and microvilli provide to the digestive process? Which of these modifications causes chyme to spiral through the lumen and slows its passage?
31. What are brush border enzymes?
32. What is a lacteal and what is its function?
33. Name three secretory products that help to protect the intestinal mucosa from bacterial damage.

For answers, see Appendix G.

The Liver and Gallbladder

- Describe the histologic anatomy of the liver.
- State the role of bile in digestion and describe how its entry into the small intestine is regulated.
- Describe the role of the gallbladder.

The *liver* and *gallbladder* are accessory organs associated with the small intestine. The liver, one of the body's most important

organs, has many metabolic and regulatory roles. However, its *digestive* function is to produce bile for export to the duodenum. Bile is a fat emulsifier. In other words, it breaks up fats into tiny particles so that they are more accessible to digestive enzymes. We will describe bile and the emulsification process when we discuss the digestion and absorption of fats later in the chapter. Although the liver also processes nutrient-laden venous blood delivered to it directly from the digestive organs, this is a metabolic rather than a digestive role. (See Chapter 24.) The gallbladder is chiefly a storage organ for bile.

Gross Anatomy of the Liver

The ruddy, blood-rich **liver** is the largest gland in the body, weighing about 1.4 kg (3 lb) in the average adult. Shaped like a wedge, it occupies most of the right hypochondriac and epigastric regions, extending farther to the right of the body midline than to the left. Located under the diaphragm, the liver lies almost entirely within the rib cage, which provides some protection (see Figure 23.1 and **Figure 23.24**).

Typically, the liver is said to have four primary lobes. The largest of these, the *right lobe*, is visible on all liver surfaces and separated from the smaller *left lobe* by a deep fissure (Figure 23.24a). The posteriormost *caudate lobe* and the *quadrate lobe*, which lies inferior to the left lobe, are visible in an inferior view of the liver (Figure 23.24b).

A mesentery, the **falciform ligament**, separates the right and left lobes anteriorly and suspends the liver from the diaphragm and anterior abdominal wall. Running along the inferior edge of the falciform ligament is the **round ligament**, or **ligamentum teres** (te′rēz; "round"), a fibrous remnant of the fetal umbilical vein. Except for the superiormost liver area (the *bare area*), which touches the diaphragm, the entire liver is enclosed by the visceral peritoneum.

As we mentioned earlier, a ventral mesentery, the lesser omentum, anchors the liver to the lesser curvature of the stomach (see Figure 23.30b). The **hepatic artery** and the **hepatic portal vein**, which enter the liver at the **porta hepatis** ("gateway to the liver"), and the common hepatic duct, which runs inferiorly from the liver, all travel through the lesser omentum to reach their destinations. The gallbladder rests in a recess on the inferior surface of the right liver lobe (Figure 23.24b).

The traditional scheme of defining liver lobes (outlined above) has been criticized because it is based on superficial features of the liver. Some anatomists emphasize that the primary lobes of the liver should be defined as the territories served by the right and left hepatic ducts. These two territories are delineated by a plane drawn from the indentation (sulcus) of the inferior vena cava to the gallbladder recess (Figure 23.24b). The areas to the right of the plane are the *right lobe* and those to its left constitute the *left lobe*. According to this scheme, the small quadrate and caudate lobes are part of the left lobe.

Bile leaves the liver through several bile ducts that ultimately fuse to form the large **common hepatic duct**, which travels downward toward the duodenum. Along its course, that duct fuses with the **cystic duct** draining the gallbladder to form the **bile duct** (see Figure 23.21).

Microscopic Anatomy of the Liver

The liver is composed of sesame seed–sized structural and functional units called **liver lobules**. Each lobule is a roughly hexagonal (six-sided) structure **(Figure 23.25a)** consisting of plates of *liver cells*, or **hepatocytes** (hep′ah-to-sīts), organized like bricks in a garden wall. The hepatocyte plates radiate outward from a **central vein** (Figure 23.25c) running in the longitudinal axis of the lobule. To make a rough "model" of a liver lobule, open a thick paperback book until its two covers meet: The pages represent the plates of hepatocytes and the hollow cylinder formed by the rolled spine represents the central vein.

If you keep in mind that the liver's main function is to filter and process the nutrient-rich blood delivered to it, the description of its anatomy that follows will make a lot of sense. At each of the six corners of a lobule is a **portal triad** (*portal tract* region), so named because three basic structures are always present there: a branch of the *hepatic artery* (supplying oxygen-rich arterial blood to the liver), a branch of the *hepatic portal vein* (carrying venous blood laden with nutrients from the digestive viscera), and a *bile duct* (Figure 23.25c).

Between the hepatocyte plates are enlarged, leaky capillaries, the **liver sinusoids**. Blood from both the hepatic portal vein and the hepatic artery percolates from the triad regions through these sinusoids and empties into the central vein. From the central veins blood eventually enters the hepatic veins, which drain the liver, and empty into the inferior vena cava. Forming part of the sinusoid walls are star-shaped **hepatic macrophages**, also called **Kupffer cells** (koop′fer) (Figure 23.25c). They remove debris such as bacteria and worn-out blood cells from the blood as it flows past.

The versatile hepatocytes have large amounts of both rough and smooth ER, Golgi apparatuses, peroxisomes, and mitochondria. Equipped in this way, the hepatocytes not only can produce some 900 ml of bile daily but also can (1) process the bloodborne nutrients in various ways (e.g., they store glucose as glycogen and use amino acids to make plasma proteins); (2) store fat-soluble vitamins; and (3) play important roles in detoxification, such as ridding the blood of ammonia by converting it to urea (Chapter 24). Thanks to these various jobs, the processed blood leaving the liver contains fewer nutrients and waste materials than the blood that entered it.

In addition to providing the hepatocytes with blood for processing and nutrition, the intimate relationship between the hepatocytes and their blood supply has consequences for liver growth and repair. The regenerative capacity of the liver is exceptional. It can regenerate to its former size even after surgical removal or loss of 70% of its normal mass. During liver injury, hepatocytes secrete *vascular endothelial growth factor* (*VEGF*) which binds to specific receptors on endothelial cells lining the sinusoids. The endothelial cells proliferate and release other growth factors, such as hepatocyte growth factor (HGF) and interleukin 6, which in turn prompt the hepatocytes to multiply and replace dead and dying liver tissue.

Secreted bile flows through tiny canals, called **bile canaliculi** (kan″ah-lik′u-li; "little canals"), that run between adjacent

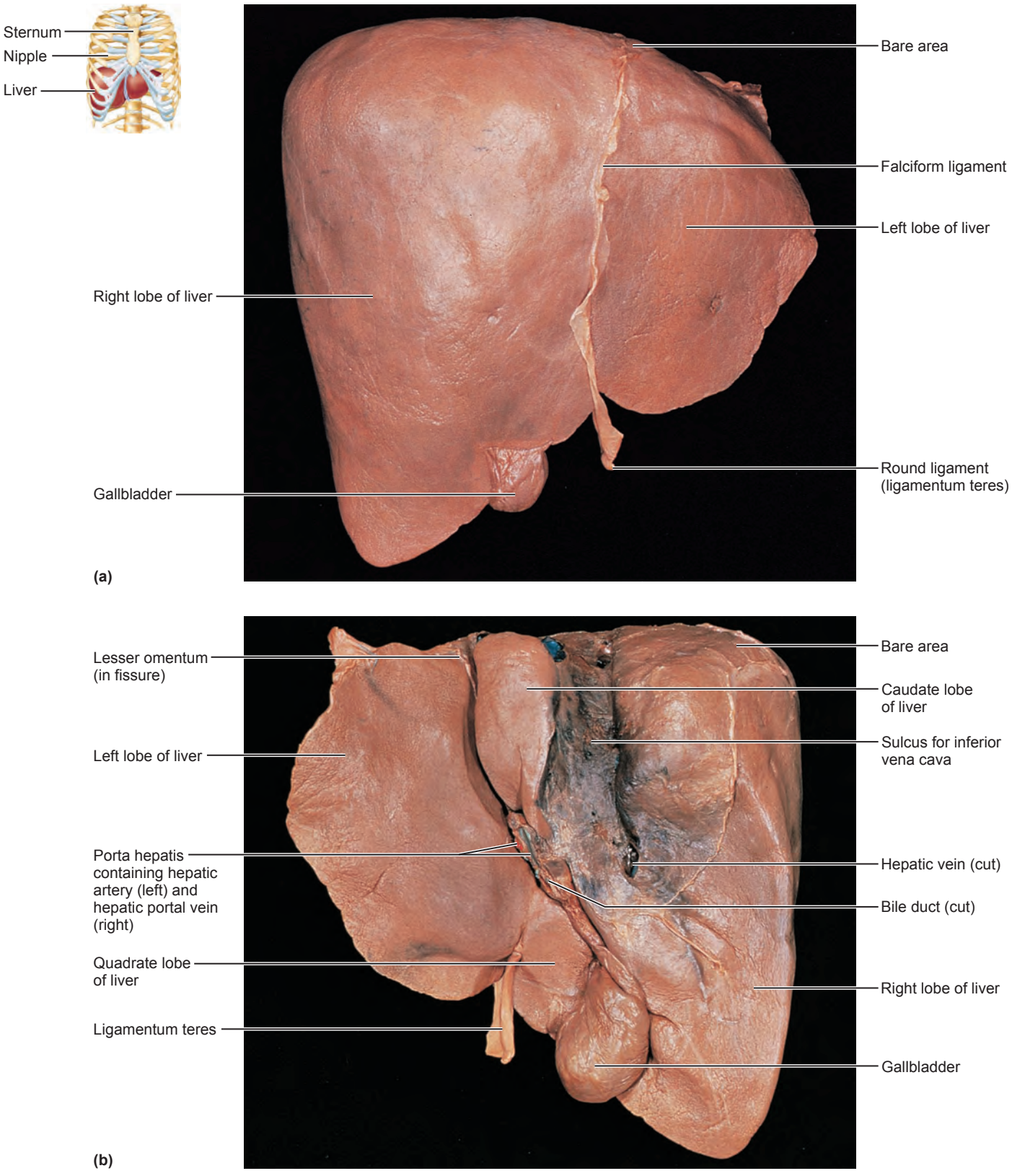


Figure 23.24 Gross anatomy of the human liver. (a) Anterior view of the liver. **(b)** Posteroinferior aspect (ventral surface) of the liver. The four liver lobes are separated by a group of fissures in this view. The porta hepatis is a deep fissure that contains the hepatic portal vein, hepatic artery, common hepatic duct, and lymphatics. (See *A Brief Atlas of the Human Body*, Figures 64 and 65.)

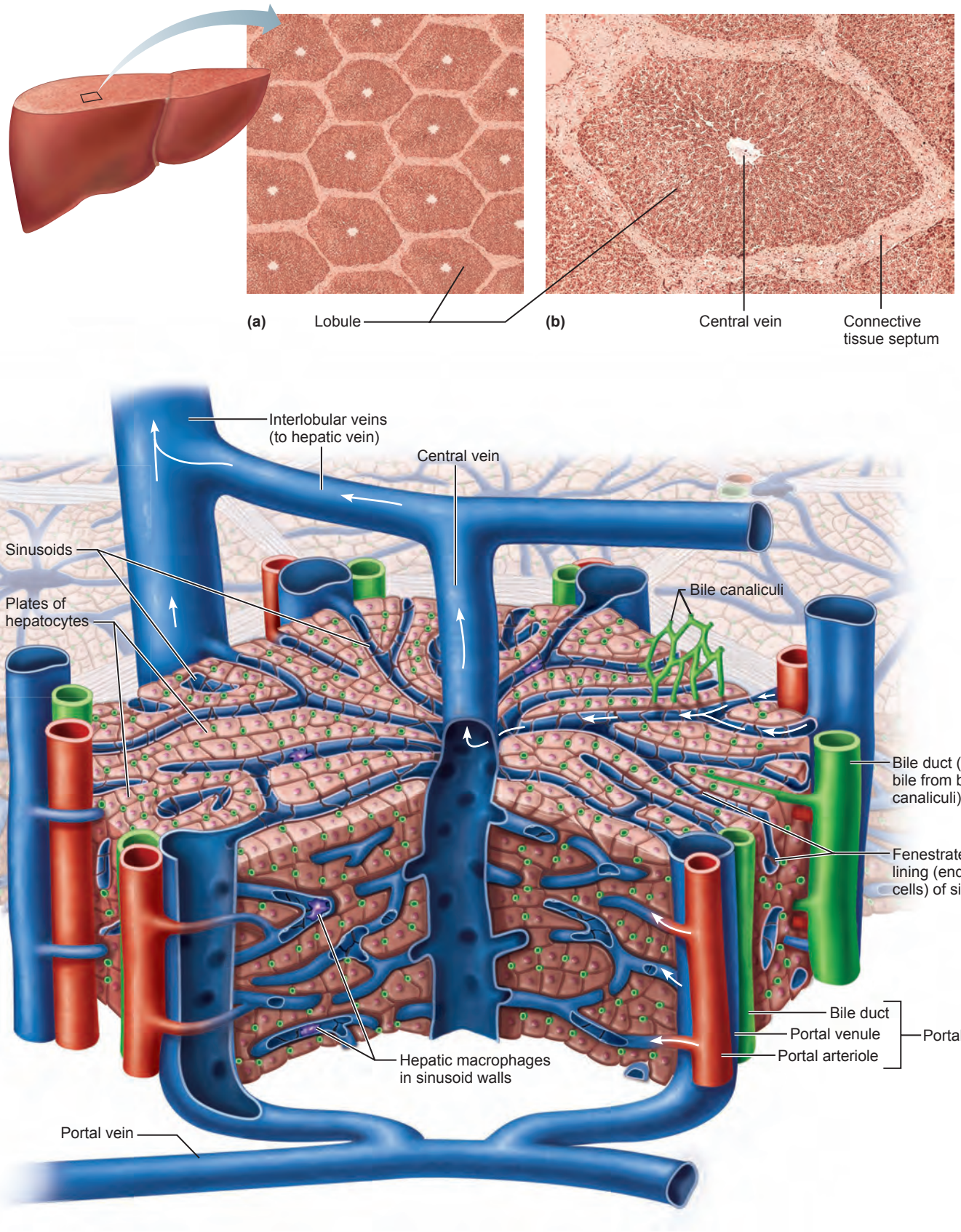


Figure 23.25 Microscopic anatomy of the liver. (a) Normal lobular pattern of the liver. **(b)** Enlarged view of one liver lobule. **(c)** Three-dimensional representation of a small portion of one liver lobule, showing portal triads and the structure of sinusoids. Arrows indicate the direction of blood flow.

hepatocytes toward the bile duct branches in the portal triads (Figure 23.25c). Although most illustrations show the canaliculi as discrete tubular structures (shown here green), their walls are actually formed by the apical membranes of adjoining hepatocytes. Notice that blood and bile flow in opposite directions in the liver lobule. Bile entering the bile ducts eventually leaves the liver via the common hepatic duct to travel toward the duodenum.

HOMEOSTATIC IMBALANCE

More common in men than in women, **hepatitis** (hep″ah-ti′tis), or inflammation of the liver, is most often due to viral infection. So far the catalogue of hepatitis-causing viruses numbers six—from the hepatitis A virus (HVA) to the hepatitis F virus (HVF). Two of these (HVA and HVE) are transmitted enterically and the infections they cause tend to be self-limiting. Those transmitted via blood—most importantly HVB and HVC—are linked to chronic hepatitis and liver cirrhosis (see discussion below). HVD is a mutated virus that needs HVB to be infectious. So far, little is known about HVF. Nonviral causes of acute hepatitis include drug toxicity and wild mushroom poisoning.

In the United States, over 40% of hepatitis cases are due to HVB, which is transmitted via blood transfusions, contaminated needles, or sexual contact. A serious problem in its own right, hepatitis B carries with it a greater menace—an elevated risk of liver cancer. However, childhood immunization using vaccine produced in bacteria is sweeping the feet out from under HVB, and the incidence of acute hepatitis from this strain has fallen dramatically since its peak in 1985.

Hepatitis A, accounting for about 32% of cases, is a more benign form frequently observed in day-care centers. It is transmitted via sewage-contaminated food, raw shellfish, water, and by the feces-mouth route, which explains why it is important for restaurant employees to scrub their hands after using the washroom. The highly successful HepA vaccine is helping to prevent hepatitis infection and shedding of the virus in the stool.

Hepatitis E is transmitted in a way similar to hepatitis A. It causes waterborne epidemics, largely in developing countries, and is a major cause of death (up to 25%) in pregnant women. It is relatively insignificant in the United States, but it is a major problem for one-third of the world's population, mainly in Africa and Asia. However, there is now hope. An experimental vaccine for HepE has proven to be 96% protective in clinical trials among soldiers in Nepal.

Hepatitis C has emerged as the most important liver disease in the United States because it produces persistent or chronic liver infections (as opposed to acute infections). More than 4 million Americans are infected and over 10,000 die annually due to sequels of HVC infection. However, the life-threatening C form of hepatitis is now being successfully treated by combination drug therapy entailing weekly injections of interferon (Pegasys, PEG-Intron) and ribavirin (Rebetol), an oral antiviral drug.

Cirrhosis (sĭr-ro′sis; "orange colored") is a progressive chronic inflammation of the liver that typically results from chronic alcoholism or severe chronic hepatitis. The alcohol-poisoned or damaged hepatocytes regenerate, but the liver's connective (scar) tissue regenerates faster. As a result, the liver becomes fatty and fibrous and its activity is depressed. As the scar tissue shrinks, it obstructs blood flow throughout the hepatic portal system, causing **portal hypertension**.

Fortunately, some veins of the portal system anastomose with veins that drain into the venae cavae (*portal-caval anastomoses*). The main ones are (1) veins in the inferior esophagus, (2) hemorrhoidal veins in the anal canal, and (3) superficial veins around the umbilicus. However, these connecting veins are small and tend to burst when forced to carry large volumes of blood. Signs of their failure include vomiting blood, and a snakelike network of distended veins surrounding the navel. This network is called *caput medusae* (kap′ut mĕ-du′se; "medusa head") after a monster in Greek mythology whose hair was made of writhing snakes. Other complications due to portal hypertension include swollen veins in the esophagus (esophageal varices) and ascites, an accumulation of fluid in the peritoneal cavity.

Liver transplants are the only clinically proven effective treatment for patients with end-stage liver disease. The one- and five-year survival rate of such transplants is approximately 90% and 75% respectively. However, donor organs are scarce and many patients die while waiting for a suitable organ. ■

Composition of Bile

Bile is a yellow-green, alkaline solution containing bile salts, bile pigments, cholesterol, triglycerides, phospholipids (lecithin and others), and a variety of electrolytes. Of these, *only* bile salts and phospholipids aid the digestive process.

Bile salts, primarily cholic and chenodeoxycholic acids, are cholesterol derivatives. Their role is to *emulsify* fats—in other words, to distribute them throughout the watery intestinal contents, just as a dish detergent breaks up a pool of fat drippings in a roasting pan. As a result, large fat globules entering the small intestine are physically separated into millions of small, more accessible fatty droplets that provide large surface areas for the fat-digesting enzymes to work on. Bile salts also facilitate fat and cholesterol absorption (discussed later) and help solubilize cholesterol, both that contained in bile and that entering the small intestine in food.

Many substances secreted in bile leave the body in feces, but bile salts are not among them. Instead, bile salts are conserved by means of a recycling mechanism called the **enterohepatic circulation**. In this process, bile salts are (1) reabsorbed into the blood by the ileum, (2) returned to the liver via the hepatic portal blood, and then (3) resecreted in newly formed bile. This pool of bile salts recirculates five or more times for a single meal.

The chief bile pigment is **bilirubin** (bil″ĭ-roo′bin), a waste product of the heme of hemoglobin formed during the breakdown of worn-out erythrocytes (see Chapter 17). The globin and iron parts of hemoglobin are saved and recycled, but bilirubin is absorbed from the blood by the liver cells, excreted into bile, and metabolized in the small intestine by resident bacteria. One of its breakdown products, *stercobilin* (ster′ko-bi″lin), gives feces a brown color. In the absence of bile, feces are gray-white in color and have fatty streaks (because essentially no fats are digested or absorbed).

The Gallbladder

The **gallbladder** is a thin-walled green muscular sac about 10 cm (4 inches) long. Roughly the size of a kiwi fruit, it snuggles in a shallow fossa on the ventral surface of the liver (see Figures 23.21 and 23.24). Its rounded fundus protrudes from the inferior margin of the liver. The gallbladder stores bile that is not immediately needed for digestion and concentrates it by absorbing some of its water and ions. (In some cases, bile released from the gallbladder is 10 to 20 times as concentrated as that entering it.) When empty, or when storing only small amounts of bile, its mucosa is thrown into honeycomb-like folds (see Figure 23.21) that, like the rugae of the stomach, allow the organ to expand as it fills. When its muscular wall contracts, bile is expelled into its duct, the *cystic duct*, and then flows into the bile duct. The gallbladder, like most of the liver, is covered by visceral peritoneum.

HOMEOSTATIC IMBALANCE

Bile is the major vehicle for cholesterol excretion from the body, and bile salts keep the cholesterol dissolved within bile. Too much cholesterol or too few bile salts leads to cholesterol crystallization, forming **gallstones**, or *biliary calculi* (bil′e-a″re kal′ku-li), which obstruct the flow of bile from the gallbladder. Then, when the gallbladder or its duct contracts, the sharp crystals cause agonizing pain that radiates to the right thoracic region. Treatments for gallstones include dissolving the crystals with drugs, pulverizing them with ultrasound vibrations (lithotripsy), vaporizing them with lasers, and the classical treatment, surgically removing the gallbladder. When the gallbladder is removed, the bile duct enlarges to assume the bile-storing role. Gallstones are easy to diagnose because they show up well with ultrasound imaging.

Bile duct blockage prevents both bile salts and bile pigments from entering the intestine. As a result, yellow bile pigments accumulate in blood and eventually are deposited in the skin, causing it to become yellow, or *jaundiced*. Jaundice caused by blocked ducts is called *obstructive jaundice*, but jaundice may also reflect liver disease (in which the liver is unable to carry out its normal metabolic duties). ■

CHECK YOUR UNDERSTANDING

34. What is a portal triad?
35. What is the importance of the enterohepatic circulation?
36. What is the role of the Kupffer cells of the liver?

For answers, see Appendix G.

The Pancreas

- State the role of pancreatic juice in digestion.
- Describe how entry of pancreatic juice into the small intestine is regulated.

The **pancreas** (pan′kre-as; *pan* = all, *creas* = flesh, meat) is a soft, tadpole-shaped gland that extends across the abdomen from its *tail* (abutting the spleen) to its *head*, which is encircled by the C-shaped duodenum (see Figures 23.1 and 23.21). Most of the pancreas is retroperitoneal and lies deep to the greater curvature of the stomach.

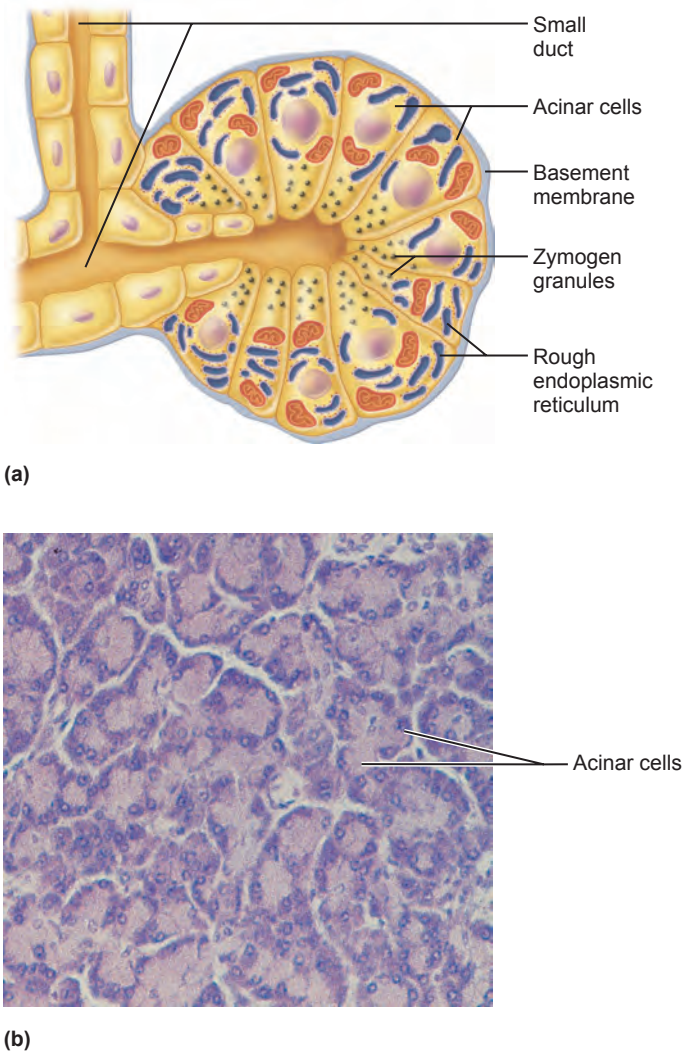


Figure 23.26 Structure of the enzyme-producing tissue of the pancreas. (a) Schematic view of one acinus (a secretory unit). The cell apices contain abundant zymogen (enzyme-containing) granules, and the dark-staining rough ER is plentiful (typical of gland cells producing large amounts of protein for export). **(b)** Photomicrograph of pancreatic acinar tissue (250×).

An accessory digestive organ, the pancreas is important to the digestive process because it produces enzymes that break down all categories of foodstuffs, which the pancreas then delivers to the duodenum. This exocrine product, called **pancreatic juice**, drains from the pancreas via the centrally located **main pancreatic duct**. The pancreatic duct generally fuses with the bile duct just as it enters the duodenum (at the hepatopancreatic ampulla). A smaller *accessory pancreatic duct* empties directly into the duodenum just proximal to the main duct.

Within the pancreas are the **acini** (as′ĭ-ni; singular: acinus), clusters of secretory cells surrounding ducts (Figure 23.26). These cells are full of rough endoplasmic reticulum and exhibit deeply staining **zymogen granules** (zi′mo-jen; "fermenting") containing the digestive enzymes they manufacture.

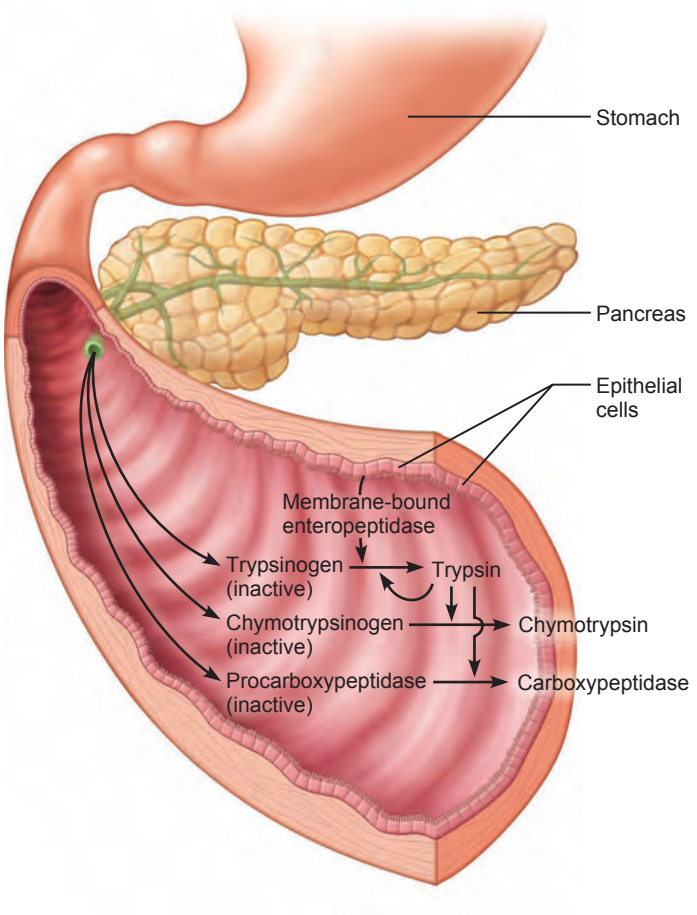


Figure 23.27 Activation of pancreatic proteases in the small intestine. Pancreatic proteases are secreted in an inactive form and are activated in the duodenum.

Scattered amid the acini are the more lightly staining *pancreatic islets* (*islets of Langerhans*). These mini-endocrine glands release insulin and glucagon, hormones that play an important role in carbohydrate metabolism, as well as several other hormones (see Chapter 16).

Composition of Pancreatic Juice

Approximately 1200 to 1500 ml of clear pancreatic juice is produced daily. It consists mainly of water, and contains enzymes and electrolytes (primarily bicarbonate ions). The acinar cells produce the enzyme-rich component of pancreatic juice. The epithelial cells lining the smallest pancreatic ducts release the bicarbonate ions that make it alkaline (about pH 8).

Normally, the amount of HCl produced in the stomach is exactly balanced by the amount of bicarbonate (HCO_3^-) secreted by the pancreas, and as HCO_3^- is secreted into the pancreatic juice, H^+ enters the blood. Consequently, the pH of venous blood returning to the heart remains relatively unchanged because alkaline blood draining from the stomach is neutralized by the acidic blood draining the pancreas.

The high pH of pancreatic fluid helps neutralize acid chyme entering the duodenum and provides the optimal environment for activity of intestinal and pancreatic enzymes. Like pepsin of the stomach, pancreatic *proteases* (protein-digesting enzymes) are produced and released in inactive forms, which are activated in the duodenum, where they do their work. This protects the pancreas from self-digestion.

For example, within the duodenum, *trypsinogen* is activated to **trypsin** by **enteropeptidase** (formerly called *enterokinase*), an intestinal brush border protease. Trypsin, in turn, activates more trypsinogen and two other pancreatic proteases (*procarboxypeptidase* and *chymotrypsinogen*) to their active forms, **carboxypeptidase** (kar-bok″se-pep′tĭ-dās) and **chymotrypsin** (ky″mo-trip′sin), respectively **(Figure 23.27)**.

Other pancreatic enzymes—**amylase**, **lipases**, and **nucleases**—are secreted in active form, but require that ions or bile be present in the intestinal lumen for optimal activity.

CHECK YOUR UNDERSTANDING

37. What is contained in zymogen granules?

38. Maryanne has pancreatitis and her pancreas is swollen and temporarily unable to produce pancreatic juice. What type of foodstuffs will probably not be digested until she recovers?

For answers, see Appendix G.

Regulation of Bile and Pancreatic Secretion and Entry into the Small Intestine

Secretion of bile and pancreatic juice and the release of these secretions to the small intestine where they "do their business" in food digestion is regulated by the same factors—neural stimuli and, more importantly, hormones (cholecystokinin and secretin).

Bile salts themselves are the major stimulus for enhanced bile secretion **(Figure 23.28)**—when a fatty meal is eaten and the enterohepatic circulation is returning large amounts of bile salts to the liver, its output of bile rises dramatically. *Secretin*, released by intestinal cells exposed to fatty chyme, also stimulates liver cells to secrete bile.

When no digestion is occurring, the hepatopancreatic sphincter (guarding the entry of bile and pancreatic juice into the duodenum) is closed and the released bile backs up the cystic duct into the gallbladder, where it is stored until needed. Although the liver makes bile continuously, bile does not usually enter the small intestine until the gallbladder contracts. Parasympathetic impulses delivered by vagus nerve fibers is a minor stimulus for gallbladder contraction, but the major stimulus is *cholecystokinin* (*CCK*), an intestinal hormone released to the blood when acidic, fatty chyme enters the duodenum (Figure 23.28). Besides causing the gallbladder to contract, CCK (1) stimulates secretion of pancreatic juice and (2) relaxes the hepatopancreatic sphincter so that bile and pancreatic juice can enter the duodenum.

Both secretin and cholecystokinin prompt the pancreas to secrete its juice. Secretin, released in response to the presence of HCl in the intestine, mainly targets the pancreatic duct cells, resulting in a watery *bicarbonate-rich* pancreatic juice. CCK, released in response to proteins and fats in chyme, stimulates the acini to release *enzyme-rich* pancreatic juice, and potentiates

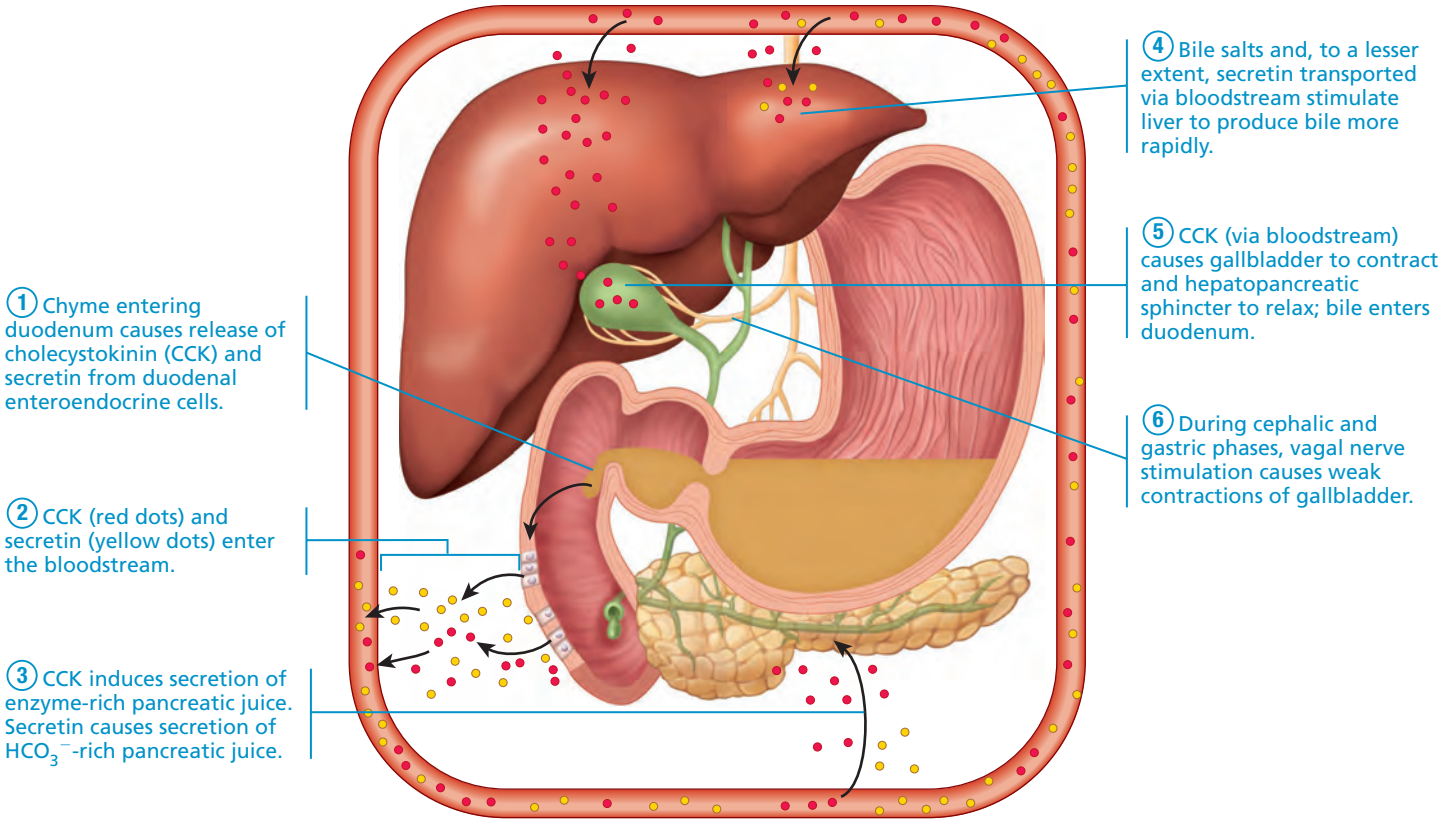


Figure 23.28 Mechanisms promoting secretion and release of bile and pancreatic juice. When digestion is not occurring, bile is stored and concentrated in the gallbladder. When acidic fatty chyme enters the small intestine, several mechanisms are initiated that accelerate the output of pancreatic juice and bile and cause the gallbladder to contract and the hepatopancreatic sphincter to relax. This allows bile and pancreatic juice to enter the small intestine. The single most important stimulus of bile secretion is an increased level of bile salts in the enterohepatic circulation.

the effect of secretin. CCK and the other digestive hormones are summarized in Table 23.1 (p. 875). Vagal stimulation prompts the release of pancreatic juice mainly during the cephalic and gastric phases of gastric secretion.

CHECK YOUR UNDERSTANDING

39. What is the functional difference between pancreatic acini and islets?

40. What is the makeup of the fluid in the pancreatic duct? In the cystic duct? In the bile duct?

41. What stimulates CCK release and what are its effects on the digestive process?

For answers, see Appendix G.

Digestive Processes Occurring in the Small Intestine

Food reaching the small intestine is unrecognizable, but it is far from being digested chemically. Carbohydrates and proteins are partially degraded, but virtually no fat digestion has occurred to this point. The process of food digestion is accelerated during the chyme's tortuous three- to six-hour journey through the small intestine, and it is here that absorption of most of the water and virtually all nutrients occurs. Like the stomach, the small intestine plays no part in ingestion or defecation.

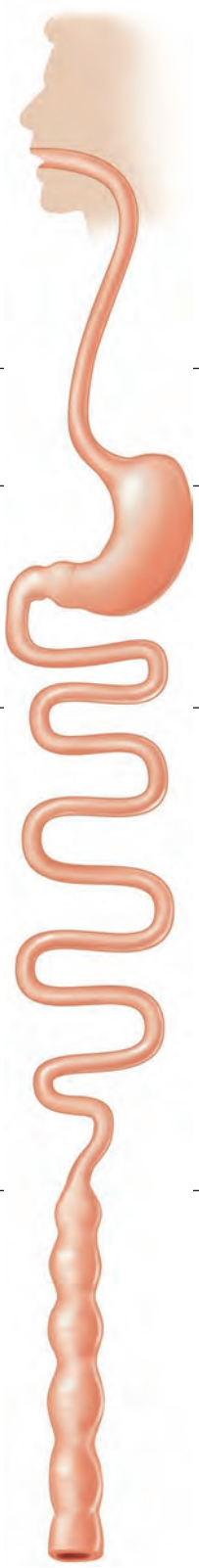
Requirements for Optimal Intestinal Digestive Activity

Although a primary function of the small intestine is digestion, intestinal juice provides little of what is needed to perform this function. Most substances required for chemical digestion—bile, digestive enzymes (except for the brush border enzymes), and bicarbonate ions (to provide the proper pH for enzymatic catalysis)—are *imported* from the liver and pancreas. Hence, anything that impairs liver or pancreatic function or delivery of their juices to the small intestine severely hinders our ability to digest food and absorb nutrients. The other primary function of the small intestine—absorption—is efficiently accomplished by its absorptive cells with their rich crop of apical microvilli.

Optimal digestive activity in the small intestine also depends on a slow, measured delivery of chyme from the stomach.

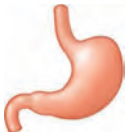
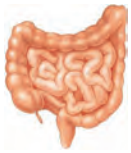
TABLE 23.2 Overview of the Functions of the Gastrointestinal Organs

ORGAN	MAJOR FUNCTIONS*	COMMENTS/ADDITIONAL FUNCTIONS
Mouth and associated accessory organs	Ingestion: food is voluntarily placed into oral cavity Propulsion: voluntary (buccal) phase of deglutition (swallowing) initiated by tongue; propels food into pharynx Mechanical digestion: mastication (chewing) by teeth and mixing movements by tongue Chemical digestion: chemical breakdown of starch is begun by salivary amylase present in saliva produced by salivary glands	Mouth serves as a receptacle; most functions performed by associated accessory organs. Mucus present in saliva helps dissolve foods so they can be tasted and moistens food so that tongue can compact it into a bolus that can be swallowed. Oral cavity and teeth cleansed and lubricated by saliva.
Pharynx and esophagus	Propulsion: peristaltic waves move food bolus to stomach, thus accomplishing involuntary (pharyngeal-esophageal) phase of deglutition	Primarily food chutes; mucus produced helps to lubricate food passageways.
Stomach	Mechanical digestion and propulsion: peristaltic waves mix food with gastric juice and propel it into the duodenum Chemical digestion: digestion of proteins begun by pepsin Absorption: absorbs a few fat-soluble substances (aspirin, alcohol, some drugs)	Also serves as storage site for food until it can be moved into the duodenum. Hydrochloric acid produced is a bacteriostatic agent and activates protein-digesting enzymes. Mucus produced helps lubricate and protect stomach from self-digestion. Intrinsic factor produced is required for intestinal absorption of vitamin B_{12}.
Small intestine and associated accessory organs (liver, gallbladder, pancreas)	Mechanical digestion and propulsion: segmentation by smooth muscle of the small intestine continually mixes contents with digestive juices and moves food along tract and through ileocecal valve at a slow rate, allowing sufficient time for digestion and absorption Chemical digestion: digestive enzymes conveyed in from pancreas and brush border enzymes attached to microvilli membranes complete digestion of all classes of foods Absorption: breakdown products of carbohydrate, protein, fat, and nucleic acid digestion, plus vitamins, electrolytes, and water, are absorbed by active and passive mechanisms	Small intestine is highly modified for digestion and absorption (circular folds, villi, and microvilli). Alkaline mucus produced by intestinal glands and bicarbonate-rich juice ducted in from pancreas help neutralize acidic chyme and provide proper environment for enzymatic activity. Bile produced by liver emulsifies fats and enhances (1) fat digestion and (2) absorption of fatty acids, monoglycerides, cholesterol, phospholipids, and fat-soluble vitamins. Gallbladder stores and concentrates bile, releasing it to small intestine in response to hormonal signals.
Large intestine	Chemical digestion: some remaining food residues are digested by enteric bacteria (which also produce vitamin K and some B vitamins) Absorption: absorbs most remaining water, electrolytes (largely NaCl), and vitamins produced by bacteria Propulsion: propels feces toward rectum by peristalsis, haustral churning, and mass movements Defecation: reflex triggered by rectal distension; eliminates feces from body	Temporarily stores and concentrates residues until defecation can occur. Copious mucus produced by goblet cells eases passage of feces through colon.



*The colored boxes beside the functions correspond to the color coding of digestive functions (gastrointestinal tract activities) illustrated in Figure 23.2.

TABLE 23.3 Control of Small Intestinal Motility

PHASE	STIMULUS	MECHANISM	EFFECT ON MOTILITY
Gastric 	↑ Gastric motility and emptying	Long neural reflexes (gastroileal reflex)	↑ Activity in ileum
		Gastrin	↑ Segmenting movements in ileum; relaxes ileocecal sphincter
Intestinal 	Distension of small intestine	Long and short neural reflexes	↑ Strength of segmentation
	Reduced intestinal volume; fasting	Long and short neural reflexes; initiated by ↑ blood levels of motilin	Initiates migrating motility complex (peristalsis); repeats until next meal

Why is this so? Entering chyme is usually hypertonic. For this reason, if large amounts of chyme were rushed into the small intestine, the osmotic water loss from the blood into the intestinal lumen would result in dangerously low blood volume. Additionally, the low pH of entering chyme must be adjusted upward and the chyme must be well mixed with bile and pancreatic juice for digestion to continue. These modifications take time, and food movement into the small intestine is carefully controlled by the pumping action of the stomach pylorus (see pp. 874–876 and Figure 23.19) to prevent the duodenum from being overwhelmed.

Since we cover the actual chemistry of digestion and absorption in detail later, next we will examine how the small intestine mixes and propels food along its length, and how its motility is regulated.

Motility of the Small Intestine

Intestinal smooth muscle mixes chyme thoroughly with bile and pancreatic and intestinal juices, and moves food residues through the ileocecal valve into the large intestine. In contrast to the peristaltic waves of the stomach, *segmentation* is the most common motion of the small intestine.

If X-ray fluoroscopy is used to examine the small intestine after it is "loaded" with a meal (the "fed state"), it looks like the intestinal contents are being massaged—the chyme is simply moved backward and forward in the lumen a few centimeters at a time by alternating contraction and relaxation of rings of smooth muscle (see Figure 23.3b). These segmenting movements of the intestine, like the peristalsis of the stomach, are initiated by intrinsic pacemaker cells in the circular smooth muscle layer. However, unlike the stomach pacemakers, which have only one rhythm, the pacemakers in the duodenum depolarize more frequently (12–14 contractions per minute) than those in the ileum (8 or 9 contractions per minute). As a result, segmentation also moves intestinal contents slowly and steadily toward the ileocecal valve at a rate that allows ample time to complete digestion and absorption.

The intensity of segmentation is altered by long and short reflexes, which parasympathetic activity enhances and sympathetic activity decreases, and by hormones **(Table 23.3)**. The more intense the contractions, the greater the mixing effect, but the basic contractile rhythms of the various intestinal regions remain unchanged.

True peristalsis occurs late in the intestinal phase only after most nutrients have been absorbed (the "fasting state"). At this point, segmenting movements wane and the duodenal mucosa begins to release the hormone *motilin*. As motilin blood levels rise, peristaltic waves are initiated in the proximal duodenum every 90 to 120 minutes and begin to sweep slowly along the intestine, moving 50–70 cm (about 2 ft) before dying out. Each successive wave is initiated a bit more distally, and this pattern of peristaltic activity is called the **migrating motility complex (MMC)**. A complete "trip" from duodenum to ileum takes about two hours. The process then repeats itself, sweeping the last remnants of the meal plus bacteria, sloughed-off mucosal cells, and other debris into the large intestine.

This "housekeeping" function is critical for preventing the overgrowth of bacteria that migrate from the large intestine into the small intestine. As food again enters the stomach with the next meal, peristalsis is replaced by segmentation.

The local enteric neurons of the GI tract wall coordinate these intestinal motility patterns and a variety of effects occur depending on which neurons are activated or inhibited. For example, a given ACh-releasing (cholinergic) sensory neuron in the small intestine, once activated, may simultaneously send messages to several different interneurons in the myenteric plexus that regulate peristalsis:

- Impulses sent proximally by effector neurons cause contraction and shortening of the circular muscle layer.
- Impulses sent distally to certain interneurons cause shortening of the longitudinal muscle layer and distension of the intestine.

As a result, as the proximal area constricts and forces chyme along the tract, the lumen of the distal part of the intestine enlarges to receive it.

Most of the time, the ileocecal sphincter is constricted and closed. However, two mechanisms—one neural and the other hormonal—cause it to relax and allow food residues to enter the cecum when ileal motility increases.

1. Enhanced activity of the stomach initiates the **gastroileal reflex** (gas″tro-il′e-ul), a long reflex that enhances the force of segmentation in the ileum.
2. Gastrin released by the stomach increases the motility of the ileum and relaxes the ileocecal sphincter. Once the chyme has passed through, it exerts backward pressure that closes the valve's flaps, preventing regurgitation into the ileum. This reflex ensures that the contents of the previous meal are swept completely out of the stomach and small intestine as the next meal is eaten.

HOMEOSTATIC IMBALANCE

Injury to the intestinal wall by severe stretching, some bacterial infections, or mechanical trauma may lead to a total shutdown of small intestine motility, a phenomenon called the intestinointestinal reflex. ■

CHECK YOUR UNDERSTANDING

42. Distension of the stomach and duodenal walls have different effects on stomach secretory activity. What are these effects?

43. Which is more important in moving food along the small intestine—peristalsis or segmentation?

44. What is the MMC and why is it important?

For answers, see Appendix G.

The Large Intestine

23

- List the major functions of the large intestine.
- Describe the regulation of defecation.

The **large intestine** frames the small intestine on three sides and extends from the ileocecal valve to the anus (see Figure 23.1). Its diameter, at about 7 cm, is greater than that of the small intestine (hence, *large* intestine), but it is less than half as long (1.5 m versus 6 m). Its major digestive function is to absorb most of the remaining water from indigestible food residues (delivered to it in a fluid state), store the residues temporarily, and then eliminate them from the body as semisolid **feces** (fe′sēz).

Gross Anatomy

The large intestine exhibits three features not seen elsewhere—teniae coli, haustra, and epiploic appendages. Except for its terminal end, the longitudinal muscle layer of its muscularis is mostly reduced to three bands of smooth muscle called **teniae coli** (ten′ne-e ko′li; "ribbons of the colon"). Their tone causes the wall of the large intestine to pucker into pocketlike sacs called **haustra** (haw′strah; "to draw up"; singular *haustrum*). Another obvious feature of the large intestine is its **epiploic appendages** (ep″ĭ-plo′ik; "membrane covered"), small fat-filled pouches of visceral peritoneum that hang from its surface (Figure 23.29a). Their significance is not known.

Subdivisions

The large intestine has the following subdivisions: cecum, appendix, colon, rectum, and anal canal. The saclike **cecum** (se′kum; "blind pouch"), which lies below the ileocecal valve in the right iliac fossa, is the first part of the large intestine (Figure 23.29a). Attached to its posteromedial surface is the blind, wormlike **vermiform appendix**. The appendix contains masses of lymphoid tissue, and as part of MALT (see p. 761) it plays an important role in body immunity. However, it has an important structural shortcoming—its twisted structure provides an ideal location for enteric bacteria to accumulate and multiply.

HOMEOSTATIC IMBALANCE

Acute inflammation of the appendix, or **appendicitis**, results from a blockage (often by feces) that traps infectious bacteria in its lumen. Unable to empty its contents, the appendix swells, squeezing off venous drainage, which may lead to ischemia and necrosis (death and decay) of the appendix. If the appendix ruptures, feces containing bacteria spray over the abdominal contents, causing *peritonitis*.

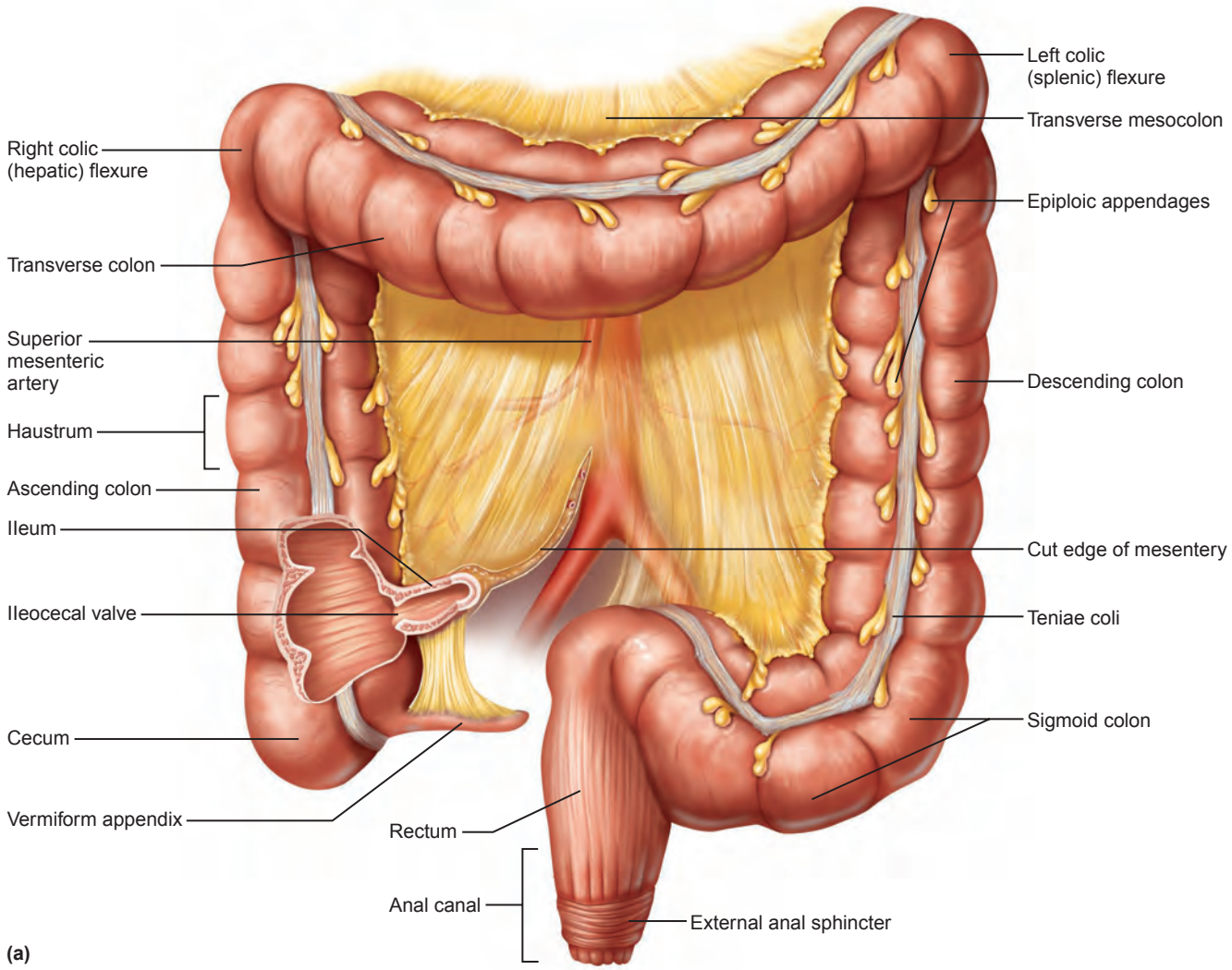
The symptoms of appendicitis are variable, but the first is usually pain in the umbilical region. Loss of appetite, nausea and vomiting, and relocalization of pain to the lower right abdominal quadrant follow. Immediate surgical removal of the appendix (appendectomy) is the accepted treatment for suspected appendicitis. Appendicitis is most common during adolescence, when the entrance to the appendix is at its widest. ■

The **colon** has several distinct regions. As the **ascending colon**, it travels up the right side of the abdominal cavity to the level of the right kidney. Here it makes a right-angle turn—the **right colic**, or **hepatic**, **flexure**—and travels across the abdominal cavity as the **transverse colon**. Directly anterior to the spleen, it bends acutely at the **left colic (splenic) flexure** and descends down the left side of the posterior abdominal wall as the **descending colon**. Inferiorly, it enters the pelvis, where it becomes the S-shaped **sigmoid colon**.

The colon is retroperitoneal, except for its transverse and sigmoid parts. These parts are intraperitoneal and anchored to the posterior abdominal wall by mesentery sheets called **mesocolons** (Figure 23.30c, d).

In the pelvis, at the level of the third sacral vertebra, the sigmoid colon joins the **rectum**, which runs posteroinferiorly just in front of the sacrum. The position of the rectum allows a number of pelvic organs (e.g., the prostate of males) to be examined digitally (with a finger) through the anterior rectal wall. This is called a **rectal exam**.

Despite its name (*rectum* = straight), the rectum has three lateral curves or bends, represented internally as three transverse folds called **rectal valves** (Figure 23.29b). These valves



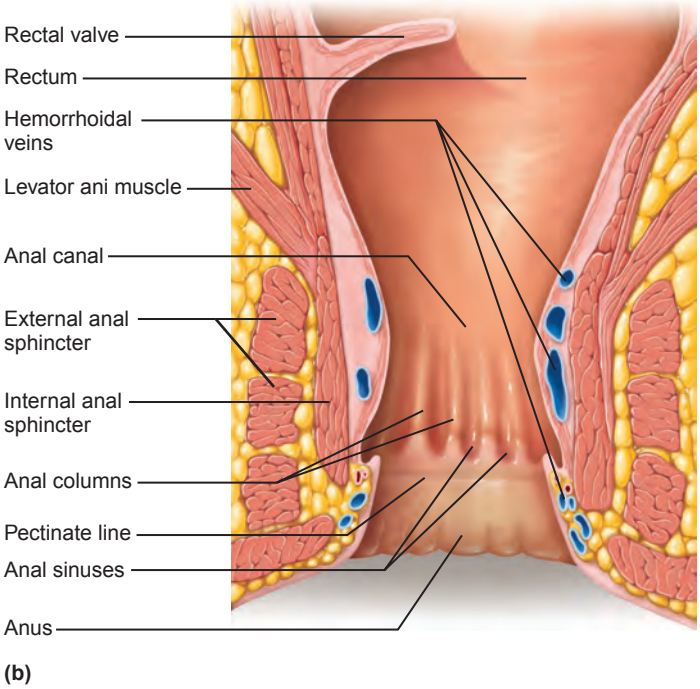


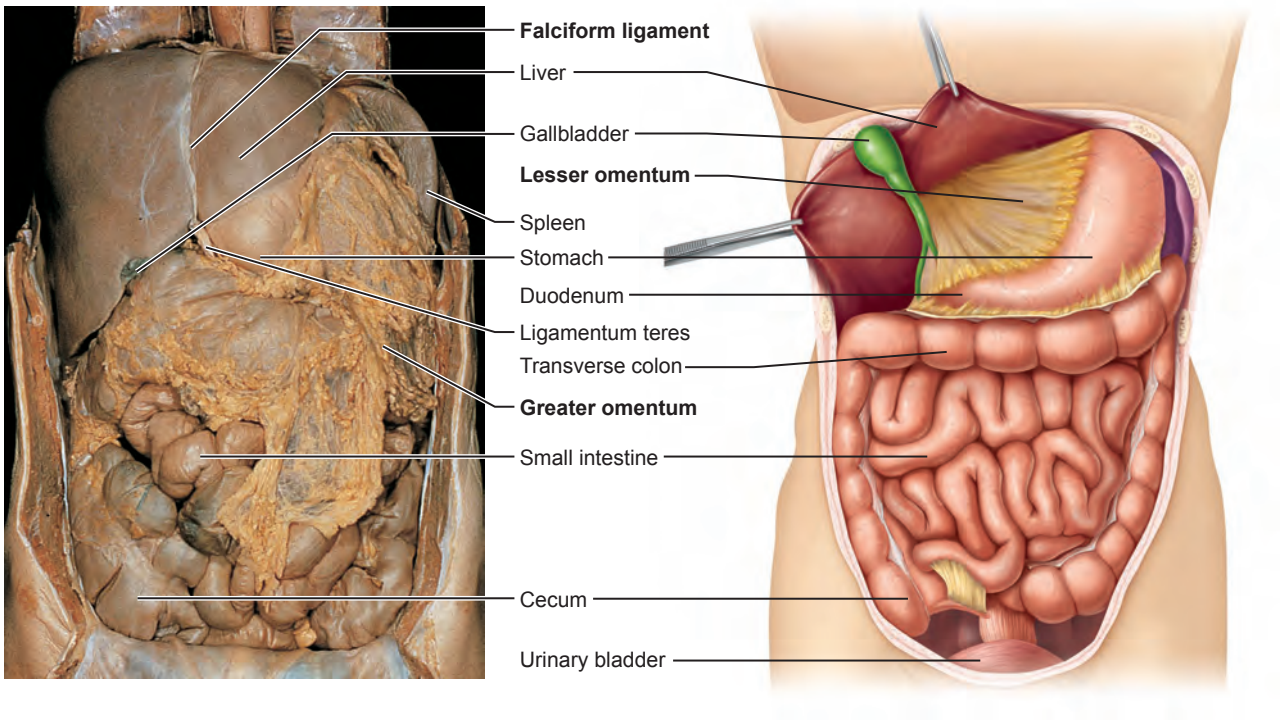
Figure 23.29 Gross anatomy of the large intestine. **(a)** Diagrammatic view. **(b)** Structure of the anal canal.

separate feces from flatus, in other words, they stop feces from being passed along with gas.

The **anal canal**, the last segment of the large intestine, lies in the perineum, entirely external to the abdominopelvic cavity. About 3 cm long, it begins where the rectum penetrates the levator ani muscle of the pelvic floor and opens to the body exterior at the **anus**. The anal canal has two sphincters, an involuntary **internal anal sphincter** composed of smooth muscle (part of the muscularis), and a voluntary **external anal sphincter** composed of skeletal muscle. The sphincters, which act rather like purse strings to open and close the anus, are ordinarily closed except during defecation.

Microscopic Anatomy

The wall of the large intestine differs in several ways from that of the small intestine. The colon *mucosa* is simple columnar epithelium except in the anal canal. Because most food is absorbed before reaching the large intestine, there are no circular folds, no



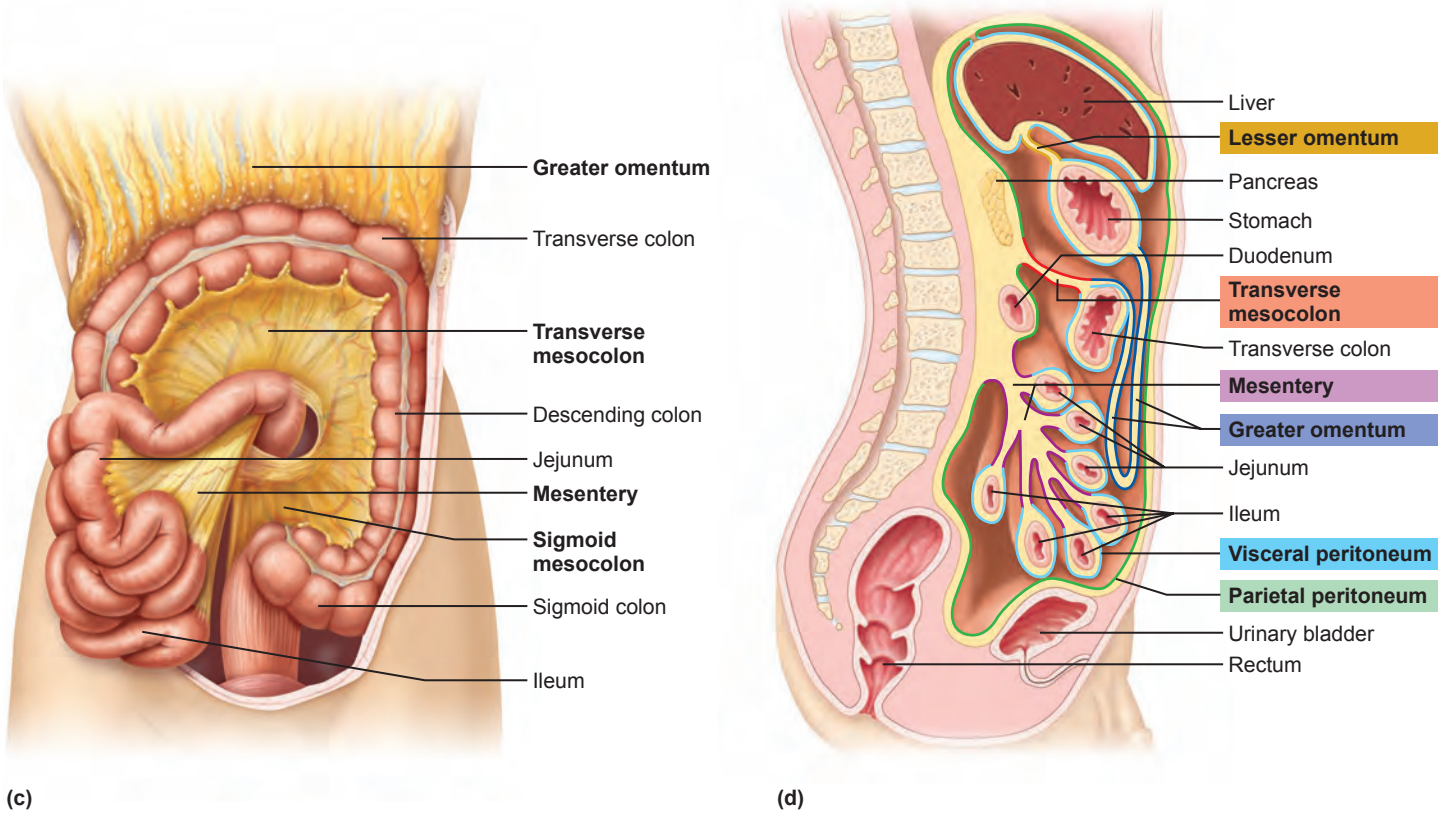


Figure 23.30 Mesenteries of the abdominal digestive organs. (a) The greater omentum, a dorsal mesentery, is shown in its normal position covering the abdominal viscera. **(b)** The liver and gallbladder have been reflected superiorly to reveal the lesser omentum, a ventral mesentery attaching the liver to the lesser curvature of the stomach. **(c)** The greater omentum has been reflected superiorly to reveal the mesentery attachments of the small and large intestine. **(d)** Sagittal section of the abdominopelvic cavity of a male.

villi, and virtually no cells that secrete digestive enzymes. However, its mucosa is thicker, its abundant crypts are deeper, and there are tremendous numbers of goblet cells in the crypts. Mucus produced by goblet cells eases the passage of feces and protects the intestinal wall from irritating acids and gases released by resident bacteria in the colon.

The mucosa of the anal canal, a stratified squamous epithelium, merges with the true skin surrounding the anus and is quite different from that of the rest of the colon, reflecting the greater abrasion that this region receives. Superiorly, it hangs in long ridges or folds called **anal columns**. **Anal sinuses**, recesses between the anal columns, exude mucus when compressed by feces, which aids in emptying the anal canal (Figure 23.29b).

The horizontal, tooth-shaped line that parallels the inferior margins of the anal sinuses is called the *pectinate line*. Superior to this line, the mucosa is innervated by visceral sensory fibers and is relatively insensitive to pain. The area inferior to the pectinate line is very sensitive to pain, a reflection of the somatic sensory fibers serving it.

Two superficial venous plexuses are associated with the anal canal, one with the anal columns and the other with the anus itself. If these (hemorrhoidal) veins are inflamed, itchy varicosities called *hemorrhoids* result.

Teniae coli and haustra are absent in the rectum and anal canal. However, consistent with its need to generate strong contractions to perform its expulsive role in defecation, the rectum's muscularis muscle layers are complete and well developed.

Bacterial Flora

Although most bacteria entering the cecum from the small intestine are dead (having been killed by the action of lysozyme, defensins, HCl, and protein-digesting enzymes), some are still "alive and kicking." Together with bacteria that enter the GI tract via the anus, these constitute the **bacterial flora** of the large intestine, an astonishing 10 million discrete types of them. These bacteria colonize the colon, metabolize some host-derived molecules (mucin, heparin, and hyaluronic acid) and ferment some of the indigestible carbohydrates (cellulose, xylan, and others), releasing irritating acids and a mixture of gases (including dimethyl sulfide, H_2, N_2, CH_4, and CO_2). Some of these gases (such as dimethyl sulfide) are quite odorous (smelly). About 500 ml of gas (flatus) is produced each day, much more when certain carbohydrate-rich foods (such as beans) are eaten. The bacterial flora also synthesize B complex vitamins and most of the vitamin K the liver requires to synthesize some of the clotting proteins.

Although the huge intestinal population of bacteria would seem to be enough inhabitants, the feces also have others, including viruses and protozoans. Of these, at least 20 are known pathogens.

Most enteric bacteria coexist peacefully with their host as long as they remain in the gut lumen. An elegant system keeps the bacteria from breaching the mucosal barrier. The epithelial cells of the gut mucosa respond to specific bacterial components by releasing chemicals that recruit immune cells, particularly dendritic cells, into the mucosa. The dendritic cells pry open tight junctions between the epithelial cells and send extensions into the lumen to sample the microbial antigens. They then migrate to the nearby lymphoid follicles (MALT) within the gut mucosa where they present the antigens to T cells. As a result, an IgA antibody–mediated response restricted to the gut lumen is triggered that prevents the bacteria from straying into tissues deep to the mucosa where they might elicit a much more widespread systemic response. Though beneficial in most ways, the coexistence of enteric bacteria with our immune system does sometimes fail. When that happens, the painful and debilitating conditions known as inflammatory bowel disease (see Related Clinical Terms, p. 905) may result.

Digestive Processes Occurring in the Large Intestine

What is finally delivered to the large intestine contains few nutrients, but it still has 12 to 24 hours more to spend there. Except for a small amount of digestion of that residue by the enteric bacteria, no further food breakdown occurs in the large intestine.

Although the large intestine harvests vitamins made by the bacterial flora and reclaims most of the remaining water and some of the electrolytes (particularly sodium and chloride), nutrient absorption is not the *major* function of this organ. As mentioned, the primary concerns of the large intestine are propulsive activities that force the fecal material toward the anus and then eliminate it from the body (defecation).

The large intestine is important for our comfort, but it is not essential for life. If the colon is removed, as may be necessitated by colon cancer, the terminal ileum is brought out to the abdominal wall in a procedure called an *ileostomy* (il″e-os′to-me), and food residues are eliminated from there into a sac attached to the abdominal wall. Another surgical technique, *ileoanal juncture*, links the ileum directly to the anal canal.

Motility of the Large Intestine

The large intestine musculature is inactive much of the time, but pressure in the ileum terminus opens the ileocecal sphincter and then closes it, preventing backward movement of the chyme. When presented with food residue the colon becomes motile, but its contractions are sluggish or short-lived. The movements most seen in the colon are **haustral contractions**, slow segmenting movements lasting about one minute that occur every 30 minutes or so.

These contractions, which occur mainly in the transverse and descending colon, reflect local controls of smooth muscle within the walls of the individual haustra. As a haustrum fills with food residue, the distension stimulates its muscle to contract, which propels the luminal contents into the next haustrum. These movements also mix the residue, which aids in water absorption.

Mass movements (mass peristalsis) are long, slow-moving, but powerful contractile waves that move over large areas of the colon three or four times daily and force the contents toward the rectum. Typically, they occur during or just after eating, which indicates that the presence of food in the stomach activates the

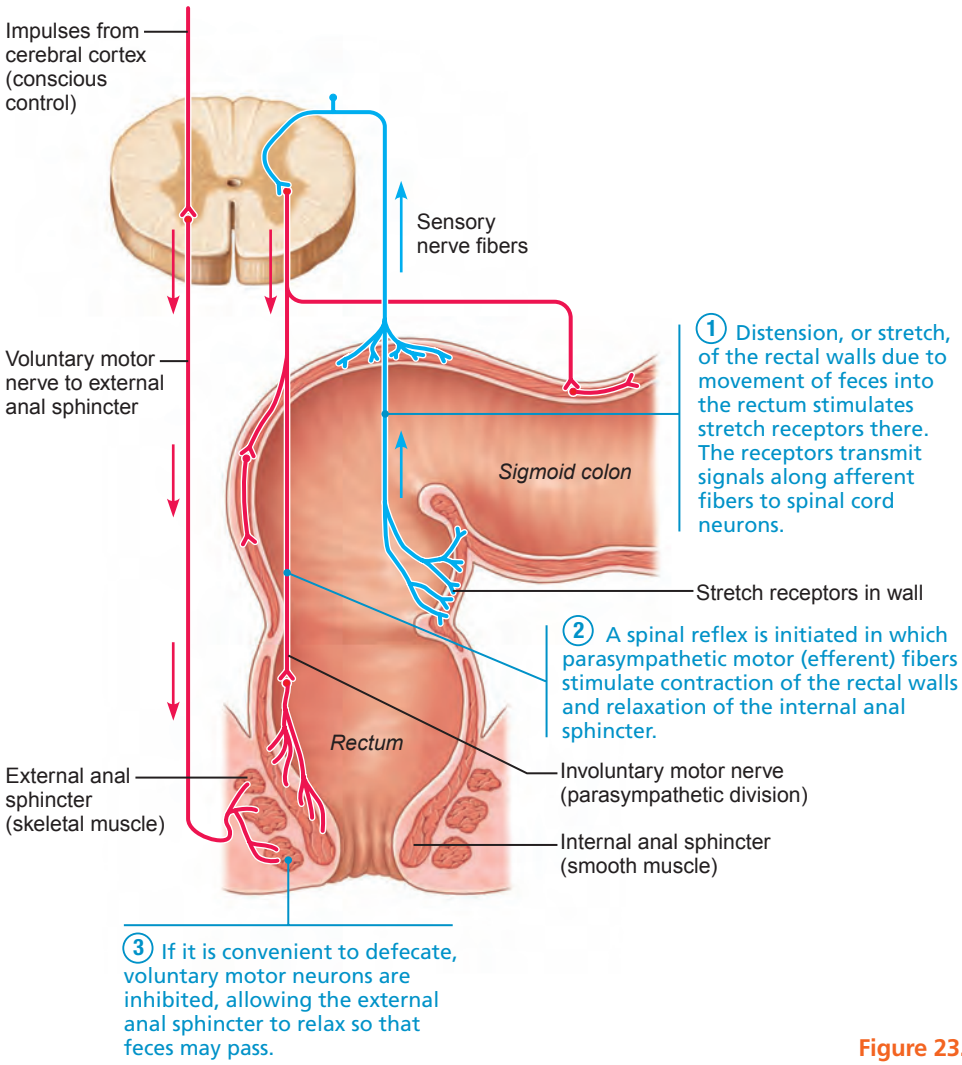


Figure 23.31 Defecation reflex.

gastroileal reflex in the small intestine and the propulsive **gastrocolic reflex** in the colon. Bulk, or fiber, in the diet increases the strength of colon contractions and softens the stool, allowing the colon to act like a well-oiled machine.

HOMEOSTATIC IMBALANCE

When the diet lacks bulk and the volume of residues in the colon is small, the colon narrows and its contractions become more powerful, increasing the pressure on its walls. This promotes formation of **diverticula** (di″ver-tik′u-lah), small herniations of the mucosa through the colon walls. This condition, called **diverticulosis**, most commonly occurs in the sigmoid colon, and affects over half of people over the age of 70. In about 20% of cases, diverticulosis progresses to **diverticulitis**, in which the diverticula become inflamed and may rupture, leaking feces into the peritoneal cavity, which can be life threatening. Foods and products that increase the bulk of the stool help to prevent attacks of diverticulitis.

Irritable bowel syndrome (*IBS*) is a functional GI disorder not explained by anatomical or biochemical abnormalities. Affected individuals have recurring (or persistent) abdominal pain that is relieved by defecation, changes in the consistency (watery to stonelike) and frequency of their stools, and varying complaints of bloating, flatulence, nausea, and depression. Stress is a common precipitating factor, and stress management is an important aspect of treatment. ■

The semisolid product delivered to the rectum, called feces or the stool, contains undigested food residues, mucus, sloughed-off epithelial cells, millions of bacteria, and just enough water to allow its smooth passage. Of the 500 ml or so of food residue entering the cecum daily, approximately 150 ml becomes feces.

Defecation

The rectum is usually empty, but when mass movements force feces into it, stretching of the rectal wall initiates the **defecation reflex**. This spinal cord–mediated parasympathetic reflex causes the sigmoid colon and the rectum to contract, and the internal anal sphincter to relax (Figure 23.31, 1 and 2). As feces are forced into the anal canal, messages reach the brain allowing us to decide whether the external (voluntary) anal sphincter should be opened or remain constricted to stop feces passage temporarily (Figure 23.31, 3). If defecation is delayed, the

reflex contractions end within a few seconds, and the rectal walls relax. With the next mass movement, the defecation reflex is initiated again—and so on, until the person chooses to defecate or the urge to defecate becomes unavoidable.

During defecation, the muscles of the rectum contract to expel the feces. We aid this process voluntarily by closing the glottis and contracting our diaphragm and abdominal wall muscles to increase the intra-abdominal pressure (a procedure called *Valsalva's maneuver*). We also contract the levator ani muscle (pp. 344–345), which lifts the anal canal superiorly. This lifting action leaves the feces below the anus—and outside the body. Involuntary or automatic defecation (incontinence of feces) occurs in infants because they have not yet gained control of their external anal sphincter. It also occurs in those with spinal cord transections.

HOMEOSTATIC IMBALANCE

Watery stools, or **diarrhea**, result from any condition that rushes food residue through the large intestine before that organ has had sufficient time to absorb the remaining water. Causes include irritation of the colon by bacteria or, less commonly, prolonged physical jostling of the digestive viscera (occurs in marathon runners). Prolonged diarrhea may result in dehydration and electrolyte imbalance (acidosis and loss of potassium).

Conversely, when food remains in the colon for extended periods, too much water is absorbed and the stool becomes hard and difficult to pass. This condition, called **constipation**, may result from lack of fiber in the diet, improper bowel habits (failing to heed the "call"), lack of exercise, emotional upset, or laxative abuse. ■

CHECK YOUR UNDERSTANDING

45. What propulsive movements are unique to the large intestine?
46. What is the result of stimulation of stretch receptors in the rectal walls?
47. In what ways are enteric bacteria important to our nutrition?

For answers, see Appendix G.

PART 3

PHYSIOLOGY OF CHEMICAL DIGESTION AND ABSORPTION

- List the enzymes involved in chemical digestion; name the foodstuffs on which they act.
- List the end products of protein, fat, carbohydrate, and nucleic acid digestion.
- Describe the process of absorption of breakdown products of foodstuffs that occurs in the small intestine.

So far in this chapter, we have examined the structure and overall function of the organs that make up the digestive system. Now let's investigate the entire chemical processing (enzymatic breakdown and absorption) of each class of foodstuffs as it moves through the GI tract. As you read along, you may find it helpful to refer to the summary in Figure 23.32.

Chemical Digestion

After foodstuffs have spent even a short time in the stomach, they are unrecognizable. Nonetheless, they are still mostly the starchy, carbohydrate-rich foods, meat proteins, butter and other fats, and so on that we ingested. Only their appearance has been changed by mechanical digestive activities. By contrast, the products of chemical digestion are the chemical building blocks of the ingested foods and are very different molecules chemically.

Mechanism of Chemical Digestion: Enzymatic Hydrolysis

Chemical digestion is a catabolic process in which large food molecules are broken down to *monomers* (chemical building blocks), which are small enough to be absorbed by the GI tract lining. Chemical digestion is accomplished by enzymes secreted by both intrinsic and accessory glands into the lumen of the alimentary canal. The enzymatic breakdown of any type of food molecule is **hydrolysis** (hi-drol′ĭ-sis) because it involves addition of a water molecule to each molecular bond to be broken (lysed).

Chemical Digestion of Carbohydrates

Most of us ingest between 200 and 600 grams of carbohydrate foods each day. **Monosaccharides** (simple sugars), the monomers of carbohydrates, are absorbed immediately without further ado. Only three of these are common in our diet: *glucose*, *fructose*, and *galactose*. The more complex carbohydrates that our digestive system is able to break down to monosaccharides are the disaccharides *sucrose* (table sugar), *lactose* (milk sugar), and *maltose* (grain sugar) and the polysaccharides *glycogen* and *starch*.

In the average diet, most digestible carbohydrates are in the form of starch, with smaller amounts of disaccharides and monosaccharides. Humans lack enzymes capable of breaking down most other polysaccharides, such as cellulose. As a result, indigestible polysaccharides do not nourish us but they do help move the food along the GI tract by providing bulk, or fiber.

Chemical digestion of starch (and perhaps glycogen) begins in the mouth (Figure 23.32). **Salivary amylase**, present in saliva, splits starch into *oligosaccharides*, smaller fragments of two to eight linked glucose molecules. Salivary amylase works best in the slightly acid to neutral environment (pH of 6.75–7.00) maintained in the mouth by the buffering effects of bicarbonate and phosphate ions in saliva. Starch digestion continues until amylase is inactivated by stomach acid and broken apart by the stomach's protein-digesting enzymes. Generally speaking, the larger the meal, the longer amylase continues to work in the stomach because foodstuffs in its relatively immobile fundus are poorly mixed with gastric juices.

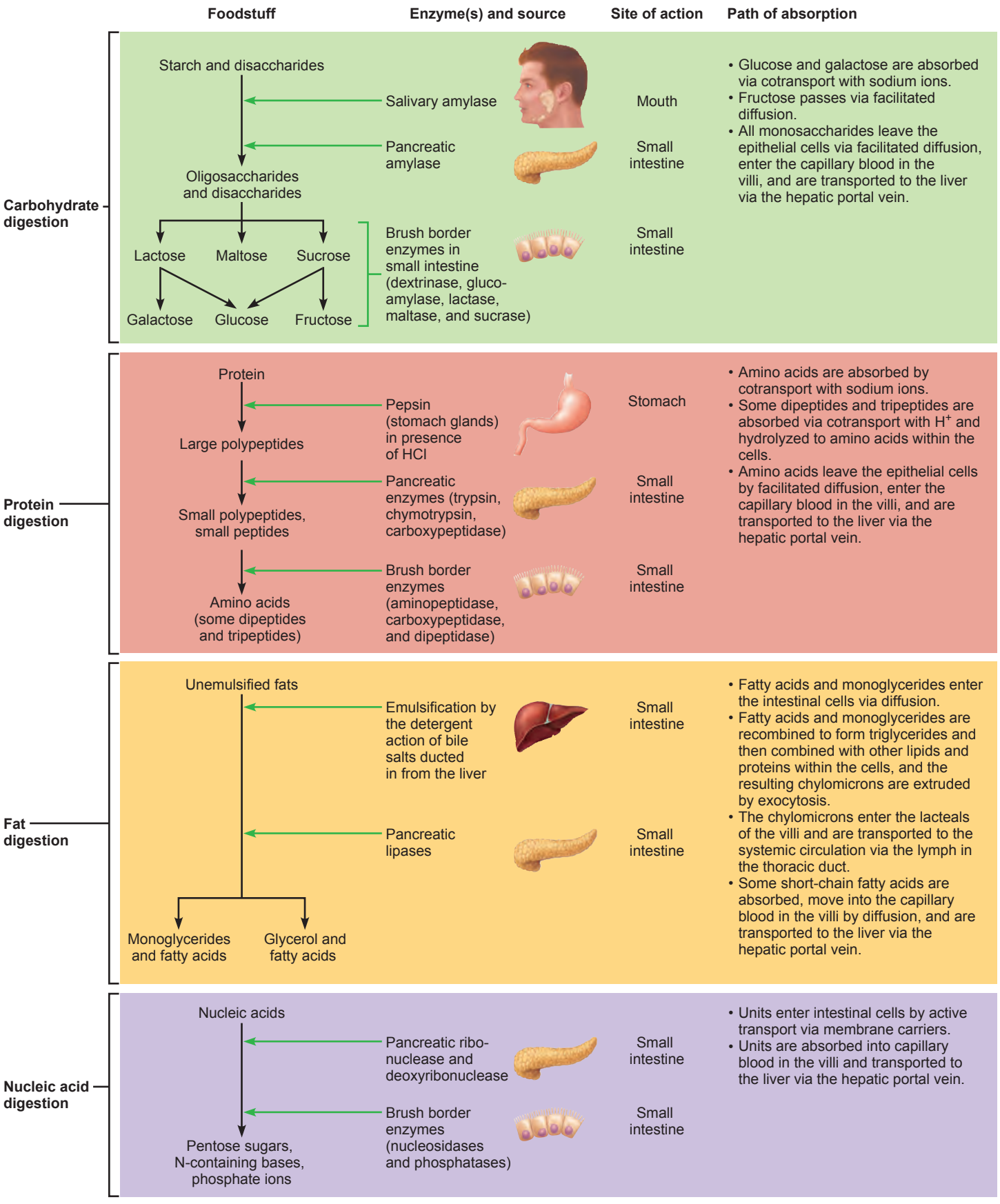


Figure 23.32 **Flowchart of chemical digestion and absorption of foodstuffs.**

Starchy foods and other digestible carbohydrates that escape being broken down by salivary amylase are acted on by **pancreatic amylase** in the small intestine. Within about 10 minutes of entering the small intestine, starch is entirely converted to various oligosaccharides, mostly maltose.

Intestinal brush border enzymes further digest these products to monosaccharides. The most important of the brush border enzymes are **dextrinase** and **glucoamylase**, which act on oligosaccharides composed of more than three simple sugars, and **maltase**, **sucrase**, and **lactase**, which hydrolyze maltose, sucrose, and lactose respectively into their constituent monosaccharides.

Because the colon does not secrete digestive enzymes, chemical digestion *officially ends* in the small intestine. As noted earlier, however, resident colon bacteria do break down and metabolize the residual complex carbohydrates and some proteins further, adding much to their own nutrition but essentially nothing to ours.

HOMEOSTATIC IMBALANCE

In some people, intestinal lactase is present at birth but then becomes deficient due to genetic factors. In such cases, the person becomes intolerant of milk products (the source of lactose), and undigested lactose creates osmotic gradients that not only prevent water from being absorbed in the small and large intestines but also pull water from the interstitial space into the intestines. The result is diarrhea. Bacterial metabolism of the undigested solutes produces large amounts of gas that result in bouts of bloating, flatulence, and cramping pain. For the most part, the solution to this problem is simple—add lactase enzyme "drops" to your milk or take a lactase tablet before meals containing milk products. ■

Chemical Digestion of Proteins

Proteins digested in the GI tract include not only dietary proteins (typically about 125 g per day), but also 15–25 g of enzyme proteins secreted into the GI tract lumen by its various glands and (probably) an equal amount of protein derived from sloughed and disintegrating mucosal cells. In healthy individuals, much of this protein is digested all the way to its **amino acid** monomers.

Protein digestion begins in the stomach when pepsinogen secreted by the chief cells is activated to **pepsin** (actually a group of protein-digesting enzymes) (Figure 23.32). Pepsin functions optimally in the acidic pH range found in the stomach: 1.5–2.5. It preferentially cleaves bonds involving the amino acids tyrosine and phenylalanine so that proteins are broken into polypeptides and small numbers of free amino acids. Pepsin, which hydrolyzes 10–15% of ingested protein, is inactivated by the high pH in the duodenum, so its proteolytic activity is restricted to the stomach. **Rennin** (the enzyme that coagulates milk protein) is not produced in adults.

Protein fragments entering the small intestine from the stomach are greeted by a host of proteolytic enzymes **(Figure 23.33)**. **Trypsin** and **chymotrypsin** secreted by the pancreas cleave the proteins into smaller peptides, which in turn become the grist for other enzymes. The pancreatic and brush border enzyme **carboxypeptidase** splits off one amino acid at a time from the end of the polypeptide chain that bears the carboxyl group. Other brush border enzymes such as **aminopeptidase** and **dipeptidase** liberate the final amino acid products. Aminopeptidase digests a protein, one amino acid at a time, by working from the amine end. Both carboxypeptidase and aminopeptidase can independently dismantle a protein, but the teamwork between these enzymes and between trypsin and chymotrypsin, which attack the more internal parts of the protein, speeds up the process tremendously.

Chemical Digestion of Lipids

Although the American Heart Association recommends a low-fat diet, the amount of lipids (fats) ingested daily varies tremendously among American adults, ranging from 30 g to 150 g or more. Triglycerides (neutral fats or triacylglycerols) are the most abundant fats in the diet. The small intestine is essentially the sole site of lipid digestion because the pancreas is the only significant source of fat-digesting enzymes, or **lipases** (see Figure 23.32).

Because triglycerides and their breakdown products are insoluble in water, fats need special "pretreatment" with bile salts to be digested and absorbed in the watery environment of the small intestine. In aqueous solutions, triglycerides aggregate to form large fat globules, and only the triglyceride molecules at the surfaces of such fatty masses are accessible to the water-soluble lipase enzymes. However, this problem is quickly resolved because as the fat globules enter the duodenum, they are coated with detergent-like bile salts.

Bile salts have both nonpolar and polar regions. Their nonpolar (hydrophobic) parts cling to the fat molecules, and their polar (ionized hydrophilic) parts allow them to repel each other and to interact with water. As a result, fatty droplets are pulled off the large fat globules, and a stable *emulsion*—an aqueous suspension of fatty droplets, each about 1 mm in diameter—is formed **(Figure 23.34, ①)**.

Emulsification does *not* break chemical bonds. It just reduces the attraction between fat molecules so that they can be more widely dispersed. This process vastly increases the number of triglyceride molecules exposed to the pancreatic lipases. Without bile, lipids would be incompletely digested in the time food is in the small intestine.

The pancreatic lipases catalyze the breakdown of fats by cleaving off two of the fatty acid chains, yielding free **fatty acids** and **monoglycerides**—glycerol with one fatty acid chain attached (Figure 23.34, ②). Fat-soluble vitamins that ride with fats require no digestion.

Chemical Digestion of Nucleic Acids

Both DNA and RNA, present in the nuclei of cells forming the ingested foods, are hydrolyzed to their **nucleotide** monomers by **pancreatic nucleases** present in pancreatic juice. The nucleotides are then broken apart by intestinal brush border enzymes (**nucleosidases** and **phosphatases**), which release their free bases, pentose sugars, and phosphate ions (see Figure 23.32).

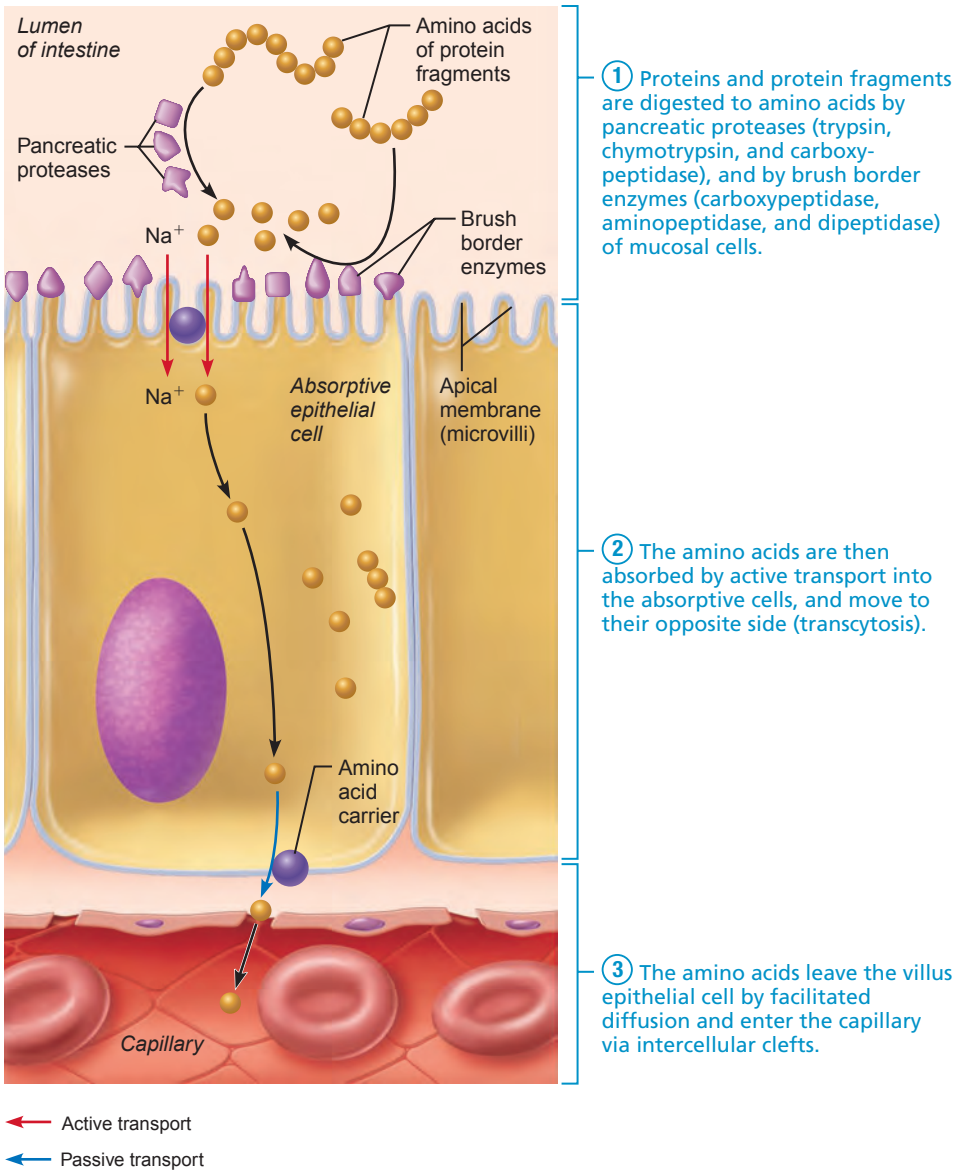


Figure 23.33 **Protein digestion and absorption in the small intestine.**

Absorption

Up to 10 L of food, drink, and GI secretions enter the alimentary canal daily, but only 1 L or less reaches the large intestine. Virtually all of the foodstuffs, 80% of the electrolytes, and most of the water (remember water follows salt) are absorbed in the small intestine. Although absorption occurs all along the length of the small intestine, most of it is completed by the time chyme reaches the ileum.

The major absorptive role of the ileum is to reclaim bile salts to be recycled back to the liver for resecretion. It is virtually impossible to exceed the absorptive capacity of the human gut, and at the end of the ileum, all that remains is some water, indigestible food materials (largely plant fibers such as cellulose), and millions of bacteria. This debris is passed on to the large intestine.

To understand absorption, remember that the fluid mosaic structure of the plasma membrane dictates that nonpolar substances, which can dissolve in the lipid core of the membrane, can be absorbed passively, and that polar substances must be absorbed by carrier mechanisms. Most nutrients are absorbed through the mucosa of the intestinal villi by *active transport* processes driven directly or indirectly (secondarily) by metabolic energy (ATP). They then enter the capillary blood in the villus to be transported in the hepatic portal vein to the liver. The exception is some lipid digestion products, which are absorbed passively by diffusion and then enter the lacteal in the villus to be carried to the blood via lymphatic fluid.

Because the epithelial cells of the intestinal mucosa are joined at their luminal surfaces by tight junctions, substances cannot move *between* the cells for the most part. Consequently, materials must pass through the epithelial cells and into the

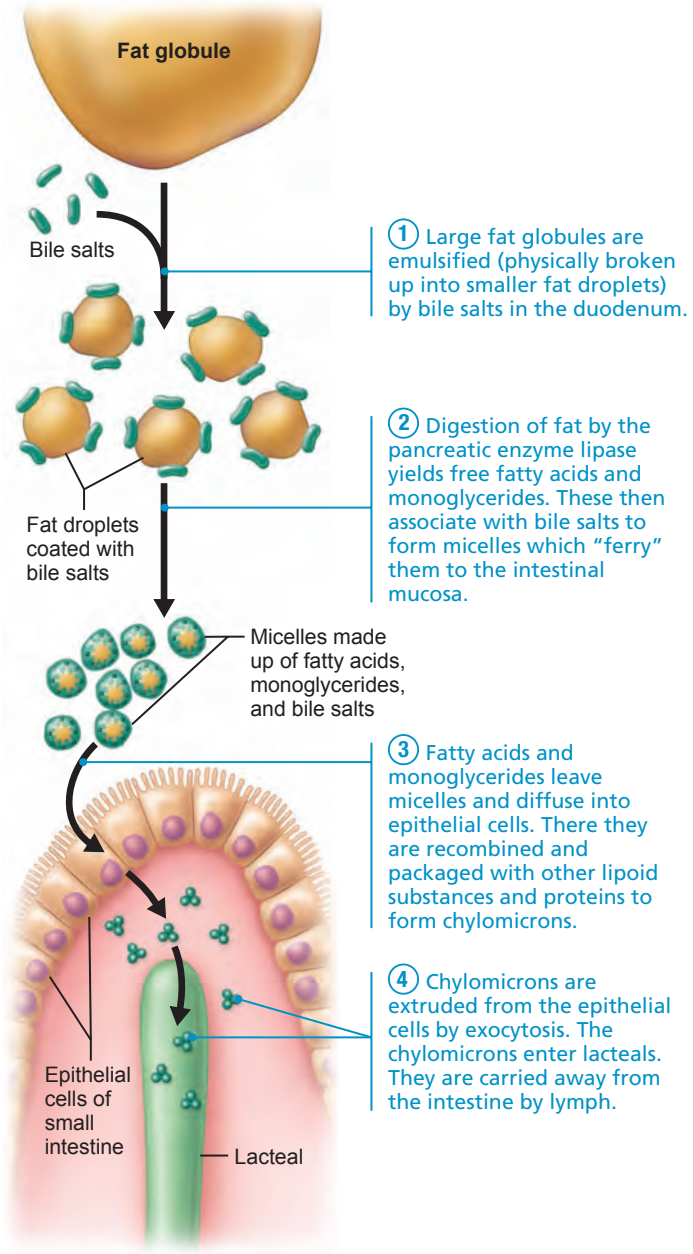


Figure 23.34 Emulsification, digestion, and absorption of fats.

interstitial fluid abutting their basolateral membranes (via transcytosis) if they are to enter the blood capillaries. As we describe the absorption of each nutrient class next, you may want to refer to the absorption summary on the right-hand side of Figure 23.32.

Carbohydrate Absorption

The monosaccharides glucose and galactose, liberated by the breakdown of starch and disaccharides, are shuttled by secondary active transport (cotransport with Na^+) into the epithelial cells by common protein carriers. They then move out of these cells by facilitated diffusion and pass into the capillaries via intercellular clefts. By contrast, fructose moves entirely by facilitated diffusion. The transport proteins, which are located very close to the disaccharidase enzymes on the microvilli, combine with the monosaccharides as soon as the disaccharides are broken down.

Protein Absorption

Several types of carriers transport the different amino acids resulting from protein digestion. Most of these carriers, like those for glucose and galactose, are coupled to the active transport of sodium. Short chains of two or three amino acids (dipeptides and tripeptides, respectively) are actively absorbed by H^+-dependent cotransport and are then digested to their amino acids within the epithelial cells before entering the capillary blood by diffusion (see Figure 23.33).

HOMEOSTATIC IMBALANCE

Whole proteins are not usually absorbed, but in rare cases intact proteins are taken up by endocytosis and released on the opposite side of the epithelial cell by exocytosis. This process is most common in newborn infants, reflecting the immaturity of their intestinal mucosa (gastric acid secretion does not reach normal levels until weeks after birth, and the mucosa is leakier than it is later.) Absorption of whole proteins accounts for many early food allergies. The immune system "sees" the intact proteins as antigenic and mounts an attack. These food allergies usually disappear as the mucosa matures. This mechanism may also provide a route for IgA antibodies present in breast milk to reach an infant's bloodstream. These antibodies confer some passive immunity on the infant, providing temporary protection against antigens to which the mother has been sensitized. ■

Lipid Absorption

Just as bile salts accelerate lipid digestion, they are also essential for the absorption of its end products. As the water-insoluble products of fat digestion—the monoglycerides and free fatty acids—are liberated by lipase activity, they quickly become associated with bile salts and *lecithin* (a phospholipid found in bile) to form micelles (Figure 23.34, (2)). **Micelles** (mi-selz′) are collections of fatty elements clustered together with bile salts in such a way that the polar (hydrophilic) ends of the molecules face the water and the nonpolar portions form the core. Also nestled in the hydrophobic core are cholesterol molecules and fat-soluble vitamins. Although micelles are similar to emulsion droplets, they are much smaller "vehicles" and easily diffuse between microvilli to come into close contact with the luminal cell surface.

Upon reaching the epithelial cells, the various lipid substances leave the micelles and move through the lipid phase of the plasma membrane by simple diffusion (Figure 23.34, (3)). Without the micelles, the lipids will simply float on the surface of the chyme (like oil on water), inaccessible to the absorptive surfaces of the epithelial cells. Generally, fat absorption is completed in the ileum, but in the absence of bile (as might occur when a gallstone blocks the cystic duct) it happens so slowly that most of the fat passes into the large intestine and is lost in feces.

Once inside the epithelial cells, the free fatty acids and monoglycerides are resynthesized into triglycerides by the smooth ER. The triglycerides are then combined with lecithin and other phospholipids and cholesterol, and coated with a "skin" of proteins to form water-soluble lipoprotein droplets called **chylomicrons** (ki″lo-mi′kronz). These are dispatched to the Golgi apparatus where they are processed for extrusion from the cell. This series of events is quite different from the absorption of amino acids and simple sugars, which pass through the epithelial cells unchanged.

The milky-white chylomicrons are too large to pass through either the plasma membranes or the basement membranes of the blood capillaries. Instead, the chylomicron-containing vesicles migrate to the basolateral membrane and are extruded by exocytosis (Figure 23.34, ④). They then enter the more permeable lacteals. Thus, most fat enters the lymphatic stream for distribution in the lymph. Eventually the chylomicrons are emptied into the venous blood in the neck region via the thoracic duct, which drains the digestive viscera.

While in the bloodstream, the triglycerides of the chylomicrons are hydrolyzed to free fatty acids and glycerol by **lipoprotein lipase**, an enzyme associated with the capillary endothelium of liver and adipose tissue. The fatty acids and glycerol can then pass through the capillary walls to be used by tissue cells for energy or stored as fats in adipose tissue. The residual chylomicron material is combined with proteins by the liver cells, and these "new" lipoproteins are used to transport cholesterol in the blood.

Passage of short-chain fatty acids is quite different from what we have just described. These fat breakdown products do not depend on the presence of bile salts or micelles, are not recombined to form triglycerides within the intestinal cells, and simply diffuse into the portal blood for distribution.

Nucleic Acid Absorption

The pentose sugars, nitrogenous bases, and phosphate ions resulting from nucleic acid digestion are transported actively across the epithelium by special carriers in the villus epithelium. They then enter the blood.

Vitamin Absorption

The small intestine absorbs dietary vitamins, and the large intestine absorbs some of the K and B vitamins made by its enteric bacterial "guests." As we already noted, fat-soluble vitamins (A, D, E, and K) dissolve in dietary fats, become incorporated into the micelles, and move across the villus epithelium passively (by diffusion). It follows that gulping pills containing fat-soluble vitamins without simultaneously eating some fat-containing food results in little or no absorption of these vitamins.

Most water-soluble vitamins (B vitamins and vitamin C) are absorbed easily by diffusion or via specific active or passive transporters. The exception is vitamin B_{12}, which is a very large, charged molecule. *Intrinsic factor*, produced by the stomach, binds to vitamin B_{12}. The vitamin B_{12}–intrinsic factor complex then binds to specific mucosal receptor sites in the terminal ileum, which trigger its active uptake by endocytosis.

Electrolyte Absorption

Absorbed electrolytes come from both ingested foods and gastrointestinal secretions. Most ions are actively absorbed along the entire length of the small intestine. However, iron and calcium absorption is largely limited to the duodenum.

As we mentioned earlier, absorption of sodium ions in the small intestine is coupled to active absorption of glucose and amino acids. For the most part, anions passively follow the electrical potential established by sodium transport. In other words, Na^+ is actively pumped out of the epithelial cells by a Na^+-K^+ pump after entering those cells. Chloride ions are also transported actively, and in the terminus of the small intestine HCO_3^- is actively secreted into the lumen in exchange for Cl^-.

Potassium ions move across the intestinal mucosa passively by facilitated diffusion (or via leaky tight junctions) in response to changing osmotic gradients. As water is absorbed from the lumen, the resulting rise in potassium levels in chyme creates a concentration gradient for its absorption. Anything that interferes with water absorption (resulting in diarrhea) not only reduces potassium absorption but also "pulls" K^+ from the interstitial space into the intestinal lumen.

For most nutrients, the amount *reaching* the intestine is the amount absorbed, regardless of the nutritional state of the body. In contrast, absorption of iron and calcium is intimately related to the body's need for them at the time.

Ionic iron, essential for hemoglobin production, is actively transported into the mucosal cells, where it binds to the protein **ferritin** (fer′i-tin). This phenomenon is called the *mucosal iron barrier*. The intracellular iron-ferritin complexes then serve as local storehouses for iron. When body reserves of iron are adequate, little (only 10% to 20%) is allowed to pass into the portal blood, and most of the stored iron is lost as the epithelial cells later slough off. However, when iron reserves are depleted (as during acute or chronic hemorrhage), iron uptake from the intestine and its release to the blood are accelerated. In the blood, iron binds to **transferrin**, a plasma protein that transports it in the circulation.

Menstrual bleeding is a major route of iron loss in females, and premenopausal women require about 50% more iron in their diets. Additionally, the intestinal epithelial cells of women have about four times as many iron transport proteins as do those of men and very little iron is lost from the body other than that lost in menses.

Calcium absorption is closely related to blood levels of ionic calcium. It is locally regulated by the active form of **vitamin D**, which promotes active calcium absorption. Decreased blood levels of ionic calcium prompt *parathyroid hormone* (*PTH*) release from the parathyroid glands. Besides facilitating the release of calcium ions from bone matrix and enhancing the reabsorption of calcium by the kidneys, PTH stimulates activation of vitamin D by the kidneys, which in turn accelerates calcium ion absorption in the small intestine.

Water Absorption

Approximately 9 L of water, mostly derived from GI tract secretions, enter the small intestine daily. Water is the most abundant substance in chyme, and 95% of it is absorbed in the small

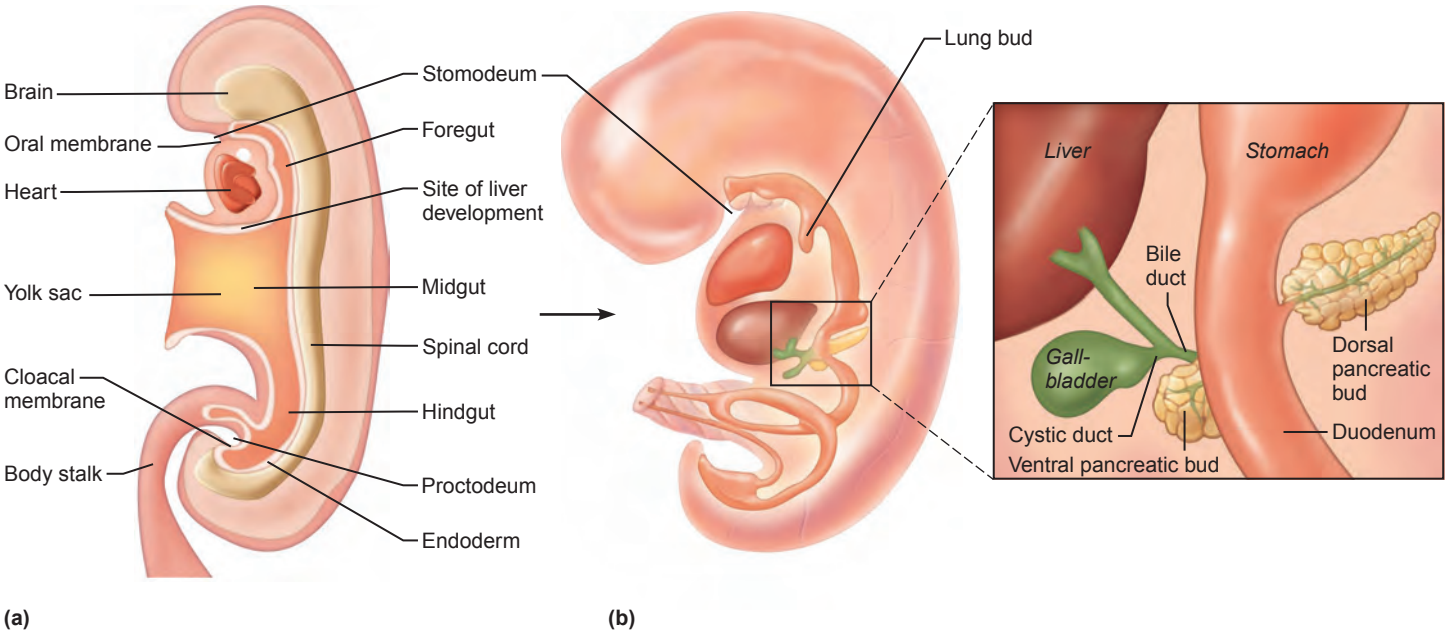


Figure 23.35 Embryonic development of the digestive system. (a) Three-week-old embryo. The endoderm has folded, and the foregut and hindgut have formed. (The midgut is still open and continuous with the yolk sac.) **(b)** By five weeks of development, the accessory organs are budding out from the endodermal layer, as shown in the enlargement.

intestine by osmosis. Most of the rest is absorbed in the large intestine, leaving only about 0.1 L to soften the feces.

The normal rate of water absorption is 300 to 400 ml per hour. Water moves freely in both directions across the intestinal mucosa, but *net osmosis* occurs whenever a concentration gradient is established by the active transport of solutes (particularly Na^+) into the mucosal cells. In this way, water uptake is effectively coupled to solute uptake and, in turn, affects the rate of absorption of substances that normally pass by diffusion. As water moves into the mucosal cells, these substances follow along their concentration gradients.

Malabsorption of Nutrients

Malabsorption, or impaired nutrient absorption, has many and varied causes. It can result from anything that interferes with the delivery of bile or pancreatic juice to the small intestine, as well as factors that damage the intestinal mucosa (severe bacterial infections and antibiotic therapy with neomycin) or reduce its absorptive surface area.

A common malabsorption syndrome is *gluten-sensitive enteropathy* or *celiac disease*, which affects one in 100 people. This chronic genetic condition is caused by an immune reaction to gluten, a protein plentiful in some grains (wheat, rye, barley). Breakdown products of gluten interact with molecules of the immune system in the GI tract, forming complexes that activate T cells, which then mount an attack on the intestinal lining. As a result, the intestinal villi are damaged and the surface area of the brush border is reduced.

The resulting bloating, diarrhea, pain, and malnutrition are usually controlled by eliminating gluten-containing grains (all grains but rice and corn) from the diet. Not many children can conceive of a world without cookies or pizza, but these are just two of the foods celiac disease victims must avoid.

CHECK YOUR UNDERSTANDING

48. What type of chemical reaction is the basis of all enzymatic food digestion?
49. Fill in the blank: Amylase is to starch as ____ is to fats.
50. What is the role of bile salts in the digestive process? In absorption?

For answers, see Appendix G.

Developmental Aspects of the Digestive System

- Describe embryonic development of the digestive system.
- Describe abnormalities of the gastrointestinal tract at different stages of life.

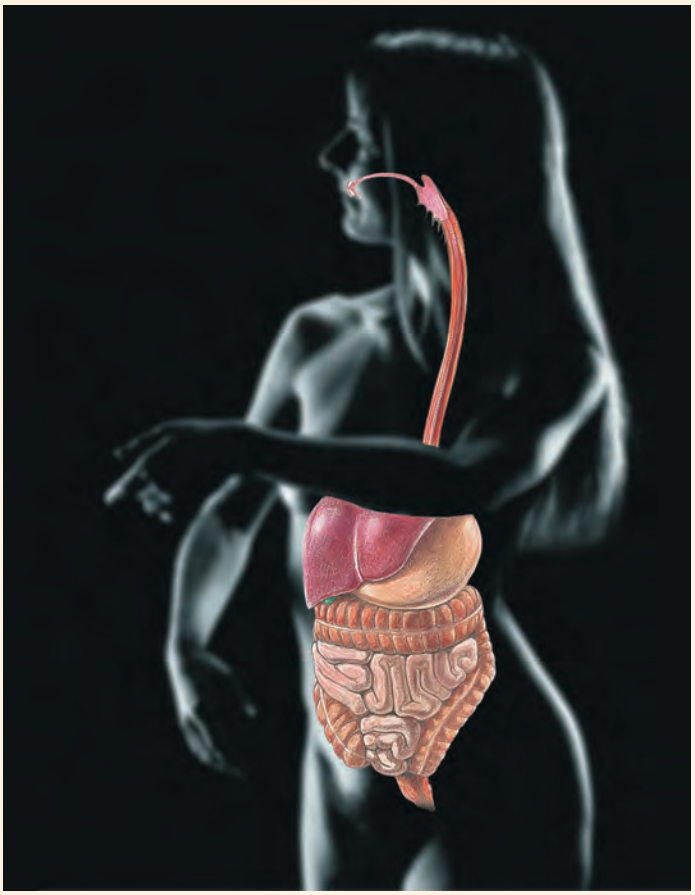
As we have described many times before, the very young embryo is flat and consists of three germ layers. From top to bottom, they are ectoderm, mesoderm, and endoderm. This flattened cell mass soon folds to form a cylindrical body, and its internal cavity becomes the cavity of the alimentary canal, which is initially closed at both ends.

The epithelial lining of the developing alimentary canal, or **primitive gut**, forms from endoderm (Figure 23.35a). The rest of the wall arises from mesoderm. The anteriormost endoderm

(Text continues on p. 904.)

System Connections

Homeostatic Interrelationships Between the Digestive System and Other Body Systems



Integumentary System

- Digestive system provides nutrients needed for energy, growth, and repair; supplies fats that provide insulation in the dermis and subcutaneous tissue
- The skin synthesizes vitamin D needed for calcium absorption from the intestine; protects by enclosure

Skeletal System

- Digestive system provides nutrients needed for energy, growth, and repair; absorbs calcium needed for bone salts
- Skeletal system protects some digestive organs by bone; cavities store some nutrients (e.g., calcium, fats)

Muscular System

- Digestive system provides nutrients needed for energy, growth, and repair; liver removes lactic acid, resulting from muscle activity, from the blood
- Skeletal muscle activity increases motility of GI tract

Nervous System

- Digestive system provides nutrients needed for normal neural functioning; nutrient signals influence neural regulation of satiety
- Neural controls of digestive function; in general, parasympathetic fibers accelerate and sympathetic fibers inhibit digestive activity; reflex and voluntary controls of defecation

Endocrine System

- Liver removes hormones from blood, ending their activity; digestive system provides nutrients needed for energy, growth, and repair; pancreas, stomach, and small intestine have hormone-producing cells
- Hormones and paracrines help regulate digestive function

Cardiovascular System

- Digestive system provides nutrients to heart and blood vessels; absorbs iron needed for hemoglobin synthesis; absorbs water necessary for normal plasma volume; liver secretes bilirubin resulting from hemoglobin breakdown in bile and stores iron for reuse
- Cardiovascular system transports nutrients absorbed by alimentary canal to all tissues of body; distributes hormones of the digestive tract

Lymphatic System/Immunity

- Digestive system provides nutrients for normal functioning; lysozyme of saliva and HCl of stomach provide nonspecific protection against bacteria
- Lacteals drain fatty lymph from digestive tract organs and convey it to blood; Peyer's patches and lymphoid tissue in mesentery house macrophages and immune cells that protect digestive tract organs against infection; plasma cells provide IgA in digestive tract secretions

Respiratory System

- Digestive system provides nutrients needed for energy metabolism, growth, and repair
- Respiratory system provides oxygen to and carries away carbon dioxide produced by digestive system organs

Urinary System

- Digestive system provides nutrients for energy fuel, growth, and repair; excretes some bilirubin produced by the liver
- Kidneys transform vitamin D to its active form, which is needed for calcium absorption

Reproductive System

- Digestive system provides nutrients for energy, growth, and repair and extra nutrition needed to support fetal growth

Closer Connections

The Digestive System and Interrelationships with the Cardiovascular, Lymphatic, and Endocrine Systems

As body systems go, the digestive system is very independent. Although the central nervous system can and does influence its activity, that is not a requirement. Indeed, most digestive system activities can be regulated entirely by local controls. Consider, for example, the following: (1) stomach and intestinal muscle is self-pacing, (2) the enteric neurons of the GI tract's intrinsic nerve plexuses carry out reflex activity that can regulate not only the organ they reside in but also adjacent and more distant GI tract organs, and (3) its enteroendocrine cells are probably even more important than neural influences in controlling digestive activity. Also unique is the fact that the digestive system operates in and regulates an environment that is actually outside the body. This is a difficult chore indeed—consider how quickly that environment can be changed by incoming foods (pizza and beer) or intestinal outflow (diarrhea).

Every cell in the body needs nutrients to stay healthy and grow, so the importance of the digestive system to virtually all body systems is clear-cut. But what systems are essential to the digestive system? If we ignore universal services, like gas exchange and renal regulation of body fluids, then the most crucial interactions are those with the cardiovascular, lymphatic, and endocrine systems. Let's take a look.

Cardiovascular and Lymphatic Systems

The important elements in this interaction are the pickup vessels. Indeed, all digestive activity would be for naught if the digested end products were not absorbed into the blood capillaries and lacteals, where they are accessible to all body cells. The lymphatic organs and tissues also offer protective services via the tonsils, Peyer's patches, and individual lymphoid follicles dispersed all along the length of the alimentary canal. Again, the fact that the alimentary canal is open at both ends makes it easy prey for both pathogenic and opportunistic bacteria and fungi.

Endocrine System

The digestive tract not only has major interactions with the endocrine system, it is itself the largest and most complex endocrine organ in the body. It makes hormones that regulate GI tract motility and secretory activity of the stomach, small intestine, liver, and pancreas (e.g., secretin, CCK), as well as cause local blood vessels to dilate to receive the digested food products being absorbed (VIP). Furthermore, some digestive organ hormones (CCK and glucagon, for example) help mediate hunger or satiety, and pancreatic hormones (insulin and glucagon) are involved in bodywide regulation of carbohydrate, fat, and amino acid metabolism.

Clinical Connections

Digestive System

Case study: Remember Mr. Gutteman, the gentleman who was dehydrating? It seems that his tremendous output of urine was only one of his current problems. Today, he complains of a headache, gnawing epigastric pain, and "the runs" (diarrhea). To pinpoint the problem, he is asked the following questions.

- Have you had these symptoms previously? (Response: "Yes, but never this bad.")
- Are you allergic to any foods? (Response: "Shellfish doesn't like me and milk gives me the runs.")

As a result of his responses, a lactose-free diet is ordered for Mr. Gutteman instead of the regular diet originally prescribed.

1. Why is the new diet prescribed? (What is believed to be his problem?)

Mr. Gutteman's problem continues despite the diet change. In fact, the frequency of diarrhea increases and by the end of the next day, he is complaining of severe abdominal pain. Again, he is asked some questions to probe his condition. One is whether he has traveled outside the country recently. He has not, reducing the possibility of infection with *Shigella* bacteria, which is associated with poor sanitation. Other questions:

- Do you drink alcohol and how much? (Response: "Little or none.")
- Have you recently eaten raw eggs or a salad containing mayonnaise at a gathering? (Response: "No.")
- Are there certain foods that seem to precipitate these attacks? (Response: "Yes, when I have coffee and a sandwich.")

2. On the basis of these responses, what do you think Mr. Gutteman's diarrhea stems from? How will it be diagnosed and treated?

(Answers in Appendix G)

(that of the foregut) touches a depressed area of the surface ectoderm called the **stomodeum** (sto″mo-de′um; "on the way to becoming the mouth"). The two membranes fuse, forming the **oral membrane**, which soon breaks through to form the opening of the mouth. Similarly, the end of the hindgut fuses with an ectodermal depression, called the **proctodeum** (*procto* = anus), to form the **cloacal membrane** (*cloaca* = sewer), which then breaks through to form the anus.

By week 5, the alimentary canal is a continuous "tube" extending from the mouth to the anus and is open to the external environment at each end. Shortly after, the glandular organs (salivary glands, liver with gallbladder, and pancreas) bud out from the mucosa at various points along its length (Figure 23.35b). These glands retain their connections, which become ducts leading into the digestive tract.

HOMEOSTATIC IMBALANCE

The digestive system is susceptible to many congenital defects that interfere with feeding. The most common are **cleft palate**, in which the palatine bones or palatine processes of the maxillae (or both) fail to fuse, and **cleft lip**, which often occur together. Of the two, cleft palate is far more serious because the child is unable to suck properly.

Another common defect is *tracheoesophageal fistula*, in which there is an opening between the esophagus and the trachea, and the esophagus often lacks a connection to the stomach. The baby chokes and becomes cyanotic during feedings because food enters the respiratory passageways. These defects are usually corrected surgically.

Cystic fibrosis (described in more detail in Chapter 22, p. 843) primarily affects the lungs, but it also impairs the activity of the pancreas. In this genetic disease, the mucous glands produce abnormally thick mucus, which blocks the ducts or passageways of involved organs. Blockage of the pancreatic duct prevents pancreatic juice from reaching the small intestine. As a result, digestion of chyme is less than optimal and most fats and fat-soluble vitamins are not digested or absorbed. Consequently the stools are bulky and fat laden. The pancreatic problems can be handled by administering pancreatic enzymes with meals. ■

During fetal life, the developing infant receives all of its nutrients through the placenta. Nonetheless, the fetal GI tract is "trained" in utero for future food digestion as the fetus naturally swallows some of the surrounding amniotic fluid. This fluid contains several chemicals that stimulate GI maturation, including gastrin and epidermal growth factor.

By contrast, feeding is a newborn baby's most important activity, and several reflexes enhance the infant's ability to obtain food: The *rooting reflex* helps the infant find the nipple, and the *sucking reflex* helps the baby hold onto the nipple and swallow.

Newborn babies tend to double their birth weight within six months, and their caloric intake and food processing ability are extraordinary. For example, a 6-week-old infant weighing about 4 kg (less than 9 lb) drinks about 600 ml of milk daily. A 65-kg adult (143 lb) would have to drink 10 L of milk to ingest a corresponding volume of fluid! However, the stomach of a newborn infant is very small, so feeding must be frequent (every 3–4 hours). Peristalsis is inefficient, and vomiting of the feeding is not unusual. As the teeth break through the gums, the infant progresses to solid foods and is usually eating an adult diet by the age of 2 years.

As a rule, the digestive system operates throughout childhood and adulthood with relatively few problems. However, contaminated food or extremely spicy or irritating foods sometimes cause an inflammation of the GI tract, called **gastroenteritis** (gas″tro-en″tĕ-ri′tis). Ulcers and gallbladder problems—inflammation or **cholecystitis** (ko″le-sis-ti′tis), and gallstones—are problems of middle age.

During old age, GI tract activity declines. Fewer digestive juices are produced, absorption is less efficient, and peristalsis slows. The result is less frequent bowel movements and, often, constipation. Taste and smell are less acute, and periodontal disease often develops. Many elderly people live alone or on a reduced income. These factors, along with increasing physical disability, tend to make eating less appealing, and many of our elderly citizens are poorly nourished.

Diverticulosis, fecal incontinence, and cancer of the GI tract are fairly common problems of the aged. Stomach and colon cancers rarely have early signs, and have often metastasized (making it inoperable) before a person seeks medical attention. Should metastasis occur, secondary cancer of the liver is almost guaranteed because of the "detour" the splanchnic venous blood takes through the liver via the hepatic portal circulation. However, when detected early, these cancers are treatable. Perhaps the best advice is to have regular dental and medical checkups. Most oral cancers are detected during routine dental examinations, 50% of all rectal cancers can be felt digitally, and nearly 80% of colon cancers can be seen and removed during a colonoscopy.

Presently, colon cancer is the second leading cancer killer (behind lung cancer) of males in the United States. Until now it was believed that most colorectal cancers derive from initially benign, knobby mucosal tumors called polyps. However, flat pancake-like growths which blend in with the surrounding tissue are more common in Americans than originally thought and are 10 times more likely to be cancerous than polyps. Researchers believe that the flat growths represent a separate pathway to colon cancer, instead of being polyp precursors. This information will likely have a big impact on gastroenterology and scheduling of tests for colon cancer. Currently it is recommended that an occult blood examination be done once a year and that colonoscopies be conducted at 3- to 10-year intervals depending on prior findings.

As we described in *A Closer Look* in Chapter 4, development of colon cancer is a gradual process that involves mutations in several regulatory genes. Recent studies have identified the mutant gene responsible for nearly 50% of all colon cancers. Dubbed *p53*, the gene normally acts as a watchdog to make sure that errors in DNA are not passed on before being corrected. When *p53* is damaged or inhibited, its tumor suppressor effect is lost and damaged DNA accumulates, resulting in carcinogenesis.

CHECK YOUR UNDERSTANDING

51. From what germ layer does the digestive system mucosa develop?
52. How does cystic fibrosis interfere with the digestive process?
53. Why are colon and stomach cancers so dangerous?

For answers, see Appendix G.

As summarized in *Making Connections*, the digestive system keeps the blood well supplied with the nutrients needed by all body tissues to fuel their energy needs and to synthesize new proteins for growth and maintenance of health. Now we are ready to examine how these nutrients are used by body cells, the topic of Chapter 24.

RELATED CLINICAL TERMS

Ascites (ah-si′tēz; *asci* = bag, bladder) Abnormal accumulation of fluid within the peritoneal cavity; if excessive, causes visible bloating of the abdomen. May result from portal hypertension caused by liver cirrhosis or by heart or kidney disease.

Barrett's esophagus A pathological change in the epithelium of the lower esophagus from stratified squamous to a metaplastic columnar epithelium. A possible sequel to untreated chronic gastroesophageal reflux due to hiatal hernia, it predisposes the individual to aggressive esophageal cancer (adenocarcinoma).

Bruxism (bruck′sizm) Grinding or clenching of teeth, usually at night during sleep in response to stress. Can wear down and crack the teeth.

Bulimia (bu-lim′e-ah; *bous* = ox; *limos* = hunger) Binge-purge behavior—episodes of massive overeating are followed by some method of purging (self-induced vomiting, taking laxatives or diuretics, or excessive exercise). Most common in women of high school or college age and in high school males in certain athletic activities (wrestling). Rooted in a pathological fear of being fat, and a need for control; provides a means of handling stress and depression. Consequences include erosion of tooth enamel and stomach trauma or rupture (from vomiting) and severe electrolyte disturbances which impair heart activity. Therapy includes hospitalization to control behavior, and nutritional counseling.

Dysphagia (dis-fa′je-ah; *dys* = difficult, abnormal; *phag* = eat) Difficulty swallowing; usually due to obstruction or physical trauma to the esophagus.

Endoscopy (en-dos′ko-pe; *endo* = within, inside; *scopy* = viewing) Visual examination of a ventral body cavity or the interior of a visceral organ with a flexible tubelike device called an endoscope, which contains a light source and a lens. A general term for a colonoscopy (viewing the colon), sigmoidoscopy (viewing the sigmoid colon), etc.

Enteritis (*enteron* = intestine) Inflammation of the intestine, especially the small intestine.

Hemochromatosis (he″mo-kro″mah-to′sis; *hemo* = blood; *chroma* = color; *osis* = condition of) A disorder in iron metabolism due to excessive/prolonged iron intake or a breakdown of the mucosal iron barrier; excess iron is deposited in the tissues, causing increased skin pigmentation and increased incidence of hepatic cancer and liver cirrhosis; also called *bronze diabetes* and *iron storage disease.*

Ileus (il′e-us) A condition in which all GI tract movement stops and the gut appears to be paralyzed. Can result from electrolyte imbalances and blockade of parasympathetic impulses by drugs (such as those commonly used during abdominal surgery); usually reversed when these interferences end. Restoration of motility is indicated by the reappearance of bowel (intestinal) sounds (gurgling, etc.).

Inflammatory bowel disease (IBD) A noncontagious, periodic inflammation of the intestinal wall now understood to be an abnormal immune and inflammatory response to bacterial antigens that normally occur in the intestine. Linked to a newly discovered T_H cell (T_H17), certain cytokines, and a deficit of antimicrobial substances normally secreted by the gut mucosa (lysozyme, defensins, and others). Afflicts up to two of every 1000 people. Symptoms include cramping, diarrhea, weight loss, and intestinal bleeding. Two subtypes occur: Crohn's disease, a syndrome characterized by relapsing and remitting periods, is more serious, with deep ulcers and fissures developing along the whole intestine, but mostly in the terminal ileum. Ulcerative colitis, by contrast, is characterized by a shallow inflammation of the large-intestinal mucosa, mainly in the rectum. They are treated with a special diet, reducing stress, antibiotics, and anti-inflammatory and immunosuppressant drugs. Extremely severe cases of ulcerative colitis are treated by colectomy (removal of a portion of the colon).

Laparoscopy (lap″ah-ros′ko-pe; *lapar* = the flank; *scopy* = observation) Examination of the peritoneal cavity and its organs with an endoscope inserted through the anterior abdominal wall. Often used to assess the condition of the digestive organs and the pelvic reproductive organs of females.

Orthodontics (or″tho-don′tiks; *ortho* = straight) Branch of dentistry that prevents and corrects misaligned teeth.

Pancreatitis (pan″kre-ah-ti′tis) A rare but extremely serious inflammation of the pancreas. May result from excessively high levels of fat in the blood or excessive alcohol ingestion, but most often results when a gallstone blocks the bile duct and pancreatic enzymes are activated in the pancreatic duct, causing the pancreatic tissue and duct to be digested. This painful condition can lead to nutritional deficiencies because pancreatic enzymes are essential to food digestion in the small intestine.

Peptic ulcers Term referring to gastric and duodenal ulcers.

Proctology (prok-tol′o-je; *procto* = rectum, anus; *logy* = study of) Branch of medicine dealing with treatment of diseases of the colon, rectum, and anus.

Pyloric stenosis (pi-lor′ik stĕ-no′sis; *stenosis* = narrowing, constriction) Congenital abnormality in which the pyloric sphincter is abnormally constricted. There is usually no problem until the baby begins to take solid food, and then projectile vomiting begins. Corrected surgically.