The food we eat contains a variety of nutrients, which are used for building new body tissues and repairing damaged tissues. Food is also vital to life because it is our only source of chemical energy. However, most of the food we eat consists of molecules that are too large to be used by body cells. Therefore, foods must be broken down into molecules that are small enough to enter body cells for their use. This is accomplished by the digestive system, which forms an extensive surface area in contact with the external environment, and is closely associated with the cardiovascular system. The combination of extensive environmental exposure and close association with blood vessels is essential for processing the food that we eat.

Q Did you ever wonder why some people are sensitive to dairy products?
24.1 Overview of the Digestive System

OBJECTIVES

- **Identify** the organs of the digestive system.
- **Describe** the basic processes performed by the digestive system.

The digestive system (dis = apart; gerere = to carry) consists of a group of organs that break down the food we eat into smaller molecules that can be used by body cells. Two groups of organs compose the digestive system (Figure 24.1): the gastrointestinal (GI) tract and the accessory digestive organs. The gastrointestinal (GI) tract, or alimentary canal (alimentary = nourishment), is a continuous tube that extends from the mouth to the anus through the thoracic and abdominopelvic cavities. Organs of the gastrointestinal tract include the mouth, most of the pharynx, esophagus, stomach, small intestine, and large intestine. The length of the GI tract is about 5–7 meters (16.5–23 ft) in a living person when the muscles along the wall of the GI tract organs are in a state of tonus (sustained contraction). It is longer in a cadaver (about 7–9 meters or 23–29.5 ft) because of the loss of muscle tone after death. The accessory digestive organs include the teeth, tongue, salivary glands, liver, gallbladder, and pancreas. Teeth aid in the physical breakdown of food, and the tongue assists in chewing and swallowing. The other accessory digestive organs, however, never come into direct contact with food. They produce or store secretions that flow into the GI tract through ducts; the secretions aid in the chemical breakdown of food.

The GI tract contains food from the time it is eaten until it is digested and absorbed or eliminated. Muscular contractions in the wall of the GI tract physically break down the food by churning it and propel the food along the tract, from the esophagus to the anus. The contractions also help to dissolve foods by mixing them with fluids secreted into the tract. Enzymes secreted by accessory digestive organs and cells that line the tract break down the food chemically.

Overall, the digestive system performs six basic processes (Figure 24.2):

1. **Ingestion.** This process involves taking foods and liquids into the mouth (eating).
2. **Secretion.** Each day, cells within the walls of the GI tract and accessory digestive organs secrete a total of about 7 liters of water, acid, buffers, and enzymes into the lumen (interior space) of the tract.
3. **Mixing and propulsion:** churning and movement of food through the GI tract.
4. **Digestion:** mechanical and chemical breakdown of food.
5. **Absorption:** passage of digested products from the GI tract into blood and lymph.
6. **Defecation:** elimination of feces from the GI tract.

**Functions of the Digestive System**

1. Ingestion: taking food into mouth.
2. Secretion: release of water, acid, buffers, and enzymes into the lumen of the GI tract.
3. Mixing and propulsion: churning and movement of food through the GI tract.
4. Digestion: mechanical and chemical breakdown of food.
5. Absorption: passage of digested products from the GI tract into blood and lymph.
6. Defecation: elimination of feces from the GI tract.

Q: Which structures of the digestive system secrete digestive enzymes?
CHAPTER 24  The Digestive System

24.2  Layers of the GI Tract

OBJECTIVE

- Describe the structure and function of the layers that form the wall of the gastrointestinal tract.

The wall of the GI tract from the lower esophagus to the anal canal has the same basic, four-layered arrangement of tissues. The four layers of the tract, from deep to superficial, are the mucosa, submucosa, muscularis, and serosa/adventitia (Figure 24.3).

Mucosa

The mucosa, or inner lining of the GI tract, is a mucous membrane. It is composed of (1) a layer of epithelium in direct contact with the contents of the GI tract, (2) a layer of connective tissue called the lamina propria, and (3) a thin layer of smooth muscle (muscularis mucosae).

1. The epithelium in the mouth, pharynx, esophagus, and anal canal is mainly nonkeratinized stratified squamous epithelium that serves a protective function. Simple columnar epithelium, which functions in secretion and absorption, lines the stomach and intestines. The tight junctions that firmly seal neighboring simple columnar epithelial cells to one another restrict leakage between the cells. The rate of renewal of GI tract epithelial cells is rapid: Every 5 to 7 days they slough off and are replaced by new cells. Located among the epithelial cells are exocrine cells that secrete mucus and fluid into the lumen of the tract, and several types of endocrine cells, collectively called enteroendocrine cells (en'-ter-o-EN-dō-krin), which secrete hormones.

Checkpoint

1. Which components of the digestive system are GI tract organs, and which are accessory digestive organs?
2. Which organs of the digestive system come in contact with food, and what are some of their digestive functions?
3. Which kinds of food molecules undergo chemical digestion, and which do not?
2. The lamina propria (lamina = thin, flat plate; proprio = one’s own) is areolar connective tissue containing many blood and lymphatic vessels, which are the routes by which nutrients absorbed into the GI tract reach the other tissues of the body. This layer supports the epithelium and binds it to the muscularis mucosae (discussed next). The lamina propria also contains the majority of the cells of the mucosa-associated lymphatic tissue (MALT). These prominent lymphatic nodules contain immune system cells that protect against disease (see Chapter 22). MALT is present all along the GI tract, especially in the tonsils, small intestine, appendix, and large intestine.

3. A thin layer of smooth muscle fibers called the muscularis mucosae (mū-KŌ-sē) throws the mucous membrane of the stomach and small intestine into many small folds, which increase the surface area for digestion and absorption. Movements of the muscularis mucosae ensure that all absorptive cells are fully exposed to the contents of the GI tract.

**Submucosa**

The submucosa consists of areolar connective tissue that binds the mucosa to the muscularis. It contains many blood and lymphatic vessels that receive absorbed food molecules. Also located in the submucosa is an extensive network of neurons known as the submucosal plexus (to be described shortly). The submucosa may also contain glands and lymphatic tissue.

**Muscularis**

The muscularis of the mouth, pharynx, and superior and middle parts of the esophagus contains skeletal muscle that produces voluntary swallowing. Skeletal muscle also forms the external anal sphincter, which permits voluntary control of defecation. Throughout the rest of the tract, the muscularis consists of smooth muscle that is generally found in two sheets: an inner sheet of circular fibers and an
outer sheet of longitudinal fibers. Involuntary contractions of the smooth muscle help break down food, mix it with digestive secretions, and propel it along the tract. Between the layers of the muscularis is a second plexus of neurons—the myenteric plexus (to be described shortly).

**Serosa**

Those portions of the GI tract that are suspended in the abdominal cavity have a superficial layer called the **serosa**. As its name implies, the serosa is a serous membrane composed of areolar connective tissue and simple squamous epithelium (mesothelium). The serosa is also called the **visceral peritoneum** because it forms a portion of the peritoneum, which we examine in detail shortly. The esophagus lacks a serosa; instead, only a single layer of areolar connective tissue called the **adventitia** forms the superficial layer of this organ.

**Checkpoint**

4. Where along the GI tract is the muscularis composed of skeletal muscle? Is control of this skeletal muscle voluntary or involuntary?

5. Name the four layers of the gastrointestinal tract, and describe their functions.

### 24.3 Neural Innervation of the GI Tract

**OBJECTIVE**

- Describe the nerve supply of the GI tract.

The gastrointestinal tract is regulated by an intrinsic set of nerves known as the enteric nervous system and by an extrinsic set of nerves that are part of the autonomic nervous system.

**Enteric Nervous System**

We first introduced you to the **enteric nervous system (ENS)**, the “brain of the gut,” in Chapter 12. It consists of about 100 million neurons that extend from the esophagus to the anus. The neurons of the ENS are arranged into two plexuses: the myenteric plexus and submucosal plexus (see Figure 24.3). The **myenteric plexus** (myo- = muscle), or **plexus of Auerbach** (OW-er-bak), is located between the longitudinal and circular smooth muscle layers of the muscularis. The **submucosal plexus**, or **plexus of Meissner** (MiZ-ner), is found within the submucosa. The plexuses of the ENS consist of motor neurons, interneurons, and sensory neurons (Figure 24.4). Because the motor neurons of the myenteric plexus supply the longitudinal and circular smooth muscle layers of the muscularis, this plexus mostly controls GI tract motility (movement), particularly the frequency and strength of contraction of the muscularis. The motor neurons of the submucosal plexus supply the secretory cells of the mucosal epithelium, controlling the secretions of the organs of the GI tract. The interneurons of the ENS interconnect the neurons of the myenteric and submucosal plexuses. The sensory neurons of the ENS supply the mucosal epithelium and contain receptors that detect stimuli in the lumen of the GI tract. The wall of the GI tract contains two major types of sensory receptors: (1) **chemoreceptors**, which respond to certain chemicals in the food present in the lumen, and (2) **mechano receptors**, such as stretch receptors, that are activated when food distends (stretches) the wall of a GI organ.

**Autonomic Nervous System**

Although the neurons of the ENS can function independently, they are subject to regulation by the neurons of the autonomic nervous system. The vagus (X) nerves supply parasympathetic fibers to most parts of the GI tract, with the exception of the last half of the large intestine, which is supplied with parasympathetic fibers from the sacral spinal cord. The parasympathetic nerves that supply the GI tract form neural connections with the ENS. Parasympathetic preganglionic neurons of the vagus or pelvic splanchnic nerves synapse with parasympathetic postganglionic neurons located in the myenteric and submucosal plexuses. Some of the parasympathetic postganglionic neurons in turn synapse with neurons in the ENS; others directly innervate smooth muscle and glands within the wall of the GI tract. In general, stimulation of the parasympathetic nerves that innervate the...
GI tract causes an increase in GI secretion and motility by increasing the activity of ENS neurons.

Sympathetic nerves that supply the GI tract arise from the thoracic and upper lumbar regions of the spinal cord. Like the parasympathetic nerves, these sympathetic nerves form neural connections with the ENS. Sympathetic postganglionic neurons synapse with neurons located in the myenteric plexus and the submucosal plexus. In general, the sympathetic nerves that supply the GI tract cause a decrease in GI secretion and motility by inhibiting the neurons of the ENS. Emotions such as anger, fear, and anxiety may slow digestion because they stimulate the sympathetic nerves that supply the GI tract.

Gastrointestinal Reflex Pathways

Many neurons of the ENS are components of GI (gastrointestinal) reflex pathways that regulate GI secretion and motility in response to stimuli present in the lumen of the GI tract. The initial components of a typical GI reflex pathway are sensory receptors (such as chemoreceptors and stretch receptors) that are associated with the sensory neurons of the ENS. The axons of these sensory neurons can synapse with other neurons located in the ENS, CNS, or ANS, informing these regions about the nature of the contents and the degree of distension (stretching) of the GI tract. The neurons of the ENS, CNS, or ANS subsequently activate or inhibit GI glands and smooth muscle, altering GI secretion and motility.

As you will see shortly, some organs lie on the posterior abdominal wall and are covered by peritoneum only on their anterior surfaces; they are not in the peritoneal cavity. Such organs, including the kidneys, ascending and descending colons of the large intestine, duodenum of the small intestine, and pancreas, are said to be retroperitoneal (retro- = behind).

Unlike the pericardium and pleurae, which smoothly cover the heart and lungs, the peritoneum contains large folds that weave between the viscera. The folds bind the organs to one another and to the walls of the abdominal cavity. They also contain blood vessels, lymphatic vessels, and nerves that supply the abdominal organs. There are five major peritoneal folds: the greater omentum, falciform ligament, lesser omentum, mesentery, and mesocolon:

1. The greater omentum (oˉ-MEN-tum = fat skin), the longest peritoneal fold, drapes over the transverse colon and coils of the small intestine like a “fatty apron” (Figure 24.5a, d). The greater omentum is a double sheet that folds back on itself, giving it a total of four layers. From attachments along the stomach and duodenum, the greater omentum extends downward anterior to the small intestine, then turns and extends upward and attaches to the transverse colon. The greater omentum normally contains a considerable amount of adipose tissue. Its adipose tissue content can greatly expand with weight gain, contributing to the characteristic “beer belly” seen in some overweight individuals. The many lymph nodes of the greater omentum contribute macrophages and antibody-producing plasma cells that help combat and contain infections of the GI tract.

2. The falciform ligament (FAL-si-form; falc- = sickle-shaped) attaches the liver to the anterior abdominal wall and diaphragm (Figure 24.5b). The liver is the only digestive organ that is attached to the anterior abdominal wall.

3. The lesser omentum arises as an anterior fold in the serosa of the stomach and duodenum, and it connects the stomach and duodenum to the liver (Figure 24.5a, c). It is the pathway for blood vessels entering the liver and contains the hepatic portal vein, common hepatic artery, and common bile duct, along with some lymph nodes.

4. A fan-shaped fold of the peritoneum, called the mesentery (MEZ-en-ter’-ē; mes- = middle), binds the jejunum and ileum of the small intestine to the posterior abdominal wall (Figure 24.5a, d). This is the most massive peritoneal fold, is typically laden with fat, and contributes extensively to the large abdomen in obese individuals. It extends from the posterior abdominal wall to wrap around the small intestine and then returns to its origin, forming a double-layered structure. Between the two layers are blood and lymphatic vessels and lymph nodes.

5. Two separate folds of peritoneum, called the mesocolon (mez’-ō-KÖ-lon), bind the transverse colon (transverse mesocolon) and sigmoid colon (sigmoid mesocolon) of the large intestine to the posterior abdominal wall (Figure 24.5a). It also carries blood and lymphatic vessels to the intestines. Together, the mesentery and mesocolon hold the intestines loosely in place, allowing movement as muscular contractions mix and move the luminal contents along the GI tract.

Checkpoint

1. How is the enteric nervous system regulated by the autonomic nervous system?
2. What is a gastrointestinal reflex pathway?

24.4 Peritoneum

OBJECTIVE

• Describe the peritoneum and its folds.

The peritoneum (per’-i-tô-NÊ-um; peri- = around) is the largest serous membrane of the body; it consists of a layer of simple squamous epithelium (mesothelium) with an underlying supporting layer of areolar connective tissue. The peritoneum is divided into the parietal peritoneum, which lines the wall of the abdominal cavity, and the visceral peritoneum, which covers some of the organs in the cavity and is their serosa (Figure 24.5a). The slim space containing lubricating serous fluid that is between the parietal and visceral portions of the peritoneum is called the peritoneal cavity. In certain diseases, the peritoneal cavity may become distended by the accumulation of several liters of fluid, a condition called ascites (a-SI-tēz).
FIGURE 24.5  Relationship of the peritoneal folds to one another and to organs of the gastrointestinal tract. The size of the peritoneal cavity in (a) is exaggerated for emphasis.

The peritoneum is the largest serous membrane in the body.
OBJECTIVES

- Identify the locations of the salivary glands, and describe the functions of their secretions.
- Describe the structure and functions of the tongue.
- Identify the parts of a typical tooth, and compare deciduous and permanent dentitions.

The mouth, also referred to as the oral or buccal cavity (BUK-al; bucca = cheeks), is formed by the cheeks, hard and soft palates, and tongue (Figure 24.6). The cheeks form the lateral walls of the oral cavity. They are covered externally by skin and internally by a mucous membrane, which consists of nonkeratinized stratified squamous epithelium. Buccinator muscles and connective tissue lie between the skin and mucous membranes of the cheeks. The anterior portions of the cheeks end at the lips.

The lips or labia (= fleshy borders) are fleshy folds surrounding the opening of the mouth. They contain the orbicularis oris muscle and are covered externally by skin and internally by a mucous membrane. The inner surface of each lip is attached to its corresponding gum by a midline fold of mucous membrane called the labial frenulum.

Q Which peritoneal fold binds the small intestine to the posterior abdominal wall?
Anteriorly, the palatoglossal arch (pal-a-to-GLOS-al) extends to the side of the base of the tongue; posteriorly, the palatopharyngeal arch (pal-a-to-FA-RIN-jē-al) extends to the side of the pharynx. The palatine tonsils are situated between the arches, and the lingual tonsils are situated at the base of the tongue. At the posterior border of the soft palate, the mouth opens into the oropharynx through the fauces (Figure 24.6).

Salivary Glands

A salivary gland (SAL-i-vār-ē) is a gland that releases a secretion called saliva into the oral cavity. Ordinarily, just enough saliva is secreted to keep the mucous membranes of the mouth and pharynx moist and to cleanse the mouth and teeth. When food enters the mouth, however, secretion of saliva increases, and it lubricates, dissolves, and begins the chemical breakdown of the food.

The mucous membrane of the mouth and tongue contains many small salivary glands that open directly, or indirectly via short ducts, to the oral cavity. These glands include labial, buccal, and palatal glands in the lips, cheeks, and palate, respectively, and lingual glands in the tongue, all of which make a small contribution to saliva.

However, most saliva is secreted by the major salivary glands, which lie beyond the oral mucosa, into ducts that lead to the oral cavity. There are three pairs of major salivary glands: the parotid,
submandibular, and sublingual glands (Figure 24.7a). The **parotid glands** (pa-ROT-id; par- = near; oto- = ear) are located inferior and anterior to the ears, between the skin and the masseter muscle. Each secretes saliva into the oral cavity via a **parotid duct** that pierces the buccinator muscle to open into the vestibule opposite the second maxillary (upper) molar tooth. The **submandibular glands** (sub’-man-DIB-ū-lar) are found in the floor of the mouth; they are medial and partly inferior to the body of the mandible. Their ducts, the **submandibular ducts**, run under the mucosa on either side of the midline of the floor of the mouth and enter the oral cavity proper lateral to the lingual frenulum. The **sublingual glands** (sub-LING-gwal) are beneath the tongue and superior to the submandibular glands. Their ducts, the **lesser sublingual ducts**, open into the floor of the mouth in the oral cavity proper.

**FIGURE 24.7**  The three major salivary glands—parotid, sublingual, and submandibular. The submandibular glands, shown in the light micrograph (b), consist mostly of serous acini (serous fluid-secreting portions of gland) and a few mucous acini (mucus-secreting portions of gland); the parotid glands consist of serous acini only; and the sublingual glands consist of mostly mucous acini and a few serous acini.

Saliva lubricates and dissolves foods and begins the chemical breakdown of carbohydrates and lipids.

**Composition and Functions of Saliva** Chemically, **saliva** is 99.5% water and 0.5% solutes. Among the solutes are ions, including sodium, potassium, chloride, bicarbonate, and phosphate. Also present are some dissolved gases and various organic substances, including urea and uric acid, mucus, immunoglobulin A, the bacteriolysine enzyme lysozyme, and salivary amylase, a digestive enzyme that acts on starch.

Not all salivary glands supply the same ingredients. The parotid glands secrete a watery (serous) liquid containing salivary amylase. Because the submandibular glands contain cells similar to those found in the parotid glands, plus some mucous cells, they secrete a fluid that contains amylase but is thickened with mucus. The sublingual glands contain mostly mucous cells, so they secrete a much thicker fluid that contributes only a small amount of salivary amylase.

Q What is the function of the chloride ions in saliva?
The water in saliva provides a medium for dissolving foods so that they can be tasted by gustatory receptors and so that digestive reactions can begin. Chloride ions in the saliva activate salivary amylase (AM-i-lās), an enzyme that starts the breakdown of starch in the mouth into maltose, maltotriose, and α-dextrin. Bicarbonate and phosphate ions buffer acidic foods that enter the mouth, so saliva is only slightly acidic (pH 6.35–6.85). Salivary glands (like the sweat glands of the skin) help remove waste molecules from the body, which accounts for the presence of urea and uric acid in saliva. Mucus lubricates food so it can be moved around easily in the mouth, formed into a ball, and swallowed. Immunoglobulin A (IgA) prevents attachment of microbes so they cannot penetrate the epithelium, and the enzyme lysozyme kills bacteria; however, these substances are not present in large enough quantities to eliminate all oral bacteria.

**Salivation** The secretion of saliva, called salivation (sal-i-VĀ-shun), is controlled by the autonomic nervous system. Amounts of saliva secreted daily vary considerably but average 1000–1500 mL (1–1.6 qt). Normally, parasympathetic stimulation promotes continuous secretion of a moderate amount of saliva, which keeps the mucous membranes moist and lubricates the movements of the tongue and lips during speech. The saliva is then swallowed and helps moisten the esophagus. Eventually, most components of saliva are reabsorbed, which prevents fluid loss. Sympathetic stimulation dominates during stress, resulting in dryness of the mouth. If the body becomes dehydrated, the salivary glands stop secreting saliva to conserve water; the resulting dryness in the mouth contributes to the sensation of thirst. Drinking not only restores the homeostasis of body water but also moistens the mouth.

The feel and taste of food also are potent stimuli of salivary gland secretions. Chemicals in the food stimulate receptors in taste buds on the tongue, and impulses are conveyed from the taste buds to two salivary nuclei in the brain stem (superior and inferior salivatory nuclei). Returning parasympathetic impulses in fibers of the facial (VII) and glossopharyngeal (IX) nerves stimulate the secretion of saliva. Saliva continues to be secreted heavily for some time after food is swallowed; this flow of saliva washes out the mouth and dilutes and buffers the remnants of irritating chemicals such as that tasty (but hot!) salsa. The smell, sight, sound, or thought of food may also stimulate secretion of saliva.

### Tongue

The **tongue** is an accessory digestive organ composed of skeletal muscle covered with mucous membrane. Together with its associated muscles, it forms the floor of the oral cavity. The tongue is divided into symmetrical lateral halves by a median septum that extends its entire length, and it is attached inferiorly to the hyoid bone, styloid process of the temporal bone, and mandible. Each half of the tongue consists of an identical complement of extrinsic and intrinsic muscles.

The **extrinsic muscles of the tongue**, which originate outside the tongue (attach to bones in the area) and insert into connective tissues in the tongue, include the hyoglossus, genioglossus, and styloglossus muscles (see Figure 11.7). The extrinsic muscles move the tongue from side to side and in and out to maneuver food for chewing, shape the food into a rounded mass, and force the food to the back of the mouth for swallowing. They also form the floor of the mouth and hold the tongue in position. The **intrinsic muscles of the tongue** originate in and insert into connective tissue within the tongue. They alter the shape and size of the tongue for speech and swallowing. The intrinsic muscles include the longitundinalis superior, longitundinalis inferior, transversus linguae, and verticalis linguae muscles. The **lingual frenulum** (lingua = the tongue), a fold of mucous membrane in the midline of the undersurface of the tongue, is attached to the floor of the mouth and aids in limiting the movement of the tongue posteriorly (see Figures 24.6 and 24.7). If a person’s lingual frenulum is abnormally short or rigid—a condition called ankyloglossia (ang´-ki-lō-GLOS-ē-a)—the person is said to be “tongue-tied” because of the resulting impairment to speech. It can be corrected surgically.

The dorsum (upper surface) and lateral surfaces of the tongue are covered with papillae (pa-PIL-ē = nipple-shaped projections), projections of the lamina propria covered with stratified squamous epithelium (see Figure 17.3). Many papillae contain taste buds, the receptors for gustation (taste). Some papillae lack taste buds, but they contain receptors for touch and increase friction between the tongue and food, making it easier for the tongue to move food in the oral cavity. The different types of taste buds are described in detail in Section 17.2. **Lingual glands** in the lamina propria of the tongue secrete both mucus and a watery serous fluid that contains the enzyme **lingual lipase** (LI-pās), which acts on as much as 30% of dietary triglycerides (fats and oils) and converts them to simpler fatty acids and diglycerides.

### Teeth

The **teeth**, or dentes (Figure 24.8), are accessory digestive organs located in sockets of the alveolar processes of the mandible and maxillae. The alveolar processes are covered by the gingivae (JIN-jī-vē), or gums, which extend slightly into each socket. The sockets are lined by the periodontal ligament (per´-ē-ō-DON-tal; odont = tooth) or periodontal membrane, which consists of dense fibrous connective tissue that anchors the teeth to the socket walls and acts as a shock absorber during chewing.

A typical tooth has three major external regions: the crown, root, and neck. The **crown** is the visible portion above the level of the gums. Embedded in the socket are one to three **roots**. The **neck** is the constricted junction of the crown and root near the gum line.
The branch of dentistry that is concerned with the prevention, diagnosis, and treatment of diseases that affect the pulp, root, periodontal ligament, and alveolar bone is known as **endodontics** (en′dō-don-tiks; endo- = within). Orthodontics (or′thō-don-tiks; ortho- = straight) is a branch of dentistry that is concerned with the prevention and correction of abnormally aligned teeth; **periodontics** (per′ō-don-tiks) is a branch of dentistry concerned with the treatment of abnormal conditions of the tissues immediately surrounding the teeth, such as gingivitis (gum disease).

Humans have two **dentitions**, or sets of teeth: deciduous and permanent. The first of these—the **deciduous teeth** (decidu- = falling out), also called **primary teeth, milk teeth, or baby teeth**—begin to erupt at about 6 months of age, and approximately two teeth appear

Internally, **dentin** forms the majority of the tooth. Dentin consists of a calcified connective tissue that gives the tooth its basic shape and rigidity. It is harder than bone because of its higher content of hydroxyapatite (70% versus 55% of dry weight).

The dentin of the crown is covered by **enamel**, which consists primarily of calcium phosphate and calcium carbonate. Enamel is also harder than bone because of its even higher content of calcium salts (about 95% of dry weight). In fact, enamel is the hardest substance in the body. It serves to protect the tooth from the wear and tear of chewing. It also protects against acids that can easily dissolve dentin. The dentin of the root is covered by **cementum**, another bonelike substance, which attaches the root to the periodontal ligament.

The dentin of a tooth encloses a space. The enlarged part of the space, the **pulp cavity**, lies within the crown and is filled with **pulp**, a connective tissue containing blood vessels, nerves, and lymphatic vessels. Narrow extensions of the pulp cavity, called **root canals**, run through the root of the tooth. Each root canal has an opening at its base, the **apical foramen**, through which blood vessels, lymphatic vessels, and nerves enter a tooth. The blood vessels bring nourishment, the lymphatic vessels offer protection, and the nerves provide sensation.

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between age 6 and adulthood. The pattern resembles the deciduous dentition, with the following exceptions. The deciduous molars are replaced by the first and second premolars (bicuspids), which have two cusps and one root and are used for crushing and grinding. The permanent molars, which erupt into the mouth posterior to the premolars, do not replace any deciduous teeth and erupt as the jaw grows to accommodate them—the first permanent molars at age 6 (six-year molars), the second permanent molars at age 12 (twelve-year molars), and the third permanent molars (wisdom teeth) after age 17 or not at all.

Often the human jaw does not have enough room posterior to the second molars to accommodate the eruption of the third molars. In this case, the third molars remain embedded in the alveolar bone and are said to be impacted. They often cause pressure and pain and

There are 20 teeth in a complete deciduous set and 32 teeth in a complete permanent set.

FIGURE 24.9 Dentitions and times of eruption. A designated letter (deciduous teeth) or number (permanent teeth) uniquely identifies each tooth. Deciduous teeth begin to erupt at 6 months of age, and approximately two teeth appear each month thereafter, until all 20 are present. Times of eruption are indicated in parentheses.

Q Which permanent teeth do not replace any deciduous teeth?
Pharynx

The pharynx, or throat, is a funnel-shaped tube that extends from the internal nares to the esophagus posteriorly and to the larynx anteriorly (see Figure 23.2). The pharynx is composed of skeletal muscle and lined by mucous membrane, and is divided into three parts: the nasopharynx, the oropharynx, and the laryngopharynx. The nasopharynx functions only in respiration, but both the oropharynx and laryngopharynx have digestive as well as respiratory functions. Swallowed food passes from the mouth into the oropharynx and laryngopharynx; the muscular contractions of these areas help propel food into the esophagus and then into the stomach.

### Checkpoint

14. To which two organ systems does the pharynx belong?
The esophagus (e-SOF-a-gus = eating gullet) is a collapsible muscular tube, about 25 cm (10 in.) long, that lies posterior to the trachea. The esophagus begins at the inferior end of the laryngopharynx, passes through the inferior aspect of the neck, and enters the mediastinum anterior to the vertebral column. Then it pierces the diaphragm through an opening called the esophageal hiatus (e-sof-a-JÉ-al hi-Ă-tus), and ends in the superior portion of the stomach (see Figure 24.1). Sometimes, part of the stomach protrudes above the diaphragm through the esophageal hiatus. This condition, termed a hiatus hernia (HER-nē-a), is described in the Medical Terminology section at the end of the chapter.

### Histology of the Esophagus

The mucosa of the esophagus consists of nonkeratinized stratified squamous epithelium, lamina propria (areolar connective tissue), and a muscularis mucosae (smooth muscle) (Figure 24.10). Near the stomach, the mucosa of the esophagus also contains mucous glands. The stratified squamous epithelium associated with the lips, mouth, tongue, oropharynx, laryngopharynx, and esophagus affords considerable protection against abrasion and wear and tear from food particles that are chewed, mixed with secretions, and swallowed. The submucosa contains areolar connective tissue, blood vessels, and mucous glands. The muscularis of the superior third of the esophagus is skeletal muscle, the intermediate third is skeletal and smooth muscle, and the inferior third is smooth muscle. At each end of the esophagus, the muscularis becomes slightly more prominent and forms two sphincters—the upper esophageal sphincter (UES) (e-sof-'a-JÉ-al), which consists of skeletal muscle, and the lower esophageal (cardiac) sphincter (LES), which consists of smooth muscle and is near the heart. The upper esophageal sphincter regulates the movement of food from the pharynx into the esophagus; the lower esophageal sphincter regulates the movement of food from the esophagus into the stomach. The superficial layer of the esophagus is known as the adventitia (ad-ven-TISH-a), rather than the serosa as in the stomach and intestines, because the areolar connective tissue of this layer is not covered by mesothelium and because the connective tissue merges with the connective tissue of surrounding structures of the mediastinum through which it passes. The adventitia attaches the esophagus to surrounding structures.

### Physiology of the Esophagus

The esophagus secretes mucus and transports food into the stomach. It does not produce digestive enzymes, and it does not carry on absorption.

**Q** In which layers of the esophagus are the glands that secrete lubricating mucus located?
Swallowing starts when the bolus is forced to the back of the oral cavity and into the oropharynx by the movement of the tongue upward and backward against the palate; these actions constitute the voluntary stage of swallowing. With the passage of the bolus into the oropharynx, the involuntary pharyngeal stage of swallowing begins (Figure 24.11b). The bolus stimulates receptors in the oropharynx, which send impulses to the deglutition center in the medulla oblongata and lower pons of the brain stem. The returning impulses cause the soft palate and uvula to move upward to close off the nasopharynx, which prevents swallowed foods and liquids from entering the nasal cavity. In addition, the epiglottis closes off the opening to the larynx, which prevents the bolus from entering the rest of the respiratory tract. The bolus moves through the oropharynx and the laryngopharynx. Once the upper esophageal sphincter relaxes, the bolus moves into the esophagus.

The esophageal stage of swallowing begins once the bolus enters the esophagus. During this phase, peristalsis (per′i-STAL-sis; stalsis = constriction), a progression of coordinated contractions and relaxations of the circular and longitudinal layers of the muscularis, pushes the bolus onward (Figure 24.11c). (Peristalsis occurs in other tubular structures, including other parts of the GI tract to the anus and the ureters, bile ducts, and uterine tubes; in the esophagus it is controlled by the medulla oblongata.)

In the section of the esophagus just superior to the bolus, the circular muscle fibers contract, constricting the esophageal wall and squeezing the bolus toward the stomach.
OBJECTIVE

- Describe the location, anatomy, histology, and functions of the stomach.

The stomach is a J-shaped enlargement of the GI tract directly inferior to the diaphragm in the abdomen. The stomach connects the esophagus to the duodenum, the first part of the small intestine (Figure 24.12). Because a meal can be eaten much more quickly than the intestines can digest and absorb it, one of the functions of the stomach is to serve as a mixing chamber and holding reservoir. At appropriate intervals after food is ingested, the stomach forces a small quantity of material into the first portion of the small intestine. The position and size of the stomach vary continually; the diaphragm pushes it inferiorly with each inhalation and pulls it superiorly with each exhalation. Empty, it is about the size of a large sausage, but it is the most distensible part of the GI tract and can accommodate a large meal.

**Clinical Connection**

**Gastroesophageal Reflux Disease**

If the lower esophageal sphincter fails to close adequately after food has entered the stomach, the stomach contents can reflux (back up) into the inferior portion of the esophagus. This condition is known as **gastroesophageal reflux disease (GERD)** (gas′-trō-e-sof-a-JÉ-al). Hydrochloric acid (HCl) from the stomach contents can irritate the esophageal wall, resulting in a burning sensation that is called **heartburn** because it is experienced in a region very near the heart; it is unrelated to any cardiac problem. Drinking alcohol and smoking can cause the sphincter to relax, worsening the problem. The symptoms of GERD often can be controlled by avoiding foods that strongly stimulate stomach acid secretion (coffee, chocolate, tomatoes, fatty foods, orange juice, peppermint, spearmint, and onions). Other acid-reducing strategies include taking over-the-counter histamine-2 (H₂) blockers such as Tagamet HB® or Pepcid AC® 30 to 60 minutes before eating to block acid secretion, and neutralizing acid that has already been secreted with antacids such as Tums® or Maalox®. Symptoms are less likely to occur if food is eaten in smaller amounts and if the person does not lie down immediately after a meal. GERD may be associated with cancer of the esophagus.

**Checkpoint**

17. What does deglutition mean?
18. What occurs during the voluntary and pharyngeal phases of swallowing?
19. Does peristalsis “push” or “pull” food along the gastrointestinal tract?

<table>
<thead>
<tr>
<th>TABLE 24.2</th>
<th>Summary of Digestive Activities in the Pharynx and Esophagus</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STRUCTURE</strong></td>
<td><strong>ACTIVITY</strong></td>
</tr>
<tr>
<td>Pharynx</td>
<td>Pharyngeal stage of deglutition.</td>
</tr>
<tr>
<td>Esophagus</td>
<td>Relaxation of upper esophageal sphincter.</td>
</tr>
<tr>
<td></td>
<td>Esophageal stage of deglutition (peristalsis).</td>
</tr>
<tr>
<td></td>
<td>Relaxation of lower esophageal sphincter.</td>
</tr>
<tr>
<td></td>
<td>Secretion of mucus.</td>
</tr>
</tbody>
</table>
Functions of the Stomach
1. Mixes saliva, food, and gastric juice to form chyme.
2. Serves as reservoir for food before release into small intestine.
3. Secretes gastric juice, which contains HCl (kills bacteria and denatures proteins), pepsin (begins the digestion of proteins), intrinsic factor (aids absorption of vitamin B<sub>12</sub>), and gastric lipase (aids digestion of triglycerides).
4. Secretes gastrin into blood.

Q After a very large meal, does your stomach still have rugae?
quantity of food. In the stomach, digestion of starch and triglycerides continues, digestion of proteins begins, the semisolid bolus is converted to a liquid, and certain substances are absorbed. The medical specialty that deals with the structure, function, diagnosis, and treatment of diseases of the stomach and intestines is called gastroenterology (gas′-trō-en-′-ter-OL-ō-jē; gastro- = stomach; -entero- = intestines; -logy = study of).

Anatomy of the Stomach

The stomach has four main regions: the cardia, fundus, body, and pyloric part (Figure 24.12). The cardia (KAR-dē-a) surrounds the opening of the esophagus into the stomach. The rounded portion superior to and to the left of the cardia is the fundus (FUN dus). Inferior to the fundus is the large central portion of the stomach, the body. The pyloric part is divisible into three regions. The first region, the pyloric antrum, connects to the body of the stomach. The second region, the pyloric canal, leads to the third region, the pylorus (pi -LOR-us; pyl- = gate; -orus = guard), which in turn connects to the duodenum. When the stomach is empty, the mucosa lies in large folds, or rugae (ROO-gē = wrinkles), that can be seen with the unaided eye. The pylorus communicates with the duodenum of the small intestine via a smooth muscle sphincter called the pyloric sphincter (valve). The concave medial border of the stomach is called the lesser curvature; the convex lateral border is called the greater curvature.

Clinical Connection

Pylorospasm and Pyloric Stenosis

Two abnormalities of the pyloric sphincter can occur in infants. In pylorospasm (pi -LOR-ō-spazm), the smooth muscle fibers of the sphincter fail to relax normally, so food does not pass easily from the stomach to the small intestine, the stomach becomes overly full, and the infant vomits often to relieve the pressure. Pylorospasm is treated by drugs that relax the muscle fibers of the pyloric sphincter. Pyloric stenosis (ste-NO-sis) is a narrowing of the pyloric sphincter that must be corrected surgically. The hallmark symptom is projectile vomiting—the spraying of liquid vomitus some distance from the infant.

Histology of the Stomach

The stomach wall is composed of the same basic layers as the rest of the GI tract, with certain modifications. The surface of the mucosa is a layer of simple columnar epithelial cells called surface mucous cells (Figure 24.13). The mucosa contains a lamina propria (areolar...
connective tissue) and a muscularis mucosae (smooth muscle) (Figure 24.13). Epithelial cells extend down into the lamina propria, where they form columns of secretory cells called gastric glands. Several gastric glands open into the bottom of narrow channels called gastric pits. Secretions from several gastric glands flow into each gastric pit and then into the lumen of the stomach.

The gastric glands contain three types of exocrine gland cells that secrete their products into the stomach lumen: mucous neck cells, chief cells, and parietal cells. Both surface mucous cells and mucous neck cells secrete mucus (Figure 24.13b). Parietal cells produce intrinsic factor (needed for absorption of vitamin B₁₂) and hydrochloric acid. The chief (zymogenic) cells secrete pepsinogen and gastric lipase. The secretions of the mucous, parietal, and chief cells form gastric juice, which totals 2000–3000 mL (roughly 2–3 qt) per day. In addition, gastric glands include a type of enteroendocrine cell, the G cell, which is located mainly in the pyloric antrum and secretes the hormone gastrin into the bloodstream. As we will see shortly, this hormone stimulates several aspects of gastric activity.

Three additional layers lie deep to the mucosa. The submucosa of the stomach is composed of areolar connective tissue. The muscularis has three layers of smooth muscle (rather than the two found in the esophagus and small and large intestines): an outer longitudinal layer, a middle circular layer, and an inner oblique layer. The oblique layer is limited primarily to the body of the stomach. The serosa is composed of simple squamous epithelium (mesothelium) and areolar connective tissue; the portion of the serosa covering the stomach is part of the visceral peritoneum. At the lesser curvature of the stomach, the visceral peritoneum extends upward to the liver as the lesser omentum. At the greater curvature of the stomach, the visceral peritoneum continues downward as the greater omentum and drapes over the intestines.
Mechanical and Chemical Digestion in the Stomach

Several minutes after food enters the stomach, waves of peristalsis pass over the stomach every 15 to 25 seconds. Few peristaltic waves are observed in the fundus, which primarily has a storage function. Instead, most waves begin at the body of the stomach and intensify as they reach the antrum. Each peristaltic wave moves gastric contents from the body of the stomach down into the antrum, a process known as propulsion. The pyloric sphincter normally remains almost, but not completely, closed. Because most food particles in the stomach initially are too large to fit through the narrow pyloric sphincter, they are forced back into the body of the stomach, a process referred to as retropulsion. Another round of propulsion then occurs, moving the food particles back down into the antrum. If the food particles are still too large to pass through the pyloric sphincter, retropulsion occurs again as the particles are squeezed back into the body of the stomach. Then yet another round of propulsion occurs and the cycle continues to repeat. The net result of these movements is that gastric contents are mixed with gastric juice, eventually becoming reduced to a soupy liquid called chyme (KIM = juice). Once the food particles in chyme are small enough, they can pass through the pyloric sphincter, a phenomenon known as gastric emptying. Gastric emptying is a slow process: only about 3 mL of chyme moves through the pyloric sphincter at a time.

Foods may remain in the fundus for about an hour without becoming mixed with gastric juice. During this time, digestion by salivary amylase from the salivary glands continues. Indeed, the churning action mixes chyme with acidic gastric juice, inactivating salivary amylase and activating lingual lipase produced by the tongue, which starts to digest triglycerides into fatty acids and diglycerides.

Although parietal cells secrete hydrogen ions (H\(^+\)) and chloride ions (Cl\(^-\)) separately into the stomach lumen, the net effect is secretion of hydrochloric acid (HCl). Proton pumps powered by H\(^+\)–K\(^+\) ATPases actively transport H\(^+\) into the lumen while bringing potassium ions (K\(^+\)) into the cell (Figure 24.14). At the same time, Cl\(^-\) and K\(^+\) diffuse out into the lumen through Cl\(^-\) and K\(^+\) channels in the apical membrane. The enzyme carbonic anhydrase, which is especially plentiful in parietal cells, catalyzes the formation of carbonic acid (H\(_2\)CO\(_3\)) from water (H\(_2\)O) and carbon dioxide (CO\(_2\)). As carbonic acid dissociates, it provides a ready source of H\(^+\) for the proton pumps but also generates bicarbonate ions (HCO\(_3^-\)). As HCO\(_3^-\) builds up in the cytosol, it exits the parietal cell in exchange for Cl\(^-\) via Cl\(^-\)–HCO\(_3^-\) antiporters in the basolateral membrane (next to the lamina propria). HCO\(_3^-\) diffuses into nearby blood capillaries. This “alkaline tide” of bicarbonate ions entering the bloodstream after a meal may be large enough to elevate blood pH slightly and make urine more alkaline.

HCl secretion by parietal cells can be stimulated by several sources: acetylcholine (ACH) released by parasympathetic neurons, gastrin secreted by G cells, and histamine, which is a paracrine substance released by mast cells in the nearby lamina propria (Figure 24.15). Acetylcholine and gastrin stimulate parietal cells to secrete more HCl in the presence of histamine. In other words, histamine acts synergistically, enhancing the effects of acetylcholine and gastrin. Receptors for all three substances are present in the plasma membrane of parietal cells. The histamine receptors on parietal cells are called H\(_2\) receptors; they mediate different responses than do the H\(_1\) receptors involved in allergic responses.

The strongly acidic fluid of the stomach kills many microbes in food. HCl partially denatures (unfolds) proteins in food and stimulates the secretion of hormones that promote the flow of bile and pancreatic juice. Enzymatic digestion of proteins also begins in the stomach. The only proteolytic (protein-digesting) enzyme in the stomach is pepsin, which is secreted by chief cells. Pepsin severs certain peptide bonds between amino acids, breaking down a protein chain of many amino acids into smaller peptide fragments. Pepsin is most effective in the very acidic environment of the stomach (pH 2); it becomes inactive at a higher pH.

What keeps pepsin from digesting the protein in stomach cells along with the food? First, pepsin is secreted in an inactive form called pepsinogen; in this form, it cannot digest the proteins in the chief cells...
that produce it. Pepsinogen is not converted into active pepsin until it comes in contact with hydrochloric acid secreted by parietal cells or active pepsin molecules. Second, the stomach epithelial cells are protected from gastric juices by a layer 1–3 mm thick of alkaline mucus secreted by surface mucous cells and mucous neck cells.

Another enzyme of the stomach is gastric lipase, which splits triglycerides (fats and oils) in fat molecules (such as those found in milk) into fatty acids and monoglycerides. A monoglyceride consists of a glycerol molecule that is attached to one fatty acid molecule. This enzyme, which has a limited role in the adult stomach, operates best at a pH of 5–6. More important than either lingual lipase or gastric lipase is pancreatic lipase, an enzyme secreted by the pancreas into the small intestine.

Only a small amount of nutrients are absorbed in the stomach because its epithelial cells are impermeable to most materials. However, mucous cells of the stomach absorb some water, ions, and short-chain fatty acids, as well as certain drugs (especially aspirin) and alcohol.

Within 2 to 4 hours after eating a meal, the stomach has emptied its contents into the duodenum. Foods rich in carbohydrate spend the least time in the stomach; high-protein foods remain somewhat longer, and emptying is slowest after a fat-laden meal containing large amounts of triglycerides.

Table 24.3 summarizes the digestive activities of the stomach.

**FIGURE 24.15** Regulation of HCl secretion.

HCl secretion by parietal cells can be stimulated by several sources: acetylcholine (ACh), gastrin, and histamine.

**Q** Among the sources that stimulate HCl secretion, which one is a paracrine agent that is released by mast cells in the lamina propria?

**TABLE 24.3** Summary of Digestive Activities in the Stomach

<table>
<thead>
<tr>
<th>STRUCTURE</th>
<th>ACTIVITY</th>
<th>RESULT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mucosa</strong></td>
<td>Surface mucous cells and mucous neck cells</td>
<td>Secrete mucus.</td>
</tr>
<tr>
<td></td>
<td>Absorption.</td>
<td>Small quantity of water, ions, short-chain fatty acids, and some drugs enter bloodstream.</td>
</tr>
<tr>
<td><strong>Parietal cells</strong></td>
<td>Secrete intrinsic factor.</td>
<td>Needed for absorption of vitamin B12 (used in red blood cell formation, or erythropoiesis).</td>
</tr>
<tr>
<td></td>
<td>Secrete hydrochloric acid.</td>
<td>Kills microbes in food; denatures proteins; converts pepsinogen into pepsin.</td>
</tr>
<tr>
<td><strong>Chief cells</strong></td>
<td>Secrete pepsinogen.</td>
<td>Pepsin (activated form) breaks down proteins into peptides.</td>
</tr>
<tr>
<td></td>
<td>Secrete gastric lipase.</td>
<td>Splits triglycerides into fatty acids and monoglycerides.</td>
</tr>
<tr>
<td><strong>G cells</strong></td>
<td>Secrete gastrin.</td>
<td>Stimulates parietal cells to secrete HCl and chief cells to secrete pepsinogen; contracts lower esophageal sphincter, increases motility of stomach, and relaxes pyloric sphincter.</td>
</tr>
<tr>
<td><strong>Muscularis</strong></td>
<td>Mixing waves (gentle peristaltic movements).</td>
<td>Churns and physically breaks down food and mixes it with gastric juice, forming chyme. Forces chyme through pyloric sphincter.</td>
</tr>
<tr>
<td><strong>Pyloric sphincter</strong></td>
<td>Opens to permit passage of chyme into duodenum.</td>
<td>Regulates passage of chyme from stomach to duodenum; prevents backflow of chyme from duodenum to stomach.</td>
</tr>
</tbody>
</table>

**Clinical Connection**

**Vomiting**

Vomiting or emesis is the forcible expulsion of the contents of the upper GI tract (stomach and sometimes duodenum) through the mouth. The strongest stimuli for vomiting are irritation and distension of the stomach; other stimuli include unpleasant sights, general anesthesia, dizziness, and certain drugs such as morphine and derivatives of digitalis. Nerve impulses are transmitted to the vomiting center in the medulla oblongata, and returning impulses propagate to the upper GI tract organs, diaphragm, and abdominal muscles. Vomiting involves squeezing the stomach between the diaphragm and abdominal muscles and expelling the contents through open esophageal sphincters. Prolonged vomiting, especially in infants and elderly people, can be serious because the loss of acidic gastric juice can lead to alkalosis (higher than normal blood pH), dehydration, and damage to the esophagus and teeth.
these accessory digestive organs and their contributions to digestion in the small intestine.

Anatomy of the Pancreas

The pancreas (pan- = all; -creas = flesh), a retroperitoneal gland that is about 12–15 cm (5–6 in.) long and 2.5 cm (1 in.) thick, lies posterior to the greater curvature of the stomach. The pancreas consists of a head, a body, and a tail and is usually connected to the duodenum of the small intestine by two ducts (Figure 24.16a). The head is the expanded portion of the organ near the curve of the duodenum; superior to and to the left of the head are the central body and the tapering tail.

Pancreatic juices are secreted by exocrine cells into small ducts that ultimately unite to form two larger ducts, the pancreatic duct and the accessory duct. These in turn convey the secretions into the small intestine. The pancreatic duct, or duct of Wirsung (VĒR-sung), is the larger of the two ducts. In most people, the pancreatic duct joins the common bile duct from the liver and gallbladder and enters the duodenum as a dilated common duct called the hepatopancreatic ampulla (hep′-a-tō-pan-krē-A-tik), or ampulla of Vater (FAH-ter). The ampulla opens on an elevation of the duodenal mucosa known as the major duodenal papilla, which lies about 10 cm (4 in.) inferior to the pyloric sphincter of the stomach. The passage of pancreatic juice and bile through the hepatopancreatic ampulla into the duodenum of the small intestine is controlled by the sphincter of the hepatopancreatic ampulla, also known as the sphincter of Oddi.

Pancreatic enzymes digest starches (polysaccharides), proteins, triglycerides, and nucleic acids.
the functions of these hormones are discussed in Chapter 18.

Composition and Functions of Pancreatic Juice

Each day the pancreas produces 1200–1500 mL (about 1.2–1.5 qt) of pancreatic juice, a clear, colorless liquid consisting mostly of water, some salts, sodium bicarbonate, and several enzymes. The sodium bicarbonate gives pancreatic juice a slightly alkaline pH (7.1–8.2) that buffers acidic gastric juice in chyme, stops the action of pepsin from the stomach, and creates the proper pH for the action of digestive enzymes in the small intestine. The enzymes in pancreatic juice include a starch-digesting enzyme called pancreatic amylase; several enzymes that digest proteins into peptides called trypsin (TRIP-sin), chymotrypsin (ki’-mō-TRIP-sin), carboxypeptidase...
The protein-digesting enzymes of the pancreas are produced in an inactive form just as pepsin is produced in the stomach as pepsino-
gen. Because they are inactive, the enzymes do not digest cells of the pancreas itself. Trypsin is secreted in an inactive form called trypsin-
gen (trip-SIN-o-jen). Pancreatic acinar cells also secrete a protein called trypsin inhibitor that combines with any trypsin formed accident-
ally in the pancreas or in pancreatic juice and blocks its enzymatic activity. When trypsinogen reaches the lumen of the small intestine, it
encounters an activating brush-border enzyme called enterokinase (en-ter-ō-KI-nās), which splits off part of the trypsinogen molecule to form trypsin. In turn, trypsin acts on the inactive precursors (called chymotrypsinogen, procarboxypeptidase, and proelastase) to produce chymotrypsin, carboxypeptidase, and elastase, respectively.

Anatomy of the Liver and Gallbladder

The liver is almost completely covered by visceral peritoneum and is completely covered by a dense irregular connective tissue layer that lies deep to the peritoneum. The liver is divided into two principal lobes—a large right lobe and a smaller left lobe—by the falciform ligament, a fold of the mesentery (Figure 24.16a). Although the right lobe is considered by many anatomists to include an inferior quadrate lobe (kwa-DRÄT) and a posterior caudate lobe (KAW-dät), based on internal morphology (primarily the distribution of blood vessels), the quadrate and caudate lobes more appropriately belong to the left lobe. The falciform ligament extends from the undersurface of the diaphragm between the two principal lobes of the liver to the superior surface of the liver, helping to suspend the liver in the abdominal cavity. In the free border of the falciform ligament is the ligamentum teres (round ligament), a remnant of the umbilical vein of the fetus (see 21.31a, b); this fibrous cord extends from the liver to the umbilicus. The right and left coronary ligaments are narrow extensions of the parietal peritoneum that suspend the liver from the diaphragm.

The parts of the gallbladder include the broad fundus, which projects inferiorly beyond the inferior border of the liver; the body, the central portion; and the neck, the tapered portion. The body and neck project superiorly.

Histology of the Liver and Gallbladder

Histologically, the liver is composed of several components (Figure 24.17a–c):

1. Hepatocytes. Hepatocytes (hepat- = liver; -cytes = cells) are the major functional cells of the liver and perform a wide array of meta-
bolic, secretory, and endocrine functions. These are specialized epithelial cells with 5 to 12 sides that make up about 80% of the volume of the liver. Hepatocytes form complex three-dimensional arrangements called hepatic laminae (LAM-i-nē). The hepatic...
Histologically, the liver is composed of hepatocytes, bile canaliculi, and hepatic sinusoids.
CHAPTER 24  The Digestive System

Gastrointestinal organs and spleen into the liver. Hepatic sinusoids converge and deliver blood into a central vein. From central veins the blood flows into the hepatic veins, which drain into the inferior vena cava (see Figure 21.29). In contrast to blood, which flows toward a central vein, bile flows in the opposite direction. Also present in the hepatic sinusoids are fixed phagocytes called stellate reticuloendothelial cells (STEL-āt re-tik′-lo-en-dō-THÉ-lē-al) or hepatic macrophages, which destroy worn-out white and red blood cells, bacteria, and other foreign matter in the venous blood draining from the gastrointestinal tract.

Together, a bile duct, branch of the hepatic artery, and branch of the hepatic vein are referred to as a portal triad (tri- = three).

The hepatocytes, bile duct system, and hepatic sinusoids can be organized into anatomical and functional units in three different ways:

1. **Hepatic lobule.** For years, anatomists described the hepatic lobule as the functional unit of the liver. According to this model, each hepatic lobule is shaped like a hexagon (six-sided structure) (Figure 24.17d, left). At its center is the central vein, and radiating out from it are rows of hepatocytes and hepatic sinusoids. Located at three corners of the hexagon is a portal triad. This model is based on a description of the liver of adult pigs. In the human liver it is difficult to

**Q Which type of cell in the liver is phagocytic?**

**Bile canaliculi.** Bile canaliculi (kan-a-LIK-ū-li = small canals) are small ducts between hepatocytes that collect bile produced by the hepatocytes. From bile canaliculi, bile passes into bile ductules and then bile ducts. The bile ducts merge and eventually form the larger right and left hepatic ducts, which unite and exit the liver as the common hepatic duct (see Figure 24.16). The common hepatic duct joins the cystic duct (cystic = bladder) from the gallbladder to form the common bile duct. From here, bile enters the duodenum of the small intestine to participate in digestion.

3. **Hepatic sinusoids.** Hepatic sinusoids are highly permeable blood capillaries between rows of hepatocytes that receive oxygenated blood from branches of the hepatic artery and nutrient-rich deoxygenated blood from branches of the hepatic portal vein. Recall that the hepatic portal vein brings venous blood from the gastrointestinal organs and spleen into the liver. Hepatic sinusoids converge and deliver blood into a central vein. From central veins the blood flows into the hepatic veins, which drain into the inferior vena cava (see Figure 21.29). In contrast to blood, which flows toward a central vein, bile flows in the opposite direction. Also present in the hepatic sinusoids are fixed phagocytes called stellate reticuloendothelial cells (STEL-āt re-tik′-lo-en-dō-THÉ-lē-al) or hepatic macrophages, which destroy worn-out white and red blood cells, bacteria, and other foreign matter in the venous blood draining from the gastrointestinal tract.

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find such well-defined hepatic lobules surrounded by thick layers of connective tissue.

2. Portal lobule. This model emphasizes the exocrine function of the liver, that is, bile secretion. Accordingly, the bile duct of a portal triad is taken as the center of the portal lobule. The portal lobule is triangular in shape and is defined by three imaginary straight lines that connect three central veins that are closest to the portal triad (Figure 24.17d, center). This model has not gained widespread acceptance.

3. Hepatic acinus. In recent years, the preferred structural and functional unit of the liver is the hepatic acinus (AS-i-nus). Each hepatic acinus is an approximately oval mass that includes portions of two neighboring hepatic lobules. The short axis of the hepatic acinus is defined by branches of the portal triad—branches of the hepatic artery, vein, and bile ducts—that run along the border of the hepatic lobules. The long axis of the acinus is defined by two imaginary curved lines, which connect the two central veins closest to the short axis (Figure 24.17d, bottom). Hepatocytes in the hepatic acinus are arranged in three zones around the short axis, with no sharp boundaries between them (Figure 24.17e). Cells in zone 1 are closest to the branches of the portal triad and the first to receive incoming oxygen, nutrients, and toxins from incoming blood. These cells are the first ones to take up glucose and store it as glycogen after a meal and break down glycogen to glucose during fasting. They are also the first to show morphological changes following bile duct obstruction or exposure to toxic substances. Zone 1 cells are the last ones to die if circulation is impaired and the first ones to regenerate. Cells in zone 3 are farthest from branches of the portal triad and are the last to show the effects of bile obstruction or exposure to toxins, the first ones to show the effects of impaired circulation, and the last ones to regenerate. Zone 3 cells also are the first to show evidence of fat accumulation. Cells in zone 2 have structural and functional characteristics intermediate between the cells in zones 1 and 3.

The hepatic acinus is the smallest structural and functional unit of the liver. Its popularity and appeal are based on the fact that it provides a logical description and interpretation of (1) patterns of glycogen storage and release and (2) toxic effects, degeneration, and regeneration relative to the proximity of the acinar zones to branches of the portal triad.

Clinical Connection

Jaundice

Jaundice (JAWN-dis = yellowed) is a yellowish coloration of the sclerae (whites of the eyes), skin, and mucous membranes due to a buildup of a yellow compound called bilirubin. After bilirubin is formed from the breakdown of the heme pigment in aged red blood cells, it is transported to the liver, where it is processed and eventually excreted into bile. The three main categories of jaundice are (1) prehepatic jaundice, due to excess production of bilirubin; (2) hepatic jaundice, due to congenital liver disease, cirrhosis of the liver, or hepatitis; and (3) extrahepatic jaundice, due to blockage of bile drainage by gallstones or cancer of the bowel or the pancreas.

Because the liver of a newborn functions poorly for the first week or so, many babies experience a mild form of jaundice called neonatal (physiological) jaundice that disappears as the liver matures. Usually, it is treated by exposing the infant to blue light, which converts bilirubin into substances the kidneys can excrete.

The mucosa of the gallbladder consists of simple columnar epithelium arranged in rugae resembling those of the stomach. The wall of the gallbladder lacks a submucosa. The middle, muscular coat of the wall consists of smooth muscle fibers. Contraction of the smooth muscle fibers ejects the contents of the gallbladder into the cystic duct. The gallbladder’s outer coat is the visceral peritoneum. The functions of the gallbladder are to store and concentrate the bile produced by the liver (up to tenfold) until it is needed in the duodenum. In the concentration process, water and ions are absorbed by the gallbladder mucosa. Bile aids in the digestion and absorption of fats.

**Blood Supply of the Liver**

The liver receives blood from two sources (Figure 24.18). From the hepatic artery it obtains oxygenated blood, and from the hepatic portal vein it receives deoxygenated blood containing newly absorbed nutrients, drugs, and possibly microbes and toxins from the gastrointestinal tract (see Figure 21.29). Branches of both the hepatic artery and the hepatic portal vein carry blood into hepatic sinusoids, where oxygen, most of the nutrients, and certain toxic substances are taken up by the hepatocytes. Products manufactured by the hepatocytes and nutrients needed by other cells are secreted back into the blood, which then drains into the central vein and eventually passes into a hepatic vein. Because blood from the gastrointestinal tract passes

**FIGURE 24.18** Hepatic blood flow: sources, path through the liver, and return to the heart.

The liver receives oxygenated blood via the hepatic artery and nutrient-rich deoxygenated blood via the hepatic portal vein.
through the liver as part of the hepatic portal circulation, the liver is often a site for metastasis of cancer that originates in the GI tract.

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### Liver Function Tests

**Liver function tests** are blood tests designed to determine the presence of certain chemicals released by liver cells. These include albumin globulin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl-transpeptidase (GGT), and bilirubin. The tests are used to evaluate and monitor liver disease or damage. Common causes of elevated liver enzymes include nonsteroidal anti-inflammatory drugs, cholesterol-lowering medications, some antibiotics, alcohol, diabetes, infections (viral hepatitis and mononucleosis), gallstones, tumors of the liver, and excessive use of herbal supplements such as kava, comfrey, pennyroyal, dandelion root, skullcap, and ephedra.

### Functions of the Liver and Gallbladder

Each day, hepatocytes secrete 800–1000 mL (about 1 qt) of **bile**, a yellow, brownish, or olive-green liquid. It has a pH of 7.6–8.6 and consists mostly of water, bile salts, cholesterol, a phospholipid called lecithin, bile pigments, and several ions.

The principal bile pigment is **bilirubin** (bil-i-ROO-bin). The phagocytosis of aged red blood cells liberates iron, globin, and bilirubin (derived from heme) (see Figure 19.5). The iron and globin are recycled; the bilirubin is secreted into the bile and is eventually broken down in the intestine. One of its breakdown products—**stercobilin** (ster-kō-BI-lin)—gives feces their normal brown color.

Bile is partially an excretory product and partially a digestive secretion. Bile salts, which are sodium salts and potassium salts of bile acids (mostly chenodeoxycholic acid and cholic acid), play a role in **emulsification** (e-mul’-si-fi-KĀ-shun), the breakdown of large lipid globules into a suspension of small lipid globules. The small lipid globules present a very large surface area that allows pancreatic lipase to more rapidly accomplish digestion of triglycerides. Bile salts also aid in the absorption of lipids following their digestion.

Although hepatocytes continually release bile, they increase production and secretion when the portal blood contains more bile acids; thus, as digestion and absorption continue in the small intestine, bile release increases. Between meals, after most absorption has occurred, bile flows into the gallbladder for storage because the sphincter of the hepatopancreatic ampulla (sphincter of Oddi; see Figure 24.16) closes off the entrance to the duodenum. The sphincter surrounds the hepatopancreatic ampulla.

In addition to secreting bile, which is needed for absorption of dietary fats, the liver performs many other vital functions:

- **Carbohydrate metabolism.** The liver is especially important in maintaining a normal blood glucose level. When blood glucose is low, the liver can break down glycogen to glucose and release the glucose into the bloodstream. The liver can also convert certain amino acids and lactic acid to glucose, and it can convert other sugars, such as fructose and galactose, into glucose. When blood glucose is high, as occurs just after eating a meal, the liver converts glucose to glycogen and triglycerides for storage.

- **Lipid metabolism.** Hepatocytes store some triglycerides; break down fatty acids to generate ATP; synthesize lipoproteins, which transport fatty acids, triglycerides, and cholesterol to and from body cells; synthesize cholesterol; and use cholesterol to make bile salts.

- **Protein metabolism.** Hepatocytes deaminate (remove the amino group, NH₃, from) amino acids so that the amino acids can be used for ATP production or converted to carbohydrates or fats. The resulting toxic ammonia (NH₃) is then converted into the much less toxic urea, which is excreted in urine. Hepatocytes also synthesize most plasma proteins, such as alpha and beta globulins, albumin, prothrombin, and fibrinogen.

- **Processing of drugs and hormones.** The liver can detoxify substances such as alcohol and excrete drugs such as penicillin, erythromycin, and sulfonamides into bile. It can also chemically alter or excrete thyroid hormones and steroid hormones such as estrogens and aldosterone.

- **Excretion of bilirubin.** As previously noted, bilirubin, derived from the heme of aged red blood cells, is absorbed by the liver from the blood and secreted into bile. Most of the bilirubin in bile is metabolized in the small intestine by bacteria and eliminated in feces.

- **Synthesis of bile salts.** Bile salts are used in the small intestine for the emulsification and absorption of lipids.

- **Storage.** In addition to glycogen, the liver is a prime storage site for certain vitamins (A, B₁₂, D, E, and K) and minerals (iron and copper), which are released from the liver when needed elsewhere in the body.

- **Phagocytosis.** The stellate reticuloendothelial (Kupffer) cells of the liver phagocytize aged red blood cells, white blood cells, and some bacteria.

- **Activation of vitamin D.** The skin, liver, and kidneys participate in synthesizing the active form of vitamin D.

The liver functions related to metabolism are discussed more fully in Chapter 25.
24.12 Small Intestine

**OBJECTIVES**

- Describe the location and structure of the small intestine.
- Identify the functions of the small intestine.

Most digestion and absorption of nutrients occur in a long tube called the small intestine. Because of this, its structure is specially adapted for these functions. Its length alone provides a large surface area for digestion and absorption, and that area is further increased by circular folds, villi, and microvilli. The small intestine begins at the pyloric sphincter of the stomach, coils through the central and inferior part of the abdominal cavity, and eventually opens into the large intestine. It averages 2.5 cm (1 in.) in diameter; its length is about 3 m (10 ft) in a living person and about 6.5 m (21 ft) in a cadaver due to the loss of smooth muscle tone after death.

**Anatomy of the Small Intestine**

The small intestine is divided into three regions (Figure 24.19). The first part of the small intestine is the *duodenum* (doo-‘ō-DĒ-num or doo-OD-e-num), the shortest region, and is retroperitoneal. It starts at the pyloric sphincter of the stomach and is in the form of a C-shaped tube that extends about 25 cm (10 in.) until it merges with the jejunum. *Duodenum* means “12”; it is so named because it is about as long as the width of 12 fingers. The *jejunum* (je-JOO-num) is the next portion and is about 1 m (3 ft) long and extends to the ileum. *Jejunum* means “empty,” which is how it is found at death. The final and longest region of the small intestine, the *ileum* (IL-ē-um = twisted), measures about 2 m (6 ft) and joins the large intestine at a smooth muscle sphincter called the *ileocecal sphincter* (valve) (il′-ē-ō-SĒ-kal).

**Histology of the Small Intestine**

The wall of the small intestine is composed of the same four layers that make up most of the GI tract: mucosa, submucosa, muscularis, and serosa (Figure 24.20b). The mucosa is composed of a layer of epithelium, lamina propria, and muscularis mucosae. The epithelial layer of the small intestinal mucosa consists of simple columnar epithelium.

**Functions of the Small Intestine**

1. Segmentations mix chyme with digestive juices and bring food into contact with mucosa for absorption; peristalsis propels chyme through small intestine.
2. Completes digestion of carbohydrates, proteins, and lipids; begins and completes digestion of nucleic acids.
3. Absorbs about 90% of nutrients and water that pass through digestive system.
FIGURE 24.20  Histology of the small intestine.

Circular folds, villi, and microvilli increase the surface area of the small intestine for digestion and absorption.

(a) Relationship of villi to circular folds

(b) Three-dimensional view of layers of the small intestine showing villi
Paneth cells may have a role in regulating the microbial population in the small intestine. Three types of enteroendocrine cells are found in the intestinal glands of the small intestine: S cells, CCK cells, and K cells, which secrete the hormones secretin (se-KRE-tin), cholecystokinin (CCK) (kō-lē-sis′-tō-KI-N-in), and glucose-dependent insulinoergic peptide (GIP) (in-soo-lin′-ō-TRÖ-pik), respectively.

The lamina propria of the small intestinal mucosa contains areolar connective tissue and has an abundance of mucosa-associated lymphoid tissue (MALT). Solitary lymphatic nodules are most numerous in the distal part of the ileum (see Figure 24.21c). Groups of
FIGURE 24.21 Histology of the duodenum and ileum.

Microvilli in the small intestine contain several brush-border enzymes that help digest nutrients.

Lumen of duodenum
Villus
Absorptive epithelium with brush border
Lamina propria

Mucosa
Intestinal gland
Muscularis mucosae
Duodenal gland in submucosa

Submucosa
Duodenal gland in submucosa

Muscularis
Serosa

(a) Wall of the duodenum

(b) Three villi from the duodenum

(c) Lymphatic nodules in ileum

Lumen of ileum
Villus
Solitary lymphatic nodule
Submucosa
Muscularis

(c) Lymphatic nodules in ileum

(d) Several microvilli from duodenum

(e) Microvilli of small intestine

Q What is the function of the fluid secreted by duodenal (Brunner’s) glands?

lymphatic nodules referred to as aggregated lymphatic follicles, or Peyer’s patches (Pl-erz), are also present in the ileum. The muscularis mucosae of the small intestinal mucosa consists of smooth muscle.

The submucosa of the duodenum contains duodenal glands, also called Brunner's glands (BRUN-erz) (Figure 24.21a), which secrete an alkaline mucus that helps neutralize gastric acid in the chyme. Sometimes the lymphatic tissue of the lamina propria extends through the muscularis mucosae into the submucosa. The muscularis of the small intestine consists of two layers of smooth muscle. The outer, thinner layer contains longitudinal fibers; the inner, thicker
layer contains circular fibers. Except for a major portion of the duodenum, which is retroperitoneal, the serosa (or visceral peritoneum) completely surrounds the small intestine.

Even though the wall of the small intestine is composed of the same four basic layers as the rest of the GI tract, special structural features of the small intestine facilitate the process of digestion and absorption. These structural features include circular folds, villi, and microvilli. **Circular folds** or *plicae circulares* are folds of the mucosa and submucosa (see Figures 24.19b and 24.20a). These permanent ridges, which are about 10 mm (0.4 in.) long, begin near the proximal portion of the duodenum and end at about the midportion of the ileum. Some extend all the way around the circumference of the intestine; others extend only part of the way around. Circular folds enhance absorption by increasing surface area and causing the chyme to spiral, rather than move in a straight line, as it passes through the small intestine.

Also present in the small intestine are **villi** (tufts of hair), which are fingerlike projections of the mucosa that are 0.5–1 mm long (see Figure 24.20b, c). The large number of villi (20–40 per square millimeter) vastly increases the surface area of the epithelium available for absorption and digestion and gives the intestinal mucosa a velvety appearance. Each villus (singular form) is covered by epithelium and has a core of lamina propria; embedded in the connective tissue of the lamina propria are an arteriole, a venule, a blood capillary network, and a **lacteal** (milky), which is a lymphatic capillary (see Figure 24.20c). Nutrients absorbed by the epithelial cells covering the villus pass through the wall of a capillary or a lacteal to enter blood or lymph, respectively.

Besides circular folds and villi, the small intestine also has **microvilli** (mi-krō-VIL-i; micro- = small), which are projections of the apical (free) membrane of the absorptive cells. Each microvillus is a 1-μm-long cylindrical, membrane-covered projection that contains a bundle of 20–30 actin filaments. When viewed through a light microscope, the microvilli are too small to be seen individually; instead they form a fuzzy line, called the **brush border**, extending into the lumen of the small intestine (Figure 24.21d). There are an estimated 200 million microvilli per square millimeter of small intestine. Because the microvilli greatly increase the surface area of the plasma membrane, larger amounts of digested nutrients can diffuse into absorptive cells in a given period. The brush border also contains several brush-border enzymes that have digestive functions (discussed shortly).

### Role of Intestinal Juice and Brush-Border Enzymes

About 1–2 liters (1–2 qt) of **intestinal juice**, a clear yellow fluid, is secreted each day. Intestinal juice contains water and mucus and is slightly alkaline (pH 7.6). The alkaline pH of intestinal juice is due to its high concentration of bicarbonate ions (HCO₃⁻). Together, pancreatic and intestinal juices provide a liquid medium that aids the absorption of substances from chyme in the small intestine. The absorptive cells of the small intestine synthesize several digestive enzymes, called **brush-border enzymes**, and insert them in the plasma membrane of the microvilli. Thus, some enzymatic digestion occurs at the surface of the absorptive cells that line the villi, rather than in the lumen exclusively, as occurs in other parts of the GI tract. Among the brush-border enzymes are four carbohydrate-digesting enzymes called α-dextrinase, maltase, sucrase, and lactase; protein-digesting enzymes called peptidases (aminopeptidase and dipeptidase); and two types of nucleotide-digesting enzymes, nucleosidases and phosphatases. Also, as absorptive cells slough off into the lumen of the small intestine, they break apart and release enzymes that help digest nutrients in the chyme.

### Mechanical Digestion in the Small Intestine

The two types of movements of the small intestine—segmentations and a type of peristalsis called migrating motility complexes—are governed mainly by the myenteric plexus. **Segmentations** are localized, mixing contractions that occur in portions of intestine distilled by a large volume of chyme. Segmentations mix chyme with the digestive juices and bring the particles of food into contact with the mucosa for absorption; they do not push the intestinal contents along the tract. A segmentation starts with the contractions of circular muscle fibers in a portion of the small intestine, an action that constricts the intestine into segments. Next, muscle fibers that encircle the middle of each segment also contract, dividing each segment again. Finally, the fibers that first contracted relax, and each small segment unites with an adjoining small segment so that large segments are formed again. As this sequence of events repeats, the chyme sloshes back and forth. Segmentations occur most rapidly in the duodenum, about 12 times per minute, and progressively slow to about 8 times per minute in the ileum. This movement is similar to alternately squeezing the middle and then the ends of a capped tube of toothpaste.

After most of a meal has been absorbed, which lessens distension of the wall of the small intestine, segmentation stops and peristalsis begins. The type of peristalsis that occurs in the small intestine, termed a **migrating motility complex** (**MMC**), begins in the lower portion of the stomach and pushes chyme forward along a short stretch of small intestine before dying out. The MMC slowly migrates down the small intestine, reaching the end of the ileum in 90–120 minutes. Then another MMC begins in the stomach. Altogether, chyme remains in the small intestine for 3–5 hours.

### Chemical Digestion in the Small Intestine

In the mouth, salivary amylase converts starch (a polysaccharide) to maltose (a disaccharide), maltotriose (a trisaccharide), and α-dextrins (short-chain, branched fragments of starch with 5–10 glucose units). In the stomach, pepsin converts proteins to peptides (small fragments of proteins), and lingual and gastric lipases convert some triglycerides into fatty acids, diglycerides, and monoglycerides. Thus, chyme entering the small intestine contains partially digested carbohydrates, proteins, and lipids. The completion of the digestion of carbohydrates, proteins, and lipids is a collective effort of pancreatic juice, bile, and intestinal juice in the small intestine.
**Digestion of Carbohydrates** Even though the action of salivary amylase may continue in the stomach for a while, the acidic pH of the stomach destroys salivary amylase and ends its activity. Thus, only a few starches are broken down by the time chyme leaves the stomach. Those starches not already broken down into maltose, maltotriose, and α-dextrins are cleaved by **pancreatic amylase**, an enzyme in pancreatic juice that acts in the small intestine. Although pancreatic amylase acts on both glycogen and starches, it has no effect on another polysaccharide called cellulose, an indigestible plant fiber that is commonly referred to as "roughage" as it moves through the digestive system. After amylase (either salivary or pancreatic) has split starch into smaller fragments, a brush-border enzyme called **α-dextrinase** acts on the resulting α-dextrins, clipping off one glucose unit at a time.

Ingested molecules of sucrose, lactose, and maltose—three disaccharides—are not acted on until they reach the small intestine. Three brush-border enzymes digest the disaccharides into monosaccharides. **Sucrase** breaks sucrose into a molecule of glucose and a molecule of fructose; **lactase** digests lactose into a molecule of glucose and a molecule of galactose; and **maltase** splits maltose and maltotriose into two or three molecules of glucose, respectively. Digestion of carbohydrates ends with the production of monosaccharides, which the digestive system is able to absorb.

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### Clinical Connection

#### Lactose Intolerance

In some people the absorptive cells of the small intestine fail to produce enough lactase, which, as you just learned, is essential for the digestion of lactose. This results in a condition called **lactase intolerance**, in which undigested lactose in chyme causes fluid to be retained in the feces; bacterial fermentation of the undigested lactose results in the production of gases. Symptoms of lactose intolerance include diarrhea, gas, bloating, and abdominal cramps after consumption of milk and other dairy products. The symptoms can be relatively minor or serious enough to require medical attention. The **hydrogen breath test** is often used to aid in diagnosis of lactose intolerance. Very little hydrogen can be detected in the breath of a normal person, but hydrogen is among the gases produced when undigested lactose in the colon is fermented by bacteria. The hydrogen is absorbed from the intestines and carried through the bloodstream to the lungs, where it is exhaled. Persons with lactose intolerance should select a diet that restricts lactose (but not calcium) and take dietary supplements to aid in the digestion of lactose.

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**Digestion of Proteins** Recall that protein digestion starts in the stomach, where proteins are fragmented into peptides by the action of pepsin. Enzymes in pancreatic juice—trypsin, chymotrypsin, carboxypeptidase, and elastase—continue to break down proteins into peptides. Although all of these enzymes convert whole proteins into peptides, their actions differ somewhat because each splits peptide bonds between different amino acids. Trypsin, chymotrypsin, and elastase all cleave the peptide bond between a specific amino acid and its neighbor; carboxypeptidase splits off the amino acid at the carboxyl end of a peptide. Protein digestion is completed by two **peptidases** in the brush border: aminopeptidase and dipeptidase. **Aminopeptidase** cleaves off the amino acid at the amino end of a peptide. **Dipeptidase** splits dipeptides (two amino acids joined by a peptide bond) into single amino acids.

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**Digestion of Lipids** The most abundant lipids in the diet are triglycerides, which consist of a molecule of glycerol bonded to three fatty acid molecules (see Figure 2.17). Enzymes that split triglycerides and phospholipids are called **lipases**. Recall that there are three types of lipases that can participate in lipid digestion: lingual lipase, gastric lipase, and pancreatic lipase. Although some lipid digestion occurs in the stomach through the action of lingual and gastric lipases, most occurs in the small intestine through the action of pancreatic lipase. Triglycerides are broken down by pancreatic lipase into fatty acids and monoglycerides. The liberated fatty acids can be either short-chain fatty acids (with fewer than 10–12 carbons) or long-chain fatty acids.

Before a large lipid globule containing triglycerides can be digested in the small intestine, it must first undergo emulsification—a process in which the large lipid globule is broken down into several small lipid globules. Recall that bile contains bile salts, the sodium salts and potassium salts of bile acids (mainly chenodeoxycholic acid and cholic acid). Bile salts are **amphipathic** (am′-fē-PATH-ik), which means that each bile salt has a hydrophobic (nonpolar) region and a hydrophilic (polar) region. The amphipathic nature of bile salts allows them to emulsify a large lipid globule: The hydrophobic regions of bile salts interact with the large lipid globule, while the hydrophilic regions of bile salts interact with the watery intestinal chyme. Consequently, the large lipid globule is broken apart into several small lipid globules, each about 1 μm in diameter. The small lipid globules formed from emulsification provide a large surface area that allows pancreatic lipase to function more effectively.

**Digestion of Nucleic Acids** Pancreatic juice contains two nucleases: ribonuclease, which digests RNA, and deoxyribonuclease, which digests DNA. The nucleotides that result from the action of the two nucleases are further digested by brush-border enzymes called **nucleosidases** (nuoo′-klē-ō-Sī-dāz-ez) and **phosphatases** (FOS-fā-tās′-ez) into pentoses, phosphates, and nitrogenous bases. These products are absorbed via active transport.

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**Absorption in the Small Intestine**

All of the chemical and mechanical phases of digestion from the mouth through the small intestine are directed toward changing food into forms that can pass through the absorptive epithelial cells lining the mucosa and into the underlying blood and lymphatic vessels. These forms are monosaccharides (glucose,
fructose, and galactose) from carbohydrates; single amino acids, dipeptides, and tripeptides from proteins; and fatty acids, glycerol, and monoglycerides from triglycerides. Passage of these digested nutrients from the gastrointestinal tract into the blood or lymph is called absorption.

Absorption of materials occurs via diffusion, facilitated diffusion, osmosis, and active transport. About 90% of all absorption of nutrients occurs in the small intestine; the other 10% occurs in the stomach and large intestine. Any undigested or unabsorbed material left in the small intestine passes on to the large intestine.

**Absorption of Monosaccharides** All carbohydrates are absorbed as monosaccharides. The capacity of the small intestine to absorb monosaccharides is huge—an estimated 120 grams per hour. As a result, all dietary carbohydrates that are digested normally are absorbed, leaving only indigestible cellulose and fibers in the feces. Monosaccharides pass from the lumen through the apical membrane via facilitated diffusion or active transport. Fructose, a monosaccharide found in fruits, is transported via facilitated diffusion; glucose and galactose are transported into absorptive cells of the villi via secondary active transport that is coupled to the active transport of Na⁺ (Figure 24.22a). The transporter has binding sites for one glucose molecule and two sodium ions; unless all three sites are filled, neither substance is transported. Galactose competes with glucose to ride the same transporter. (Because both Na⁺ and glucose or galactose move in the same direction, this is a symporter.) Monosaccharides then move out of the absorptive cells through their basolateral surfaces via facilitated diffusion and enter the capillaries of the villi (Figure 24.22b).

**Absorption of Amino Acids, Dipeptides, and Tripeptides** Most proteins are absorbed as amino acids via active transport processes that occur mainly in the duodenum and jejunum. About half of the absorbed amino acids are present in food; the other half come from the body itself as proteins in digestive juices and dead cells that slough off the mucosal surface! Normally, 95–98% of the protein present in the small intestine is digested and absorbed. Different transporters carry different types of amino acids. Some amino acids enter absorptive cells of the villi via Na⁺-dependent secondary active transport processes that are similar to the glucose transporter; other amino acids are actively transported by themselves. At least one symporter brings in dipeptides and tripeptides together with H⁺; the peptides then are hydrolyzed to single amino acids inside the absorptive cells. Amino acids move out of the absorptive cells via diffusion and enter capillaries of the villus (Figure 24.22). Both monosaccharides and amino acids are transported in the blood to the liver by way of the hepatic portal system. If not removed by hepatocytes, they enter the general circulation.

**Absorption of Lipids and Bile Salts** All dietary lipids are absorbed via simple diffusion. Adults absorb about 95% of the lipids present in the small intestine; due to their lower production of bile, newborn infants absorb only about 85% of lipids. As a result of their emulsification and digestion, triglycerides are mainly broken down into monoglycerides and fatty acids, which can be either short-chain fatty acids or long-chain fatty acids. Small short-chain fatty acids are hydrophobic, contain less than 10–12 carbon atoms, and are more water-soluble. Thus, they can dissolve in the watery intestinal chyme, pass through the absorptive cells via simple diffusion, and follow the same route taken by monosaccharides and amino acids into a blood capillary of a villus (Figure 24.22a).

Large short-chain fatty acids (with more than 10–12 carbon atoms), long-chain fatty acids, and monoglycerides are larger and hydrophobic, and since they are not water-soluble, they have difficulty being suspended in the watery environment of the intestinal chyme. Besides their role in emulsification, bile salts also help to make these large short-chain fatty acids, long-chain fatty acids, and monoglycerides more soluble. The bile salts in intestinal chyme surround them, forming tiny spheres called micelles (mi-SElz = small morsels), each of which is 2–10 nm in diameter and includes 20–50 bile salt molecules (Figure 24.22a). Micelles are formed due to the amphipathic nature of bile salts: The hydrophobic regions of bile salts interact with the large short-chain fatty acids, long-chain fatty acids, and monoglycerides, and the hydrophilic regions of bile salts interact with the watery intestinal chyme. Once formed, the micelles move from the interior of the small intestinal lumen to the brush border of the absorptive cells. At that point, the large short-chain fatty acids, long-chain fatty acids, and monoglycerides diffuse out of the micelles into the absorptive cells, leaving the micelles behind in the chyme. The micelles continually repeat this ferrying function as they move from the brush border back through the chyme to the interior of the small intestinal lumen to pick up more of the large short-chain fatty acids, long-chain fatty acids, and monoglycerides. Micelles also solubilize other large hydrophobic molecules such as fat-soluble vitamins (A, D, E, and K) and cholesterol that may be present in intestinal chyme, and aid in their absorption. These fat-soluble vitamins and cholesterol molecules are packed in the micelles along with the long-chain fatty acids and monoglycerides.

Once inside the absorptive cells, long-chain fatty acids and monoglycerides are recombined to form triglycerides, which aggregate into globules along with phospholipids and cholesterol and become coated with proteins. These large spherical masses, about 80 nm in diameter, are called chylomicrons (ki-lo-Mi-krons). Chylomicrons leave the absorptive cell via exocytosis. Because they are so large and bulky, chylomicrons cannot enter blood capillaries—the pores in the walls of blood capillaries are too small. Instead, chylomicrons enter lacteals, which have much larger pores than blood capillaries. From lacteals, chylomicrons are transported by way of lymphatic vessels to the thoracic duct and enter the blood at the junction of the left internal jugular and left subclavian veins (Figure 24.22b). The hydrophilic protein coat that surrounds each chylomicron keeps the chylomicrons suspended in blood and prevents them from sticking to each other.

Within 10 minutes after absorption, about half of the chylomicrons have already been removed from the blood as they pass through blood capillaries in the liver and adipose tissue. This
**Absorption of digested nutrients in the small intestine.** For simplicity, all digested foods are shown in the lumen of the small intestine, even though some nutrients are digested by brush-border enzymes.

Long-chain fatty acids and monoglycerides are absorbed into lacteals; other products of digestion enter blood capillaries.

To blood capillary of a villus

Hepatic portal vein

Liver

To lacteal of a villus

Thoracic duct

Junction of left internal jugular and left subclavian veins

**Q** A monoglyceride may be larger than an amino acid. Why can monoglycerides be absorbed by simple diffusion, but amino acids cannot?
removal is accomplished by an enzyme attached to the apical surface of capillary endothelial cells, called lipoprotein lipase, that breaks down triglycerides in chylomicrons and other lipoproteins into fatty acids and glycerol. The fatty acids diffuse into hepatocytes and adipose cells and combine with glycerol during resynthesis of triglycerides. Two or three hours after a meal, few chylomicrons remain in the blood.

After participating in the emulsification and absorption of lipids, most of the bile salts are reabsorbed by active transport in the final segment of the small intestine (ileum) and returned by the blood to the liver through the hepatic portal system for recycling. This cycle of bile salt secretion by hepatocytes into bile, reabsorption by the ileum, and resecretion into bile is called the enterohepatic circulation (en′-ter-o-he-PAT-ik). Insufficient bile salts, due either to obstruction of the bile ducts or removal of the gallbladder, can result in the loss of up to 40% of dietary lipids in feces due to diminished lipid absorption. There are several benefits to including some healthy fats in the diet. For example, fats delay gastric emptying, which helps a person feel full. Fats also enhance the feeling of fullness by triggering the release of a hormone called cholecystokinin. Finally, fats are necessary for the absorption of fat-soluble vitamins.

Absorption of Electrolytes Many of the electrolytes absorbed by the small intestine come from gastrointestinal secretions, and some are part of ingested foods and liquids. Recall that electrolytes are compounds that separate into ions in water and conduct electricity. Sodium ions are actively transported out of absorptive cells by basolateral sodium–potassium pumps (Na⁺–K⁺ ATPases) after they have moved into absorptive cells via diffusion and secondary active transport. Thus, most of the sodium ions (Na⁺) in gastrointestinal secretions are reclaimed and not lost in the feces. Negatively charged bicarbonate, chloride, iodide, and nitrate ions can passively follow Na⁺ or be actively transported. Calcium ions also are absorbed actively in a process stimulated by calcitriol. Other electrolytes such as iron, potassium, magnesium, and phosphate ions also are absorbed via active transport mechanisms.

Absorption of Vitamins As you have just learned, the fat-soluble vitamins A, D, E, and K are included with ingested dietary lipids in micelles and are absorbed via simple diffusion. Most water-soluble vitamins, such as most B vitamins and vitamin C, also are absorbed via simple diffusion. Vitamin B₁₂, however, combines with intrinsic factor produced by the stomach, and the combination is absorbed in the ileum via an active transport mechanism.

Absorption of Water The total volume of fluid that enters the small intestine each day—about 9.3 liters (9.8 qt)—comes from ingestion of liquids (about 2.3 liters) and from various gastrointestinal secretions (about 7.0 liters). Figure 24.23 depicts the amounts of fluid ingested, secreted, absorbed, and excreted by the GI tract. The small intestine absorbs about 8.3 liters of the fluid; the remainder passes

**Figure 24.23** Daily volumes of fluid ingested, secreted, absorbed, and excreted from the GI tract.

All water absorption in the GI tract occurs via osmosis.
into the large intestine, where most of the rest of it—about 0.9 liter—is also absorbed. Only 0.1 liter (100 mL) of water is excreted in the feces each day.

All water absorption in the GI tract occurs via osmosis from the lumen of the intestines through absorptive cells and into blood capillaries. Because water can move across the intestinal mucosa in both directions, the absorption of water from the small intestine depends on the absorption of electrolytes and nutrients to maintain an osmotic balance with the blood. The absorbed electrolytes, monosaccharides, and amino acids establish a concentration gradient for water that promotes water absorption via osmosis.

*Table 24.4* summarizes the digestive activities of the pancreas, liver, gallbladder, and small intestine and *Table 24.5* summarizes the digestive enzymes and their functions in the digestive system.

### Table 24.4 Summary of Digestive Activities in the Pancreas, Liver, Gallbladder, and Small Intestine

<table>
<thead>
<tr>
<th>STRUCTURE</th>
<th>ACTIVITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreas</td>
<td>Delivers pancreatic juice into duodenum via pancreatic duct to assist absorption (see Table 24.5 for pancreatic enzymes and their functions).</td>
</tr>
<tr>
<td>Liver</td>
<td>Produces bile (bile salts) necessary for emulsification and absorption of lipids.</td>
</tr>
<tr>
<td>Gallbladder</td>
<td>Stores, concentrates, and delivers bile into duodenum via common bile duct.</td>
</tr>
<tr>
<td>Small intestine</td>
<td>Major site of digestion and absorption of nutrients and water in gastrointestinal tract.</td>
</tr>
<tr>
<td>Mucosa/submucosa</td>
<td></td>
</tr>
<tr>
<td>Intestinal glands</td>
<td>Secrete intestinal juice to assist absorption.</td>
</tr>
<tr>
<td>Absorptive cells</td>
<td>Digest and absorb nutrients.</td>
</tr>
<tr>
<td>Goblet cells</td>
<td>Secrete mucus.</td>
</tr>
<tr>
<td>Enteroendocrine cells (S, CCK, K)</td>
<td>Secrete secretin, cholecystokinin, and glucose-dependent insulinotropic peptide.</td>
</tr>
<tr>
<td>Paneth cells</td>
<td>Secrete lysozyme (bactericidal enzyme), and phagocytosis.</td>
</tr>
<tr>
<td>Duodenal (Brunner’s) glands</td>
<td>Secrete alkaline fluid to buffer stomach acids and mucus for protection and lubrication.</td>
</tr>
<tr>
<td>Circular folds</td>
<td>Folds of mucosa and submucosa that increase surface area for digestion and absorption.</td>
</tr>
<tr>
<td>Villi</td>
<td>Fingerlike projections of mucosa that are sites of absorption of digested food and increase surface area for digestion and absorption.</td>
</tr>
<tr>
<td>Microvilli</td>
<td>Microscopic, membrane-covered projections of absorptive epithelial cells that contain brush-border enzymes (listed in Table 24.5) and that increase surface area for digestion and absorption.</td>
</tr>
<tr>
<td>Muscularis</td>
<td></td>
</tr>
<tr>
<td>Segmentation</td>
<td>Type of peristalsis: alternating contractions of circular smooth muscle fibers that produce segmentation and resegmentation of sections of small intestine; mixes chyme with digestive juices and brings food into contact with mucosa for absorption.</td>
</tr>
<tr>
<td>Migrating motility complex (MMC)</td>
<td>Type of peristalsis: waves of contraction and relaxation of circular and longitudinal smooth muscle fibers passing the length of the small intestine; moves chyme toward ileocecal sphincter.</td>
</tr>
</tbody>
</table>
**24.13 Large Intestine**

**OBJECTIVE**

- Describe the anatomy, histology, and functions of the large intestine.

The large intestine is the terminal portion of the GI tract. The overall functions of the large intestine are the completion of absorption, the production of certain vitamins, the formation of feces, and the expulsion of feces from the body. The medical specialty that deals with the diagnosis and treatment of disorders of the rectum and anus is called proctology (prok-TOL-ō-ji; proct- = rectum).
Structurally, the four major regions of the large intestine are the cecum, colon, rectum, and anal canal (Figure 24.24a).

The opening from the ileum into the large intestine is guarded by a fold of mucous membrane called the ileocecal sphincter (valve), which allows materials from the small intestine to pass into the large intestine. Hanging inferior to the ileocecal valve is the cecum, a small region of the large intestine (Figure 24.24a).

Anatomy of the Large Intestine

The large intestine (Figure 24.24), which is about 1.5 m (5 ft) long and 6.5 cm (2.5 in.) in diameter in living humans and cadavers, extends from the ileum to the anus. It is attached to the posterior abdominal wall by its mesocolon, which is a double layer of peritoneum (see Figure 24.5a).

Q Which portions of the colon are retroperitoneal?

Functions of the Large Intestine

1. Haustral churning, peristalsis, and mass peristalsis drive contents of colon into rectum.
2. Bacteria in large intestine convert proteins to amino acids, break down amino acids, and produce some B vitamins and vitamin K.
3. Absorption of some water, ions, and vitamins.
4. Formation of feces.
5. Defecation (emptying rectum).

Clinical Connection

Appendicitis

Inflammation of the appendix, termed appendicitis, is preceded by obstruction of the lumen of the appendix by chyme, inflammation, a foreign body, a carcinoma of the cecum, stenosis, or kinking of the organ. It is characterized by high fever, elevated white blood cell count, and a neutrophil count higher than 75%. The infection that follows may result in edema and ischemia and may progress to gangrene and perforation within 24 hours. Typically, appendicitis begins with referred pain in the umbilical region of the abdomen, followed by anorexia (loss of appetite for food), nausea, and vomiting. After several hours the pain localizes in the right lower quadrant (RLQ) and is continuous, dull or severe, and intensified by coughing, sneezing, or body movements. Early appendectomy (removal of the appendix) is recommended because it is safer to operate than to risk rupture, peritonitis, and gangrene. Although it required major abdominal surgery in the past, today appendectomies are usually performed laparoscopically.
pouch about 6 cm (2.4 in.) long. Attached to the cecum is a twisted, coiled tube, measuring about 8 cm (3 in.) in length, called the **appendix** or **vermiform appendix** (VER-mi-form; vermiform = worm-shaped; appendix = appendage). The mesentery of the appendix, called the **mesoappendix** (mez-6-a-PEN-diks), attaches the appendix to the inferior part of the mesentery of the ileum.

The open end of the cecum merges with a long tube called the **colon** (= food passage), which is divided into ascending, transverse, descending, and sigmoid portions. Both the ascending and descending colon are retroperitoneal; the transverse and sigmoid colon are not. True to its name, the **ascending colon** ascends on the right side of the abdomen, reaches the inferior surface of the liver, and turns abruptly to the left to form the **right colic (hepatic) flexure**. The colon continues across the abdomen to the left side as the **transverse colon**. It curves beneath the inferior end of the spleen on the left side as the **left colic (splenic) flexure** and passes inferiorly to the level of the iliac crest as the **descending colon**. The **sigmoid colon** (sigm- = S-shaped) begins near the left iliac crest, projects medially to the midline, and terminates as the rectum at about the level of the third sacral vertebra.

The **rectum** is about 15 cm (6 in.) in length and lies anterior to the sacrum and coccyx. The terminal 2–3 cm (1 in.) of the large intestine is called the **anal canal** (Figure 24.24b). The mucous membrane of the anal canal is arranged in longitudinal folds called **anal columns** that contain a network of arteries and veins. The opening of the anal canal to the exterior, called the **anus**, is guarded by an **internal anal sphincter** of smooth muscle (involuntary) and an **external anal sphincter** of skeletal muscle (voluntary). Normally these sphincters keep the anus closed except during the elimination of feces.

**Histology of the Large Intestine**

The wall of the large intestine contains the typical four layers found in the rest of the GI tract: mucosa, submucosa, muscularis, and serosa. The mucosa consists of simple columnar epithelium, lamina propria (areolar connective tissue), and muscularis mucosae (smooth muscle) (Figure 24.25a). The epithelium contains mostly absorptive and goblet cells (Figure 24.25b, d). The absorptive cells function primarily in water absorption; the goblet cells secrete mucus that lubricates the passage of the colonic contents. Both absorptive and goblet cells are located in long, straight, tubular intestinal glands (crypts of Lieberkühn) that extend the full thickness of the mucosa. Solitary lymphatic nodules are also found in the lamina propria of the mucosa and may extend through the muscularis mucosae into the submucosa. Compared to the small intestine, the mucosa of the large intestine does not have as many structural adaptations that increase surface area. There are no circular folds or villi; however, microvilli are present on the absorptive cells. Consequently, much more absorption occurs in the small intestine than in the large intestine.
The submucosa of the large intestine consists of areolar connective tissue. The muscularis consists of an external layer of longitudinal smooth muscle and an internal layer of circular smooth muscle. Unlike other parts of the GI tract, portions of the longitudinal muscles are thickened, forming three conspicuous bands called the teniae coli (TE-nē-ē KŌ-li; teniae = flat bands) that run most of the length of the large intestine (see Figure 24.24a). The teniae coli are separated by portions of the wall with less or no longitudinal muscle. Tonic contractions of the bands gather the colon into a series of pouches called haustra (HAWS-tra = shaped like pouches; singular is haustrum), which give the colon a puckered appearance. A single layer of circular smooth muscle lies between teniae coli. The serosa of the large intestine is part of the visceral peritoneum. Small pouches of visceral peritoneum filled with fat are attached to teniae coli and are called omental (fatty) appendices.

**Clinical Connection**

**Polyps in the Colon**

**Polyps** in the colon are generally slow-developing benign growths that arise from the mucosa of the large intestine. Often, they do not cause symptoms. If symptoms do occur, they include diarrhea, blood in the feces, and mucus discharged from the anus. The polyps are removed by colonoscopy or surgery because some of them may become cancerous.

**What is the function of the goblet cells in the large intestine?**
Mechanical Digestion in the Large Intestine

The passage of chyme from the ileum into the cecum is regulated by the action of the ileocecal sphincter. Normally, the valve remains partially closed so that the passage of chyme into the cecum usually occurs slowly. Immediately after a meal, a gastroileal reflex (gas'-trö-IL-ē-al) intensifies peristalsis in the ileum and forces any chyme into the cecum. The hormone gastrin also relaxes the sphincter. Whenever the cecum is distended, the degree of contraction of the ileocecal sphincter intensifies.

Movements of the colon begin when substances pass the ileocecal sphincter. Because chyme moves through the small intestine at a fairly constant rate, the time required for a meal to pass into the colon is determined by gastric emptying time. As food passes through the ileocecal sphincter, it fills the cecum and accumulates in the ascending colon.

One movement characteristic of the large intestine is haustral churning. In this process, the haustra remain relaxed and become distended while they fill up. When the distension reaches a certain point, the walls contract and squeeze the contents into the next haustrum. Peristalsis also occurs, although at a slower rate (3–12 contractions per minute) than in more proximal portions of the tract. A final type of movement is mass peristalsis, a strong peristaltic wave that begins at about the middle of the transverse colon and quickly drives the contents of the colon into the rectum. Because food in the stomach initiates this gastrocolic reflex in the colon, mass peristalsis usually takes place three or four times a day, during or immediately after a meal.

Chemical Digestion in the Large Intestine

The final stage of digestion occurs in the colon through the activity of bacteria that inhabit the lumen. Mucus is secreted by the glands of the large intestine, but no enzymes are secreted. Chyme is prepared for elimination by the action of bacteria, which ferment any remaining carbohydrates and release hydrogen, carbon dioxide, and methane gases. These gases contribute to flatus (gas) in the colon, termed flatulence when it is excessive. Bacteria also convert any remaining proteins to amino acids and break down the amino acids into simpler substances: indole, skatole, hydrogen sulfide, and fatty acids. Some of the indole and skatole is eliminated in the feces and contributes to their odor; the rest is absorbed and transported to the liver, where these compounds are converted to less toxic compounds and excreted in the urine. Bacteria also decompose bilirubin to simpler pigments, including stercobilin, which gives feces their brown color. Bacterial products that are absorbed in the colon include several vitamins needed for normal metabolism, among them some B vitamins and vitamin K.

Absorption and Feces Formation in the Large Intestine

By the time chyme has remained in the large intestine 3–10 hours, it has become solid or semisolid because of water absorption and is now called feces. Chemically, feces consist of water, inorganic salts, sloughed-off epithelial cells from the mucosa of the gastrointestinal tract, bacteria, products of bacterial decomposition, unabsorbed digested materials, and indigestible parts of food.

Although 90% of all water absorption occurs in the small intestine, the large intestine absorbs enough to make it an important organ in maintaining the body’s water balance. Of the 0.5–1.0 liter of water that enters the large intestine, all but about 100–200 mL is normally absorbed via osmosis. The large intestine also absorbs ions, including sodium and chloride, and some vitamins.

### Clinical Connection

#### Occult Blood

The term occult blood refers to blood that is hidden; it is not detectable by the human eye. The main diagnostic value of occult blood testing is to screen for colorectal cancer. Two substances often examined for occult blood are feces and urine. Several types of products are available for at-home testing for hidden blood in feces. The tests are based on color changes when reagents are added to feces. The presence of occult blood in urine may be detected at home by using dip-and-read reagent strips.

#### The Defecation Reflex

Mass peristaltic movements push fecal material from the sigmoid colon into the rectum. The resulting distension of the rectal wall stimulates stretch receptors, which initiates a defecation reflex that results in defecation, the elimination of feces from the rectum through the anus. The defecation reflex occurs as follows: In response to distension of the rectal wall, the receptors send sensory nerve impulses to the sacral spinal cord. Motor impulses from the cord travel along parasympathetic nerves back to the descending colon, sigmoid colon, rectum, and anus. The resulting contraction of the longitudinal rectal muscles shortens the rectum, thereby increasing the pressure within it. This pressure, along with voluntary contractions of the diaphragm and abdominal muscles, plus parasympathetic stimulation, opens the internal anal sphincter.

### Clinical Connection

#### Dietary Fiber

Dietary fiber consists of indigestible plant carbohydrates—such as cellulose, lignin, and pectin—found in fruits, vegetables, grains, and beans. Insoluble fiber, which does not dissolve in water, includes the woody or structural parts of plants such as the skins of fruits and vegetables and the bran coating around wheat and corn kernels. Insoluble fiber passes through the GI tract largely unchanged but speeds up the passage of material through the tract. Soluble fiber, which does dissolve in water, forms a gel that slows the passage of material through the tract. It is found in abundance in beans, oats, barley, broccoli, prunes, apples, and citrus fruits.

People who choose a fiber-rich diet may reduce their risk of developing obesity, diabetes, atherosclerosis, gallstones, hemorrhoids, diverticulitis, appendicitis, and colorectal cancer. Soluble fiber also may help lower blood cholesterol. The liver normally converts cholesterol to bile salts, which are released into the small intestine to help fat digestion. Having accomplished their task, the bile salts are reabsorbed by the small intestine and recycled back to the liver. Since soluble fiber binds to bile salts to prevent their reabsorption, the liver makes more bile salts to replace those lost in feces. Thus, the liver uses more cholesterol to make more bile salts and blood cholesterol level is lowered.

The external anal sphincter is voluntarily controlled. If it is voluntarily relaxed, defecation occurs and the feces are expelled through...
The amount of bowel movements that a person has over a given period of time depends on various factors such as diet, health, and stress. The normal range of bowel activity varies from two or three bowel movements per day to three or four bowel movements per week.

**Diarrhea** (di-à-RE-à; dia- = through; -rrhea = flow) is an increase in the frequency, volume, and fluid content of the feces caused by increased motility of and decreased absorption by the intestines. When chyme passes too quickly through the small intestine and feces pass too quickly through the large intestine, there is not enough time for absorption. Frequent diarrhea can result in dehydration and electrolyte imbalances. Excessive motility may be caused by lactase intolerance, stress, and microbes that irritate the gastrointestinal mucosa.

**Constipation** (kon-sti-PÅ-shun; con- = together; -stip- = to press) refers to infrequent or difficult defecation caused by decreased motility of the intestines. Because the feces remain in the colon for prolonged periods, excessive water absorption occurs, and the feces become dry and hard. Constipation may be caused by poor habits (delaying defecation), spasms of the colon, insufficient fiber in the diet, inadequate fluid intake, lack of exercise, emotional stress, and certain drugs. A common treatment is a mild laxative, such as milk of magnesia, which induces defecation. However, many physicians maintain that laxatives are habit-forming, and that adding fiber to the diet, increasing the amount of exercise, and increasing fluid intake are safer ways of controlling this common problem.

Table 24.6 summarizes the digestive activities in the large intestine, and Table 24.7 summarizes the functions of all digestive system organs.

### Table 24.6 Summary of Digestive Activities in the Large Intestine

<table>
<thead>
<tr>
<th>STRUCTURE</th>
<th>ACTIVITY</th>
<th>FUNCTION(S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumen</td>
<td>Bacterial activity.</td>
<td>Breaks down undigested carbohydrates, proteins, and amino acids into products that can be expelled in feces or absorbed and detoxified by liver; synthesizes certain B vitamins and vitamin K.</td>
</tr>
<tr>
<td>Mucosa</td>
<td>Secretes mucus.</td>
<td>Lubricates colon; protects mucosa.</td>
</tr>
<tr>
<td>Absorption.</td>
<td>Water absorption solidifies feces and contributes to body's water balance; solutes absorbed include ions and some vitamins.</td>
<td></td>
</tr>
<tr>
<td>Muscularis</td>
<td>Hastral churning.</td>
<td>Moves contents from haustrum to haustrum by muscular contractions.</td>
</tr>
<tr>
<td>Peristalsis.</td>
<td>Moves contents along length of colon by contractions of circular and longitudinal muscles.</td>
<td></td>
</tr>
<tr>
<td>Mass peristalsis.</td>
<td>Forces contents into sigmoid colon and rectum.</td>
<td></td>
</tr>
<tr>
<td>Defecation reflex.</td>
<td>Eliminates feces by contractions in sigmoid colon and rectum.</td>
<td></td>
</tr>
</tbody>
</table>

### Table 24.7 Summary of Organs of the Digestive System and Their Functions

<table>
<thead>
<tr>
<th>ORGAN</th>
<th>FUNCTION(S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tongue</td>
<td>Maneuvers food for mastication, shapes food into a bolus, maneuvers food for deglutition, detects sensations for taste, and initiates digestion of triglycerides.</td>
</tr>
<tr>
<td>Salivary glands</td>
<td>Saliva produced by these glands softens, moistens, and dissolves foods; cleanses mouth and teeth; initiates the digestion of starch.</td>
</tr>
<tr>
<td>Teeth</td>
<td>Cut, tear, and pulverize food to reduce solids to smaller particles for swallowing.</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Pancreatic juice buffers acidic gastric juice in chyme, stops the action of pepsin from the stomach, creates the proper pH for digestion in the small intestine, and participates in the digestion of carbohydrates, proteins, triglycerides, and nucleic acids.</td>
</tr>
<tr>
<td>Liver</td>
<td>Produces bile, which is required for the emulsification and absorption of lipids in the small intestine.</td>
</tr>
<tr>
<td>Gallbladder</td>
<td>Stores and concentrates bile and releases it into the small intestine.</td>
</tr>
<tr>
<td>Mouth</td>
<td>See the functions of the tongue, salivary glands, and teeth, all of which are in the mouth. Additionally, the lips and cheeks keep food between the teeth during mastication, and buccal glands lining the mouth produce saliva.</td>
</tr>
<tr>
<td>Pharynx</td>
<td>Receives a bolus from the oral cavity and passes it into the esophagus.</td>
</tr>
<tr>
<td>Esophagus</td>
<td>Receives a bolus from the pharynx and moves it into the stomach; this requires relaxation of the upper esophageal sphincter and secretion of mucus.</td>
</tr>
<tr>
<td>Stomach</td>
<td>Mixing waves combine saliva, food, and gastric juice, which activates pepsin, initiates protein digestion, kills microbes in food, helps absorb vitamin B₁₂, contracts the lower esophageal sphincter, increases stomach motility, relaxes the pyloric sphincter, and moves chyme into the small intestine.</td>
</tr>
<tr>
<td>Small intestine</td>
<td>Segmentation mixes chyme with digestive juices; peristalsis propels chyme toward the ileocecal sphincter; digestive secretions from the small intestine, pancreas, and liver complete the digestion of carbohydrates, proteins, lipids, and nucleic acids; circular folds, villi, and microvilli help absorb about 90% of digested nutrients.</td>
</tr>
<tr>
<td>Large intestine</td>
<td>Hastral churning, peristalsis, and mass peristalsis drive the colonic contents into the rectum; bacteria produce some B vitamins and vitamin K; absorption of some water, ions, and vitamins occurs; defecation.</td>
</tr>
</tbody>
</table>
**24.14 Phases of Digestion**

**OBJECTIVE**

- Explain the three phases of digestion.
- Describe the major hormones regulating digestive activities.

Digestive activities occur in three overlapping phases: the cephalic phase, the gastric phase, and the intestinal phase.

**Cephalic Phase**

During the cephalic phase of digestion, the smell, sight, thought, or initial taste of food activates neural centers in the cerebral cortex, hypothalamus, and brain stem. The brain stem then activates the facial (VII), glossopharyngeal (IX), and vagus (X) nerves. The facial and glossopharyngeal nerves stimulate the salivary glands to secrete saliva, while the vagus nerves stimulate the gastric glands to secrete gastric juice. The purpose of the cephalic phase of digestion is to prepare the mouth and stomach for food that is about to be eaten.

**Gastric Phase**

Once food reaches the stomach, the gastric phase of digestion begins. Neural and hormonal mechanisms regulate the gastric phase of digestion to promote gastric secretion and gastric motility.

- **Neural regulation.** Food of any kind distends the stomach and stimulates stretch receptors in its walls. Chemoreceptors in the stomach monitor the pH of the stomach chyme. When the stomach walls are distended or pH increases because proteins have entered the stomach and buffered some of the stomach acid, the stretch receptors and chemoreceptors are activated, and a neural negative feedback loop is set in motion (Figure 24.26). From the stretch receptors and chemoreceptors, nerve impulses propagate to the submucosal plexus, where they activate parasympathetic and enteric neurons. The resulting nerve impulses cause waves of peristalsis and continue to stimulate the flow of gastric juice from gastric glands. The peristaltic waves mix the food with gastric juice; when the waves become strong enough, a small quantity of chyme undergoes gastric emptying into the duodenum.

**Checkpoint**

39. What are the major regions of the large intestine?
40. How does the muscularis of the large intestine differ from that of the rest of the gastrointestinal tract? What are haustra?
41. Describe the mechanical movements that occur in the large intestine.
42. What is defecation, and how does it occur?
43. What activities occur in the large intestine to change its contents into feces?

**Figure 24.26** Neural negative feedback regulation of the pH of gastric juice and gastric motility during the gastric phase of digestion.

Food entering the stomach stimulates secretion of gastric juice and causes vigorous waves of peristalsis.

Q: Why does food initially cause the pH of the gastric juice to rise?
the duodenum. The pH of the stomach chyme decreases (becomes more acidic) and the distension of the stomach walls lessens because chyme has passed into the small intestine, suppressing secretion of gastric juice.

- **Hormonal regulation.** Gastric secretion during the gastric phase is also regulated by the hormone gastrin. Gastrin is released from the G cells of the gastric glands in response to several stimuli: distension of the stomach by chyme, partially digested proteins in chyme, the high pH of chyme due to the presence of food in the stomach, caffeine in gastric chyme, and acetylcholine released from parasympathetic neurons. Once it is released, gastrin enters the bloodstream, makes a round-trip through the body, and finally reaches its target organs in the digestive system. Gastrin stimulates gastric glands to secrete large amounts of gastric juice. It also strengthens the contraction of the pyloric sphincter, which promotes gastric emptying. Gastrin secretion is inhibited when the pH of gastric juice drops below 2.0 and is stimulated when the pH rises. This negative feedback mechanism helps provide an optimal low pH for the functioning of pepsin, the killing of microbes, and the denaturing of proteins in the stomach.

**Intestinal Phase**

The intestinal phase of digestion begins once food enters the small intestine. In contrast to reflexes initiated during the cephalic and gastric phases, which stimulate stomach secretory activity and motility, those occurring during the intestinal phase have inhibitory effects that slow the exit of chyme from the stomach. This prevents the duodenum from being overloaded with more chyme than it can handle. In addition, responses occurring during the intestinal phase promote the continued digestion of foods that have reached the small intestine. These activities of the intestinal phase of digestion are regulated by neural and hormonal mechanisms.

- **Neural regulation.** Distension of the duodenum by the presence of chyme causes the entero gastric reflex (en’-ter-ō-GAS-trik). Stretch receptors in the duodenal wall send nerve impulses to the medulla oblongata, where they inhibit parasympathetic stimulation and stimulate the sympathetic nervous to the stomach. As a result, gastric motility is inhibited and there is an increase in the contraction of the pyloric sphincter, which decreases gastric emptying.

- **Hormonal regulation.** The intestinal phase of digestion is mediated by two major hormones secreted by the small intestine: cholecystokinin and secretin. Cholecystokinin (CCK) is secreted by the CCK cells of intestinal glands in the small intestine in response to chyme containing amino acids from partially digested proteins and fatty acids from partially digested triglycerides. CCK stimulates secretion of pancreatic juice that is rich in digestive enzymes. It also causes contraction of the wall of the gallbladder, which squeezes stored bile out of the gallbladder into the cystic duct and through the common bile duct. In addition, CCK causes relaxation of the sphincter of the hepatopancreatic ampulla (sphincter of Oddi), which allows pancreatic juice and bile to flow into the duodenum. CCK also slows gastric emptying by promoting contraction of the pyloric sphincter, produces satiety (a feeling of fullness) by acting on the hypothalamus in the brain, promotes normal growth and maintenance of the pancreas, and enhances the effects of secretin. Acidic chyme entering the duodenum stimulates the release of secretin from the S cells of the intestinal glands in the small intestine. In turn, secretin stimulates the flow of pancreatic juice that is rich in bicarbonate (HCO₃⁻) ions to buffer the acidic chyme that enters the duodenum from the stomach. In addition to this major effect, secretin inhibits secretion of gastric juice, promotes normal growth and maintenance of the pancreas, and enhances the effects of CCK. Overall, secretin causes buffering of acid in chyme that reaches the duodenum and slows production of acid in the stomach.

Table 24.8 summarizes the major hormones that control digestion.

<table>
<thead>
<tr>
<th>HORMONE</th>
<th>STIMULUS AND SITE OF SECRETION</th>
<th>ACTIONS</th>
</tr>
</thead>
</table>
| **Gastrin**| Distension of stomach, partially digested proteins and caffeine in stomach, and high pH of stomach chyme stimulate gastrin secretion by enteroendocrine G cells, located mainly in mucosa of pyloric antrum of stomach. | **Major effects:** Promotes secretion of gastric juice, increases gastric motility, promotes growth of gastric mucosa.  
**Minor effects:** Constricts lower esophageal sphincter, relaxes pyloric sphincter. |
| **Secretin**| Acidic (high H⁺ level) chyme that enters small intestine stimulates secretion of secretin by enteroendocrine S cells in the mucosa of duodenum. | **Major effects:** Stimulates secretion of pancreatic juice and bile that are rich in HCO₃⁻ (bicarbonate ions).  
**Minor effects:** Inhibits secretion of gastric juice, promotes normal growth and maintenance of pancreas, enhances effects of CCK. |
| **Cholecystokinin (CCK)** | Partially digested proteins (amino acids), triglycerides, and fatty acids that enter small intestine stimulate secretion of CCK by enteroendocrine CCK cells in mucosa of small intestine; CCK is also released in brain. | **Major effects:** Stimulates secretion of pancreatic juice rich in digestive enzymes, causes ejection of bile from gallbladder and opening of sphincter of the hepatopancreatic ampulla (sphincter of Oddi), induces satiety (feeling full to satisfaction).  
**Minor effects:** Inhibits gastric emptying, promotes normal growth and maintenance of pancreas, enhances effects of secretin. |
Other Hormones of the Digestive System

Besides gastrin, CCK, and secretin, there are many other hormones of the digestive system. For example, ghrelin, which is secreted by the stomach, plays a role in increasing appetite. Glucose-dependent insulinotropic peptide (GIP) and glucagon-like peptide (GLP), which are secreted by the small intestine in response to the presence of food, stimulate the release of insulin from the pancreas, thereby increasing the blood glucose concentration. GIP and GLP are collectively referred to as incretins; they provide a type of feedforward control that anticipates the increase in blood glucose occurring after a typical meal. At least 10 other so-called gut hormones are secreted by and have effects on the GI tract. They include motilin, substance P, and bombesin, which stimulate motility of the intestines; vasoactive intestinal polypeptide (VIP), which stimulates secretion of ions and water by the intestines and inhibits gastric acid secretion; gastrin-releasing peptide, which stimulates release of gastrin; and somatostatin, which inhibits gastrin release. Some of these hormones are thought to act as local hormones (paracrines), whereas others are secreted into the blood or even into the lumen of the GI tract. The physiological roles of these and other gut hormones are still under investigation.

Checkpoint

44. What is the purpose of the cephalic phase of digestion?
45. Describe the role of gastrin in the gastric phase of digestion.
46. Outline the steps of the enterogastric reflex.
47. Explain the roles of CCK and secretin in the intestinal phase of digestion.

24.15 Development of the Digestive System

OBJECTIVE

• Describe the development of the digestive system.

During the fourth week of development, the cells of the endoderm form a cavity called the primitive gut, the forerunner of the gastrointestinal tract (see Figure 29.12b). Soon afterward the mesoderm forms and splits into two layers (somatic and splanchnic), as shown in Figure 29.9d. The splanchnic mesoderm associates with the endoderm of the primitive gut; as a result, the primitive gut has a double-layered wall. The endodermal layer gives rise to the epithelial lining and glands of most of the gastrointestinal tract; the mesodermal layer produces the smooth muscle and connective tissue of the tract.

24.16 Aging and the Digestive System

OBJECTIVE

• Describe the effects of aging on the digestive system.

Overall changes of the digestive system associated with aging include decreased secretory mechanisms, decreased motility of the digestive organs, loss of strength and tone of the muscular tissue and its supporting structures, changes in neurosensory feedback regarding enzyme and hormone release, and diminished response to pain and...
Internal sensations. In the upper portion of the GI tract, common changes include reduced sensitivity to mouth irritations and sores, loss of taste, periodontal disease, difficulty in swallowing, hiatal hernia, gastritis, and peptic ulcer disease. Changes that may appear in the small intestine include duodenal ulcers, malabsorption, and maldigestion. Other pathologies that increase in incidence with age between the teeth be removed every 24 hours with dental floss. The most common complication of peptic ulcers is bleeding, which can lead to anemia if enough blood is lost. In acute cases, peptic ulcers can lead to shock and death. Three distinct causes of PUD are recognized: (1) the bacterium Helicobacter pylori (hel-i-kō-BAK-ter pi-LÔ-rē); (2) nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin; and (3) hypersecretion of HCl, as occurs in Zollinger–Ellison syndrome (ZOL-in-er EL-i-son), a gastrin-producing tumor, usually of the pancreas. Helicobacter pylori (previously named Campylobacter pylori) is the most frequent cause of PUD. The bacterium produces an enzyme called urease, which splits urea into ammonia and carbon dioxide. While shielding the bacterium from the acidity of the stomach, the ammonia also damages the protective mucous layer of the stomach and the underlying gastric cells. The microbe also produces catalase, an enzyme that may protect H. pylori from phagocytosis by neutrophils, plus several adhesion proteins that allow the bacterium to attach itself to gastric cells.

Several therapeutic approaches are helpful in the treatment of PUD. Cigarette smoke, alcohol, caffeine, and NSAIDs should be avoided because they can impair mucosal defensive mechanisms, which increases mucosal susceptibility to the damaging effects of HCl. In cases associated with H. pylori, treatment with an antibiotic drug often resolves the problem. Oral antacids such as Tums® or Maalox® can help temporarily by buffering gastric acid. When hypersecretion of HCl is the cause of PUD, H₂ blockers (such as Tagamet®) or proton pump inhibitors such as omeprazole (Prilosec®), which block secretion of H⁺ from parietal cells, may be used.

Disorders: Homeostatic Imbalances

Dental Caries

Dental caries (KĀR-ēz), or tooth decay, involves a gradual demineralization (softening) of the enamel and dentin. If untreated, microorganisms may invade the pulp, causing inflammation and infection, with subsequent death of the pulp and abscess of the alveolar bone surrounding the root’s apex, requiring root canal therapy (see Section 24.5).

Dental caries begin when bacteria, acting on sugars, produce acids that demineralize the enamel. Dextran, a sticky polysaccharide produced from sucrose, causes the bacteria to stick to the teeth. Masses of bacterial cells, dextran, and other debris adhering to teeth constitute dental plaque (PLAK). Saliva cannot reach the tooth surface to buffer the acid because the plaque covers the teeth. Brushing the teeth after eating removes the plaque from flat surfaces before the bacteria can produce acids. Dentists also recommend that the plaque between the teeth be removed every 24 hours with dental floss.

Periodontal Disease

Periodontal disease is a collective term for a variety of conditions characterized by inflammation and degeneration of the gingivae, alveolar bone, periodontal ligament, and cementum. In one such condition, called pyorrhea, initial symptoms include enlargement and inflammation of the soft tissue and bleeding of the gums. Without treatment, the soft tissue may deteriorate and the alveolar bone may be resorbed, causing loosening of the teeth and recession of the gums. Periodontal diseases are often caused by poor oral hygiene; by local irritants, such as bacteria, impacted food, and cigarette smoke; or by a poor “bite.”

Peptic Ulcer Disease

In the United States, 5–10% of the population develops peptic ulcer disease (PUD). An ulcer is a craterlike lesion in a membrane; ulcers that develop in areas of the GI tract exposed to acidic gastric juice are called peptic ulcers. The most common complication of peptic ulcers is bleeding, which can lead to anemia if enough blood is lost. In acute cases, peptic ulcers can lead to shock and death. Three distinct causes of PUD are recognized: (1) the bacterium Helicobacter pylori (hel-i-kō-BAK-ter pi-LÔ-rē); (2) nonsteroidal anti-inflammatory drugs (NSAIDs) such as aspirin; and (3) hypersecretion of HCl, as occurs in Zollinger–Ellison syndrome (ZOL-in-er EL-i-son), a gastrin-producing tumor, usually of the pancreas. Helicobacter pylori (previously named Campylobacter pylori) is the most frequent cause of PUD. The bacterium produces an enzyme called urease, which splits urea into ammonia and carbon dioxide. While shielding the bacterium from the acidity of the stomach, the ammonia also damages the protective mucous layer of the stomach and the underlying gastric cells. The microbe also produces catalase, an enzyme that may protect H. pylori from phagocytosis by neutrophils, plus several adhesion proteins that allow the bacterium to attach itself to gastric cells.

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Diverticular Disease

In diverticular disease (di’-ver-TIK-ū-lar), saclike outpouchings of the wall of the colon, termed diverticula, occur in places where the muscularis has weakened and may become inflamed. Development of diverticula is known as diverticulosis (di-ver-tik-ū-sis). Many people who develop diverticulosis have no symptoms and experience no complications. Of those people known to have diverticulosis, 10–25% eventually develop an inflammation known as diverticulitis (di’-ver-tik-ū-lī-tis). This condition may be characterized by pain, either constipation or increased frequency of defecation, nausea, vomiting, and low-grade fever. Because diets low in fiber contribute to development of diverticulitis, patients who change to high-fiber diets...
FOCUS on HOMEOSTASIS

CONTRIBUTIONS OF THE DIGESTIVE SYSTEM

- Small intestine absorbs vitamin D, which skin and kidneys modify to produce the hormone calcitriol.
- Excess dietary calories are stored as triglycerides in adipose cells in dermis and subcutaneous layer.

INTEGUMENTARY SYSTEM

- Small intestine absorbs dietary calcium and phosphorus salts needed to build bone extracellular matrix.

SKELETAL SYSTEM

- Liver can convert lactic acid (produced by muscles during exercise) to glucose.

MUSCULAR SYSTEM

- Gluconeogenesis (synthesis of new glucose molecules) in liver plus digestion and absorption of dietary carbohydrates provide glucose, needed for ATP production by neurons.

NERVOUS SYSTEM

- Liver inactivates some hormones, ending their activity.
- Pancreatic islets release insulin and glucagon.
- Cells in mucosa of stomach and small intestine release hormones that regulate digestive activities.
- Liver produces angiotensinogen.

ENDOCRINE SYSTEM

- The digestive system breaks down dietary nutrients into forms that can be absorbed and used by body cells for producing ATP and building body tissues.
- Absorbs water, minerals, and vitamins needed for growth and function of body tissues.
- Eliminates wastes from body tissues in feces.

FOR ALL BODY SYSTEMS

- GI tract absorbs water that helps maintain blood volume and iron that is needed for synthesis of hemoglobin in red blood cells.
- Bilirubin from hemoglobin breakdown is partially excreted in feces.
- Liver synthesizes most plasma proteins.

CARDIOVASCULAR SYSTEM

- Acidity of gastric juice destroys bacteria and most toxins in stomach.
- Lymphatic nodules in lamina propria of mucosa of gastrointestinal tract (MALT) destroy microbes.

LYMPHATIC SYSTEM and IMMUNITY

- Pressure of abdominal organs against diaphragm helps expel air quickly during forced exhalation.

RESPIRATORY SYSTEM

- Absorption of water by GI tract provides water needed to excrete waste products in urine.

URINARY SYSTEM

- Digestion and absorption provide adequate nutrients, including fats, for normal development of reproductive structures, for production of gametes (oocytes and sperm), and for fetal growth and development during pregnancy.

REPRODUCTIVE SYSTEMS

- GI tract absorbs vitamin D, which skin and kidneys modify to produce the hormone calcitriol.
- Excess dietary calories are stored as triglycerides in adipose cells in dermis and subcutaneous layer.
show marked relief of symptoms. In severe cases, affected portions of the colon may require surgical removal. If diverticula rupture, the release of bacteria into the abdominal cavity can cause peritonitis.

**Colorectal Cancer**

**Colorectal cancer** is among the deadliest of malignancies, ranking second to lung cancer in males and third after lung cancer and breast cancer in females. Genetics plays a very important role; an inherited predisposition contributes to more than half of all cases of colorectal cancer. Intake of alcohol and diets high in animal fat and protein are associated with increased risk of colorectal cancer; dietary fiber, retinoids, calcium, and selenium may be protective. Signs and symptoms of colorectal cancer include diarrhea, constipation, cramping, abdominal pain, and rectal bleeding, either visible or occult (hidden in feces). Precancerous growths on the mucosal surface, called polyps, also increase the risk of developing colorectal cancer. Screening for colorectal cancer includes testing for blood in the feces, digital rectal examination, sigmoidoscopy, colonoscopy, and barium enema. Tumors may be removed endoscopically or surgically.

**Hepatitis**

**Hepatitis** is an inflammation of the liver that can be caused by viruses, drugs, and chemicals, including alcohol. Clinically, several types of viral hepatitis are recognized.

**Hepatitis A (infectious hepatitis)** is caused by the hepatitis A virus (HAV) and is spread via fecal contamination of objects such as food, clothing, toys, and eating utensils (fecal–oral route). It is generally a mild disease of children and young adults characterized by loss of appetite, malaise, nausea, diarrhea, fever, and chills. Eventually, jaundice appears. This type of hepatitis does not cause lasting liver damage. Most people recover in 4 to 6 weeks. A vaccine is available.

**Hepatitis B** is caused by the hepatitis B virus (HBV) and is spread primarily by sexual contact and contaminated syringes and transfusion equipment. It can also be spread via saliva and tears. Hepatitis B virus can be present for years or even a lifetime, and it can produce cirrhosis and possibly cancer of the liver. Individuals who harbor the active hepatitis B virus also become carriers. A vaccine is available.

**Hepatitis C**, caused by the hepatitis C virus (HCV), is clinically similar to hepatitis B. Hepatitis C can cause cirrhosis and possibly liver cancer. In developed nations, donated blood is screened for the presence of hepatitis B and C.

**Hepatitis D** is caused by the hepatitis D virus (HDV). It is transmitted like hepatitis B, and in fact a person must have been co-infected with hepatitis B before contracting hepatitis D. Hepatitis D results in severe liver damage and has a higher fatality rate than infection with hepatitis B virus alone. HBV vaccine is protective.

**Hepatitis E** is caused by the hepatitis E virus and is spread like hepatitis A. Although it does not cause chronic liver disease, hepatitis E virus has a very high mortality rate among pregnant women.

### Medical Terminology

- **Achalasia** (ak-ˈa-LÄ-zē-a; α- = without; -chalasis = relaxation) A condition caused by malfunction of the myenteric plexus in which the lower esophageal sphincter fails to relax normally as food approaches. A whole meal may become lodged in the esophagus and enter the stomach very slowly. Distension of the esophagus results in chest pain that is often confused with pain originating from the heart.

- **Bariatric surgery** (bar-ˈē-AT-rik; baros- = weight; -iatreia = medical treatment) A surgical procedure that limits the amount of food that can be ingested and absorbed in order to bring about a significant weight loss in obese individuals. The most commonly performed type of bariatric surgery is called gastric bypass surgery. In one variation of this procedure, the stomach is reduced in size by making a small pouch at the top of the stomach about the size of a walnut. The pouch, which is only 5–10% of the stomach, is sealed off from the rest of the stomach using surgical staples or a plastic band. The pouch is connected to the jejunum of the small intestine, thus bypassing the rest of the stomach and the duodenum. The result is that smaller amounts of food are ingested and fewer nutrients are absorbed in the small intestine. This leads to weight loss.

- **Barrett’s esophagus** A pathological change in the epithelium of the esophagus from nonkeratinized stratified squamous epithelium to columnar epithelium so that the lining resembles that of the stomach or small intestine due to long-term exposure of the esophagus to stomach acid; increases the risk of developing cancer of the esophagus.

- **Borborygmus** (bor-ˈbō-RIG-mus) A rumbling noise caused by the propulsion of gas through the intestines.

- **Bulimia** (bū-LEM-ē-a; bu- = ox; limia = hunger or binge–purge syndrome) A disorder that typically affects young, single, middle-class white females, characterized by overeating at least twice a week followed by purging by self-induced vomiting, strict dieting or fasting, vigorous exercise, or use of laxatives or diuretics; it occurs in response to fears of being overweight or to stress, depression, and physiological disorders such as hypothalamic tumors.

- **Canker sore** (KANG-ker) Painful ulcer on the mucous membrane of the mouth that affects females more often than males, usually between ages 10 and 40; may be an autoimmune reaction or a food allergy.

- **Cirrhosis** (si-RŌ-sis) Distorted or scarred liver as a result of chronic inflammation due to hepatitis, chemicals that destroy hepatocytes, parasites that infect the liver, or alcoholism; the hepatocytes are replaced by fibrous or adipose connective tissue. Symptoms include jaundice, edema in the legs, uncontrolled bleeding, and increased sensitivity to drugs.

- **Colitis** (kō-LĪ-tis) Inflammation of the mucosa of the colon and rectum in which absorption of water and salts is reduced, producing watery, bloody feces and, in severe cases, dehydration and salt depletion. Spasms of the irritated muscularis produce cramps. It is thought to be an autoimmune condition.

- **Colonoscopy** (kō-lon-OS-kō-pē; -skopes = to view) The visual examination of the lining of the colon using an elongated, flexible, fiber-optic endoscope...
called digestion. The organs involved in the breakdown of food are collectively known as the digestive system.

2. The organs involved in the breakdown of food are collectively known as the digestive system.

24.1 Overview of the Digestive System

1. The digestive system is composed of two main groups of organs: the gastrointestinal (GI) tract and accessory digestive organs.
2. The GI tract is a continuous tube extending from the mouth to the anus.
3. The accessory digestive organs include the teeth, tongue, salivary glands, liver, gallbladder, and pancreas.

4. Digestion includes six basic processes: ingestion, secretion, mixing and propulsion, mechanical and chemical digestion, absorption, and defecation.

5. Mechanical digestion consists of mastication and movements of the gastrointestinal tract that aid chemical digestion.
6. Chemical digestion is a series of hydrolysis reactions that break down large carbohydrates, lipids, proteins, and nucleic acids in foods into smaller molecules that are usable by body cells.

**24.2 Layers of the GI Tract**
1. The basic arrangement of layers in most of the gastrointestinal tract, from deep to superficial, is the mucosa, submucosa, muscularis, and serosa.
2. Associated with the lamina propria of the mucosa are extensive patches of lymphatic tissue called mucosa-associated lymphoid tissue (MALT).

**24.3 Neural Innervation of the GI Tract**
1. The gastrointestinal tract is regulated by an intrinsic set of nerves known as the enteric nervous system (ENS) and by an extrinsic set of nerves that are part of the autonomic nervous system (ANS).
2. The ENS consists of neurons arranged into two plexuses: the myenteric plexus and the submucosal plexus.
3. The myenteric plexus, which is located between the longitudinal and circular smooth muscle layers of the muscularis, regulates GI tract motility.
4. The submucosal plexus, which is located in the submucosa, regulates GI secretion.
5. Although the neurons of the ENS can function independently, they are subject to regulation by the neurons of the ANS.
6. Parasympathetic fibers of the vagus (X) nerves and pelvic splanchnic nerves increase GI tract secretion and motility by increasing the activity of ENS neurons.
7. Sympathetic fibers from the thoracic and upper lumbar regions of the spinal cord decrease GI tract secretion and motility by inhibiting ENS neurons.

**24.4 Peritoneum**
1. The peritoneum is the largest serous membrane of the body; it lines the wall of the abdominal cavity and covers some abdominal organs.
2. Folds of the peritoneum include the mesentery, mesocolon, falciform ligament, lesser omentum, and greater omentum.

**24.5 Mouth**
1. The mouth is formed by the cheeks, hard and soft palates, lips, and tongue.
2. The vestibule is the space bounded externally by the cheeks and lips and internally by the teeth and gums.
3. The oral cavity proper extends from the vestibule to the fauces.
4. The tongue, together with its associated muscles, forms the floor of the oral cavity. It is composed of skeletal muscle covered with mucous membrane. The upper surface and sides of the tongue are covered with papillae, some of which contain taste buds. Glands in the tongue secrete lingual lipase, which digests triglycerides into fatty acids and diglycerides once in the acid environment of the stomach.
5. The major portion of saliva is secreted by the major salivary glands, which lie outside the mouth and pour their contents into ducts that empty into the oral cavity. There are three pairs of major salivary glands: parotid, submandibular, and sublingual glands.
6. Saliva lubricates food and starts the chemical digestion of carbohydrates. Salivation is controlled by the nervous system.
7. The teeth (dentes) project into the mouth and are adapted for mechanical digestion.
8. A typical tooth consists of three principal regions: crown, root, and neck. Teeth are composed primarily of dentin and are covered by enamel, the hardest substance in the body. There are two dentitions: deciduous and permanent.
9. Through mastication, food is mixed with saliva and shaped into a soft, flexible mass called a bolus. Salivary amylase then begins the digestion of starches, and lingual lipase acts on triglycerides.

**24.6 Pharynx**
1. The pharynx is a funnel-shaped tube that extends from the internal nares to the esophagus posteriorly and to the larynx anteriorly.
2. The pharynx has both respiratory and digestive functions.

**24.7 Esophagus**
1. The esophagus is a collapsible, muscular tube that connects the pharynx to the stomach.
2. It contains an upper and a lower esophageal sphincter.

**24.8 Deglutition**
1. Deglutition, or swallowing, moves a bolus from the mouth to the stomach.
2. Swallowing consists of voluntary, pharyngeal (involuntary), and esophageal (involuntary) stages.

**24.9 Stomach**
1. The stomach connects the esophagus to the duodenum.
2. The principal anatomical regions of the stomach are the cardia, fundus, body, and pylorus.
3. Adaptations of the stomach for digestion include rugae; glands that produce mucus, hydrochloric acid, pepsin, gastric lipase, and intrinsic factor; and a three-layered muscularis.
4. Mechanical digestion consists of propulsion and retropulsion.
5. Chemical digestion consists mostly of the conversion of proteins into peptides by pepsin.
6. The stomach wall is impermeable to most substances.
7. Among the substances the stomach can absorb are water, certain ions, drugs, and alcohol.

**24.10 Pancreas**
1. The pancreas consists of a head, a body, and a tail and is connected to the duodenum via the pancreatic duct and accessory duct.
2. Endocrine pancreatic islets secrete hormones, and exocrine acini secrete pancreatic juice.
3. Pancreatic juice contains enzymes that digest starch (pancreatic amylase), proteins (trypsin, chymotrypsin, carboxypeptidase, and elastase), triglycerides (pancreatic lipase), and nucleic acids (ribonuclease and deoxyribonuclease).

**24.11 Liver and Gallbladder**
1. The liver has left and right lobes; the left lobe includes a quadrate lobe and a caudate lobe. The gallbladder is a sac located in a depression on the posterior surface of the liver that stores and concentrates bile.
2. The lobes of the liver are made up of lobules that contain hepatocytes (liver cells), sinusoids, stellate reticuloendothelial (Kupffer) cells, and a central vein.

3. Hepatocytes produce bile that is carried by a duct system to the gallbladder for concentration and temporary storage.

4. Bile’s contribution to digestion is the emulsification of dietary lipids.

5. The liver also functions in carbohydrate, lipid, and protein metabolism; processing of drugs and hormones; excretion of bilirubin; synthesis of bile salts; storage of vitamins and minerals; phagocytosis; and activation of vitamin D.

24.12 Small Intestine
1. The small intestine extends from the pyloric sphincter to the ileocecal sphincter. It is divided into duodenum, jejunum, and ileum.
2. Its glands secrete fluid and mucus, and the circular folds, villi, and microvilli of its wall provide a large surface area for digestion and absorption.
3. Brush-border enzymes digest $\alpha$-dextrins, maltose, sucrose, lactose, peptides, and nucleotides at the surface of mucosal epithelial cells.
4. Pancreatic and intestinal brush-border enzymes break down starches into maltose, maltotriose, and $\alpha$-dextrins (pancreatic amylase), $\alpha$-dextrins into glucose ($\alpha$-dextrinase), maltose to glucose (maltase), sucrose to glucose and fructose (sucrase), lactose to glucose and galactose (lactase), and proteins into peptides (trypsin, chymotrypsin, and elastase). Also, enzymes break off amino acids at the carboxyl ends of peptides (carboxypeptidases) and break off amino acids at the amino ends of peptides (aminopeptidases). Finally, enzymes split dipeptides into amino acids (dipeptidases), triglycerides to fatty acids and monoglycerides (lipases), and nucleotides to pentoses and nitrogenous bases (nucleosidases and phosphatases).
5. Mechanical digestion in the small intestine involves segmentation and migrating motility complexes.
6. Absorption occurs via diffusion, facilitated diffusion, osmosis, and active transport; most absorption occurs in the small intestine.
7. Monosaccharides, amino acids, and short-chain fatty acids pass into the blood capillaries.
8. Long-chain fatty acids and monoglycerides are absorbed from micelles, resynthesized to triglycerides, and formed into chylomicrons.
9. Chylomicrons move into lymph in the lacteal of a villus.
10. The small intestine also absorbs electrolytes, vitamins, and water.

24.13 Large Intestine
1. The large intestine extends from the ileocecal sphincter to the anus.
2. Its regions include the cecum, colon, rectum, and anal canal.
3. The mucosa contains many goblet cells, and the muscularis consists of teniae coli and hastrae.
4. Mechanical movements of the large intestine include hastral churning, peristalsis, and mass peristalsis.
5. The last stages of chemical digestion occur in the large intestine through bacterial action. Substances are further broken down, and some vitamins are synthesized.
6. The large intestine absorbs water, ions, and vitamins.
7. Feces consist of water, inorganic salts, epithelial cells, bacteria, and undigested foods.
8. The elimination of feces from the rectum is called defecation.
9. Defecation is a reflex action aided by voluntary contractions of the diaphragm and abdominal muscles and relaxation of the external anal sphincter.

24.14 Phases of Digestion
1. Digestive activities occur in three overlapping phases: cephalic, gastric, and intestinal.
2. During the cephalic phase of digestion, salivary glands secrete saliva and gastric glands secrete gastric juice in order to prepare the mouth and stomach for food that is about to be eaten.
3. The presence of food in the stomach causes the gastric phase of digestion, which promotes gastric juice secretion and gastric motility.
4. During the intestinal phase of digestion, food is digested in the small intestine. In addition, gastric motility and gastric secretion decrease in order to slow the exit of chyme from the stomach, which prevents the small intestine from being overloaded with more chyme than it can handle.
5. The activities that occur during the various phases of digestion are coordinated by neural pathways and by hormones. Table 24.8 summarizes the major hormones that control digestion.

24.15 Development of the Digestive System
1. The endoderm of the primitive gut forms the epithelium and glands of most of the GI tract.
2. The mesoderm of the primitive gut forms the smooth muscle and connective tissue of the GI tract.

24.16 Aging and the Digestive System
1. General changes include decreased secretory mechanisms, decreased motility, and loss of tone.
2. Specific changes may include loss of taste, pyorrhea, hernias, peptic ulcer disease, constipation, hemorrhoids, and diverticular diseases.

Critical Thinking Questions

1. Why would you not want to completely suppress HCl secretion in the stomach?
2. Trey has cystic fibrosis, a genetic disorder that is characterized by the production of excessive mucus, affecting several body systems (e.g., respiratory, digestive, reproductive). In the digestive system, the excess mucus blocks bile ducts in the liver and pancreatic ducts. How would this affect Trey’s digestive processes?
3. Antonio had dinner at his favorite Italian restaurant. His menu consisted of a salad, a large plate of spaghetti, garlic bread, and wine. For dessert, he consumed “death by chocolate” cake and a cup of coffee. He topped off his evening with a cigarette and brandy. He returned home and, while lying on his couch watching television, he experienced a pain in his chest. He called 911 because he was certain he was having a heart attack. Antonio was told his heart was fine, but he needed to watch his diet. What happened to Antonio?
Answers to Figure Questions

24.1 Digestive enzymes are produced by the salivary glands, tongue, stomach, pancreas, and small intestine.

24.2 In the context of the digestive system, absorption is the movement of the products of digestion from the lumen of the GI tract into blood or lymph.

24.3 The lamina propria has the following functions: (1) It contains blood vessels and lymphatic vessels, which are the routes by which nutrients are absorbed from the GI tract; (2) it supports the mucosal epithelium and binds it to the muscularis mucosae; and (3) it contains mucosa-associated lymphatic tissue (MALT), which helps protect against disease.

24.4 The neurons of the myenteric plexus regulate GI tract motility, and the neurons of the submucosal plexus regulate GI secretion.

24.5 Mesentery binds the small intestine to the posterior abdominal wall.

24.6 The uvula helps prevent foods and liquids from entering the nasal cavity during swallowing.

24.7 Chloride ions in saliva activate salivary amylase.

24.8 The main component of teeth is connective tissue, specifically dentin.

24.9 The first, second, and third molars do not replace any deciduous teeth.

24.10 The esophageal mucosa and submucosa contain mucus-secreting glands.

24.11 Both. Initiation of swallowing is voluntary and the action is carried out by skeletal muscles. Completion of swallowing—moving a bolus along the esophagus and into the stomach—is involuntary and involves peristalsis by smooth muscle.

24.12 After a large meal, the rugae stretch and disappear as the stomach fills.

24.13 Parietal cells in gastric glands secrete HCl, which is a component of gastric juice. HCl kills microbes in food, denatures proteins, and converts pepsinogen into pepsin.

24.14 Hydrogen ions secreted into gastric juice are derived from carbonic acid (H₂CO₃).

24.15 Histamine is a paracrine agent released by mast cells in the lamina propria.

24.16 The pancreatic duct contains pancreatic juice (fluid and digestive enzymes); the common bile duct contains bile; the hepatopancreatic ampulla contains pancreatic juice and bile.

24.17 The phagocytic cell in the liver is the stellate reticuloendothelial (Kupffer) cell.

24.18 While a meal is being absorbed, nutrients, O₂, and certain toxic substances are removed by hepatocytes from blood flowing through liver sinusoids.

24.19 The ileum is the longest part of the small intestine.

24.20 Nutrients being absorbed in the small intestine enter the blood via capillaries or the lymph via lacteals.

24.21 The fluid secreted by duodenal (Brunner’s) glands—alkaline mucus—neutralizes gastric acid and protects the mucosal lining of the duodenum.

24.22 Because monoglycerides are hydrophobic (nonpolar) molecules, they can dissolve in and diffuse through the lipid bilayer of the plasma membrane.

24.23 The stomach and pancreas are the two digestive system organs that secrete the largest volumes of fluid.

24.24 The ascending and descending portions of the colon are retroperitoneal.

24.25 Goblet cells in the large intestine secrete mucus to lubricate colonic contents.

24.26 The pH of gastric juice rises due to the buffering action of some amino acids in food proteins.
The food we eat is our only source of energy for running, walking, and even breathing. Many molecules needed to maintain cells and tissues can be made from simpler precursors by the body’s metabolic reactions; others—the essential amino acids, essential fatty acids, vitamins, and minerals—must be obtained from our food. As you learned in Chapter 24, carbohydrates, lipids, and proteins in food are digested by enzymes and absorbed in the gastrointestinal tract. The products of digestion that reach body cells are monosaccharides, fatty acids, glycerol, monoglycerides, and amino acids. Some minerals and many vitamins are part of enzyme systems that catalyze the breakdown and synthesis of carbohydrates, lipids, and proteins. Food molecules absorbed by the gastrointestinal (GI) tract have three main fates:

1. Most food molecules are used to supply energy for sustaining life processes, such as active transport, DNA replication, protein synthesis, muscle contraction, maintenance of body temperature, and mitosis.

2. Some food molecules serve as building blocks for the synthesis of more complex structural or functional molecules, such as muscle proteins, hormones, and enzymes.

3. Other food molecules are stored for future use. For example, glycogen is stored in liver cells, and triglycerides are stored in adipose cells.

In this chapter we discuss how metabolic reactions harvest the chemical energy stored in foods; how each group of food molecules contributes to the body’s growth, repair, and energy needs; how energy balance is maintained in the body; and how body temperature is regulated. Finally, we explore some aspects of nutrition to discover why you should opt for fish instead of a burger the next time you eat out.

Did you ever wonder how fasting and starvation affect the body?
25.1 Metabolic Reactions

OBJECTIVES

- Define metabolism.
- Explain the role of ATP in anabolism and catabolism.

Metabolism (me-TAB-ō-lizm; metabol- = change) refers to all of the chemical reactions that occur in the body. There are two types of metabolism: catabolism and anabolism. Those chemical reactions that break down complex organic molecules into simpler ones are collectively known as catabolism (ka-TAB-ō-lizm; cata- = downward). Overall, catabolic (decomposition) reactions are exergonic; they produce more energy than they consume, releasing the chemical energy stored in organic molecules. Important sets of catabolic reactions occur in glycolysis, the Krebs cycle, and the electron transport chain, each of which will be discussed later in the chapter.

Chemical reactions that combine simple molecules and monomers to form the body’s complex structural and functional components are collectively known as anabolism (a-NAB-ō-lizm; ana- = upward). Examples of anabolic reactions are the formation of peptide bonds between amino acids during protein synthesis, the building of fatty acids into phospholipids that form the plasma membrane bilayer, and the linkage of glucose monomers to form glycogen. Anabolic reactions are endergonic; they consume more energy than they produce.

Metabolism is an energy-balancing act between catabolic (decomposition) reactions and anabolic (synthesis) reactions. The molecule that participates most often in energy exchanges in living cells is ATP (adenosine triphosphate), which couples energy-releasing catabolic reactions to energy-requiring anabolic reactions.

The metabolic reactions that occur depend on which enzymes are active in a particular cell at a particular time, or even in a particular part of the cell. Catabolic reactions can be occurring in the mitochondria of a cell at the same time as anabolic reactions are taking place in the endoplasmic reticulum.

A molecule synthesized in an anabolic reaction has a limited lifetime. With few exceptions, it will eventually be broken down and its component atoms recycled into other molecules or excreted from the body. Recycling of biological molecules occurs continuously in living tissues, more rapidly in some than in others. Individual cells may be refurbished molecule by molecule, or a whole tissue may be rebuilt cell by cell.

Coupling of Catabolism and Anabolism by ATP

The chemical reactions of living systems depend on the efficient transfer of manageable amounts of energy from one molecule to another. The molecule that most often performs this task is ATP, the “energy currency” of a living cell. Like money, it is readily available to “buy” cellular activities; it is spent and earned over and over. A typical cell has about a billion molecules of ATP, each of which typically lasts for less than a minute before being used. Thus, ATP is not a long-term storage form of currency, like gold in a vault, but rather convenient cash for moment-to-moment transactions.

Recall from Chapter 2 that a molecule of ATP consists of an adenine molecule, a ribose molecule, and three phosphate groups bonded to one another (see Figure 2.26). Figure 25.1 shows how ATP links anabolic and catabolic reactions. When the terminal phosphate group is split off ATP, adenosine diphosphate (ADP) and a phosphate group (symbolized as \( P \)) are formed. Some of the energy released is used to drive anabolic reactions such as the formation of glycogen from glucose. In addition, energy from complex molecules is used in catabolic reactions to combine ADP and a phosphate group to resynthesize ATP:

\[
ADP + P + \text{energy} \rightarrow ATP
\]

About 40% of the energy released in catabolism is used for cellular functions; the rest is converted to heat, some of which helps maintain normal body temperature. Excess heat is lost to the environment. Compared with machines, which typically convert only 10–20% of energy into work, the 40% efficiency of the body’s metabolism is impressive. Still, the body has a continuous need to take in and process external sources of energy so that cells can synthesize enough ATP to sustain life.

Checkpoint

1. What is metabolism? Distinguish between anabolism and catabolism, and give examples of each.
2. How does ATP link anabolism and catabolism?

**Figure 25.1** Role of ATP in linking anabolic and catabolic reactions. When complex molecules and polymers are split apart (catabolism, at left), some of the energy is transferred to form ATP and the rest is given off as heat. When simple molecules and monomers are combined to form complex molecules (anabolism, at right), ATP provides the energy for synthesis, and again some energy is given off as heat.

The coupling of energy-releasing and energy-requiring reactions is achieved through ATP.

Q In a pancreatic cell that produces digestive enzymes, does anabolism or catabolism predominate?
25.2 Energy Transfer

OBJECTIVES

• Describe oxidation–reduction reactions.
• Explain the role of ATP in metabolism.

Various catabolic reactions transfer energy into the “high-energy” phosphate bonds of ATP. Although the amount of energy in these bonds is not exceptionally large, it can be released quickly and easily. Before discussing metabolic pathways, it is important to understand how this transfer of energy occurs. Two important aspects of energy transfer are oxidation–reduction reactions and mechanisms of ATP generation.

Oxidation–Reduction Reactions

Oxidation (ok’si-DÅ-shun) is the removal of electrons from an atom or molecule; the result is a decrease in the potential energy of the atom or molecule. Because most biological oxidation reactions involve the loss of hydrogen atoms, they are called dehydrogenation reactions. An example of an oxidation reaction is the conversion of lactic acid into pyruvic acid:

\[
\begin{align*}
\text{COOH} & \quad \text{Oxidation} \quad \text{Oxidized} \\
\text{H} & \quad \text{C} \quad \text{OH} \quad \text{Remove 2 H} (\text{H}^+ + \text{H}^-) \\
\text{CH}_3 & \quad \text{Lactic acid} \\
\text{COOH} & \quad \text{C} \quad \text{OH} \quad \text{Pyruvic acid} \\
\text{H} & \quad \text{C} \quad \text{O} \quad \text{Reduced} \\
\text{CH}_3 & \quad \text{Lactic acid} \\
\end{align*}
\]

In the preceding reaction, 2H (H^+ + H^-) means that two neutral hydrogen atoms (2H) are removed as one hydrogen ion (H^+) plus one hydride ion (H^-).

Reduction (ré-DUK-shun) is the opposite of oxidation; it is the addition of electrons to a molecule. Reduction results in an increase in the potential energy of the molecule. An example of a reduction reaction is the conversion of pyruvic acid into lactic acid:

\[
\begin{align*}
\text{COOH} & \quad \text{Reduction} \quad \text{Reduced} \\
\text{C} & \quad \text{O} \quad \text{Add 2 H} (\text{H}^+ + \text{H}^-) \\
\text{CH}_3 & \quad \text{Pyruvic acid} \\
\text{H} & \quad \text{C} \quad \text{OH} \quad \text{Lactic acid} \\
\text{C} & \quad \text{O} \quad \text{Oxidized} \\
\text{CH}_3 & \quad \text{Lactic acid} \\
\end{align*}
\]

When a substance is oxidized, the liberated hydrogen atoms do not remain free in the cell but are transferred immediately by coenzymes to another compound. Two coenzymes are commonly used by animal cells to carry hydrogen atoms: nicotinamide adenine dinucleotide (NAD), a derivative of the B vitamin niacin, and flavin adenine dinucleotide (FAD), a derivative of vitamin B_2 (riboflavin). The oxidation and reduction states of NAD^+ and FAD can be represented as follows:

\[
\begin{align*}
\text{NAD}^+ & \quad \text{Oxidized} \quad +2 \text{H} (\text{H}^+ + \text{H}^-) \\
\text{NADH} + \text{H}^+ & \quad \text{Reduced} \quad -2 \text{H} (\text{H}^+ + \text{H}^-) \\
\text{FAD} & \quad \text{Oxidized} \quad +2 \text{H} (\text{H}^+ + \text{H}^-) \\
\text{FADH}_2 & \quad \text{Reduced} \quad -2 \text{H} (\text{H}^+ + \text{H}^-)
\end{align*}
\]

When NAD^+ is reduced to NADH + H^+, the NAD^+ gains a hydride ion (H^-), neutralizing its charge, and the H^+ is released into the surrounding solution. When NADH is oxidized to NAD^+, the loss of the hydride ion results in one less hydrogen atom and an additional positive charge. FAD is reduced to FADH\_2 when it gains a hydrogen ion and a hydride ion, and FADH\_2 is oxidized to FAD when it loses the same two ions.

Oxidation and reduction reactions are always coupled; each time one substance is oxidized, another is simultaneously reduced. Such paired reactions are called oxidation-reduction or redox reactions. For example, when lactic acid is oxidized to form pyruvic acid, the two hydrogen atoms removed in the reaction are used to reduce NAD^+.

This coupled redox reaction may be written as follows:

\[
\begin{align*}
\text{Lactic acid} & \quad \text{Reduced} \\
\text{NAD}^+ & \quad \text{Oxidized} \\
\text{Pyruvic acid} & \quad \text{NADH} + \text{H}^+ \\
\end{align*}
\]

An important point to remember about oxidation-reduction reactions is that oxidation is usually an exergonic (energy-releasing) reaction. Cells use multistep biochemical reactions to release energy from energy-rich, highly reduced compounds (with many hydrogen atoms) to lower-energy, highly oxidized compounds (with many oxygen atoms or multiple bonds). For example, when a cell oxidizes a molecule of glucose (C\_6H\_12O\_6), the energy in the glucose molecule is removed in a stepwise manner. Ultimately, some of the energy is captured by transferring it to ATP, which then serves as an energy source for energy-requiring reactions within the cell. Compounds with many hydrogen atoms such as glucose contain more chemical potential energy than oxidized compounds. For this reason, glucose is a valuable nutrient.

Mechanisms of ATP Generation

Some of the energy released during oxidation reactions is captured within a cell when ATP is formed. Briefly, a phosphate group (\(\hat{P}\)) is added to ADP, with an input of energy, to form ATP. The two high-energy phosphate bonds that can be used to transfer energy are indicated by “squiggles” (\(\sim\)):

\[
\begin{align*}
\text{Adenosine} & \quad \hat{P} \sim \hat{P} \sim \text{energy} \\
\text{ADP} & \quad \text{ATP}
\end{align*}
\]

The high-energy phosphate bond that attaches the third phosphate group contains the energy stored in this reaction. The addition of a phosphate group to a molecule, called phosphorylation (fos-i-LÅ-shun), increases its potential energy. Organisms use three mechanisms of phosphorylation to generate ATP:

1. **Substrate-level phosphorylation** generates ATP by transferring a high-energy phosphate group from an intermediate phosphorylated metabolic compound—a substrate—directly to ADP. In human cells, this process occurs in the cytosol.
2. **Oxidative phosphorylation** removes electrons from organic compounds and passes them through a series of electron acceptors, called the **electron transport chain**, to molecules of oxygen \((O_2)\). This process occurs in the inner mitochondrial membrane of cells.

3. **Photophosphorylation** occurs only in chlorophyll-containing plant cells or in certain bacteria that contain other light-absorbing pigments.

### Checkpoint

3. How is a hydride ion different from a hydrogen ion? What is the involvement of both ions in redox reactions?

4. What are three ways that ATP can be generated?

### 25.3 Carbohydrate Metabolism

**OBJECTIVE**

- Describe the fate, metabolism, and functions of carbohydrates.

As you learned in Chapter 24, both polysaccharides and disaccharides are hydrolyzed into the monosaccharides **glucose** (about 80%), fructose, and galactose during the digestion of carbohydrates. (Some fructose is converted into glucose as it is absorbed through the intestinal epithelial cells.) Hepatocytes (liver cells) convert most of the remaining fructose and practically all of the galactose to glucose.

So the story of carbohydrate metabolism is really the story of glucose metabolism. Because negative feedback systems maintain blood glucose at about 90 mg/100 mL of plasma (5 mmol/liter), a total of 2–3 g of glucose normally circulates in the blood.

### The Fate of Glucose

Because glucose is the body’s preferred source for synthesizing ATP, its use depends on the needs of body cells, which include the following:

- **ATP production.** In body cells that require immediate energy, glucose is oxidized to produce ATP. Glucose not needed for immediate ATP production can enter one of several other metabolic pathways.

- **Amino acid synthesis.** Cells throughout the body can use glucose to form several amino acids, which then can be incorporated into proteins.

- **Glycogen synthesis.** Hepatocytes and muscle fibers can perform glycogenesis (gli’-kö-JEN-e-sis; glyco- = sugar or sweet; -genesis = to generate), in which hundreds of glucose monomers are combined to form the polysaccharide glycogen. Total storage capacity of glycogen is about 125 g in the liver and 375 g in skeletal muscles.

- **Triglyceride synthesis.** When the glycogen storage areas are filled up, hepatocytes can transform the glucose to glycerol and fatty acids that can be used for lipogenesis (lip-ö-JEN-e-sis), the synthesis of triglycerides. Triglycerides then are deposited in adipose tissue, which has virtually unlimited storage capacity.

### Glucose Movement into Cells

Before glucose can be used by body cells, it must first pass through the plasma membrane and enter the cytosol. Glucose absorption in the gastrointestinal tract (and kidney tubules) is accomplished via secondary active transport (Na\(^+\)–glucose symporters). Glucose entry into most other body cells occurs via GluT molecules, a family of transporters that bring glucose into cells via facilitated diffusion (see Section 3.3). A high level of insulin increases the insertion of one type of GluT, called GluT4, into the plasma membranes of most body cells, thereby increasing the rate of facilitated diffusion of glucose into cells. In neurons and hepatocytes, however, another type of GluT is always present in the plasma membrane, so glucose entry is always “turned on.” On entering a cell, glucose becomes phosphorylated. Because GluT cannot transport phosphorylated glucose, this reaction traps glucose within the cell.

### Glucose Catabolism

The oxidation of glucose to produce ATP is also known as **cellular respiration**, and it involves four sets of reactions: glycolysis, the formation of acetyl coenzyme A, the Krebs cycle, and the electron transport chain (Figure 25.2).

1. **Glycolysis.** A set of reactions in which one glucose molecule is oxidized and two molecules of pyruvic acid are produced. The reactions also produce two molecules of ATP and two energy-containing NADH + H\(^+\).

2. **Formation of acetyl coenzyme A.** A transition step that prepares pyruvic acid for entrance into the Krebs cycle. This step also produces energy-containing NADH + H\(^+\) plus carbon dioxide (CO\(_2\)).

3. **Krebs cycle reactions.** These reactions oxidize acetyl coenzyme A and produce CO\(_2\), ATP, NADH + H\(^+\), and FADH\(_2\).

4. **Electron transport chain reactions.** These reactions oxidize NADH + H\(^+\) and FADH\(_2\) and transfer their electrons through a series of electron carriers.

Because glycolysis does not require oxygen, it can occur under **aerobic** (with oxygen) or **anaerobic** (without oxygen) conditions. By contrast, the reactions of the Krebs cycle and electron transport chain require oxygen and are collectively referred to as **aerobic respiration**. Thus, when oxygen is present, all four phases occur: glycolysis, formation of acetyl coenzyme A, the Krebs cycle, and the electron transport chain. However, if oxygen is not available or at a low concentration, pyruvic acid is converted to a substance called **lactic acid** (see Figure 25.5) and the remaining steps of cellular respiration do not occur. When glycolysis occurs by itself under anaerobic conditions, it is referred to as **anaerobic glycolysis**.

**Glycolysis** During glycolysis (gli-KOL-i-sis; -lysis = breakdown), chemical reactions split a 6-carbon molecule of glucose into two 3-carbon molecules of pyruvic acid (Figure 25.3). Even though glycolysis
25.3 Carbohydrate Metabolism

The oxidation of glucose involves glycolysis, the formation of acetyl coenzyme A, the Krebs cycle, and the electron transport chain.

**FIGURE 25.2** Overview of cellular respiration (oxidation of glucose). A modified version of this figure appears in several places in this chapter to indicate the relationships of particular reactions to the overall process of cellular respiration.

The oxidation of glucose involves glycolysis, the formation of acetyl coenzyme A, the Krebs cycle, and the electron transport chain.

**Q** Which of the four processes shown here produces the most ATP?

**FIGURE 25.3** The role of glycolysis in cellular respiration.

During glycolysis, each molecule of glucose is converted to two molecules of pyruvic acid.

**Q** For each glucose molecule that undergoes glycolysis, how many ATP molecules are generated?
consumes two ATP molecules, it produces four ATP molecules, for a net gain of two ATP molecules for each glucose molecule that is oxidized.

**Figure 25.4** shows the 10 reactions that glycolysis comprises. In the first half of the sequence (reactions 1 through 5), energy in the form of ATP is “invested” and the 6-carbon glucose is split into two 3-carbon molecules of glyceraldehyde 3-phosphate. *Phosphofructokinase* (fos′-fō-fruk′-tō-KL-nās), the enzyme that catalyzes step 3, is the key regulator of the rate of glycolysis. The activity of this enzyme is high

**FIGURE 25.4  The 10 reactions of glycolysis.**  1 Glucose is phosphorylated, using a phosphate group from an ATP molecule to form glucose 6-phosphate. 2 Glucose 6-phosphate is converted to fructose 6-phosphate. 3 A second ATP is used to add a second phosphate group to fructose 6-phosphate to form fructose 1,6-bisphosphate. 4 and 5 Fructose splits into two 3-carbon molecules, glyceraldehyde 3-phosphate (G 3-P) and dihydroxyacetone phosphate, each having one phosphate group. 6 Oxidation occurs as two molecules of NAD$^+$ accept two pairs of electrons and hydrogen ions from two molecules of G 3-P to form two molecules of NADH. Body cells use the two NADH produced in this step to generate ATP in the electron transport chain. A second phosphate group attaches to G 3-P, forming 1,3-bisphosphoglyceric acid (BPG). 7 through 10 These reactions generate four molecules of ATP and produce two molecules of pyruvic acid (pyruvate*).

Glycolysis results in a net gain of two ATP, two NADH, and two H$^+$.

**Q  Why is the enzyme that catalyzes step 3 called a kinase?**

*The carboxyl groups (–COOH) of intermediates in glycolysis and in the citric acid cycle are mostly ionized at the pH of body fluids to –COO$^-$. The suffix “-ic acid” indicates the non-ionized form, whereas the ending “-ate” indicates the ionized form. Although the “-ate” names are more correct, we will use the “acid” names because these terms are more familiar.*
The Fate of Pyruvic Acid  The fate of pyruvic acid produced during glycolysis depends on the availability of oxygen (Figure 25.5). If oxygen is scarce (anaerobic conditions)—for example, in skeletal muscle fibers during strenuous exercise—then pyruvic acid is reduced via an anaerobic pathway by the addition of two hydrogen atoms to form lactic acid (lactate):

\[2 \text{Pyruvic acid} + 2 \text{NADH} + 2 \text{H}^+ \rightarrow 2 \text{Lactic acid} + 2 \text{NAD}^+\]

This reaction regenerates the NAD\(^+\) that was used in the oxidation of glyceraldehyde 3-phosphate (see step 6 in Figure 25.4) and thus allows glycolysis to continue. As lactic acid is produced, it rapidly diffuses out of the cell and enters the blood. Hepatocytes remove lactic acid from the blood and convert it back to pyruvic acid. Recall that a buildup of lactic acid is one factor that contributes to muscle fatigue.

When oxygen is plentiful (aerobic conditions), most cells convert pyruvic acid to acetyl coenzyme A. This molecule links glycolysis, which occurs in the cytosol, with the Krebs cycle, which occurs in the matrix of mitochondria. Pyruvic acid enters the mitochondrial matrix with the help of a special transporter protein. Because they lack mitochondria, red blood cells can only produce ATP through glycolysis.

Formation of Acetyl Coenzyme A  Each step in the oxidation of glucose requires a different enzyme, and often a coenzyme as well. The coenzyme used at this point in cellular respiration is coenzyme A (CoA), which is derived from pantothenic acid, a B vitamin. During the transitional step between glycolysis and the Krebs cycle, pyruvic acid is prepared for entrance into the cycle. The enzyme pyruvate dehydrogenase (pi-ROO-vât dé-Hi-drō-jen-ås), which is located exclusively in the mitochondrial matrix, converts pyruvic acid to a 2-carbon fragment called an acetyl group by removing a molecule of carbon dioxide (Figure 25.5). The loss of a molecule of CO\(_2\) by a substance is called decarboxylation (dé-kar-bok-si-LÅ-shun). This is the first reaction in cellular respiration that releases CO\(_2\). During this reaction, pyruvic acid is also oxidized. Each pyruvic acid loses two hydrogen atoms in the form of one hydride ion (H\(^-\)) plus one hydrogen ion (H\(^+\)). The coenzyme NAD\(^+\) is reduced as it picks up the H\(^-\) from pyruvic acid; the H\(^+\) is released into the mitochondrial matrix. The reduction of NAD\(^+\) to NADH + H\(^+\) is indicated in Figure 25.5 by the curved arrow entering and then leaving the reaction. Recall that the oxidation of one glucose molecule produces two molecules of pyruvic acid, so for each molecule of glucose, two molecules of carbon dioxide are lost and two NADH + H\(^+\) are produced. The acetyl group attaches to coenzyme A, producing a molecule called acetyl coenzyme A (acetyl CoA).

Q In which part of the cell does glycolysis occur?

The Krebs Cycle  Once the pyruvic acid has undergone decarboxylation and the remaining acetyl group has attached to CoA, the resulting compound (acetyl CoA) is ready to enter the Krebs cycle (Figure 25.6). The Krebs cycle—named for the biochemist Hans Krebs, who described these reactions in the 1930s—is also
known as the *citric acid cycle*, for the first molecule formed when an acetyl group joins the cycle. The reactions occur in the matrix of mitochondria and consist of a series of oxidation–reduction reactions and decarboxylation reactions that release CO₂. In the Krebs cycle, the oxidation–reduction reactions transfer chemical energy, in the form of electrons, to two coenzymes—NAD⁺ and FAD. The pyruvic acid derivatives are oxidized, and the coenzymes are reduced. In addition, one step generates ATP. Figure 25.7 shows the reactions of the Krebs cycle in more detail.

Each time that an acetyl CoA molecule enters the Krebs cycle, the cycle undergoes one complete “turn,” starting with the production of citric acid and ending with the formation of oxaloacetic acid (Figure 25.7). For each turn of the Krebs cycle, three NADH, three H⁺, and one FADH₂ are produced by oxidation–reduction reactions, and one molecule of ATP is generated by substrate-level phosphorylation. Because each glucose molecule provides two acetyl CoA molecules, there are two turns of the Krebs cycle per molecule of glucose catabolized. This results in the production of six molecules of NADH, six H⁺, and two molecules of FADH₂ by oxidation–reduction reactions, and two molecules of ATP by substrate-level phosphorylation. The formation of NADH and FADH₂ is the most important outcome of the Krebs cycle because these reduced coenzymes contain the energy originally stored in glucose and then in pyruvic acid. They will later yield many molecules of ATP from the electron transport chain.

Liberation of CO₂ occurs as pyruvic acid is converted to acetyl CoA and during the two decarboxylation reactions of the Krebs cycle (see Figure 25.6). Because each molecule of glucose generates two molecules of pyruvic acid, six molecules of CO₂ are liberated from each original glucose molecule catabolized along this pathway. The molecules of CO₂ diffuse out of the mitochondria, through the cytosol and plasma membrane, and then into the blood. Blood transports the CO₂ to the lungs, where it eventually is exhaled.

The Electron Transport Chain The electron transport chain is a series of electron carriers, integral membrane proteins in the inner mitochondrial membrane. This membrane is folded into
FIGURE 25.7 The eight reactions of the Krebs cycle.  

1. **Entry of the acetyl group.** The chemical bond that attaches the acetyl group to coenzyme A (CoA) breaks, and the 2-carbon acetyl group attaches to a 4-carbon molecule of oxaloacetic acid to form a 6-carbon molecule called citric acid. CoA is free to combine with another acetyl group from pyruvic acid and repeat the process.  

2. **Isomerization.** Citric acid undergoes isomerization to isocitric acid, which has the same molecular formula as citrate. Notice, however, that the hydroxyl group (–OH) is attached to a different carbon.  

3. **Oxidative decarboxylation.** Isocitric acid is oxidized and loses a molecule of CO₂, forming alpha-ketoglutaric acid. The H⁺ from the oxidation is passed on to NAD⁺, which is reduced to NADH + H⁺.  

4. **Oxidative decarboxylation.** Alpha-ketoglutaric acid is oxidized, loses a molecule of CO₂, and picks up CoA to form succinyl-CoA.  

5. **Substrate-level phosphorylation.** CoA is displaced by a phosphate group, which is then transferred to guanosine diphosphate (GDP) to form guanosine triphosphate (GTP). GTP can donate a phosphate group to ADP to form ATP.  

6. **Dehydrogenation.** Succinic acid is oxidized to fumaric acid as two of its hydrogen atoms are transferred to the coenzyme flavin adenine dinucleotide (FAD), which is reduced to FADH₂.  

7. **Hydration.** Fumaric acid is converted to malic acid by the addition of a molecule of water.  

8. **Dehydrogenation.** In the final step in the cycle, malic acid is oxidized to re-form oxaloacetic acid. Two hydrogen atoms are removed and one is transferred to NAD⁺, which is reduced to NADH + H⁺. The regenerated oxaloacetic acid can combine with another molecule of acetyl CoA, beginning a new cycle.  

The three main results of the Krebs cycle are the production of reduced coenzymes (NADH and FADH₂), which contain stored energy; the generation of GTP, a high-energy compound that is used to produce ATP; and the formation of CO₂, which is transported to the lungs and exhaled.

**Q** Why is the production of reduced coenzymes important in the Krebs cycle?
cristae that increase its surface area, accommodating thousands of copies of the transport chain in each mitochondrion. Each carrier in the chain is reduced as it picks up electrons and oxidized as it gives up electrons. As electrons pass through the chain, a series of exergonic reactions release small amounts of energy; this energy is used to form ATP. In cellular respiration, the final electron acceptor of the chain is oxygen. Because this mechanism of ATP generation links chemical reactions (the passage of electrons along the transport chain) with the pumping of hydrogen ions, it is called chemiosmosis (kem′-ē-oz-MÔ-sis; chemi- = chemical; -osmosis = pushing). Together, chemiosmosis and the electron transport chain constitute oxidative phosphorylation.

Briefly, chemiosmosis works as follows (Figure 25.8):

1. Energy from NADH + H+ passes along the electron transport chain and is used to pump H+ from the matrix of the mitochondrion into the space between the inner and outer mitochondrial membranes. This mechanism is called a proton pump because H+ ions consist of a single proton.

2. A high concentration of H+ accumulates between the inner and outer mitochondrial membranes.

3. ATP synthesis then occurs as hydrogen ions flow back into the mitochondrial matrix through a special type of H+ channel in the inner membrane.

**FIGURE 25.8 Chemiosmosis.**

In chemiosmosis, ATP is produced when hydrogen ions diffuse back into the mitochondrial matrix.

**ELECTRON CARRIERS** Several types of molecules and atoms serve as electron carriers:

- **Flavin mononucleotide (FMN)** (FLA-′vin mon′-ô-NOO-klê-ô-tid) is a flavoprotein derived from riboflavin (vitamin B2).

- **Cytochromes** (SI-tô-krômz) are proteins with an iron-containing group (heme) capable of existing alternately in a reduced form (Fe2+) and an oxidized form (Fe3+). The cytochromes involved in the electron transport chain include cytochrome b (cyt b), cytochrome c1 (cyt c1), cytochrome c (cyt c), cytochrome a (cyt a), and cytochrome a3 (cyt a3).

- **Iron–sulfur (Fe-S) centers** contain either two or four iron atoms bound to sulfur atoms that form an electron transfer center within a protein.

- **Copper (Cu) atoms** bound to two proteins in the chain also participate in electron transfer.

- **Coenzyme Q (Q)**, is a nonprotein, low-molecular-weight carrier that is mobile in the lipid bilayer of the inner membrane.

**STEPS IN ELECTRON TRANSPORT AND CHEMIOSMOTIC ATP GENERATION**

Within the inner mitochondrial membrane, the carriers of the electron transport chain are clustered into three complexes, each of which acts as a proton pump that expels H+ from the mitochondrial matrix and helps create an electrochemical gradient of H+. Each of the three proton pumps transports electrons and pumps H+ through the inner mitochondrial membrane, driven by the proton motive force. As H+ flow back, they generate ATP because the H+ channels also include an enzyme called ATP synthase (SIN-thås). The enzyme uses the proton motive force to synthesize ATP from ADP and P. The process of chemiosmosis is responsible for most of the ATP produced during cellular respiration.

For every molecule of NADH + H+ that drops off hydrogen atoms to the electron transport chain, two or three molecules of ATP (average = 2.5) are produced via oxidative phosphorylation. For every molecule of FADH2 that drops off hydrogen atoms to the electron transport chain, only one or two molecules of ATP (average = 1.5) are produced via oxidative phosphorylation. This is due to the fact that FADH2 drops off its hydrogen atoms at a lower step along the electron transport chain than NADH + H+.

**Summary of Cellular Respiration** The various electron transfers in the electron transport chain generate either 26 or 28 ATP molecules from each molecule of glucose that is catabolized: either 23 or 25 from the 10 molecules of NADH + H+ and three from the two molecules of FADH2. The discrepancy in the number of ATP formed from NADH + H+ via oxidative phosphorylation is due to the fact...
that the two NADH + H⁺ molecules produced in the cytosol during glycolysis cannot enter mitochondria. Instead they donate their electrons to one of two transfer shuttles, known as the malate shuttle and the glycerol phosphate shuttle. In cells of the liver, kidneys, and heart, use of the malate shuttle results in an average of 2.5 molecules of ATP synthesized for each molecule of NADH + H⁺. In other body cells, such as skeletal muscle fibers and neurons, use of the glycerol phosphate shuttle results in an average of 1.5 molecules of ATP synthesized for each molecule of NADH + H⁺.

Recall that four ATP molecules are produced via substrate-level phosphorylation (two from glycolysis and two from the Krebs cycle). If the four ATP produced via substrate-level phosphorylation are added to the 26 or 28 ATP produced via oxidative phosphorylation, a total of either 30 or 32 ATP is generated for each molecule of glucose catabolized during cellular respiration. The overall reaction is

\[
\text{C}_6\text{H}_{12}\text{O}_6 + 6\text{O}_2 + 30 \text{ or } 32\text{ ADPs} + 30 \text{ or } 32\text{ P} \rightarrow 6\text{CO}_2 + 6\text{H}_2\text{O} + 30 \text{ or } 32\text{ ATPs}
\]

Glucose  Oxygen
Carbon dioxide  Water

Table 25.1 summarizes the ATP yield during cellular respiration. A schematic depiction of the principal reactions of cellular respiration is presented in Figure 25.10.

Glycolysis, the Krebs cycle, and especially the electron transport chain provide all of the ATP for cellular activities. Because the Krebs cycle and electron transport chain are aerobic processes, cells cannot carry on their activities for long if oxygen is lacking.

**Glucose Anabolism**

Even though most of the glucose in the body is catabolized to generate ATP, glucose may take part in or be formed via several anabolic...
epinephrine from the adrenal medullae. Glucose 1-phosphate is then converted to glucose 6-phosphate and finally to glucose, which leaves hepatocytes via glucose transporters (GluT) in the plasma membrane. Phosphorylated glucose molecules cannot ride aboard the GluT transporters, however, and need to be dephosphorylated by phosphatase, the enzyme that catalyzes this reaction. When body activities require ATP, glycogen stored in hepatocytes is broken down into glucose and released into the blood to be transported to cells, where it will be catabolized by the processes of cellular respiration already described. The process of splitting glycogen into its glucose subunits is called glycogenolysis (gli-′ko-je-NOL-e-sis). (Note: Do not confuse glycogenolysis, the breakdown of glycogen to glucose, with glycolysis, the 10 reactions that convert glucose to pyruvic acid.)

Glycogenolysis is not a simple reversal of the steps of glycogenesis (Figure 25.11). It begins by splitting off glucose molecules from the branched glycogen molecule via phosphorylation to form glucose 1-phosphate. Phosphorylase, the enzyme that catalyzes this reaction, is activated by glucagon from pancreatic alpha cells and reacts. One is the synthesis of glycogen; another is the synthesis of new glucose molecules from some of the products of protein and lipid breakdown.

Glucose Storage: Glycogenesis If glucose is not needed immediately for ATP production, it combines with many other molecules of glucose to form glycogen, a polysaccharide that is the only stored form of carbohydrate in the body. The hormone insulin, from pancreatic beta cells, stimulates hepatocytes and skeletal muscle cells to carry out glycogenesis (gli-′ko-JEN-e-sis), the synthesis of glycogen (Figure 25.11). The body can store about 500 g (about 1.1 lb) of glycogen, roughly 75% in skeletal muscle fibers and the rest in liver cells. During glycogenesis, glucose is first phosphorylated to glucose 6-phosphate by hexokinase. Glucose 6-phosphate is converted to glucose 1-phosphate, then to uridine diphosphate glucose, and finally to glycogen.

Glucose Release: Glycogenolysis When body activities require ATP, glycogen stored in hepatocytes is broken down into glucose and released into the blood to be transported to cells, where it will be catabolized by the processes of cellular respiration already described. The process of splitting glycogen into its glucose subunits is called glycogenolysis (gli-′ko-je-NOL-e-sis). (Note: Do not confuse glycogenolysis, the breakdown of glycogen to glucose, with glycolysis, the 10 reactions that convert glucose to pyruvic acid.)

Glycogenolysis is not a simple reversal of the steps of glycogenesis (Figure 25.11). It begins by splitting off glucose molecules from the branched glycogen molecule via phosphorylation to form glucose 1-phosphate. Phosphorylase, the enzyme that catalyzes this reaction, is activated by glucagon from pancreatic alpha cells and

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**TABLE 25.1 Summary of ATP Produced in Cellular Respiration**

<table>
<thead>
<tr>
<th>SOURCE</th>
<th>ATP YIELD PER GLUCOSE MOLECULE (PROCESS)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GLYCOLYSIS</strong></td>
<td></td>
</tr>
<tr>
<td>Oxidation of one glucose molecule to two pyruvic acid molecules</td>
<td>2 ATPs (substrate-level phosphorylation).</td>
</tr>
<tr>
<td>Production of 2 NADH + H⁺</td>
<td>3 or 5 ATPs (oxidative phosphorylation).</td>
</tr>
<tr>
<td><strong>FORMATION OF TWO MOLECULES OF ACETYL COENZYME A</strong></td>
<td></td>
</tr>
<tr>
<td>2 NADH + 2 H⁺</td>
<td>5 ATPs (oxidative phosphorylation).</td>
</tr>
<tr>
<td><strong>KREBS CYCLE AND ELECTRON TRANSPORT CHAIN</strong></td>
<td></td>
</tr>
<tr>
<td>Oxidation of succinyl-CoA to succinic acid</td>
<td>2 GTPs that are converted to 2 ATPs (substrate-level phosphorylation).</td>
</tr>
<tr>
<td>Production of 6 NADH + 6 H⁺</td>
<td>15 ATPs (oxidative phosphorylation).</td>
</tr>
<tr>
<td>Production of 2 FADH₂</td>
<td>3 ATPs (oxidative phosphorylation).</td>
</tr>
<tr>
<td>Total</td>
<td>30 or 32 ATPs per glucose molecule.</td>
</tr>
</tbody>
</table>

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**FIGURE 25.10** Summary of the principal reactions of cellular respiration. ETC = electron transport chain and chemiosmosis.

Except for glycolysis, which occurs in the cytosol, all other reactions of cellular respiration occur within mitochondria.

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Q How many molecules of O₂ are used, and how many molecules of CO₂ are produced during the complete oxidation of one glucose molecule?
Formation of Glucose from Proteins and Fats: Gluconeogenesis

When your liver runs low on glycogen, it is time to eat. If you don’t, your body starts catabolizing triglycerides (fats) and proteins. Actually, the body normally catabolizes some of its triglycerides and proteins, but large-scale triglyceride and protein catabolism does not happen unless you are starving, eating very few carbohydrates, or suffering from an endocrine disorder.

The glycerol part of triglycerides, lactic acid, and certain amino acids can be converted in the liver to glucose (Figure 25.12). The process by which glucose is formed from these noncarbohydrate sources is called gluconeogenesis (gloo’-kō-nee-ō-JEN-e-sis; neo- = new). An easy way to distinguish this term from glycogenesis or glycogenolysis is to remember that in this case glucose is not converted back from glycogen, but is instead newly formed. About 60% of the amino acids in the body can be used for gluconeogenesis. Lactic acid and amino acids such as alanine, cysteine, glycine, serine, and threonine are converted to pyruvic acid, which then may be synthesized into glucose or enter the Krebs cycle. Glycerol may be converted into glyceraldehyde 3-phosphate, which may form pyruvic acid or be used to synthesize glucose.

Gluconeogenesis is stimulated by cortisol, the main glucocorticoid hormone of the adrenal cortex, and by glucagon from the pancreas. In addition, cortisol stimulates the breakdown of proteins into amino acids, thus expanding the pool of amino acids available for gluconeogenesis. Thyroid hormones (thyroxine and triiodothyronine) also mobilize proteins and may mobilize triglycerides from adipose tissue, thereby making glycerol available for gluconeogenesis.

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Q Other than hepatocytes, which body cells can synthesize glycogen? Why are they unable to release glucose into the blood?

converts glucose 6-phosphate into glucose, is absent in skeletal muscle cells. Thus, hepatocytes, which have phosphatase, can release glucose derived from glycogen to the bloodstream, but skeletal muscle cells cannot. In skeletal muscle cells, glycogen is broken down into glucose 1-phosphate, which is then catabolized for ATP production via glycolysis and the Krebs cycle. However, the lactic acid produced by glycolysis in muscle cells can be converted to glucose in the liver. In this way, muscle glycogen can be an indirect source of blood glucose.

Q What cells can carry out gluconeogenesis and glycogenesis?
Fat-soluble vitamins. Chylomicrons enter lacteals of intestinal villi and are carried by lymph into venous blood and then into the systemic circulation. Their presence gives blood plasma a milky appearance, but they remain in the blood for only a few minutes. As chylomicrons circulate through the capillaries of adipose tissue, one of their apo-proteins, apo C-2, activates endothelial lipoprotein lipase, an enzyme that removes fatty acids from chylomicron triglycerides. The free fatty acids are then taken up by adipocytes for synthesis and storage as triglycerides and by muscle cells for ATP production. Hepatocytes remove chylomicron remnants from the blood via receptor-mediated endocytosis, in which another chylomicron apoprotein, apo E, is the docking protein.

Very-low-density lipoproteins (VLDLs), which form in hepatocytes, contain mainly endogenous (made in the body) lipids. VLDLs contain about 10% proteins, 50% triglycerides, 20% phospholipids, and 20% cholesterol. VLDLs transport triglycerides synthesized in hepatocytes to adipocytes for storage. Like chylomicrons, they lose triglycerides as their apo C-2 activates endothelial lipoprotein lipase, and the resulting fatty acids are taken up by adipocytes for storage and by muscle cells for ATP production. As they deposit some of their triglycerides in adipose cells, VLDLs are converted to LDLs.

Low-density lipoproteins (LDLs) contain 25% proteins, 5% triglycerides, 20% phospholipids, and 50% cholesterol. They carry about 75% of the total cholesterol in blood and deliver it to cells throughout the body for use in repair of cell membranes and synthesis of steroid hormones and bile salts. LDLs contain a single apoprotein, apo B100, which is the docking protein that binds to LDL receptors on cell membranes.

**Figure 25.13** A lipoprotein. Shown here is a VLDL.

A single layer of amphipathic phospholipids, cholesterol, and proteins surrounds a core of nonpolar lipids.

Q Which type of lipoprotein delivers cholesterol to body cells?
the plasma membrane of body cells so that LDL can enter the cell via receptor-mediated endocytosis. Within the cell, the LDL is broken down, and the cholesterol is released to serve the cell’s needs. Once a cell has sufficient cholesterol for its activities, a negative feedback system inhibits the cell’s synthesis of new LDL receptors.

When present in excessive numbers, LDLs also deposit cholesterol in and around smooth muscle fibers in arteries, forming fatty plaques that increase the risk of coronary artery disease (see Disorders: Homeostatic Imbalances at the end of Chapter 20). For this reason, the cholesterol in LDLs, called LDL-cholesterol, is known as “bad” cholesterol. Because some people have too few LDL receptors, their body cells remove LDL from the blood less efficiently; as a result, their plasma LDL level is abnormally high, and they are more likely to develop fatty plaques. Eating a high-fat diet increases the production of VLDLs, which elevate the plasma level and increases the formation of fatty plaques.

High-density lipoproteins (HDLs), which contain 40–45% proteins, 5–10% triglycerides, 30% phospholipids, and 20% cholesterol, remove excess cholesterol from body cells and the blood and transport it to the liver for elimination. Because HDLs prevent accumulation of cholesterol in the blood, a high HDL level is associated with decreased risk of coronary artery disease. For this reason, HDL-cholesterol is known as “good” cholesterol.

### Sources and Significance of Blood Cholesterol

There are two sources of cholesterol in the body. Some is present in foods (eggs, dairy products, organ meats, beef, pork, and processed luncheon meats), but most is synthesized by hepatocytes. Fatty foods that don’t contain any cholesterol at all can still dramatically increase blood cholesterol level in two ways. First, a high intake of dietary fats stimulates reabsorption of cholesterol-containing bile back into the blood, so less cholesterol is lost in the feces. Second, when saturated fats are broken down in the body, hepatocytes use some of the breakdown products to make cholesterol.

A lipid profile test usually measures total cholesterol (TC), HDL-cholesterol, and triglycerides (VLDLs). LDL-cholesterol then is calculated by using the following formula: LDL-cholesterol = TC − HDL-cholesterol − (triglycerides/5). In the United States, blood cholesterol is usually measured in milligrams per deciliter (mg/dL); a deciliter is 0.1 liter or 100 mL. For adults, desirable levels of blood cholesterol are total cholesterol under 200 mg/dL, LDL-cholesterol under 130 mg/dL, and HDL-cholesterol over 40 mg/dL. Normally, triglycerides are in the range of 10–190 mg/dL.

As total cholesterol level increases, the risk of coronary artery disease begins to rise. When total cholesterol is above 200 mg/dL (5.2 mmol/liter), the risk of a heart attack doubles with every 50 mg/dL (1.3 mmol/liter) increase in total cholesterol. Total cholesterol of 200–239 mg/dL and LDL of 130–159 mg/dL are borderline-high; total cholesterol above 239 mg/dL and LDL above 159 mg/dL are classified as high blood cholesterol. The ratio of total cholesterol to HDL-cholesterol predicts the risk of developing coronary artery disease. For example, a person with a total cholesterol of 180 mg/dL and HDL of 60 mg/dL has a risk ratio of 3. Ratios above 4 are considered undesirable; the higher the ratio, the greater the risk of developing coronary artery disease.

Among the therapies used to reduce blood cholesterol level are exercise, diet, and drugs. Regular physical activity at aerobic and nearly aerobic levels raises HDL level. Dietary changes are aimed at reducing the intake of total fat, saturated fats, and cholesterol. Drugs used to treat high blood cholesterol levels include cholestyramine (Questran) and colestipol (Colestid), which promote excretion of bile in the feces; nicotinic acid (Liponicin); and the “statin” drugs—atorvastatin (Lipitor), lovastatin (Mevacor), and simvastatin (Zocor), which block the key enzyme (HMG-CoA reductase) needed for cholesterol synthesis.

### The Fate of Lipids

Lipids, like carbohydrates, may be oxidized to produce ATP. If the body has no immediate need to use lipids in this way, they are stored in adipose tissue (fat depots) throughout the body and in the liver. A few lipids are used as structural molecules or to synthesize other essential substances. Some examples include phospholipids, which are constituents of plasma membranes; lipoproteins, which are used to transport cholesterol throughout the body; thromboplastin, which is needed for blood clotting; and myelin sheaths, which speed up nerve impulse conduction. Two essential fatty acids that the body cannot synthesize are linoleic acid and linolenic acid. Dietary sources include vegetable oils and leafy vegetables. The various functions of lipids in the body may be reviewed in Table 2.7.

### Triglyceride Storage

A major function of adipose tissue is to remove triglycerides from chylomicrons and VLDLs and store them until they are needed for ATP production in other parts of the body. Triglycerides stored in adipose tissue constitute 98% of all body energy reserves. They are stored more readily than glycogen, in part because triglycerides are hydrophobic and do not exert osmotic pressure on cell membranes. Adipose tissue also insulates and protects various parts of the body. Adipocytes in the subcutaneous layer contain about 50% of the stored triglycerides. Other adipose tissues account for the other half: about 12% around the kidneys, 10–15% in the omenta, 15% in genital areas, 5–8% between muscles, and 5% behind the eyes, in the sulci of the heart, and attached to the outside of the large intestine. Triglycerides in adipose tissue are continually broken down and resynthesized. Thus, the triglycerides stored in adipose tissue today are not the same molecules that were present last month because they are continually released from storage, transported in the blood, and redeposited in other adipose tissue cells.

### Lipid Catabolism: Lipolysis

In order for muscle, liver, and adipose tissue to oxidize the fatty acids derived from triglycerides to produce ATP, the triglycerides must first be split into glycerol and fatty acids, a process called lipolysis (li-POL-i-sis). Lipolysis is catalyzed by enzymes called lipases. Epinephrine and norepinephrine enhance triglyceride breakdown into fatty acids and glycerol. These hormones are released when sympathetic tone increases, as occurs, for example, during exercise. Other lipolytic...
hormones include cortisol, thyroid hormones, and insulinlike growth factors. By contrast, insulin inhibits lipolysis.

The glycerol and fatty acids that result from lipolysis are catabolized via different pathways (Figure 25.14). Glycerol is converted by many cells of the body to glyceraldehyde 3-phosphate, one of the compounds also formed during the catabolism of glucose. If ATP supply in a cell is high, glyceraldehyde 3-phosphate is converted into glucose, an example of gluconeogenesis. If ATP supply in a cell is low, glyceraldehyde 3-phosphate enters the catabolic pathway to pyruvic acid.

Fatty acids are catabolized differently than glycerol and yield more ATP. The first stage in fatty acid catabolism is a series of reactions, collectively called beta oxidation (BÂ-ta), that occurs in the matrix of mitochondria. Enzymes remove two carbon atoms at a time from the long chain of carbon atoms composing a fatty acid and attach the resulting two-carbon fragment to coenzyme A, forming acetyl CoA. Then, acetyl CoA enters the Krebs cycle (Figure 25.14). A 16-carbon fatty acid such as palmitic acid can yield as many as 129 ATPs on its complete oxidation via beta oxidation, the Krebs cycle, and the electron transport chain.

As part of normal fatty acid catabolism, hepatocytes can take two acetyl CoA molecules at a time and condense them to form acetoacetic acid (as´-ē-to¯-a-SĒ-tik). This reaction liberates the bulky CoA portion, which cannot diffuse out of cells. Some acetoacetic acid is converted into beta-hydroxybutyric acid (hī-drok-sē-bū-TIR-ik) and acetone (AS-e-tō-n). The formation of these three substances, collectively known as ketone bodies (KĒ-tō-n), is called ketogenesis (kē-to¯-JEN-e-sis) (Figure 25.14). Because ketone bodies freely diffuse through plasma membranes, they leave hepatocytes and enter the bloodstream.

Other cells take up acetoacetic acid and attach its four carbons to two coenzyme A molecules to form two acetyl CoA molecules, which can then enter the Krebs cycle for oxidation. Heart muscle and the cortex (outer part) of the kidneys use acetoacetic acid in preference to glucose for generating ATP. Hepatocytes, which make acetoacetic acid, cannot use it for ATP production because they lack the enzyme that transfers acetoacetic acid back to coenzyme A.

**Lipid Anabolism: Lipogenesis**

Liver cells and adipose cells can synthesize lipids from glucose or amino acids through lipogenesis (Figure 25.14), which is stimulated by insulin. Lipogenesis occurs when individuals consume more calories than are needed to satisfy their ATP needs. Excess dietary carbohydrates, proteins, and fats all have the same fate—they are converted into triglycerides. Certain amino acids can undergo the following reactions: amino acids → acetyl CoA → fatty acids → triglycerides. The use of glucose to form lipids takes place via two pathways: (1) glucose → glyceraldehyde 3-phosphate → glycerol and (2) glucose → glyceraldehyde 3-phosphate → ketone bodies.

**Figure 25.14** Pathways of lipid metabolism. Glycerol may be converted to glyceraldehyde 3-phosphate, which can then be converted to glucose or enter the Krebs cycle for oxidation. Fatty acids undergo beta oxidation and enter the Krebs cycle via acetyl coenzyme A. The synthesis of lipids from glucose or amino acids is called lipogenesis.

**Q** What types of cells can carry out lipogenesis, beta oxidation, and lipolysis? What type of cell can carry out ketogenesis?
→ acetyl CoA → fatty acids. The resulting glycerol and fatty acids can undergo anabolic reactions to become stored triglycerides, or they can go through a series of anabolic reactions to produce other lipids such as lipoproteins, phospholipids, and cholesterol.

\[\text{Clinical Connection}\]

Ketosis

The level of ketone bodies in the blood normally is very low because other tissues use them for ATP production as fast as they are generated from the breakdown of fatty acids in the liver. During periods of excessive beta oxidation, however, the production of ketone bodies exceeds their uptake and use by body cells. This might occur after a meal rich in triglycerides, or during fasting or starvation, because few carbohydrates are available for catabolism. Excessive beta oxidation may also occur in poorly controlled or untreated diabetes mellitus for two reasons: (1) Because adequate glucose cannot get into cells, triglycerides are used for ATP production, and (2) because insulin normally inhibits lipolysis, a lack of insulin accelerates the pace of lipolysis. When the concentration of ketone bodies in the blood rises above normal—a condition called ketosis—the ketone bodies, most of which are acids, must be buffered. If too many accumulate, they decrease the concentration of buffers, such as bicarbonate ions, and blood pH falls. Extreme or prolonged ketosis can lead to acidosis (ketoacidosis), an abnormally low blood pH. The decreased blood pH in turn causes depression of the central nervous system, which can result in disorientation, coma, and even death if the condition is not treated. When a diabetic becomes seriously insulin-deficient, one of the telltale signs is the sweet smell on the breath from the ketone body acetone.

Checkpoint

13. What are the functions of the apoproteins in lipoproteins?
14. Which lipoprotein particles contain “good” and “bad” cholesterol, and why are these terms used?
15. Where are triglycerides stored in the body?
16. Explain the principal events of the catabolism of glycerol and fatty acids.
17. What are ketone bodies? What is ketosis?
18. Define lipogenesis and explain its importance.

25.5 Protein Metabolism

OBJECTIVE

- Describe the fate, metabolism, and functions of proteins.

During digestion, proteins are broken down into amino acids. Unlike carbohydrates and triglycerides, which are stored, proteins are not warehoused for future use. Instead, amino acids are either oxidized to produce ATP or used to synthesize new proteins for body growth and repair. Excess dietary amino acids are not excreted in the urine or feces but instead are converted into glucose (gluconeogenesis) or triglycerides (lipogenesis).

The Fate of Proteins

The active transport of amino acids into body cells is stimulated by insulinlike growth factors (IGFs) and insulin. Almost immediately after digestion, amino acids are reassembled into proteins. Many proteins function as enzymes; others are involved in transportation (hemoglobin) or serve as antibodies, clotting chemicals (fibrinogen), hormones (insulin), or contractile elements in muscle fibers (actin and myosin). Several proteins serve as structural components of the body (collagen, elastin, and keratin). The various functions of proteins in the body may be reviewed in Table 2.8.

Protein Catabolism

A certain amount of protein catabolism occurs in the body each day, stimulated mainly by cortisol from the adrenal cortex. Proteins from worn-out cells (such as red blood cells) are broken down into amino acids. Some amino acids are converted into other amino acids, peptide bonds are re-formed, and new proteins are synthesized as part of the recycling process. Hepatocytes convert some amino acids to fatty acids, ketone bodies, or glucose. Cells throughout the body oxidize a small amount of amino acids to generate ATP via the Krebs cycle and the electron transport chain. However, before amino acids can be oxidized, they must first be converted to molecules that are part of the Krebs cycle or can enter the Krebs cycle, such as acetyl CoA (Figure 25.15). Before amino acids can enter the Krebs cycle, their amino group (NH$_3$) must first be removed—a process called deamination (dē-am′-ĭ-nā-shun). Deamination occurs in hepatocytes and produces ammonia (NH$_3$). The liver cells then convert the highly toxic ammonia to urea, a relatively harmless substance that is excreted in the urine. The conversion of amino acids into glucose (gluconeogenesis) may be reviewed in Figure 25.12; the conversion of amino acids into fatty acids (lipogenesis) or ketone bodies (ketogenesis) is shown in Figure 25.14.

Protein Anabolism

Protein anabolism, the formation of peptide bonds between amino acids to produce new proteins, is carried out on the ribosomes of almost every cell in the body, directed by the cells’ DNA and RNA (see Figure 3.29). Insulinlike growth factors, thyroid hormones (T$_3$ and T$_4$), insulin, estrogen, and testosterone all stimulate protein synthesis. Because proteins are a main component of most cell structures, adequate dietary protein is especially essential during the growth years, during pregnancy, and when tissue has been damaged by disease or injury. Once dietary intake of protein is adequate, eating more protein will not increase bone or muscle mass; only a regular program of forceful, weight-bearing muscular activity accomplishes that goal.

Of the 20 amino acids in the human body, 10 are essential amino acids: They must be present in the diet because they cannot be synthesized in the body in adequate amounts. It is essential to include them in your diet. Humans are unable to synthesize eight amino acids
Q What group is removed from an amino acid before it can enter the Krebs cycle, and what is this process called?

**Clinical Connection**

**Phenylketonuria**

Phenylketonuria (PKU) (fen′-il-ki′-tô-NOO-rē-a) is a genetic error of protein metabolism characterized by elevated blood levels of the amino acid phenylalanine. Most children with phenylketonuria have a mutation in the gene that codes for the enzyme phenylalanine hydroxylase, the enzyme needed to convert phenylalanine into the amino acid tyrosine, which can enter the Krebs cycle (Figure 25.15). Because the enzyme is deficient, phenylalanine cannot be metabolized, and what is not used in protein synthesis builds up in the blood. If untreated, the disorder causes vomiting, rashes, seizures, growth deficiency, and severe mental retardation. Newborns are screened for PKU, and mental retardation can be prevented by restricting the affected child to a diet that supplies only the amount of phenylalanine needed for growth, although learning disabilities may still ensue. Because the artificial sweetener aspartame (NutraSweet) contains phenylalanine, its consumption must be restricted in children with PKU.
KEY MOLECULES AT METABOLIC CROSSROADS

OBJECTIVE

- Describe the reactions of key molecules and the products formed during metabolism.

Although there are thousands of different chemicals in cells, three molecules—glucose 6-phosphate, pyruvic acid, and acetyl coenzyme A—play pivotal roles in metabolism (Figure 25.16). These molecules stand at “metabolic crossroads”; as you will learn shortly, the reactions that occur (or do not occur) depend on the nutritional or activity status of the individual. Reactions 1 through 7 in Figure 25.16 occur in the cytosol, reactions 8 and 9 occur inside mitochondria, and reactions indicated by 10 occur on smooth endoplasmic reticulum.

Checkpoint

19. What is deamination and why does it occur?
20. What are the possible fates of the amino acids from protein catabolism?
21. How are essential and nonessential amino acids different?

Q Which substance is the gateway into the Krebs cycle for molecules that are being oxidized to generate ATP?
The Role of Glucose 6-Phosphate

Shortly after glucose enters a body cell, a kinase converts it to **glucose 6-phosphate**. Four possible fates await glucose 6-phosphate (see Figure 25.16):

1. **Synthesis of glycogen.** When glucose is abundant in the bloodstream, as it is just after a meal, a large amount of glucose 6-phosphate is used to synthesize glycogen, the storage form of carbohydrate in animals. Subsequent breakdown of glycogen into glucose 6-phosphate occurs through a slightly different series of reactions. Synthesis and breakdown of glycogen occur mainly in skeletal muscle fibers and hepatocytes.

2. **Release of glucose into the bloodstream.** If the enzyme glucose 6-phosphatase is present and active, glucose 6-phosphate can be dephosphorylated to glucose. Once glucose is released from the phosphatase group, it can leave the cell and enter the bloodstream. Hepatocytes are the main cells that can provide glucose to the bloodstream in this way.

3. **Synthesis of nucleic acids.** Glucose 6-phosphate is the precursor used by cells throughout the body to make ribose 5-phosphate, a 5-carbon sugar that is needed for synthesis of RNA (ribonucleic acid) and DNA (deoxyribonucleic acid). The same sequence of reactions also produces NADPH. This molecule is a hydrogen and electron donor in certain reduction reactions, such as synthesis of fatty acids and steroid hormones.

4. **Glycolysis.** Some ATP is produced anaerobically via glycolysis, in which glucose 6-phosphate is converted to pyruvic acid, another key molecule in metabolism. Most body cells carry out glycolysis.

The Role of Pyruvic Acid

Each 6-carbon molecule of glucose that undergoes glycolysis yields two 3-carbon molecules of **pyruvic acid** (pi-ROO-vik). This molecule, like glucose 6-phosphate, stands at a metabolic crossroads: Given enough oxygen, the aerobic (oxygen-consuming) reactions of cellular respiration can proceed; if oxygen is in short supply, anaerobic reactions can occur (Figure 25.16):

5. **Production of lactic acid.** When oxygen is in short supply in a tissue, as in actively contracting skeletal or cardiac muscle, some pyruvic acid is changed to lactic acid. The lactic acid then diffuses into the bloodstream and is taken up by hepatocytes, which eventually convert it back to pyruvic acid.

6. **Production of alanine.** Carbohydrate and protein metabolism are linked by pyruvic acid. Through transamination, an amino group (–NH2) can either be added to pyruvic acid (a carbohydrate) to produce the amino acid alanine, or be removed from alanine to generate pyruvic acid.

7. **Gluconeogenesis.** Pyruvic acid and certain amino acids also can be converted to oxaloacetic acid, one of the Krebs cycle intermediates, which in turn can be used to form glucose 6-phosphate. This sequence of gluconeogenesis reactions bypasses certain one-way reactions of glycolysis.

The Role of Acetyl Coenzyme A

When the ATP level in a cell is low but oxygen is plentiful, most pyruvic acid streams toward ATP-producing reactions—the Krebs cycle and electron transport chain—via conversion to **acetyl coenzyme A**.

8. **Entry into the Krebs cycle.** Acetyl CoA is the vehicle for 2-carbon acetyl groups to enter the Krebs cycle. Oxidative Krebs cycle reactions convert acetyl CoA to CO2 and produce reduced coenzymes (NADH and FADH2) that transfer electrons into the electron transport chain. Oxidative reactions in the electron transport chain in turn generate ATP. Most fuel molecules that will be oxidized to generate ATP—glucose, fatty acids, and ketone bodies—are first converted to acetyl CoA.

9. **Synthesis of lipids.** Acetyl CoA also can be used for synthesis of certain lipids, including fatty acids, ketone bodies, and cholesterol. Because pyruvic acid can be converted to acetyl CoA, carbohydrates can be turned into triglycerides; this metabolic pathway stores some excess carbohydrate calories as fat. Mammals, including humans, cannot reconvert acetyl CoA to pyruvic acid, however, so fatty acids cannot be used to generate glucose or other carbohydrate molecules.

**Table 25.2** is a summary of carbohydrate, lipid, and protein metabolism.

<table>
<thead>
<tr>
<th>Checkpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>22. What are the possible fates of glucose 6-phosphate, pyruvic acid, and acetyl coenzyme A in a cell?</td>
</tr>
</tbody>
</table>

25.7 Metabolic Adaptations

**OBJECTIVE**

- Compare metabolism during the absorptive and postabsorptive states.

Regulation of metabolic reactions depends both on the chemical environment within body cells, such as the levels of ATP and oxygen, and on signals from the nervous and endocrine systems. Some aspects of metabolism depend on how much time has passed since the last meal. During the **absorptive state**, ingested nutrients are entering the bloodstream, and glucose is readily available for ATP production. During the **postabsorptive state**, absorption of nutrients from the GI tract is complete, and energy needs must be met by fuels already in the body. A typical meal requires about 4 hours for complete absorption; given three meals a day, the absorptive state exists for about 12 hours each day. Assuming no between-meal snacks, the other 12 hours—typically late morning, late afternoon, and most of the night—are spent in the postabsorptive state.
**Catabolism of amino acids.** Some amino acids enter hepatocytes (liver cells), where they are deaminated to keto acids. The keto acids in turn can either enter the Krebs cycle for ATP production or be used to synthesize glucose or fatty acids.

**Protein synthesis.** Many amino acids enter body cells, such as muscle cells and hepatocytes, for synthesis of proteins.

**Catabolism of few dietary lipids.** During the absorptive state, only a small portion of dietary lipids are catabolized for energy; most dietary lipids are stored in adipose tissue.

Another key event of the absorptive state is that absorbed nutrients in excess of the body’s energy needs are converted into nutrient stores—namely glycogen and fat. This function is reflected by the following absorptive state reactions (Figure 25.17):

**Glycogenesis.** Some of the glucose that may be in excess of the body’s needs is taken up by the liver and skeletal muscle and then converted into glycogen (glycogenesis).

**Lipogenesis.** The liver can also convert excess glucose or amino acids to fatty acids for use in the synthesis of triglycerides (lipogenesis). Adipocytes also take up glucose not picked up by the liver and convert it into triglycerides for storage. Overall, about 40% of the glucose absorbed from a meal is converted to triglycerides, and about 10% is stored as glycogen in skeletal muscles and the liver.
Before glucose can be used by body cells, it must first pass through the plasma membrane and enter the cytosol. Glucose entry into most body cells occurs via glucose transporter (GLUT) molecules, a family of transporters that bring glucose into cells via facilitated diffusion. A high level of insulin increases the insertion of one type of GLUT, called GLUT4, into the plasma membranes of most body cells (especially muscle fiber and adipocytes), increasing the rate of facilitated diffusion of glucose into cells. In neurons and hepatocytes, however, other types of GLUTs are always present in the plasma membrane, so glucose entry is always “turned on.” Upon entering a cell, glucose becomes phosphorylated. Because GLUT cannot transport phosphorylated glucose, this reaction traps glucose within the cell.

Table 25.3 summarizes the hormonal regulation of metabolism in the absorptive state.

**Regulation of Metabolism during the Absorptive State**

Soon after a meal, glucose-dependent insulinotropic peptide (GIP), plus the rising blood levels of glucose and certain amino acids, stimulates pancreatic beta cells to release the hormone insulin. In general, insulin increases the activity of enzymes needed for anabolism and the synthesis of storage molecules; at the same time, it decreases the activity of enzymes needed for catabolic or breakdown reactions. Insulin promotes the entry of glucose and amino acids into cells of many tissues, and it stimulates the conversion of glucose to glycogen (glycogen synthesis) in both liver and muscle cells. In liver and adipose tissue, insulin enhances the synthesis of triglycerides (lipogenesis), and in cells throughout the body, insulin stimulates protein synthesis. (See Section 18.10 to review the effects of insulin.) Insulin-like growth factors and the thyroid hormones (T3 and T4) also stimulate protein synthesis.

**Transport of triglycerides from liver to adipose tissue.** Some fatty acids and triglycerides synthesized in the liver remain there, but hepatocytes package most into very low-density lipoproteins (VLDLs), which carry lipids to adipose tissue for storage.

Before glucose can be used by body cells, it must first pass through the plasma membrane and enter the cytosol. Glucose entry into most body cells occurs via glucose transporter (GLUT) molecules, a family of transporters that bring glucose into cells via facilitated diffusion. A high level of insulin increases the insertion of one type of GLUT, called GLUT4, into the plasma membranes of most body cells (especially muscle fiber and adipocytes), increasing the rate of facilitated diffusion of glucose into cells. In neurons and hepatocytes, however, other types of GLUTs are always present in the plasma membrane, so glucose entry is always “turned on.” Upon entering a cell, glucose becomes phosphorylated. Because GLUT cannot transport phosphorylated glucose, this reaction traps glucose within the cell. Table 25.3 summarizes the hormonal regulation of metabolism in the absorptive state.

**Metabolism during the Postabsorptive State**

About 4 hours after the last meal, absorption of nutrients from the small intestine is complete, and the blood glucose level starts to fall because glucose continues to leave the bloodstream and enter body
### 25.7 Metabolic Adaptations

**Important for the nervous system and for red blood cells for the following reasons:**

- The dominant fuel molecule for ATP production in the nervous system is glucose because fatty acids are unable to pass the blood–brain barrier.
- Red blood cells derive all of their ATP from glycolysis of glucose because they have no mitochondria, so the Krebs cycle and the electron transport chain are not available to them.

### Postabsorptive State Reactions

A key feature of the postabsorptive state is that the blood glucose concentration is maintained at a normal level due to the breakdown of the body’s nutrient stores (glycogen and fat) and the formation of new glucose from noncarbohydrate sources (gluconeogenesis). The reactions of the postabsorptive state that produce glucose are as follows (Figure 25.18):

1. **Glycogenolysis in the liver.** During the postabsorptive state, a major source of blood glucose is liver glycogenolysis, which can provide about 4-hour supply of glucose. Once glycogenolysis occurs in the liver, the glucose is released into the blood.

2. **Glycogenolysis in muscle.** Glycogenolysis can also occur in skeletal muscle. However, in skeletal muscle, the glucose that cells while none is being absorbed from the GI tract. Thus, the main metabolic challenge during the postabsorptive state is to maintain the normal blood glucose level of 70–110 mg/100 mL (3.9–6.1 mmol/liter). Homeostasis of blood glucose concentration is especially important for the nervous system and for red blood cells for the following reasons:

- The dominant fuel molecule for ATP production in the nervous system is glucose because fatty acids are unable to pass the blood–brain barrier.
- Red blood cells derive all of their ATP from glycolysis of glucose because they have no mitochondria, so the Krebs cycle and the electron transport chain are not available to them.

### Table 25.3

**Hormonal Regulation of Metabolism in the Absorptive State**

<table>
<thead>
<tr>
<th>PROCESS</th>
<th>LOCATION(S)</th>
<th>MAIN STIMULATING HORMONE(S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facilitated diffusion of glucose into cells</td>
<td>Most cells.</td>
<td>Insulin.*</td>
</tr>
<tr>
<td>Active transport of amino acids into cells</td>
<td>Most cells.</td>
<td>Insulin.</td>
</tr>
<tr>
<td>Glycogenesis (glycogen synthesis)</td>
<td>Hepatocytes and muscle fibers.</td>
<td>Insulin.</td>
</tr>
<tr>
<td>Protein synthesis</td>
<td>All body cells.</td>
<td>Insulin, thyroid hormones, and insulinlike growth factors.</td>
</tr>
<tr>
<td>Lipogenesis (triglyceride synthesis)</td>
<td>Adipose cells and hepatocytes.</td>
<td>Insulin.</td>
</tr>
</tbody>
</table>

*Facilitated diffusion of glucose into hepatocytes (liver cells) and neurons is always “turned on” and does not require insulin.

### Figure 25.18

**Principal metabolic pathways during the postabsorptive state.**

The principal function of postabsorptive state reactions is to maintain a normal blood glucose level.
is formed from glycogenolysis is catabolized to provide ATP for muscle contraction: Glycogen is broken down to glucose 6-phosphate, which undergoes glycolysis. If anaerobic conditions exist in the skeletal muscle, the pyruvic acid is converted to lactic acid, which is released into the blood. The liver takes up the lactic acid, converts it back to glucose, and then releases glucose into the blood.

3 Lipolysis. In adipose tissue, triglycerides are broken down into fatty acids and glycerol, which are released into the blood. The glycerol is taken up by the liver and then converted into glucose, which in turn is released into the bloodstream.

4 Protein catabolism. Modest breakdown of proteins in skeletal muscle and other tissues releases amino acids, which then can be converted to glucose by the liver. The glucose in turn is released into the bloodstream.

5 Gluconeogenesis. During the postabsorptive state, new glucose is formed from noncarbohydrate sources. Examples of gluconeogenesis include the formation of glucose from lactic acid, glycerol, or an amino acid.

Another hallmark feature of the postabsorptive state is that glucose sparing occurs. Glucose sparing means that most body cells switch to other fuels besides glucose as their main source of energy, leaving more glucose in the blood for the brain and red blood cells. The following reactions produce ATP without using glucose (Figure 25.18):

6 Catabolism of fatty acids. The fatty acids released by lipolysis of triglycerides cannot be used for glucose production because acetyl CoA cannot be readily converted to pyruvic acid. But most cells can catabolize the fatty acids directly, feed them into the Krebs cycle as acetyl CoA, and produce ATP through the electron transport chain.

7 Catabolism of lactic acid. Cardiac muscle can produce ATP aerobically from lactic acid.

8 Catabolism of amino acids. In hepatocytes, amino acids may be catabolized directly to produce ATP.

9 Catabolism of ketone bodies. Hepatocytes also convert fatty acids to ketone bodies (acetoacetic acid, beta-hydroxybutyric acid, and acetone), which can be used by the heart, kidneys, and other tissues for ATP production.

Metabolism during Fasting and Starvation

The term fasting means going without food for many hours or a few days; starvation implies weeks or months of food deprivation or inadequate food intake. People can survive without food for 2 months or more if they drink enough water to prevent dehydration. Although glycogen stores are depleted within a few hours of beginning a fast, catabolism of stored triglycerides and structural proteins can provide energy for several weeks. The amount of adipose tissue the body contains determines the life span possible without food.

During fasting and starvation, nervous tissue and RBCs continue to use glucose for ATP production. There is a ready supply of amino acids for gluconeogenesis because lowered insulin and increased cortisol levels slow the pace of protein synthesis and promote protein catabolism. Most cells in the body, especially skeletal muscle cells (because of their high protein content), can spare a fair amount of

### TABLE 25.4 Hormonal Regulation of Metabolism in the Postabsorptive State

<table>
<thead>
<tr>
<th>PROCESS</th>
<th>LOCATION(S)</th>
<th>MAIN STIMULATING HORMONE(S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glycogenolysis (glycogen breakdown)</td>
<td>Hepatocytes and skeletal muscle fibers.</td>
<td>Glucagon and epinephrine.</td>
</tr>
<tr>
<td>Lipolysis (triglyceride breakdown)</td>
<td>Adipocytes.</td>
<td>Epinephrine, norepinephrine, cortisol, insulinlike growth factors, thyroid hormones, and others.</td>
</tr>
<tr>
<td>Protein breakdown</td>
<td>Most body cells, but especially skeletal muscle fibers.</td>
<td>Cortisol.</td>
</tr>
<tr>
<td>Gluconeogenesis (synthesis of glucose from noncarbohydrates)</td>
<td>Hepatocytes and kidney cortex cells.</td>
<td>Glucagon and cortisol.</td>
</tr>
</tbody>
</table>
protein before their performance is adversely affected. During the first few days of fasting, protein catabolism outpaces protein synthesis by about 75 grams daily as some of the “old” amino acids are being deaminated and used for gluconeogenesis and “new” (dietary) amino acids are lacking.

By the second day of a fast, blood glucose level has stabilized at about 65 mg/100 mL (3.6 mmol/liter); at the same time the level of fatty acids in plasma has risen fourfold. Lipolysis of triglycerides in adipose tissue releases glycerol, which is used for gluconeogenesis, and fatty acids. The fatty acids diffuse into muscle fibers and other body cells, where they are used to produce acetyl CoA, which enters the Krebs cycle. ATP then is synthesized as oxidation proceeds via the Krebs cycle and the electron transport chain.

The most dramatic metabolic change that occurs with fasting and starvation is the increase in the formation of ketone bodies by hepatocytes. During fasting, only small amounts of glucose undergo glycolysis to pyruvic acid, which in turn can be converted to oxaloacetic acid. Acetyl CoA enters the Krebs cycle by combining with oxaloacetic acid (see Figure 25.16); when oxaloacetic acid is scarce due to fasting, only some of the available acetyl CoA can enter the Krebs cycle. Surplus acetyl CoA is used for ketogenesis, mainly in hepatocytes. Ketone body production thus increases as catabolism of fatty acids rises. Lipid-soluble ketone bodies can diffuse through plasma membranes and across the blood–brain barrier and be used as an alternative fuel for ATP production, especially by cardiac and skeletal muscle fibers and neurons. Normally, only a trace of ketone bodies (0.01 mmol/liter) are present in the blood, so they are a negligible fuel source. After 2 days of fasting, however, the level of ketones is 100–300 times higher and supplies roughly a third of the brain’s energy needs. The presence of ketones actually reduces the use of glucose for ATP production, which in turn decreases the demand for gluconeogenesis and slows the catabolism of muscle proteins later in starvation to about 20 grams daily.

**Energy balance** refers to the precise matching of energy intake (in food) to energy expenditure over time. When the energy content of food balances the energy used by all cells of the body, body weight remains constant (unless there is a gain or loss of water). In many people, weight stability persists despite large day-to-day variations in activity and food intake. In the more affluent nations, however, a large fraction of the population is overweight. Easy access to tasty, high-calorie foods and a “couch-potato” lifestyle both promote weight gain. Being overweight increases the risk of dying from a variety of cardiovascular and metabolic disorders, including hypertension, varicose veins, diabetes mellitus, arthritis, and certain cancers.

### Food Calories

As you learned in Chapter 4, when catabolic reactions occur, energy is released. About 40% of this energy is used to perform biological work, such as active transport and muscle contraction. The remaining 60% is converted to heat, some of which helps maintain normal body temperature. Excess heat is lost to the environment. When the body catabolizes the organic compounds in food, the heat energy released can be measured in units called calories. A **calorie (cal)** is defined as the amount of energy in the form of heat required to raise the temperature of 1 gram of water 1°C. Because the calorie is a relatively small unit, the **kilocalorie (kcal)** or **Calorie (Cal)** (always spelled with an uppercase C) is often used to express the energy content of foods. A kilocalorie equals 1000 calories. Thus, when we say that a particular food item contains 500 Calories, we are actually referring to kilocalories.

Essentially all of the kilocalories in our food come from the catabolism of carbohydrates, proteins, and fats. The catabolism of carbohydrates or proteins yields about the same amount of energy—about 4 kcal/g. The catabolism of fat yields much more energy—about 9 kcal/g. Some foods or beverages may contain alcohol, and the catabolism of alcohol also yields energy—about 7 kcal/g. The energy content of carbohydrates, proteins, fats, and alcohol is summarized in Table 25.5.

The number of kilocalories from a component in a particular food can be calculated by multiplying the number of grams of that component by its energy content. For example, suppose that one slice of pizza contains 27 g of carbohydrate, 14 g of fat, and 12 g of protein. To calculate the number of kcal from carbohydrate in this slice of pizza, multiply the number of grams of carbohydrate in the pizza by the energy content of carbohydrates: 27 g carbohydrate × 4 kcal/g = 108 kcal. To calculate the number of kcal from fat in the slice of pizza, multiple the number of grams of fat in the pizza by the energy content of fat: 14 g fat × 9 kcal/g = 126 kcal. To calculate the

### Table 25.5: Energy Content of Various Nutrients and Alcohol

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Energy Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrate</td>
<td>4 kcal/g</td>
</tr>
<tr>
<td>Protein</td>
<td>4 kcal/g</td>
</tr>
<tr>
<td>Fat</td>
<td>9 kcal/g</td>
</tr>
<tr>
<td>Alcohol</td>
<td>7 kcal/g</td>
</tr>
</tbody>
</table>

### Checkpoint

23. What are the roles of insulin, glucagon, epinephrine, insulinlike growth factors, thyroxine, cortisol, estrogen, and testosterone in regulation of metabolism?

24. Why is ketogenesis more significant during fasting or starvation than during normal absorptive and postabsorptive states?
Based on the caloric content of these foods, your body will have to work harder (via exercise, for example) to release more energy in order to catabolize the chocolate cake compared with the apple.

Beverages can also be a source of calories. For example, a cola soft drink (12 ounces) contains 40 g of carbohydrate, 0 g of protein, and 0 g of fat, so the energy content of this soda is 160 kcal (40 g carbohydrate \( \times 4 \text{ kcal/g} \)). A typical serving of vodka (1.5 ounces) contains 0 g of carbohydrate, 0 g of protein, 0 g of fat, and 14 g of alcohol, so the energy content of this drink is 98 calories (14 g \( \times 7 \text{ kcal/g} \)). If juice, soda, or cocktail mix is added to the vodka, these solutions usually contain carbohydrates that contribute additional calories. Table 25.7 lists the caloric content of several beverages.

### Table 25.6: Caloric Content of Various Foods

<table>
<thead>
<tr>
<th>FOOD</th>
<th>SERVING SIZE</th>
<th>ENERGY (kcal)</th>
<th>CARBOHYDRATE (g)</th>
<th>FAT (g)</th>
<th>PROTEIN (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apple</td>
<td>1</td>
<td>80</td>
<td>19</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Broccoli (raw)</td>
<td>1/2 cup</td>
<td>16</td>
<td>3</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Baked potato (plain)</td>
<td>1</td>
<td>160</td>
<td>35</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Wheat bread</td>
<td>1 slice</td>
<td>65</td>
<td>12</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Vegetable soup</td>
<td>1 cup</td>
<td>100</td>
<td>20</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Baked chicken</td>
<td>3 ounces</td>
<td>158</td>
<td>0</td>
<td>6</td>
<td>26</td>
</tr>
<tr>
<td>Lean ground beef (10% fat)</td>
<td>3 ounces</td>
<td>178</td>
<td>0</td>
<td>10</td>
<td>22</td>
</tr>
<tr>
<td>Baked trout</td>
<td>3 ounces</td>
<td>101</td>
<td>0</td>
<td>1</td>
<td>23</td>
</tr>
<tr>
<td>McDonald’s® Big Mac</td>
<td>1</td>
<td>541</td>
<td>45</td>
<td>29</td>
<td>25</td>
</tr>
<tr>
<td>Wendy’s® Biggie Fry</td>
<td>1</td>
<td>530</td>
<td>68</td>
<td>25</td>
<td>6</td>
</tr>
<tr>
<td>Chick-fil-A® chicken sandwich</td>
<td>1</td>
<td>408</td>
<td>38</td>
<td>16</td>
<td>28</td>
</tr>
<tr>
<td>Burger King® Whopper</td>
<td>1</td>
<td>710</td>
<td>52</td>
<td>42</td>
<td>31</td>
</tr>
<tr>
<td>Pizza Hut® super supreme pizza</td>
<td>1 slice</td>
<td>282</td>
<td>27</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td>Cinnabon® roll</td>
<td>1</td>
<td>808</td>
<td>115</td>
<td>32</td>
<td>15</td>
</tr>
<tr>
<td>Chocolate cake</td>
<td>1 slice</td>
<td>247</td>
<td>35</td>
<td>11</td>
<td>2</td>
</tr>
<tr>
<td>Butter</td>
<td>1 tablespoon</td>
<td>108</td>
<td>0</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Sour cream</td>
<td>2 tablespoons</td>
<td>62</td>
<td>1</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Mayonnaise</td>
<td>1 tablespoon</td>
<td>99</td>
<td>0</td>
<td>11</td>
<td>0</td>
</tr>
</tbody>
</table>

Number of kcal from protein in the slice of pizza, multiply the number of grams of protein in the pizza by the energy content of protein: 12 g protein \( \times 4 \text{ kcal/g} = 48 \text{ kcal} \). Finally, to calculate the total kcal in the slice of pizza, add together all of the kcal from carbohydrate, fat, and protein: 108 kcal + 126 kcal + 48 kcal = 282 kcal.

Table 25.6 lists the caloric content of several familiar foods. The higher the caloric content of a particular food, the greater the amount of energy released as it is catabolized. For example, the energy content of one medium apple is 80 kcal; this means that 80 kcal is the amount of energy released as the apple is catabolized. The energy content of a slice of chocolate cake is 247 kcal; this means that 247 kcal is the amount of energy released as the chocolate cake is catabolized. Suppose that you eat the apple or the chocolate cake. Based on the caloric content of these foods, your body will have to work harder (via exercise, for example) to release more energy in order to catabolize the chocolate cake compared with the apple.

### Table 25.7: Caloric Content of Various Beverages

<table>
<thead>
<tr>
<th>BEVERAGE</th>
<th>SERVING SIZE</th>
<th>ENERGY (kcal)</th>
<th>CARBOHYDRATE (g)</th>
<th>(FAT) (g)</th>
<th>PROTEIN (g)</th>
<th>ALCOHOL (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cola soft drink</td>
<td>12 ounces</td>
<td>160</td>
<td>40</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Whole milk</td>
<td>1 cup</td>
<td>148</td>
<td>11</td>
<td>8</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>Orange juice</td>
<td>1 cup</td>
<td>108</td>
<td>25</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>White wine</td>
<td>5 ounces</td>
<td>102</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>Red wine</td>
<td>5 ounces</td>
<td>110</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>Beer</td>
<td>12 ounces</td>
<td>143</td>
<td>13</td>
<td>0</td>
<td>0</td>
<td>13</td>
</tr>
<tr>
<td>Vodka</td>
<td>1.5 ounces</td>
<td>98</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>Whiskey</td>
<td>1.5 ounces</td>
<td>98</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>14</td>
</tr>
<tr>
<td>Bourbon</td>
<td>1.5 ounces</td>
<td>98</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>14</td>
</tr>
</tbody>
</table>
Metabolic Rate

The overall rate at which metabolic reactions use energy is termed the metabolic rate. As you have already learned, some of the energy is used to produce ATP, and some is released as heat. Thus, the higher the metabolic rate, the higher the rate of heat production.

Several factors affect the metabolic rate:

- **Hormones.** Thyroid hormones (thyroxine and triiodothyronine) are the main regulators of basal metabolic rate (BMR), the metabolic rate under basal conditions (described shortly). BMR increases as the blood levels of thyroid hormones rise. The response to changing levels of thyroid hormones is slow, however, taking several days to appear. Thyroid hormones increase BMR in part by stimulating cellular respiration. As cells use more oxygen to produce ATP, more heat is given off, and body temperature rises. This effect of thyroid hormones on BMR is called the calorogenic effect. Other hormones have minor effects on BMR. Testosterone, insulin, and growth hormone can increase the metabolic rate by 5–15%.

- **Exercise.** During strenuous exercise, the metabolic rate may increase to as much as 15 times the basal rate. In well-trained athletes, the rate may increase up to 20 times.

- **Nervous system.** During exercise or in a stressful situation, the sympathetic division of the autonomic nervous system is stimulated. Its postganglionic neurons release norepinephrine (NE), and it also stimulates release of the hormones epinephrine and norepinephrine by the adrenal medulla. Both epinephrine and norepinephrine increase the metabolic rate of body cells.

- **Body temperature.** The higher the body temperature, the higher the metabolic rate. Each 1°C rise in core temperature increases the rate of biochemical reactions by about 10%. As a result, metabolic rate may be increased substantially during a fever.

- **Ingestion of food.** The ingestion of food raises the metabolic rate 10–20% due to the energy “costs” of digesting, absorbing, and storing nutrients. This effect, food-induced thermogenesis, is greatest after eating a high-protein meal and is less after eating carbohydrates and lipids.

- **Age.** The metabolic rate of a child, in relation to its size, is about double that of an elderly person due to the high rates of reactions related to growth.

- **Other factors.** Other factors that affect metabolic rate include gender (lower in females, except during pregnancy and lactation), climate (lower in tropical regions), sleep (lower), and malnutrition (lower).

Basal Metabolic Rate

Because many factors affect metabolic rate, it is measured under standard conditions, with the body in a quiet, resting, and fasting condition called the basal state. The measurement obtained under these conditions is the basal metabolic rate (BMR). The most common way to determine BMR is by measuring the amount of oxygen used per kilocalorie of food metabolized. When the body uses 1 liter of oxygen to catabolize a typical dietary mixture of triglycerides, carbohydrates,

and proteins, about 4.8 kcal of energy is released. BMR is 1200–1800 kcal/day in adults, or about 24 kcal/kg of body mass in adult males and 22 kcal/kg in adult females. The added calories needed to support daily activities, such as digestion and walking, range from 500 kcal for a small, relatively sedentary person to over 3000 kcal for a person in training for Olympic-level competitions or mountain climbing.

Total Metabolic Rate

The total metabolic rate (TMR) is the total energy expenditure by the body per unit of time. Three components contribute to the TMR:

1. **Basal metabolic rate.** The basal metabolic rate accounts for about 60% of the TMR.

2. **Physical activity.** Physical activity typically adds 30–35% but can be lower in sedentary people. The energy expenditure is partly from voluntary exercise, such as walking, and partly from non-exercise activity thermogenesis (NEAT), the energy costs for maintaining muscle tone, posture while sitting or standing, and involuntary fidgeting movements. Table 25.8 lists various activities and the calories that they burn per hour.

3. **Food-induced thermogenesis.** Food-induced thermogenesis—the heat produced while food is being digested, absorbed, and stored—represents 5–10% of the TMR.

Adipose Tissue and Stored Chemical Energy

The major site of stored chemical energy in the body is adipose tissue. When energy use exceeds energy input, triglycerides in adipose tissue...
are catabolized to provide the extra energy, and when energy input exceeds energy expenditure, triglycerides are stored. Over time, the amount of stored triglycerides indicates the excess of energy intake over energy expenditure. Even small differences add up over time. A gain of 20 lb (9 kg) between ages 25 and 55 represents only a tiny imbalance, about 0.3% more energy intake in food than energy expenditure.

**Regulation of Body Temperature**

**OBJECTIVES**

- **Describe** the various mechanisms of heat transfer.
- **Explain** how normal body temperature is maintained by negative feedback loops involving the hypothalamic thermostat.
Your body produces more or less heat depending on the rates of its metabolic reactions. Because homeostasis of body temperature can be maintained only if the rate of heat loss from the body equals the rate of heat production by metabolism, it is important to understand the ways in which heat can be lost, gained, or conserved. Heat is a form of energy that can be measured as temperature. Despite wide fluctuations in environmental temperature, homeostatic mechanisms can maintain a normal range for internal body temperature. If the rate of body heat production equals the rate of heat loss, the body maintains a constant core temperature near 37°C (98.6°F). Core temperature is the temperature in body structures deep to the skin and subcutaneous layer. Shell temperature is the temperature near the body surface—in the skin and subcutaneous layer. Depending on the environmental temperature, shell temperature is 1–6°C lower than core temperature. A core temperature that is too high kills by denaturing body proteins; a core temperature that is too low causes cardiac arrhythmias that result in death.

Mechanisms of Heat Transfer

Maintaining normal body temperature depends on the ability to lose heat to the environment at the same rate as it is produced by metabolic reactions. Heat can be transferred between the body and its surroundings in four ways: via conduction, convection, radiation, and evaporation.

1. **Conduction** is the heat exchange that occurs between molecules of two materials that are in direct contact with each other. At rest, about 3% of body heat is lost via conduction to cooler, solid materials in contact with the body, such as a chair, clothing, and jewelry. Heat can also be gained via conduction—for example, while soaking in a hot tub. Because water conducts heat 20 times more effectively than air, heat loss or heat gain via conduction is much greater when the body is submerged in cold or hot water.

2. **Convection** is the transfer of heat by the movement of air or water between areas of different temperatures. The contact of air or water with your body results in heat transfer by both conduction and convection. When cool air makes contact with the body, the air becomes warmed and therefore less dense and is carried away by convection currents created as the less dense air rises. The faster the air moves—for example, by a breeze or a fan—the faster the rate of convection. At rest, about 15% of body heat is lost to the air via conduction and convection.

3. **Radiation** is the transfer of heat in the form of infrared rays between a warmer object and a cooler one without physical contact. Your body loses heat by radiating more infrared waves than it absorbs from cooler objects. If surrounding objects are warmer than you are, you absorb more heat than you lose by radiation. In a room at 21°C (70°F), about 60% of heat loss occurs via radiation in a resting person.

4. **Evaporation** is the conversion of a liquid to a vapor. Every milliliter of evaporating water takes with it a great deal of heat—about 0.58 kcal/mL. Under typical resting conditions, about 22% of heat loss occurs through evaporation of about 700 mL of water per day—300 mL in exhaled air and 400 mL from the skin surface.

Because we are not normally aware of this water loss through the skin and mucous membranes of the mouth and respiratory system, it is termed **insensible water loss**. The rate of evaporation is inversely related to relative humidity, the ratio of the actual amount of moisture in the air to the maximum amount it can hold at a given temperature. The higher the relative humidity, the lower the rate of evaporation. At 100% humidity, heat is gained via condensation of water on the skin surface as fast as heat is lost via evaporation. Evaporation provides the main defense against overheating during exercise. Under extreme conditions, a maximum of about 3 liters of sweat can be produced each hour, removing more than 1700 kcal of heat if all of it evaporates. (Note: Sweat that drips off the body rather than evaporating removes very little heat.)

**Hypothalamic Thermostat**

The control center that functions as the body's thermostat is a group of neurons in the anterior part of the hypothalamus, the **preoptic area**. This area receives input from thermoreceptors in the skin (peripheral thermoreceptors) and in the hypothalamus itself (central thermoreceptors). Neurons of the preoptic area generate action potentials at a higher frequency when blood temperature increases and at a lower frequency when blood temperature decreases.

Action potentials from the preoptic area propagate to two other parts of the hypothalamus known as the heat-losing center and the heat-promoting center, which, when stimulated by the preoptic area, set into operation a series of responses that lower body temperature and raise body temperature, respectively.

**Thermoregulation**

If core temperature declines, mechanisms that help conserve heat and increase heat production act via negative feedback to raise the body temperature to normal (Figure 25.19). Peripheral thermoreceptors and central thermoreceptors send input to the preoptic area of the hypothalamus, which in turn activates the heat-promoting center. In response, the hypothalamus discharges action potentials and secretes thyrotropin-releasing hormone (TRH), which in turn stimulates thyrotrophs in the anterior pituitary gland to release thyroid-stimulating hormone (TSH). Action potentials from the hypothalamus and TSH then activate several effectors, which respond in the following ways to increase the core temperature to the normal value:

- **Vasoconstriction.** Action potentials from the heat-promoting center stimulate sympathetic nerves that cause blood vessels of the skin to constrict. Vasoconstriction decreases the flow of warm blood, and thus the transfer of heat, from the internal organs to the skin. Slowing the rate of heat loss allows the internal body temperature to increase as metabolic reactions continue to produce heat.

- **Release of epinephrine and norepinephrine.** Action potentials in sympathetic nerves leading to the adrenal medulla stimulate the release of epinephrine and norepinephrine into the blood. The hormones in turn bring about an increase in cellular metabolism, which increases heat production.
Core temperature is the temperature in body structures deep to the skin and subcutaneous layer; shell temperature is the temperature near the body surface.

Q What factors can increase metabolic rate and thus increase the rate of heat production?
• **Shivering.** The heat-promoting center stimulates parts of the brain that increase muscle tone and hence heat production. As muscle tone increases in one muscle (the agonist), the small contractions stretch muscle spindles in its antagonist, initiating a stretch reflex. The resulting contraction in the antagonist stretches muscle spindles in the agonist, and it too develops a stretch reflex. This repetitive cycle—called shivering—greatly increases the rate of heat production. During maximal shivering, body heat production can rise to about four times the basal rate in just a few minutes.

• **Release of thyroid hormones.** The thyroid gland responds to TSH by releasing more thyroid hormones into the blood. As increased levels of thyroid hormones slowly increase the metabolic rate, body temperature rises.

If core body temperature rises above normal, a negative feedback loop opposite to the one depicted in Figure 25.19 goes into action. The higher temperature of the blood stimulates peripheral and central thermoreceptors that send input to the preoptic area, which in turn stimulates the heat-losing center and inhibits the heat-promoting center. Action potentials from the heat-losing center cause dilation of blood vessels in the skin. The skin becomes warm, and the excess heat is lost to the environment via radiation and conduction as an increased volume of blood flows from the warmer core of the body into the cooler skin. At the same time, metabolic rate decreases, and shivering does not occur. The high temperature of the blood stimulates sweat glands of the skin via hypothalamic activation of sympathetic nerves. As the water in perspiration evaporates from the surface of the skin, the skin is cooled. All of these responses counteract heat-promoting effects and help return body temperature to normal.

### Hypothermia

**Hypothermia** (hi’-pō-THER-mè-a) is a lowering of core body temperature to 35°C (95°F) or below. Causes of hypothermia include an overwhelming cold stress (immersion in icy water), metabolic diseases (hypoglycemia, adrenal insufficiency, or hypothyroidism), drugs (alcohol, antidepressants, sedatives, or tranquilizers), burns, and malnutrition. Hypothermia is characterized by the following as core body temperature falls: sensation of cold, shivering, confusion, vasoconstriction, muscle rigidity, bradycardia, acidosis, hypoventilation, hypotension, loss of spontaneous movement, coma, and death (usually caused by cardiac arrhythmias). Because the elderly have reduced metabolic protection against a cold environment coupled with a reduced perception of cold, they are at greater risk for developing hypothermia.

### Guidelines for Healthy Eating

Each gram of protein or carbohydrate in food provides about 4 Calories; 1 gram of fat (lipids) provides about 9 Calories. We do not know with certainty what levels and types of carbohydrate, fat, and protein are optimal in the diet. Different populations around the world eat radically different diets that are adapted to their particular lifestyles. However, many experts recommend the following distribution of calories: 50–60% from carbohydrates, with less than 15% from simple sugars; less than 30% from fats (triglycerides are the main type of dietary fat), with no more than 10% as saturated fats; and about 12–15% from proteins.

On June 2, 2011, the United States Department of Agriculture (USDA) introduced a revised icon called MyPlate based on revised guidelines for healthy eating. It replaces the USDA MyPyramid, which first appeared in 2005. As shown in Figure 25.20, the plate is divided into four different-sized colored sections:

- **Green** (vegetables)
- **Red** (fruits)
- **Orange** (grains)
- **Purple** (protein)

The blue cup (dairy) adjacent to the plate icon is a reminder to include three daily servings of dairy.
Minerals

Minerals are inorganic elements that occur naturally in the earth's crust. In the body they appear in combination with one another, in combination with organic compounds, or as ions in solution. Minerals constitute about 4% of total body mass and are concentrated most heavily in the skeleton. Minerals with known functions in the body include calcium, phosphorus, potassium, sulfur, sodium, chloride, magnesium, iron, iodide, manganese, copper, cobalt, zinc, fluoride, selenium, and chromium. Table 25.9 describes the vital functions of these minerals. Note that the body generally uses the ions of the minerals rather than the non-ionized form. Some minerals, such as chlorine, are toxic or even fatal if ingested in the non-ionized form. Other minerals—aluminum, boron, silicon, and molybdenum—are present but their functions are unclear. Typical diets supply adequate amounts of potassium, sodium, chloride, and magnesium. Some attention must be paid to eating foods that provide enough calcium, phosphorus, iron, and iodide. Excess amounts of most minerals are excreted in the urine and feces.

Calcium and phosphorus form part of the matrix of bone. Because minerals do not form long-chain compounds, they are otherwise poor building materials. A major role of minerals is to help regulate enzymatic reactions. Calcium, iron, magnesium, and manganese are constituents of some coenzymes. Magnesium also serves as a catalyst for the conversion of ADP to ATP. Minerals such as sodium and phosphorus work in buffer systems, which help control the pH of body fluids. Sodium also helps regulate the osmosis of water and, along with other ions, is involved in the generation of nerve impulses.

Vitamins

Organic nutrients required in small amounts to maintain growth and normal metabolism are called vitamins. Unlike carbohydrates, lipids, or proteins, vitamins do not provide energy or serve as the body’s building materials. Most vitamins with known functions are coenzymes.

Most vitamins cannot be synthesized by the body and must be ingested in food. Other vitamins, such as vitamin K, are produced by bacteria in the GI tract and then absorbed. The body can assemble...
TABLE 25.9 Minerals Vital to the Body

<table>
<thead>
<tr>
<th>MINERAL</th>
<th>COMMENTS</th>
<th>IMPORTANCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphorus</td>
<td>About 80% found in bones and teeth as phosphate salts. Blood phosphate level controlled by parathyroid hormone (PTH). Excess excreted in urine; small amount eliminated in feces. Sources: dairy products, meat, fish, poultry, nuts.</td>
<td>Formation of bones and teeth. Phosphates (H₂PO₄⁻, HPO₄²⁻, and PO₄³⁻) constitute a major buffer system of blood. Role in muscle contraction and nerve activity. Component of many enzymes. Involved in energy transfer (ATP). Component of DNA and RNA.</td>
</tr>
<tr>
<td>Potassium</td>
<td>Major cation (K⁺) in intracellular fluid. Excess excreted in urine. Present in most foods (meats, fish, poultry, fruits, nuts).</td>
<td>Needed for generation and conduction of action potentials in neurons and muscle fibers.</td>
</tr>
<tr>
<td>Sulfur</td>
<td>Component of many proteins (such as insulin and chondroitin sulfate), electron carriers in electron transport chain, and some vitamins (thiamine and biotin). Excreted in urine. Sources: beef, liver, lamb, fish, poultry, eggs, cheese, beans.</td>
<td>As component of hormones and vitamins, regulates various body activities. Needed for ATP production by electron transport chain.</td>
</tr>
<tr>
<td>Sodium</td>
<td>Most abundant cation (Na⁺) in extracellular fluids; some found in bones. Excreted in urine and perspiration. Normal intake of NaCl (table salt) supplies more than required amounts.</td>
<td>Strongly affects distribution of water through osmosis. Part of bicarbonate buffer system. Functions in nerve and muscle action potential conduction.</td>
</tr>
<tr>
<td>Magnesium</td>
<td>Important cation (Mg²⁺) in intracellular fluid. Excreted in urine and feces. Widespread in various foods, such as green leafy vegetables, seafood, and whole-grain cereals.</td>
<td>Required for normal functioning of muscle and nervous tissue. Participates in bone formation. Constituent of many coenzymes.</td>
</tr>
<tr>
<td>Iron</td>
<td>About 66% found in hemoglobin of blood. Normal losses of iron occur by shedding of hair, epithelial cells, and mucosal cells, and in sweat, urine, feces, bile, and blood lost during menstruation. Sources: meat, liver, shellfish, egg yolk, beans, legumes, dried fruits, nuts, cereals.</td>
<td>As component of hemoglobin, reversibly binds O₂. Component of cytochromes involved in electron transport chain.</td>
</tr>
<tr>
<td>Iodide</td>
<td>Essential component of thyroid hormones. Excreted in urine. Sources: seafood, iodized salt, vegetables grown in iodine-rich soils.</td>
<td>Required by thyroid gland to synthesize thyroid hormones, which regulate metabolic rate.</td>
</tr>
<tr>
<td>Manganese</td>
<td>Some stored in liver and spleen. Most excreted in feces. Sources: spinach, romaine lettuce, pineapple.</td>
<td>Activates several enzymes. Needed for hemoglobin synthesis, urea formation, growth, reproduction, lactation, bone formation, and possibly production and release of insulin, and inhibition of cell damage.</td>
</tr>
<tr>
<td>Copper</td>
<td>Some stored in liver and spleen. Most excreted in feces. Sources: eggs, whole-wheat flour, beans, beets, liver, fish, spinach, asparagus.</td>
<td>Required with iron for synthesis of hemoglobin. Component of coenzymes in electron transport chain and enzyme necessary for melanin formation.</td>
</tr>
<tr>
<td>Cobalt</td>
<td>Constituent of vitamin B₁₂. Sources: liver, kidney, milk, eggs, cheese, meat.</td>
<td>As part of vitamin B₁₂, required for erythropoiesis.</td>
</tr>
<tr>
<td>Zinc</td>
<td>Important component of certain enzymes. Widespread in many foods, especially meats.</td>
<td>As component of carbonic anhydrase, important in carbon dioxide metabolism. Necessary for normal growth and wound healing, normal taste sensations and appetite, and normal sperm counts in males. As component of peptidases, involved in protein digestion.</td>
</tr>
<tr>
<td>Fluoride</td>
<td>Component of bones, teeth, other tissues. Sources: seafood, tea, gelatin.</td>
<td>Appears to improve tooth structure and inhibit tooth decay.</td>
</tr>
<tr>
<td>Selenium</td>
<td>Important component of certain enzymes. Sources: seafood, meat, chicken, tomatoes, egg yolk, milk, mushrooms, garlic, cereal grains grown in selenium-rich soil.</td>
<td>Needed for synthesis of thyroid hormones, sperm motility, and proper functioning of immune system. Also functions as antioxidant. Prevents chromosome breakage and may play role in preventing certain birth defects, miscarriage, prostate cancer, and coronary artery disease.</td>
</tr>
<tr>
<td>Chromium</td>
<td>Found in high concentrations in brewer's yeast. Also found in wine and some brands of beer.</td>
<td>Needed for normal activity of insulin in carbohydrate and lipid metabolism.</td>
</tr>
</tbody>
</table>
In addition to their other functions, three vitamins—C, E, and beta-carotene (a provitamin)—are termed antioxidant vitamins because they inactivate oxygen free radicals. Recall that free radicals are highly reactive ions or molecules that carry an unpaired electron in their outermost electron shell (see Figure 2.3). Free radicals damage cell membranes, DNA, and other cellular structures and contribute to the formation of artery-narrowing atherosclerotic plaques. Some free radicals arise naturally in the body, and others come from environmental hazards such as tobacco smoke and radiation. Antioxidant vitamins are thought to play a role in protecting against some kinds of cancer, reducing the buildup of atherosclerotic plaque, delaying some effects of aging, and decreasing the chance of cataract formation in the lens of the eyes. Table 25.10 lists the major vitamins, their sources, their functions, and related deficiency disorders.

### Table 25.10 The Principal Vitamins

<table>
<thead>
<tr>
<th>VITAMIN</th>
<th>COMMENT AND SOURCE</th>
<th>FUNCTIONS</th>
<th>DEFICIENCY SYMPTOMS AND DISORDERS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fat-soluble</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>Formed from provitamin beta-carotene (and other provitamins) in GI tract. Stored in liver. Sources of carotene and other provitamins: orange, yellow, and green vegetables. Sources of vitamin A: liver, milk.</td>
<td>Maintains general health and vigor of epithelial cells. Beta-carotene acts as antioxidant to inactivate free radicals. Essential for formation of light-sensitive pigments in photoreceptors of retina. Aids in growth of bones and teeth by helping to regulate activity of osteoblasts and osteoclasts.</td>
<td>Deficiency results in atrophy and keratinization of epithelium, leading to dry skin and hair; increased incidence of ear, sinus, respiratory, urinary, and digestive system infections; inability to gain weight; drying of cornea; and skin sores. <strong>Night blindness</strong> (decreased ability for dark adaptation). Slow and faulty development of bones and teeth.</td>
</tr>
<tr>
<td>D</td>
<td>Sunlight converts 7-dehydrocholesterol in skin to cholecalciferol (vitamin D3). A liver enzyme then converts cholecalciferol to 25-hydroxycholecalciferol. A second enzyme in kidneys converts 25-hydroxycholecalciferol to calcitriol (1,25-dihydroxycholecalciferol), the active form of vitamin D. Most excreted in bile. Dietary sources: fish-liver oils, egg yolk, fortified milk.</td>
<td>Essential for absorption of calcium and phosphorus from GI tract. Works with parathyroid hormone (PTH) to maintain Ca(^{2+}) homeostasis.</td>
<td>Defective utilization of calcium by bones leads to <strong>rickets</strong> in children and <strong>osteomalacia</strong> in adults. Possible loss of muscle tone.</td>
</tr>
<tr>
<td>E (tocopherols)</td>
<td>Stored in liver, adipose tissue, and muscles. Sources: fresh nuts and wheat germ, seed oils, green leafy vegetables.</td>
<td>Inhibits catabolism of certain fatty acids that help form cell structures, especially membranes. Involved in formation of DNA, RNA, and red blood cells. May promote wound healing, contribute to normal structure and functioning of nervous system, and prevent scarring. May help protect liver from toxic chemicals such as carbon tetrachloride. Acts as antioxidant to inactivate free radicals.</td>
<td>May cause oxidation of monounsaturated fats, resulting in abnormal structure and function of mitochondria, lysosomes, and plasma membranes. Possible consequence is hemolytic anemia.</td>
</tr>
<tr>
<td>K</td>
<td>Produced by intestinal bacteria. Stored in liver and spleen. Dietary sources: spinach, cauliflower, cabbage, liver.</td>
<td>Coenzyme essential for synthesis of several clotting factors by liver, including prothrombin.</td>
<td>Delayed clotting time results in excessive bleeding.</td>
</tr>
<tr>
<td>VITamin</td>
<td>COMMENT AND SOURCE</td>
<td>FUNCTIONS</td>
<td>DEFICIENCY SYMPTOMS AND DISORDERS</td>
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<tr>
<td><strong>Water-soluble</strong></td>
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<tr>
<td>B₁₂ (thiamine)</td>
<td>Dissolved in body fluids. Most not stored in body. Excess intake eliminated in urine.</td>
<td>Acts as coenzyme for many different enzymes that break carbon-to-carbon bonds and are involved in carbohydrate metabolism of pyruvic acid to CO₂ and H₂O. Essential for synthesis of neurotransmitter acetylcholine.</td>
<td>Improper carbohydrate metabolism leads to buildup of pyruvic and lactic acids and insufficient production of ATP for muscle and nerve cells. Deficiency leads to (1) beriberi, partial paralysis of smooth muscle of GI tract, causing digestive disturbances; skeletal muscle paralysis; and atrophy of limbs; (2) polyneuritis, due to degeneration of myelin sheaths; impaired reflexes, impaired sense of touch, stunted growth in children, and poor appetite.</td>
</tr>
<tr>
<td><strong>B₂ (riboflavin)</strong></td>
<td>Small amounts supplied by bacteria of GI tract. Dietary sources: yeast, liver, beef, veal, lamb, eggs, whole-grain products, asparagus, peas, beets, peanuts.</td>
<td>Component of certain coenzymes (for example, FAD and FMN) in carbohydrate and protein metabolism, especially in cells of eye, integument, mucosa of intestine, and blood.</td>
<td>Deficiency may lead to improper utilization of oxygen, resulting in blurred vision, cataracts, and corneal ulcerations. Also dermatitis and cracking of skin, lesions of intestinal mucosa, and one type of anemia.</td>
</tr>
<tr>
<td><strong>Niacin (nicotinamide)</strong></td>
<td>Derived from amino acid tryptophan. Sources: yeast, meats, liver, fish, whole-grain products, peas, beans, nuts.</td>
<td>Essential component of NAD and NADP, coenzymes in oxidation-reduction reactions. In lipid metabolism, inhibits production of cholesterol and assists in triglyceride breakdown.</td>
<td>Principal deficiency is pellagra, characterized by dermatitis, diarrhea, and psychological disturbances.</td>
</tr>
<tr>
<td><strong>B₆ (pyridoxine)</strong></td>
<td>Synthesized by bacteria of GI tract. Stored in liver, muscle, and brain. Other sources: salmon, yeast, tomatoes, yellow corn, spinach, whole grain products, liver, yogurt.</td>
<td>Essential coenzyme for normal amino acid metabolism. Assists production of circulating antibodies. May function as coenzyme in triglyceride metabolism.</td>
<td>Most common deficiency symptom is dermatitis of eyes, nose, and mouth. Other symptoms are retarded growth and nausea.</td>
</tr>
<tr>
<td><strong>B₁₂ (cyanocobalamin)</strong></td>
<td>Only B vitamin not found in vegetables; only vitamin containing cobalt. Absorption from GI tract depends on intrinsic factor secreted by gastric mucosa. Sources: liver, kidney, milk, eggs, cheese, meat.</td>
<td>Coenzyme necessary for red blood cell formation, formation of amino acid methionine, entrance of some amino acids into Krebs cycle, and manufacture of choline (used to synthesize acetylcholine).</td>
<td>Pernicious anemia, neuropsychiatric abnormalities (ataxia, memory loss, weakness, personality and mood changes, and abnormal sensations), and impaired activity of osteoblasts.</td>
</tr>
<tr>
<td><strong>Pantothenic acid</strong></td>
<td>Some produced by bacteria of GI tract. Stored primarily in liver and kidneys. Other sources: kidneys, liver, yeast, green vegetables, cereal.</td>
<td>Constituent of coenzyme A, which is essential for transfer of acetyl group from pyruvic acid into Krebs cycle, conversion of lipids and amino acids into glucose, and synthesis of cholesterol and steroid hormones.</td>
<td>Fatigue, muscle spasms, insufficient production of adrenal steroid hormones, vomiting, and insomnia.</td>
</tr>
<tr>
<td><strong>Folic acid (folate, folacin)</strong></td>
<td>Synthesized by bacteria of GI tract. Dietary sources: green leafy vegetables, broccoli, asparagus, breads, dried beans, citrus fruits.</td>
<td>Component of enzyme systems synthesizing nitrogenous bases of DNA and RNA. Essential for normal production of red and white blood cells.</td>
<td>Production of abnormally large red blood cells (macrocytic anemia). Higher risk of neural tube defects in babies born to folate-deficient mothers.</td>
</tr>
<tr>
<td><strong>Biotin</strong></td>
<td>Synthesized by bacteria of GI tract. Dietary sources include yeast, liver, egg yolk, kidneys.</td>
<td>Essential coenzyme for conversion of pyruvic acid to oxaloacetic acid and synthesis of fatty acids and purines.</td>
<td>Mental depression, muscular pain, dermatitis, fatigue, and nausea.</td>
</tr>
<tr>
<td><strong>C (ascorbic acid)</strong></td>
<td>Rapidly destroyed by heat. Some stored in glandular tissue and plasma. Sources: citrus fruits, tomatoes, green vegetables.</td>
<td>Promotes protein synthesis, including laying down of collagen in formation of connective tissue. As coenzyme, may combine with poisons, rendering them harmless until excreted. Works with antibodies, promotes wound healing, and functions as an antioxidant.</td>
<td>Scurvy; anemia; many symptoms related to poor collagen formation, including tender swollen gums, loosening of teeth (alveolar processes also deteriorate), poor wound healing, bleeding (vessel walls are fragile because of connective tissue degeneration), and retardation of growth.</td>
</tr>
</tbody>
</table>
Disorders: Homeostatic Imbalances

Anorexia Nervosa

**Anorexia nervosa** is a chronic disorder characterized by self-induced weight loss, negative perception of body image, and physiological changes that result from nutritional depletion. Patients with anorexia nervosa have a fixation on weight control and often insist on having a bowel movement every day despite inadequate food intake. They often abuse laxatives, which worsens the fluid and electrolyte imbalances and nutrient deficiencies. The disorder is found predominantly in young, single females, and it may be inherited. Abnormal patterns of menstruation, amenorrhea (absence of menstruation), and a low-basal metabolic rate reflect the depressive effects of starvation. Individuals may become emaciated and may ultimately die of starvation. Hypotension, and changes that result from nutritional depletion. Patients with anorexia nervosa have a fixation on weight control and often insist on having a bowel movement every day despite inadequate food intake. They often abuse laxatives, which worsens the fluid and electrolyte imbalances and nutrient deficiencies. The disorder is found predominantly in young, single females, and it may be inherited. Abnormal patterns of menstruation, amenorrhea (absence of menstruation), and a lowered basal metabolic rate reflect the depressive effects of starvation. Individuals may become emaciated and may ultimately die of starvation or one of its complications. Also associated with the disorder are osteoporosis, depression, and brain abnormalities coupled with impaired mental performance. Treatment consists of psychotherapy and dietary regulation.

Fever

A **fever** is an elevation of core temperature caused by a resetting of the hypothalamic thermostat. The most common causes of fever are viral or bacterial infections and bacterial toxins; other causes are ovulation, excessive secretion of thyroid hormones, tumors, and reactions to vaccines. When phagocytes ingest certain bacteria, they are stimulated to secrete a **pyrogen** (pi-rō′-gen; pyro- = fire; -gen = produce), a fever-producing substance. One pyrogen is interleukin-1. It circulates to the hypothalamus and induces neurons of the preoptic area to secrete prostaglandins. Some prostaglandins can reset the hypothalamic thermostat at a higher temperature, and temperature-regulating reflex mechanisms then act to bring the core body temperature up to this new setting. **Antipyretics** are agents that relieve or reduce fever. Examples include aspirin, acetaminophen (Tylenol), and ibuprofen (Advil), all of which reduce fever by inhibiting synthesis of certain prostaglandins.

Suppose that due to production of pyrogens the thermostat is reset at 39°C (103°F). Now the heat-promoting mechanisms (vasoconstriction, increased metabolism, shivering) are operating at full force. Thus, even though core temperature is climbing higher than normal—say, 38°C (101°F)—the skin remains cold, and shivering occurs. This condition, called a **chill**, is a definite sign that core temperature is rising. After several hours, core temperature reaches the setting of the thermostat, and the chills disappear. But now the body will continue to regulate temperature at 39°C (103°F). When the pyrogens disappear, the thermostat is reset at normal—37.0°C (98.6°F). Because core temperature is high in the beginning, the heat-losing mechanisms (vasodilation and sweating) go into operation to decrease core temperature. The skin becomes warm, and the person begins to sweat. This phase of the fever is called the **crisis**, and it indicates that core temperature is falling.

Although death results if core temperature rises above 44–46°C (112–114°F), up to a point, fever is beneficial. For example, a higher temperature intensifies the effects of interferons and the phagocytic activities of macrophages while hindering replication of some pathogens. Because fever increases heart rate, infection-fighting white blood cells are delivered to sites of infection more rapidly. In
addition, antibody production and T cell proliferation increase. Moreover, heat speeds up the rate of chemical reactions, which may help body cells repair themselves more quickly.

**Obesity**

**Obesity** is body weight more than 20% above a desirable standard due to an excessive accumulation of adipose tissue. More than one-third of the adult population in the United States is obese. (An athlete may be overweight due to higher-than-normal amounts of muscle tissue without being obese.) Even moderate obesity is hazardous to health; it is a risk factor in cardiovascular disease, hypertension, pulmonary disease, non-insulin-dependent diabetes mellitus, arthritis, certain cancers (breast, uterus, and colon), varicose veins, and gall-bladder disease.

In a few cases, obesity may result from trauma of or tumors in the food-regulating centers in the hypothalamus. In most cases of obesity, no specific cause can be identified. Contributing factors include genetic factors, eating habits taught early in life, overeating to relieve tension, and social customs. Studies indicate that some obese people burn fewer calories during digestion and absorption of a meal, a smaller food-induced thermogenesis effect. Additionally, obese people who lose weight require about 15% fewer calories to maintain normal body weight than do people who have never been obese. Interestingly, people who gain weight easily when deliberately fed excess calories exhibit less NEAT (nonexercise activity thermogenesis, such as occurs with fidgeting) than people who resist weight gains in the face of extra calories. Although leptin suppresses appetite and produces satiety in experimental animals, it is not deficient in most obese people.

Most surplus calories in the diet are converted to triglycerides and stored in adipose cells. Initially, the adipocytes increase in size, but at a maximal size, they divide. As a result, proliferation of adipocytes occurs in extreme obesity. The enzyme endothelial lipoprotein lipase regulates triglyceride storage. The enzyme is very active in abdominal fat but less active in hip fat. Accumulation of fat in the abdomen is associated with higher blood cholesterol level and other cardiac risk factors because adipose cells in this area appear to be more metabolically active.

Treatment of obesity is difficult because most people who are successful at losing weight gain it back within 2 years. Yet even modest weight loss is associated with health benefits. Treatments for obesity include behavior modification programs, very-low-calorie diets, drugs, and surgery. Behavior modification programs, offered at many hospitals, strive to alter eating behaviors and increase exercise activity. The nutrition program includes a “heart-healthy” diet that includes abundant vegetables but is low in fats, especially saturated fats. A typical exercise program suggests walking for 30 minutes a day, five to seven times a week. Regular exercise enhances both weight loss and weight-loss maintenance. Very-low-calorie (VLC) diets include 400 to 800 kcal/day in a commercially made liquid mixture. The VLC diet is usually prescribed for 12 weeks, under close medical supervision. Two drugs are available to treat obesity. Sibutramine is an appetite suppressant that works by inhibiting reuptake of serotonin and norepinephrine in brain areas that govern eating behavior. Orlistat works by inhibiting the lipases released into the lumen of the GI tract. With less lipase activity, fewer dietary triglycerides are absorbed. For those with extreme obesity who have not responded to other treatments, a surgical procedure may be considered. The two operations most commonly performed—gastric bypass and gastroplasty—both greatly reduce the stomach size so that it can hold just a tiny quantity of food.
Chapter Review

Review

Introduction

1. Our only source of energy for performing biological work is the food we eat. Food also provides essential substances that we cannot synthesize.

2. Most food molecules absorbed by the gastrointestinal tract are used to supply energy for life processes, serve as building blocks during synthesis of complex molecules, or are stored for future use.

25.1 Metabolic Reactions

1. Metabolism refers to all chemical reactions of the body and is of two types: catabolism and anabolism.

2. Catabolism is the term for reactions that break down complex organic compounds into simple ones. Overall, catabolic reactions are exergonic; they produce more energy than they consume.

3. Chemical reactions that combine simple molecules into more complex ones that form the body’s structural and functional components are collectively known as anabolism. Overall, anabolic reactions are endergonic; they consume more energy than they produce.

4. The coupling of anabolism and catabolism occurs via ATP.

25.2 Energy Transfer

1. Oxidation is the removal of electrons from a substance; reduction is the addition of electrons to a substance.

2. Two coenzymes that carry hydrogen atoms during coupled oxidation-reduction reactions are nicotinamide adenine dinucleotide (NAD) and flavin adenine dinucleotide (FAD).

3. ATP can be generated via substrate-level phosphorylation, oxidative phosphorylation, and photophosphorylation.

25.3 Carbohydrate Metabolism

1. During digestion, polysaccharides and disaccharides are hydrolyzed into the monosaccharides glucose (about 80%), fructose, and galactose; the latter two are then converted to glucose. Some glucose is oxidized by cells to provide ATP. Glucose also can be used to synthesize amino acids, glycogen, and triglycerides.

2. Glucose moves into most body cells via facilitated diffusion through glucose transporters (GluT) and becomes phosphorylated to glucose 6-phosphate. In muscle cells, this process is stimulated by insulin. Glucose entry into neurons and hepatocytes is always “turned on.”

3. Cellular respiration, the complete oxidation of glucose to CO₂ and H₂O, involves glycolysis, the Krebs cycle, and the electron transport chain.

4. Glycolysis is the breakdown of glucose into two molecules of pyruvic acid; there is a net production of two molecules of ATP.

5. When oxygen is in short supply, pyruvic acid is reduced to lactic acid; under aerobic conditions, pyruvic acid enters the Krebs cycle. Pyruvic acid is prepared for entrance into the Krebs cycle by conversion to a 2-carbon acetyl group followed by the addition of coenzyme A to form acetyl coenzyme A. The Krebs cycle involves decarboxylations, oxidations, and reductions of various organic acids. Each molecule of pyruvic acid that is converted to acetyl coenzyme A and then enters the Krebs cycle produces three molecules of CO₂, four molecules of NADH and four H⁺, one molecule of FADH₂, and one molecule of ATP. The energy originally stored in glucose and then in pyruvic acid is transferred primarily to the reduced coenzymes NADH and FADH₂.

6. The electron transport chain involves a series of oxidation-reduction reactions in which the energy in NADH and FADH₂ is liberated and transferred to ATP. The electron carriers include FMN, cytochromes, iron-sulfur centers, copper atoms, and coenzyme Q. The electron transport chain yields a maximum of 26 or 28 molecules of ATP and six molecules of H₂O.

7. Table 25.1 summarizes the ATP yield during cellular respiration. The complete oxidation of glucose can be represented as follows:

\[
C_6H_{12}O_6 + 6O_2 \rightarrow 6CO_2 + 6H_2O + 30 or 32 ATPs
\]

8. The conversion of glucose to glycogen for storage in the liver and skeletal muscle is called glycogenesis. It is stimulated by insulin.

9. The conversion of glycogen to glucose is called glycogenolysis. It occurs between meals and is stimulated by glucagon and epinephrine.

10. Gluconeogenesis is the conversion of noncarbohydrate molecules into glucose. It is stimulated by cortisol and glucagon.

25.4 Lipid Metabolism

1. Lipoproteins transport lipids in the bloodstream. Types of lipoproteins include chylomicrons, which carry dietary lipids to adipose tissue; very-low-density lipoproteins (VLDLs), which carry triglycerides from the liver to adipose tissue; low-density lipoproteins (LDLs), which deliver cholesterol to body cells; and high-density lipoproteins (HDLs), which remove excess cholesterol from body cells and transport it to the liver for elimination.

2. Cholesterol in the blood comes from two sources: from food and from synthesis by the liver.

3. Lipids may be oxidized to produce ATP or stored as triglycerides in adipose tissue, mostly in the subcutaneous layer.

4. A few lipids are used as structural molecules or to synthesize essential molecules.

5. Adipose tissue contains lipases that catalyze the deposition of triglycerides from chylomicrons and hydrolyze triglycerides into fatty acids and glycerol.

6. In lipolysis, triglycerides are split into fatty acids and glycerol and released from adipose tissue under the influence of epinephrine, norepinephrine, cortisol, thyroid hormones, and insulin-like growth factors.

7. Glycerol can be converted into glucose by conversion into glyceraldehyde 3-phosphate.

8. In beta oxidation of fatty acids, carbon atoms are removed in pairs from fatty acid chains; the resulting molecules of acetyl coenzyme A enter the Krebs cycle.

9. The conversion of glucose or amino acids into lipids is called lipogenesis; it is stimulated by insulin.

25.5 Protein Metabolism

1. During digestion, proteins are hydrolyzed into amino acids, which enter the liver via the hepatic portal vein.

2. Amino acids, under the influence of insulin-like growth factors and insulin, enter body cells via active transport.

3. Inside cells, amino acids are synthesized into proteins that function as enzymes, hormones, structural elements, and so forth; are stored as fat or glycogen; or are used for energy.

4. Before amino acids can be catabolized, they must be deaminated and converted to substances that can enter the Krebs cycle.
5. Amino acids may also be converted into glucose, fatty acids, and ketone bodies.
6. Protein synthesis is stimulated by insulin-like growth factors, thyroid hormones, insulin, estrogen, and testosterone.
7. Table 25.2 summarizes carbohydrate, lipid, and protein metabolism.

25.6 Key Molecules at Metabolic Crossroads
1. Three molecules play a key role in metabolism: glucose 6-phosphate, pyruvic acid, and acetyl coenzyme A.
2. Glucose 6-phosphate may be converted to glucose, glycogen, ribose 5-phosphate, and pyruvic acid.
3. When ATP is low and oxygen is plentiful, pyruvic acid is converted to acetyl coenzyme A; when oxygen supply is low, pyruvic acid is converted to lactic acid. Carbohydrate and protein metabolism are linked by pyruvic acid.
4. Acetyl coenzyme A is the molecule that enters the Krebs cycle; it is also used to synthesize fatty acids, ketone bodies, and cholesterol.

25.7 Metabolic Adaptations
1. During the absorptive state, ingested nutrients enter the blood and lymph from the GI tract.
2. During the absorptive state, blood glucose is oxidized to form ATP, and glucose transported to the liver is converted to glycogen or triglycerides. Most triglycerides are stored in adipose tissue. Amino acids in hepatocytes are converted to carbohydrates, fats, and proteins. Table 25.3 summarizes the hormonal regulation of metabolism during the absorptive state.
3. During the postabsorptive state, absorption is complete and the ATP needs of the body are satisfied by nutrients already present in the body. The major task is to maintain normal blood glucose level by converting glycogen in the liver and skeletal muscle into glucose, converting glycerol into glucose, and converting amino acids into glucose. Fatty acids, ketone bodies, and amino acids are oxidized to supply ATP. Table 25.4 summarizes the hormonal regulation of metabolism during the postabsorptive state.
4. Fasting is going without food for a few days; starvation implies weeks or months of inadequate food intake. During fasting and starvation, fatty acids and ketone bodies are increasingly utilized for ATP production.

25.8 Energy Balance
1. Energy balance is the precise matching of energy intake to energy expenditure over time.
2. A calorie (cal) is the amount of energy required to raise the temperature of 1 g of water 1°C. Because the calorie is a relatively small unit, the kilocalorie (kcal) or Calorie (Cal) is often used to measure the body's metabolic rate and to express the energy content of foods; a kilocalorie equals 1000 calories.
3. Metabolic rate is the overall rate at which metabolic reactions use energy. Factors that affect metabolic rate include hormones, exercise, the nervous system, body temperature, ingestion of food, age, gender, climate, sleep, and malnutrition.
4. Measurement of the metabolic rate under basal conditions is called the basal metabolic rate (BMR).

Critical Thinking Questions
1. Jane Doe's deceased body was found at her dining room table. Her death was considered suspicious. Lab results from the medical investigation revealed cyanide in her blood. How did the cyanide cause her death?

2. During a recent physical, 55-year-old Glenn's blood serum lab results showed the following: total cholesterol = 300 mg/dL; LDL = 175 mg/dL; HDL = 20 mg/dL. Interpret these results for Glenn and indicate to him what changes, if any, he needs to make in his lifestyle. Why are these changes important?
3. Marissa has joined a weight loss program. As part of the program, she regularly submits a urine sample which is tested for ketones. She went to the clinic today, had her urine checked, and was confronted by the nurse who accused Marissa of “cheating” on her diet. How did the nurse know Marissa was not following her diet?

Answers to Figure Questions

25.1 In pancreatic acinar cells, anabolism predominates because the primary activity is synthesis of complex molecules (digestive enzymes).
25.2 The electron transport chain produces the most ATP.
25.3 The reactions of glycolysis consume two molecules of ATP but generate four molecules of ATP, for a net gain of two.
25.4 Kinases are enzymes that phosphorylate (add phosphate to) their substrate.
25.5 Glycolysis occurs in the cytosol.
25.6 CO₂ is given off during the production of acetyl coenzyme A and during the Krebs cycle. It diffuses into the blood, is transported by the blood to the lungs, and is exhaled.
25.7 The production of reduced coenzymes is important in the Krebs cycle because they will subsequently yield ATP in the electron transport chain.
25.8 The energy source that powers the proton pumps is electrons provided by NADH + H⁺.
25.9 The concentration of H⁺ is highest in the space between the inner and outer mitochondrial membranes.
25.10 During the complete oxidation of one glucose molecule, six molecules of O₂ are used and six molecules of CO₂ are produced.
25.11 Skeletal muscle fibers can synthesize glycogen, but they cannot release glucose into the blood because they lack the enzyme phosphatase required to remove the phosphate group from glucose.

25.12 Hepatocytes can carry out gluconeogenesis and glycogenesis.
25.13 LDLs deliver cholesterol to body cells.
25.14 Hepatocytes and adipose cells carry out lipogenesis, beta oxidation, and lipolysis; hepatocytes carry out ketogenesis.
25.15 Before an amino acid can enter the Krebs cycle, an amino group must be removed via deamination.
25.16 Acetyl coenzyme A is the gateway into the Krebs cycle for molecules being oxidized to generate ATP.
25.17 Reactions of the absorptive state are mainly anabolic.
25.18 Processes that directly elevate blood glucose during the postabsorptive state include lipolysis (in adipocytes and hepatocytes), gluconeogenesis (in hepatocytes), and glycogenolysis (in hepatocytes).
25.19 Exercise, the sympathetic nervous system, hormones (epinephrine, norepinephrine, thyroxine, testosterone, growth hormone), elevated body temperature, and ingestion of food increase metabolic rate, which results in an increase in body temperature.
25.20 The blue cup is a reminder to include three daily servings of dairy such as milk, yogurt, and cheese.