The Digestive System

New Terminology

Alimentary tube (AL-i-**MEN**-tah-ree TOOB)
Chemical digestion (**KEM**-i-kuhl dye-**JES**-chun)
Common bile duct (**KOM**-mon BYL DUKT)
Defecation reflex (DEF-e-**KAY**-shun)
Duodenum (dew-**AH**-den-um)
Emulsify (e-**MULL**-si-fye)
Enamel (e-**NAM**-uhl)
Essential amino acids (e-**SEN**-shul ah-**ME**-noh **ASS**-ids)
External anal sphincter (eks-**TER**-nuhl **AY**-nuhl **SFINK**-ter)
Ileocecal valve (ILL-ee-oh-**SEE**-kuhl VALV)
Internal anal sphincter (in-**TER**-nuhl **AY**-nuhl **SFINK**-ter)
Lower esophageal sphincter (e-SOF-uh-**JEE**-uhl **SFINK**-ter)
Mechanical digestion (muh-**KAN**-i-kuhl dye-**JES**-chun)
Non-essential amino acids (NON-e-**SEN**-shul ah-**ME**-noh **ASS**-ids)
Normal flora (**NOR**-muhl **FLOOR**-ah)
Periodontal membrane (PER-ee-oh-**DON**-tal)
Pyloric sphincter (pye-**LOR**-ik **SFINK**-ter)
Rugae (**ROO**-gay)
Villi (**VILL**-eye)

Related Clinical Terminology

Appendicitis (uh-PEN-di-**SIGH**-tis)
Diverticulitis (DYE-ver-TIK-yoo-**LYE**-tis)
Gastric ulcer (**GAS**-trik **UL**-ser)
Hepatitis (HEP-uh-**TIGH**-tis)
Lactose intolerance (**LAK**-tohs in-**TAHL**-er-ense)
Lithotripsy (LITH-oh-**TRIP**-see)
Paralytic ileus (**PAR**-uh-LIT-ik **ILL**-ee-us)
Peritonitis (per-i-toh-**NIGH**-tis)
Pyloric stenosis (pye-**LOR**-ik ste-**NOH**-sis)

*Terms that appear in **bold type** in the chapter text are defined in the glossary, which begins on page 547.*

A hurried breakfast when you are late for work or school . . . Thanksgiving dinner . . . going on a diet to lose 5 pounds . . . what do these experiences all have in common? Food. We may take food for granted, celebrate with it, or wish we wouldn't eat quite so much of it. Although food is not as immediate a need for human beings as is oxygen, it is a very important part of our lives. Food provides the raw materials or nutrients that cells use to reproduce and to build new tissue. The energy needed for cell reproduction and tissue building is released from food in the process of cell respiration. In fact, a supply of nutrients from regular food intake is so important that the body can even store any excess for use later. Those "extra 5 pounds" are often stored fat in adipose tissue.

The food we eat, however, is not in a form that our body cells can use. A turkey sandwich, for example, consists of complex proteins, fats, and carbohydrates. The function of the **digestive system** is to change these complex organic nutrient molecules into simple organic and inorganic molecules that can then be absorbed into the blood or lymph to be transported to cells. In this chapter we will discuss the organs of digestion and the contribution each makes to digestion and absorption.

DIVISIONS OF THE DIGESTIVE SYSTEM

The two divisions of the digestive system are the alimentary tube and the accessory organs (Fig. 16–1). The **alimentary tube** extends from the mouth to the anus. It consists of the oral cavity, pharynx, esophagus, stomach, small intestine, and large intestine. Digestion takes place within the oral cavity, stomach, and small intestine; most absorption of nutrients takes place in the small intestine. Undigestible material, primarily cellulose, is eliminated by the large intestine (also called the colon).

The **accessory organs** of digestion are the teeth, tongue, salivary glands, liver, gallbladder, and pancreas. Digestion does not take place *within* these organs, but each contributes something *to* the digestive process.

TYPES OF DIGESTION

The food we eat is broken down in two complementary processes: mechanical digestion and chemical digestion. **Mechanical digestion** is the physical breaking up of food into smaller pieces. Chewing is an example of this. As food is broken up, more of its surface area is exposed for the action of digestive enzymes. Enzymes are discussed in Chapter 2. The work of the digestive enzymes is the **chemical digestion** of broken-up food particles, in which complex chemical molecules are changed into much simpler chemicals that the body can utilize. Such enzymes are specific with respect to the fat, protein, or carbohydrate food molecules each can digest. For example, protein-digesting enzymes work only on proteins, not on carbohydrates or fats. Each enzyme is produced by a particular digestive organ and functions at a specific site. However, the enzyme's site of action may or may not be its site of production. These digestive enzymes and their functions are discussed in later sections.

END PRODUCTS OF DIGESTION

Before we describe the organs of digestion, let us see where the process of digestion will take us, or rather, will take our food. The three types of complex organic molecules found in food are carbohydrates, proteins, and fats. Each of these complex molecules is digested to a much more simple substance that the body can then use. Carbohydrates, such as starches and disaccharides, are digested to monosaccharides such as glucose, fructose, and galactose. Proteins are digested to amino acids, and fats are digested to fatty acids and glycerol. Also part of food, and released during digestion, are vitamins, minerals, and water.

We will now return to the beginning of the alimentary tube and consider the digestive organs and the process of digestion.

ORAL CAVITY

Food enters the **oral cavity** (or **buccal cavity**) by way of the mouth. The boundaries of the oral cavity are the hard and soft palates superiorly; the cheeks laterally; and the floor of the mouth inferiorly. Within the oral cavity are the teeth and tongue and the openings of the ducts of the salivary glands.

TEETH

The function of the **teeth** is, of course, chewing. This is the process that mechanically breaks food into smaller pieces and mixes it with saliva. An individual

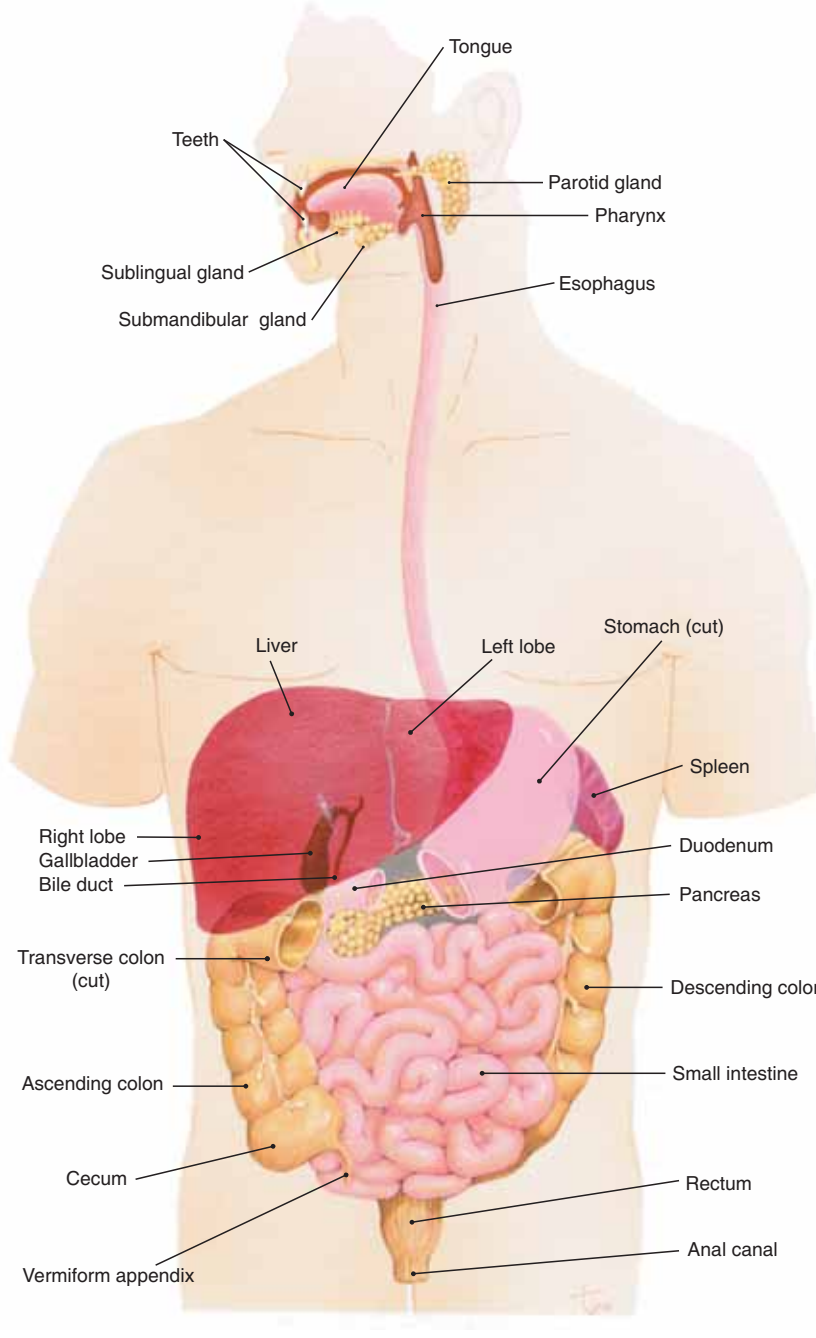


Figure 16–1. The digestive organs shown in anterior view of the trunk and left lateral view of the head. (The spleen is not a digestive organ but is included to show its location relative to the stomach, pancreas, and colon.) **QUESTION:** In which parts of the digestive system does digestion actually take place?

develops two sets of teeth: deciduous and permanent. The **deciduous teeth** begin to erupt through the gums at about 6 months of age, and the set of 20 teeth is usually complete by the age of 2 years. These teeth are gradually lost throughout childhood and replaced by the **permanent teeth**, the first of which are molars that emerge around the age of 6 years. A complete set of permanent teeth consists of 32 teeth; the types of teeth are incisors, canines, premolars, and molars. The wisdom teeth are the third molars on either side of each jawbone. In some people, the wisdom teeth may not emerge from the jawbone because there is no room for them along the gum line. These wisdom teeth are said to be impacted and may put pressure on

the roots of the second molars. In such cases, extraction of a wisdom tooth may be necessary to prevent damage to other teeth.

The structure of a tooth is shown in Fig. 16–2. The crown is visible above the gum (**gingiva**). The root is enclosed in a socket in the mandible or maxillae. The **periodontal membrane** lines the socket and produces a bone-like cement that anchors the tooth. The outermost layer of the crown is **enamel**, which is made by cells called ameloblasts. Enamel provides a hard chewing surface and is more resistant to decay than are other parts of the tooth. Within the enamel is **dentin**, which is very similar to bone and is produced by cells called odontoblasts. Dentin also forms the roots of a tooth. The innermost portion of a tooth is the **pulp cavity**, which contains blood vessels and nerve endings of the trigeminal nerve (5th cranial). Erosion of the enamel and dentin layers by bacterial acids (dental caries or cavities) may result in bacterial invasion of the pulp cavity and a very painful toothache.

TONGUE

The **tongue** is made of skeletal muscle that is innervated by the hypoglossal nerves (12th cranial). On the upper surface of the tongue are small projections called **papillae**, many of which contain taste buds (see also Chapter 9). The sensory nerves for taste are also cranial nerves: the facial (7th) and glossopharyngeal (9th). As you know, the sense of taste is important because it makes eating enjoyable, but the tongue has other functions as well.

Chewing is efficient because of the action of the tongue in keeping the food between the teeth and mixing it with saliva. Elevation of the tongue is the first step in swallowing. This is a voluntary action, in which the tongue contracts and meets the resistance of the hard palate. The mass of food, called a bolus, is thus pushed backward toward the pharynx. The remainder of swallowing is a reflex, which is described in the section on the pharynx.

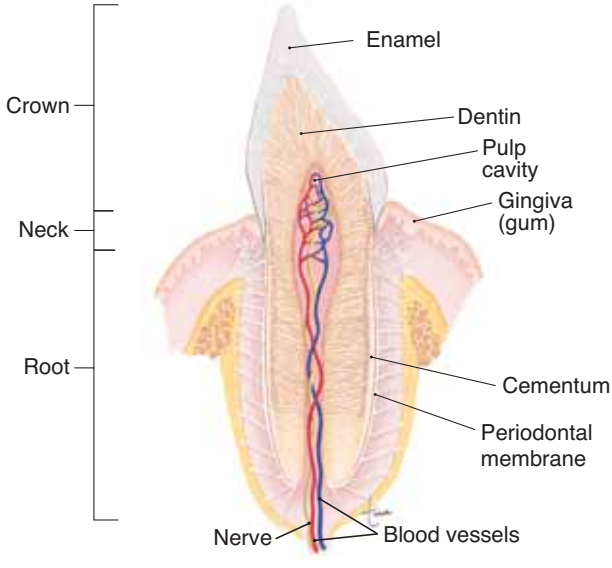


Figure 16–2. Tooth structure. Longitudinal section of a tooth showing internal structure.
QUESTION: Which parts of a tooth are living? How do you know?

SALIVARY GLANDS

The digestive secretion in the oral cavity is **saliva**, produced by three pairs of **salivary glands**, which are shown in Fig. 16–3. The **parotid glands** are just below and in front of the ears. The **submandibular** (also called submaxillary) glands are at the posterior corners of the mandible, and the **sublingual** glands are below the floor of the mouth. Each gland has at least one duct that takes saliva to the oral cavity.

Secretion of saliva is continuous, but the amount varies in different situations. The presence of food (or anything else) in the mouth increases saliva secretion. This is a parasympathetic response mediated by the facial and glossopharyngeal nerves. The sight or smell of food also increases secretion of saliva. Sympathetic stimulation in stress situations decreases secretion, making the mouth dry and swallowing difficult.

Saliva is mostly water, which is important to dissolve food for tasting and to moisten food for swallowing. The digestive enzyme in saliva is salivary amylase, which breaks down starch molecules to shorter chains of glucose molecules, or to maltose, a disaccharide. Most of us, however, do not chew our food long enough for the action of salivary amylase to be truly effective. As you will see, another amylase from the pancreas is also available to digest starch. Table 16–1 summarizes the functions of digestive secretions.

Saliva is made from blood plasma and thus contains many of the chemicals that are found in plasma. Considerable research is focused on detecting in saliva chemical markers for diseases such as cancer, with the

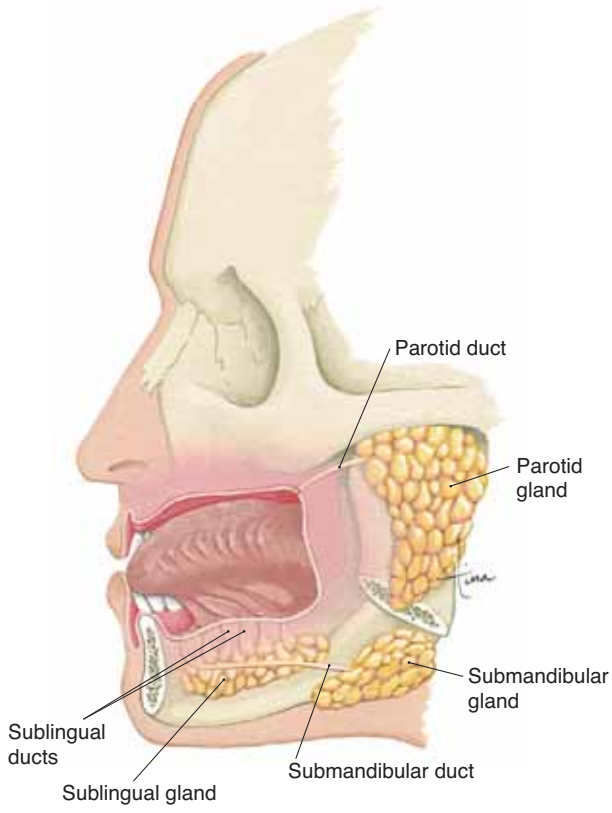


Figure 16–3. The salivary glands shown in left lateral view.
QUESTION: Why are these exocrine glands? What is saliva made from?

goal of using saliva rather than blood for diagnostic tests.

PHARYNX

As described in the preceding chapter, the oropharynx and laryngopharynx are food passageways connecting the oral cavity to the esophagus. No digestion takes place in the pharynx. Its only related function is swallowing, the mechanical movement of food. When the bolus of food is pushed backward by the tongue, the constrictor muscles of the pharynx contract as part of the swallowing reflex. The reflex center for swallowing is in the medulla, which coordinates the many actions that take place: constriction of the pharynx, cessation of breathing, elevation of the soft palate to block the nasopharynx, elevation of the larynx and closure of the epiglottis, and peristalsis of the esophagus. As you can see, swallowing is rather complicated, but because it is a reflex we don't have to think about making it happen correctly. Talking or laughing while eating, however, may interfere with the reflex and cause food to go into the "wrong pipe," the larynx. When that happens, the cough reflex is usually effective in clearing the airway.

ESOPHAGUS

The **esophagus** is a muscular tube that takes food from the pharynx to the stomach; no digestion takes place here. Peristalsis of the esophagus propels food in one direction and ensures that food gets to the stomach even if the body is horizontal or upside down. At the junction with the stomach, the lumen (cavity) of the esophagus is surrounded by the **lower esophageal sphincter** (LES or cardiac sphincter), a circular smooth muscle. The LES relaxes to permit food to enter the stomach, then contracts to prevent the backup of stomach contents. If the LES does not close completely, gastric juice may splash up into the esophagus; this is a painful condition we call heartburn, or gastroesophageal reflux disease (GERD). Most people experience heartburn once in a while, and it is merely uncomfortable, but chronic GERD is more serious. The lining of the esophagus cannot withstand the corrosive action of gastric acid and will be damaged, perhaps resulting in bleeding or even perforation. Medications are available to treat this condition.

STRUCTURAL LAYERS OF THE ALIMENTARY TUBE

Before we continue with our discussion of the organs of digestion, we will first examine the typical structure of the alimentary tube. When viewed in cross-section, the alimentary tube has four layers (Fig. 16–4): the mucosa, submucosa, external muscle layer, and serosa. Each layer has a specific structure, and its functions contribute to the functioning of the organs of which it is a part.

MUCOSA

The **mucosa**, or lining, of the alimentary tube is made of epithelial tissue, areolar connective tissue, and two

Table 16–1 THE PROCESS OF DIGESTION

Organ	Enzyme or Other Secretion	Function	Site of Action
Salivary glands	Amylase	• Converts starch to maltose	Oral cavity
Stomach	Pepsin	• Converts proteins to polypeptides	Stomach
	HCl	• Changes pepsinogen to pepsin; maintains pH 1–2; destroys pathogens	Stomach
Liver	Bile salts	• Emulsify fats	Small intestine
Pancreas	Amylase	• Converts starch to maltose	Small intestine
	Trypsin	• Converts polypeptides to peptides	Small intestine
	Lipase	• Converts emulsified fats to fatty acids and glycerol	Small intestine
Small intestine	Peptidases	• Convert peptides to amino acids	Small intestine
	Sucrase	• Converts sucrose to glucose and fructose	Small intestine
	Maltase	• Converts maltose to glucose (2)	Small intestine
	Lactase	• Converts lactose to glucose and galactose	Small intestine

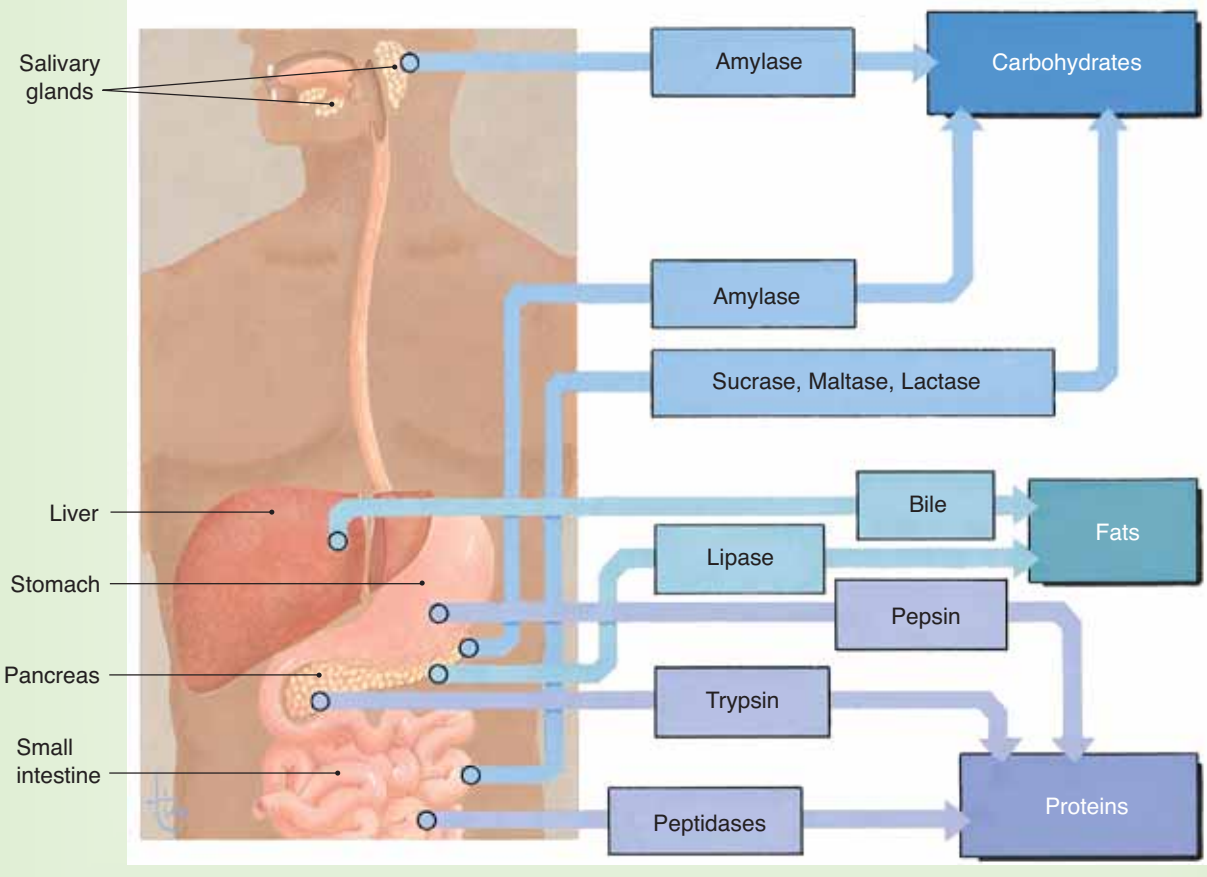


Table Figure 16–A Functions of digestive secretions.
QUESTION: Proteins are digested by secretions from which organs? How did you decide?

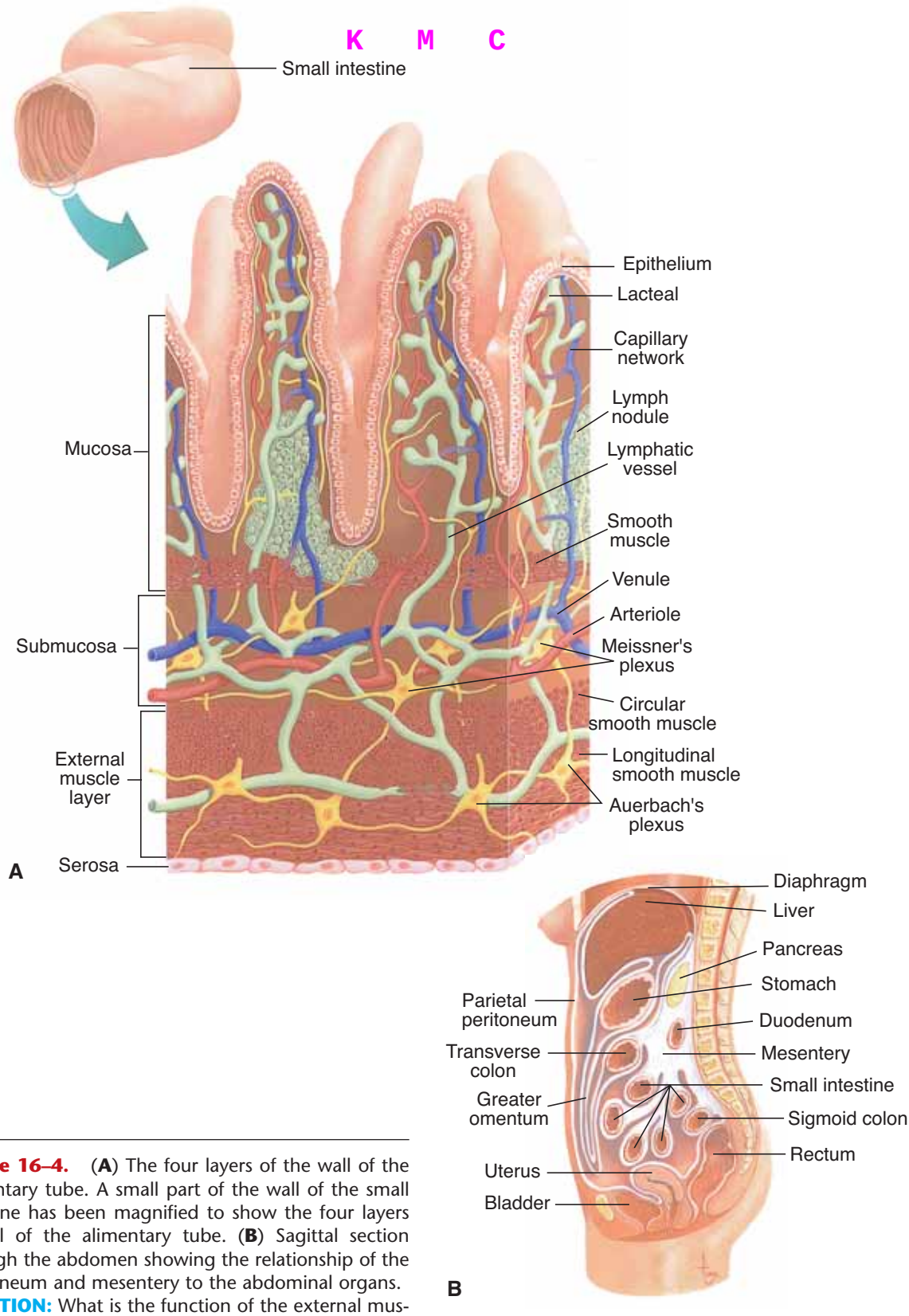


Figure 16–4. (**A**) The four layers of the wall of the alimentary tube. A small part of the wall of the small intestine has been magnified to show the four layers typical of the alimentary tube. (**B**) Sagittal section through the abdomen showing the relationship of the peritoneum and mesentery to the abdominal organs. **QUESTION:** What is the function of the external muscle layer?

thin layers of smooth muscle. In the esophagus the epithelium is stratified squamous epithelium; in the stomach and intestines it is simple columnar epithelium. The epithelium secretes mucus, which lubricates the passage of food, and also secretes the digestive enzymes of the stomach and small intestine. Just below the epithelium, within the areolar connective tissue, are lymph nodules that contain lymphocytes to produce antibodies, and macrophages to phagocytize bacteria or other foreign material that get through the epithelium. The thin layers of smooth muscle create folds in the mucosa, and ripples, so that all of the epithelial cells are in touch with the contents of the organ. In the stomach and small intestine this is important for absorption.

SUBMUCOSA

The **submucosa** is made of areolar connective tissue with many blood vessels and lymphatic vessels. Many millions of nerve fibers are also present, part of what is called the **enteric nervous system**, or the "brain of the gut," which extends the entire length of the alimentary tube. The nerve networks in the submucosa are called **Meissner's plexus** (or submucosal plexus), and they innervate the mucosa to regulate secretions. Parasympathetic impulses increase secretions, whereas sympathetic impulses decrease secretions. Sensory neurons are also present to the smooth muscle (a stretched or cramping gut is painful), as are motor neurons to blood vessels, to regulate vessel diameter and blood flow.

EXTERNAL MUSCLE LAYER

The external muscle layer typically contains two layers of smooth muscle: an inner, circular layer and an outer, longitudinal layer. Variations from the typical do occur, however. In the esophagus, this layer is striated muscle in the upper third, which gradually changes to smooth muscle in the lower portions. The stomach has three layers of smooth muscle, rather than two.

Contractions of this muscle layer help break up food and mix it with digestive juices. The one-way contractions of **peristalsis** move the food toward the anus. **Auerbach's plexus** (or myenteric plexus) is the portion of the enteric nervous system in this layer, and some of its millions of neurons are autonomic. Sympathetic impulses decrease contractions and peristalsis, whereas parasympathetic impulses increase contractions and peristalsis, promoting normal digestion. The parasympathetic nerves are the vagus (10th cranial) nerves; they truly live up to the meaning of *vagus*, which is "wanderer."

SEROSA

Above the diaphragm, for the esophagus, the serosa, the outermost layer, is fibrous connective tissue. Below the diaphragm, the serosa is the **mesentery** or visceral peritoneum, a serous membrane. Lining the abdominal cavity is the parietal peritoneum, usually simply called the **peritoneum**. The peritoneum-mesentery is actually one continuous membrane (see Fig. 16–4). The serous fluid between the peritoneum and mesentery prevents friction when the alimentary tube contracts and the organs slide against one another.

The preceding descriptions are typical of the layers of the alimentary tube. As noted, variations are possible, and any important differences are mentioned in the sections that follow on specific organs.

STOMACH

The **stomach** is located in the upper left quadrant of the abdominal cavity, to the left of the liver and in front of the spleen. Although part of the alimentary tube, the stomach is not a tube, but rather a sac that extends from the esophagus to the small intestine. Because it is a sac, the stomach is a reservoir for food, so that digestion proceeds gradually and we do not have to eat constantly. Both mechanical and chemical digestion take place in the stomach.

The parts of the stomach are shown in Fig. 16–5. The cardiac orifice is the opening of the esophagus, and the fundus is the portion above the level of this opening. The body of the stomach is the large central portion, bounded laterally by the greater curvature and medially by the lesser curvature. The pylorus is adjacent to the duodenum of the small intestine, and the **pyloric sphincter** surrounds the junction of the two organs. The fundus and body are mainly storage areas, whereas most digestion takes place in the pylorus.

When the stomach is empty, the mucosa appears wrinkled or folded. These folds are called **rugae**; they flatten out as the stomach is filled and permit expansion of the lining without tearing it. The **gastric pits** are the glands of the stomach and consist of several

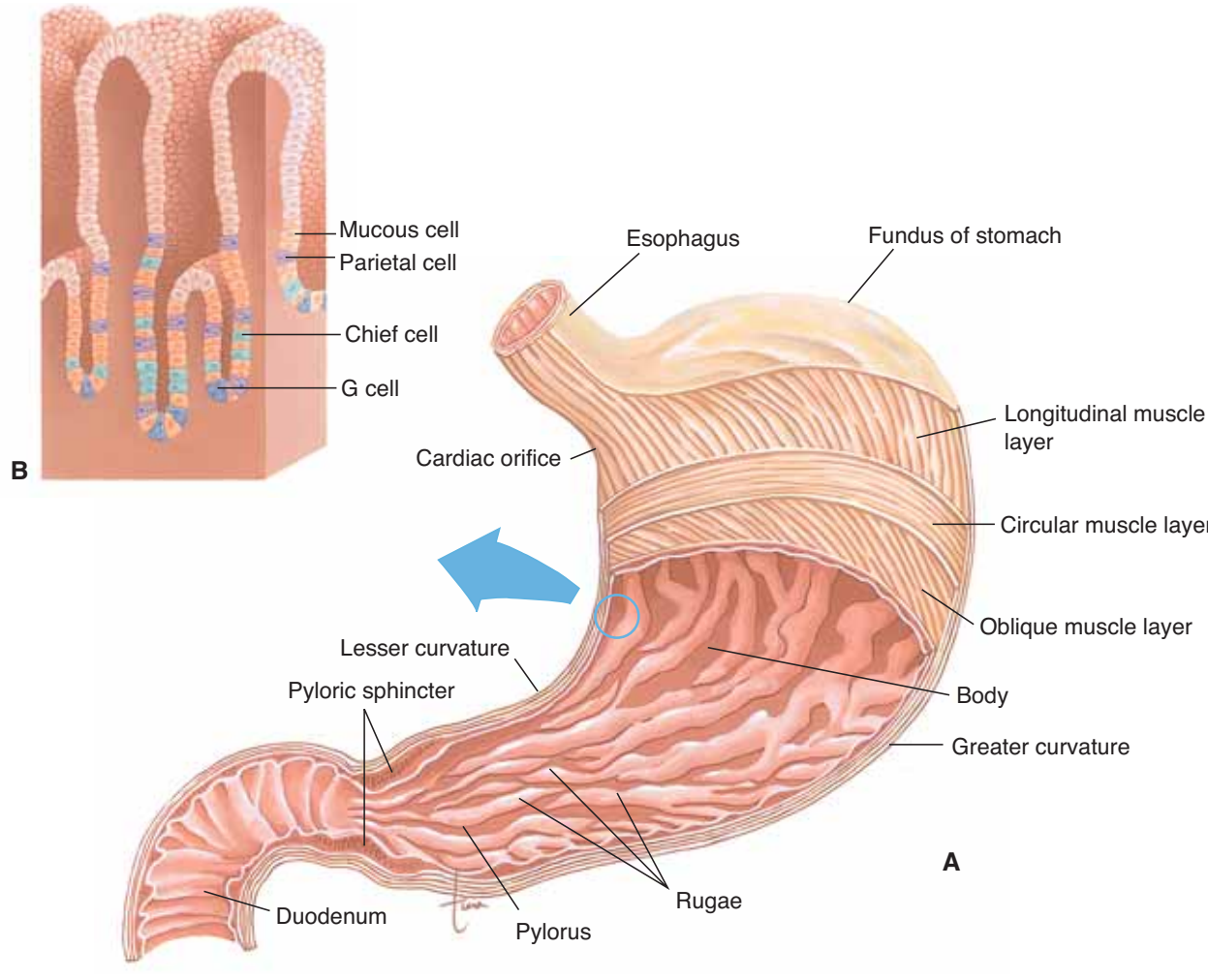


Figure 16–5. (**A**) The stomach in anterior view. The stomach wall has been sectioned to show the muscle layers and the rugae of the mucosa. (**B**) Gastric pits (glands) showing the types of cells present. See text for functions.
QUESTION: What is the function of the pyloric sphincter?

types of cells; their collective secretions are called gastric juice. **Mucous cells** secrete mucus, which coats the stomach lining and helps prevent erosion by the gastric juice. **Chief cells** secrete **pepsinogen**, an inactive form of the enzyme **pepsin**. **Parietal cells** produce hydrochloric acid (HCl); these cells have enzymes called **proton pumps**, which secrete H^+ ions into the stomach cavity. The H^+ ions unite with Cl^- ions that have diffused from the parietal cells to form HCl in the lumen of the stomach. HCl converts pepsinogen to pepsin, which then begins the digestion of proteins to polypeptides, and also gives gastric juice its pH of 1 to 2. This very acidic pH is necessary for pepsin to function and also kills most microorganisms that enter the stomach. The parietal cells also secrete intrinsic factor, which is necessary for the absorption of vitamin B_{12}. Enteroendocrine cells called G cells secrete the hormone gastrin.

Gastric juice is secreted in small amounts at the sight or smell of food. This is a parasympathetic response that ensures that some gastric juice will be present in the stomach when food arrives. The pres-

ence of food in the stomach causes the G cells to secrete **gastrin**, a hormone that stimulates the secretion of greater amounts of gastric juice.

The external muscle layer of the stomach consists of three layers of smooth muscle: circular, longitudinal, and oblique layers. These three layers are innervated by the myenteric plexuses of the enteric nervous system. Stimulatory impulses are carried from the CNS by the vagus nerves (10th cranial) and provide for very efficient mechanical digestion to change food into a thick liquid called chyme. The pyloric sphincter is usually contracted when the stomach is churning food; it relaxes at intervals to permit small amounts of chyme to pass into the duodenum. This sphincter then contracts again to prevent the backup of intestinal contents into the stomach (see Box 16–1: Disorders of the Stomach).

SMALL INTESTINE

The **small intestine** is about 1 inch (2.5 cm) in diameter and approximately 20 feet (6 m) long and extends from the stomach to the cecum of the large intestine. Within the abdominal cavity, the large intestine encircles the coils of the small intestine (see Fig. 16–1).

The **duodenum** is the first 10 inches (25 cm) of the small intestine. The common bile duct enters the duodenum at the ampulla of Vater (or hepatopancreatic ampulla). The **jejunum** is about 8 feet long, and the **ileum** is about 11 feet in length. In a living person, however, the small intestine is always contracted and is therefore somewhat shorter.

Digestion is completed in the small intestine, and the end products of digestion are absorbed into the blood and lymph. The mucosa (see Fig. 16–4) has simple columnar epithelium that includes cells with microvilli and goblet cells that secrete mucus. Enteroendocrine cells secrete the hormones of the small intestine. Lymph nodules called Peyer's patches are especially abundant in the ileum to destroy absorbed pathogens. The external muscle layer has the typical circular and longitudinal smooth muscle layers that mix the chyme with digestive secretions and propel the chyme toward the colon. Stimulatory impulses to the enteric nerves of these muscle layers are carried by the vagus nerves. The waves of peristalsis, however, can take place without stimulation by the central nerv-

Box 16–1 DISORDERS OF THE STOMACH

Vomiting is the expulsion of stomach and intestinal contents through the esophagus and mouth. Stimuli include irritation of the stomach, motion sickness, food poisoning, or diseases such as meningitis. The vomiting center is in the medulla, which coordinates the simultaneous contraction of the diaphragm and the abdominal muscles. This squeezes the stomach and upper intestine, expelling their contents. As part of the reflex, the lower esophageal sphincter relaxes, and the glottis closes. If the glottis fails to close, as may happen in alcohol or drug intoxication, aspiration of vomitus may occur and result in fatal obstruction of the respiratory passages.

Pyloric stenosis means that the opening of the pyloric sphincter is narrowed, and emptying of the stomach is impaired. This is most often a congenital disorder caused by hypertrophy of the pyloric sphincter. For reasons unknown, this condition is more common in male infants than in female infants. When the stomach does not empty efficiently, its internal pressure increases. Vomiting relieves the pressure; this is a classic symptom of pyloric stenosis. Correcting this condition requires surgery to widen the opening in the sphincter.

A **gastric ulcer** is an erosion of the mucosa of the stomach. Because the normal stomach lining is adapted to resist the corrosive action of gastric juice, ulcer formation is the result of oversecretion of HCl or undersecretion of mucus.

As erosion reaches the submucosa, small blood vessels are ruptured and bleed. If vomiting occurs, the vomitus has a "coffee-ground" appearance due to the presence of blood acted on by gastric juice. A more serious complication is perforation of the stomach wall, with leakage of gastric contents into the abdominal cavity, and **peritonitis**.

The bacterium called *Helicobacter pylori* is the cause of most gastric ulcers. For many patients, a few weeks of antibiotic therapy to eradicate this bacterium has produced rapid healing of their ulcers. This bacterium also seems to be responsible for virtually all cases of stomach cancer.

The medications that decrease the secretion of HCl are useful for ulcer patients not helped by antibiotics.

ous system; the enteric nervous system can function independently and promote normal peristalsis.

There are three sources of digestive secretions that function within the small intestine: the liver, the pancreas, and the small intestine itself. We will return to the small intestine after considering these other organs.

LIVER

The **liver** (Fig. 16–6) consists of two large lobes, right and left, and fills the upper right and center of the abdominal cavity, just below the diaphragm. The structural unit of the liver is the **liver lobule**, a roughly hexagonal column of liver cells (hepatocytes). Between adjacent lobules are branches of the hepatic artery and portal vein. The capillaries of a lobule are sinusoids, large and very permeable vessels between the rows of liver cells. The sinusoids receive blood from both the hepatic artery and portal vein, and it is with this mixture of blood that the liver cells carry out their functions. The hepatic artery brings oxygenated blood, and the portal vein brings blood from the digestive organs and spleen (see Fig. 13–7). Each lobule has a central vein. The central veins of all the lobules unite to form the hepatic veins, which take blood out of the liver to the inferior vena cava.

The cells of the liver have many functions (which are discussed in a later section), but their only digestive function is the production of **bile**. Bile enters the small bile ducts, called bile canaliculi, on the liver cells, which unite to form larger ducts and finally merge to form the **hepatic duct**, which takes bile out of the liver (see Fig. 16–6). The hepatic duct unites with the cystic duct of the gallbladder to form the **common bile duct**, which takes bile to the duodenum.

Bile is mostly water and has an excretory function in that it carries bilirubin and excess cholesterol to the intestines for elimination in feces. The digestive function of bile is accomplished by **bile salts**, which **emulsify** fats in the small intestine. Emulsification means that large fat globules are broken into smaller globules. This is mechanical, not chemical, digestion; the fat is still fat but now has more surface area to facilitate chemical digestion.

Production of bile is stimulated by the hormone **secretin**, which is produced by the duodenum when food enters the small intestine. Table 16–2 summarizes the regulation of secretion of all digestive secretions.

GALLBLADDER

The **gallbladder** is a sac about 3 to 4 inches (7.5 to 10 cm) long located on the undersurface of the right lobe of the liver. Bile in the hepatic duct of the liver flows through the **cystic duct** into the gallbladder (see Fig. 16–6), which stores bile until it is needed in the small intestine. The gallbladder also concentrates bile by absorbing water (see Box 16–2: Gallstones).

When fatty foods enter the duodenum, the enteroendocrine cells of the duodenal mucosa secrete the hormone **cholecystokinin**. This hormone stimulates contraction of the smooth muscle in the wall of the gallbladder, which forces bile into the cystic duct, then into the common bile duct, and on into the duodenum.

PANCREAS

The **pancreas** is located in the upper left abdominal quadrant between the curve of the duodenum and the spleen and is about 6 inches (15 cm) in length. The endocrine functions of the pancreas were discussed in Chapter 10, so only the exocrine functions will be considered here. The exocrine glands of the pancreas are called acini (singular: acinus) (Fig. 16–7). They produce enzymes that are involved in the digestion of all three types of complex food molecules.

The pancreatic enzyme **amylase** digests starch to maltose. You may recall that this is the "backup" enzyme for salivary amylase, though pancreatic amylase is responsible for most digestion of starch. **Lipase** converts emulsified fats to fatty acids and glycerol. The emulsifying or fat-separating action of bile salts increases the surface area of fats so that lipase works effectively. Trypsinogen is an inactive enzyme that is changed to active **trypsin** in the duodenum. Trypsin digests polypeptides to shorter chains of amino acids.

The pancreatic enzyme juice is carried by small ducts that unite to form larger ducts, then finally the main **pancreatic duct**. An accessory duct may also be present. The main pancreatic duct emerges from the medial side of the pancreas and joins the common bile duct to the duodenum (see Fig. 16–7).

The pancreas also produces a **bicarbonate juice** (containing sodium bicarbonate), which is alkaline.

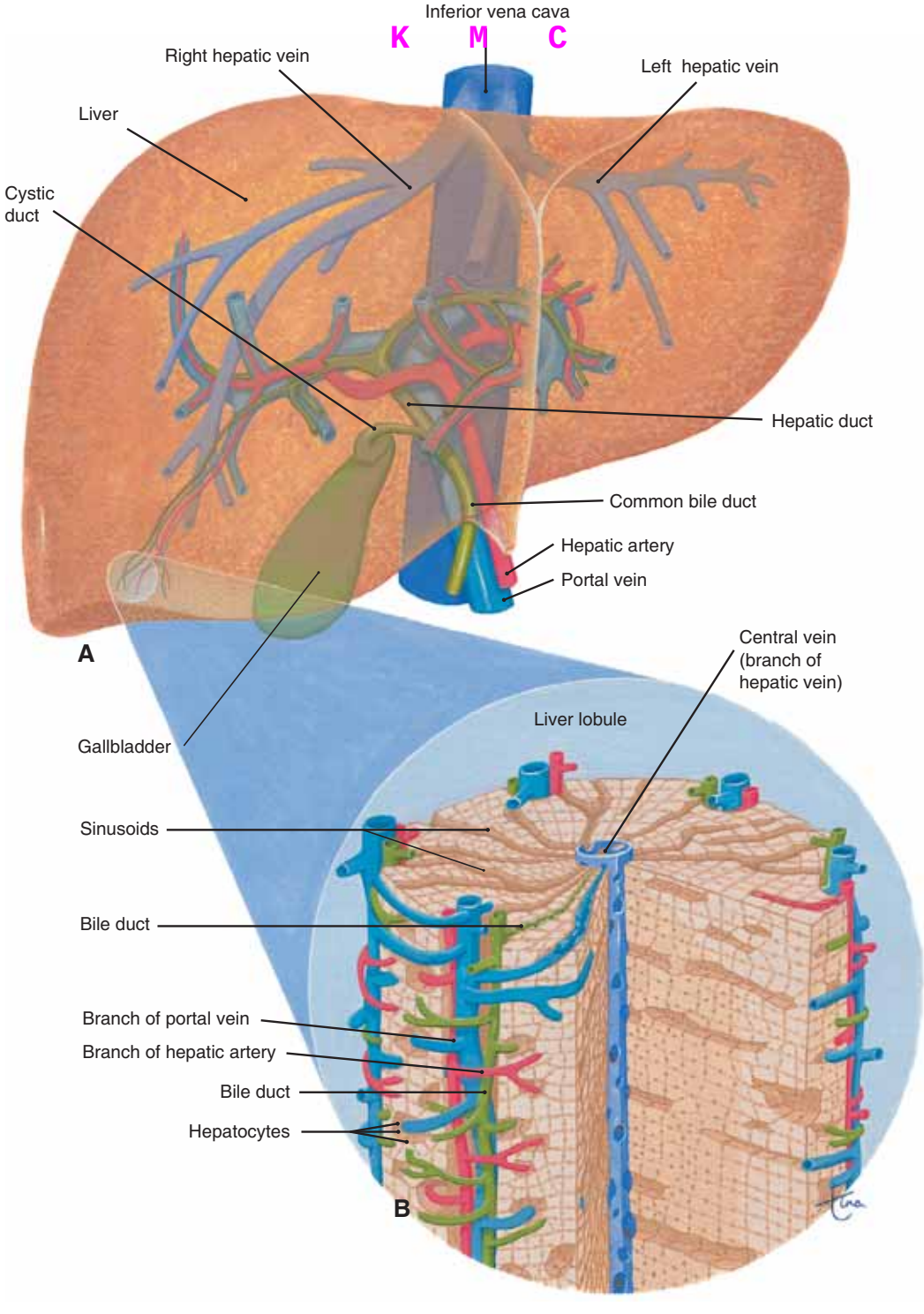


Figure 16–6. (**A**) The liver and gallbladder with blood vessels and bile ducts. (**B**) Magnified view of one liver lobule. See text for description.
QUESTION: In part B, trace the pathway of blood flow through a liver lobule.

Table 16–2 REGULATION OF DIGESTIVE SECRETIONS

Secretion	Nervous Regulation	Chemical Regulation
Saliva	Presence of food in mouth or sight of food; parasympathetic impulses along 7th and 9th cranial nerves	None
Gastric juice	Sight or smell of food; parasympathetic impulses along 10th cranial nerves	Gastrin—produced by the G cells of the gastric mucosa when food is present in the stomach
Bile		
Secretion by the liver	None	Secretin—produced by the enteroendocrine cells of the duodenum when chyme enters
Contraction of the gallbladder	None	Cholecystokinin—produced by the enteroendocrine cells of the duodenum when chyme enters
Enzyme pancreatic juice	None	Cholecystokinin—from the duodenum
Bicarbonate pancreatic juice	None	Secretin—from the duodenum
Intestinal juice	Presence of chyme in the duodenum; parasympathetic impulses along 10th cranial nerves	None

Because the gastric juice that enters the duodenum is very acidic, it must be neutralized to prevent damage to the duodenal mucosa. This neutralizing is accomplished by the sodium bicarbonate in pancreatic juice, and the pH of the duodenal chyme is raised to about 7.5.

Secretion of pancreatic juice is stimulated by the hormones secretin and cholecystokinin, which are produced by the duodenal mucosa when chyme enters the small intestine. **Secretin** stimulates the production of bicarbonate juice by the pancreas, and **cholecystokinin** stimulates the secretion of the pancreatic enzymes.

COMPLETION OF DIGESTION AND ABSORPTION

SMALL INTESTINE

The secretion of the epithelium of the intestinal glands (or crypts of Lieberkühn) is stimulated by the

Box 16–2 GALLSTONES

One of the functions of the gallbladder is to concentrate bile by absorbing water. If the bile contains a high concentration of cholesterol, absorption of water may lead to precipitation and the formation of cholesterol crystals. These crystals are **gallstones**.

If the gallstones are small, they will pass through the cystic duct and common bile duct to the duodenum without causing symptoms. If large, however, the gallstones cannot pass out of the gallbladder, and may cause mild to severe pain that often radiates to the right shoulder. Obstructive jaundice may occur if bile backs up into the liver and bilirubin is reabsorbed into the blood.

Several treatments are available for gallstones. Medications that dissolve gallstones work slowly, over the course of several months, and are useful if biliary obstruction is not severe. An instrument that generates shock waves (called a lithotripter) may be used to pulverize the stones into smaller pieces that may easily pass into the duodenum; this procedure is called **lithotripsy**. Surgery to remove the gallbladder (cholecystectomy) is required in some cases. The hepatic duct is then connected directly to the common bile duct, and dilute bile flows into the duodenum. Following such surgery, the patient should avoid meals high in fats.

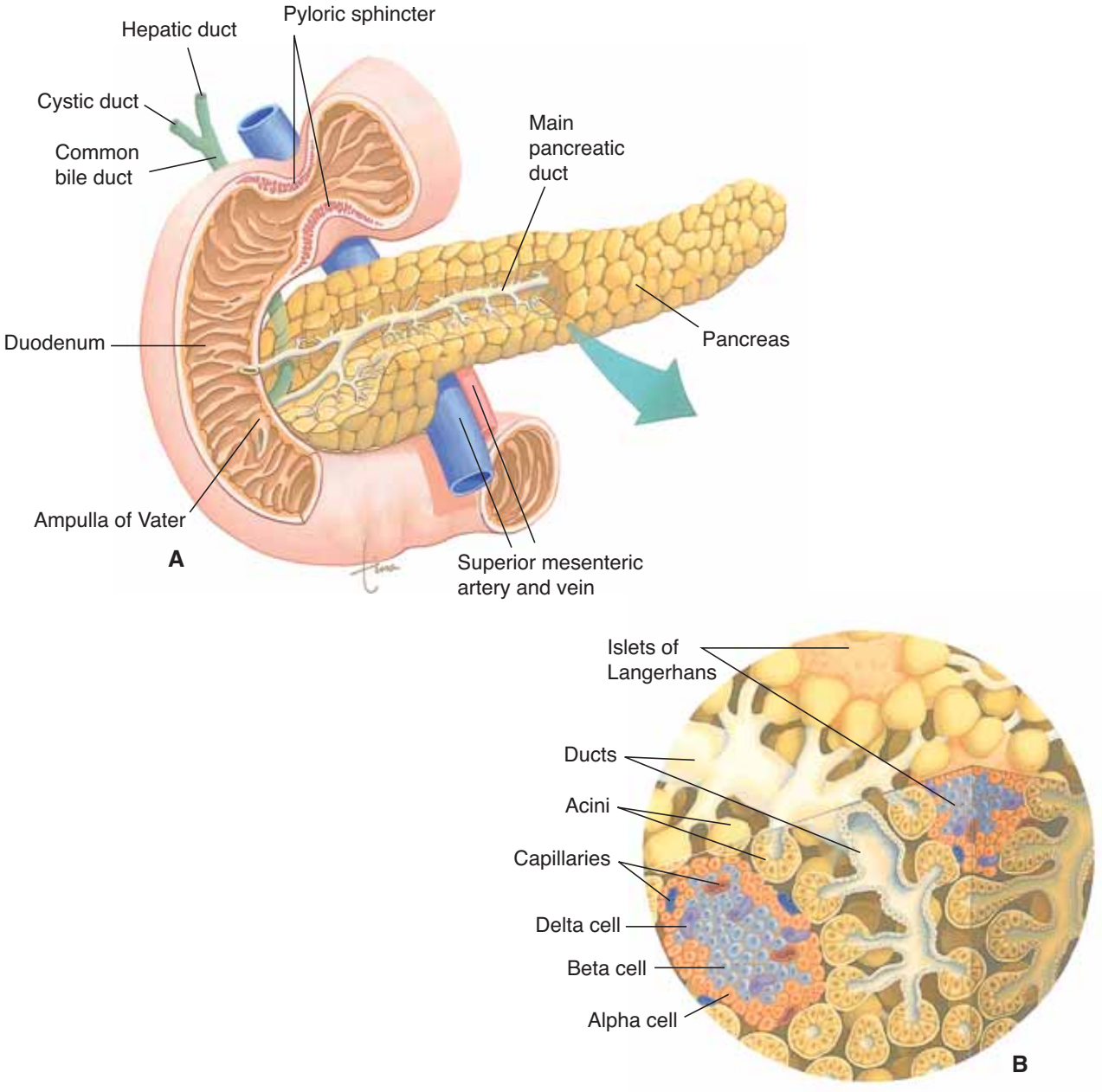


Figure 16–7. (**A**) The pancreas, sectioned to show the pancreatic ducts. The main pancreatic duct joins the common bile duct. (**B**) Microscopic section showing acini with their ducts and several islets of Langerhans.
QUESTION: In part B, what do the acini secrete?

presence of food in the duodenum. The intestinal enzymes are the peptidases and sucrase, maltase, and lactase. **Peptidases** complete the digestion of protein by breaking down short polypeptide chains to amino acids. **Sucrase**, **maltase**, and **lactase**, respectively, digest the disaccharides sucrose, maltose, and lactose to monosaccharides.

The enteroendocrine cells of the intestinal glands secrete the hormones of the small intestine. Secretion is stimulated by food entering the duodenum.

A summary of the digestive secretions and their functions is found in Table 16–1. Regulation of these secretions is shown in Table 16–2.

ABSORPTION

Most absorption of the end products of digestion takes place in the small intestine (although the stomach does absorb water and alcohol). The process of absorption requires a large surface area, which is provided by several structural modifications of the small intestine; these are shown in Fig. 16–8. **Plica circulares**, or circular folds, are macroscopic folds of the mucosa and submucosa, somewhat like accordion pleats. The mucosa is further folded into projections called **villi**, which give the inner surface of the intestine a velvet-like appearance. Each columnar cell (except the mucus-secreting goblet cells) of the villi also has **microvilli** on its free surface. Microvilli are microscopic folds of the cell membrane, and are collectively

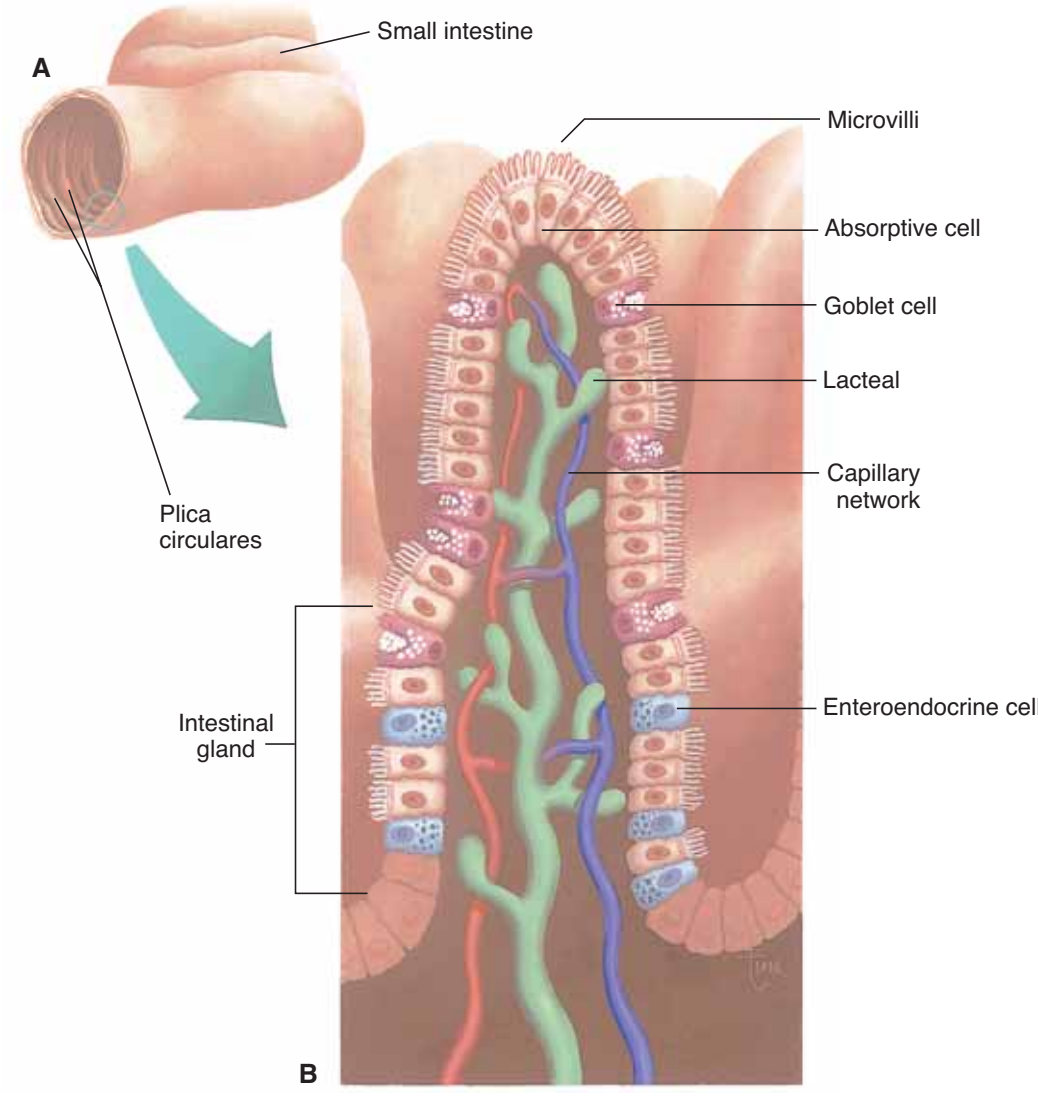


Figure 16–8. The small intestine. (**A**) Section through the small intestine showing plica circulares. (**B**) Microscopic view of a villus showing the internal structure. The enteroendocrine cells secrete the intestinal hormones.
QUESTION: What is the purpose of the villi? What other structures have the same purpose?

called the brush border. All of these folds greatly increase the surface area of the intestinal lining. It is estimated that if the intestinal mucosa could be flattened out, it would cover more than 2000 square feet (half a basketball court).

The absorption of nutrients takes place from the lumen of the intestine into the vessels within the villi. Refer to Fig. 16–8 and notice that within each villus is a **capillary network** and a **lacteal**, which is a dead-end lymph capillary. Water-soluble nutrients are absorbed into the blood in the capillary networks. Monosaccharides, amino acids, positive ions, and the water-soluble vitamins (vitamin C and the B vitamins) are absorbed by active transport. Negative ions may be absorbed by either passive or active transport mechanisms. Water is absorbed by osmosis following the absorption of minerals, especially sodium. Certain nutrients have additional special requirements for their absorption: For example, vitamin B_{12} requires the intrinsic factor produced by the parietal cells of the gastric mucosa, and the efficient absorption of calcium ions requires parathyroid hormone and vitamin D.

Fat-soluble nutrients are absorbed into the lymph in the lacteals of the villi. Bile salts are necessary for the efficient absorption of fatty acids and the fat-soluble vitamins (A, D, E, and K). Once absorbed, fatty acids are recombined with glycerol to form triglycerides. These triglycerides then form globules that include cholesterol and protein; these lipid–protein complexes are called **chylomicrons**. In the form of chylomicrons, most absorbed fat is transported by the lymph and eventually enters the blood in the left subclavian vein.

Blood from the capillary networks in the villi does not return directly to the heart but first travels through the portal vein to the liver. You may recall the importance of portal circulation, discussed in Chapter 13. This pathway enables the liver to regulate the blood levels of glucose and amino acids, store certain vitamins, and remove potential poisons from the blood (see Box 16–3: Disorders of the Intestines).

Box 16–3 DISORDERS OF THE INTESTINES

Duodenal ulcers are erosions of the duodenal wall caused by the gastric juice that enters from the stomach. The most serious consequences are bleeding and perforation.

Paralytic ileus is the cessation of contraction of the smooth muscle layer of the intestine. This is a possible complication of abdominal surgery, but it may also be the result of peritonitis or inflammation elsewhere in the abdominal cavity. In the absence of peristalsis, intestinal obstruction may occur. Bowel movements cease, and vomiting occurs to relieve the pressure within the alimentary tube. Treatment involves suctioning the intestinal contents to eliminate any obstruction and to allow the intestine to regain its normal motility.

Lactose intolerance is the inability to digest lactose because of deficiency of the enzyme lactase. Lactase deficiency may be congenital, a consequence of prematurity, or acquired later in life. The delayed form is quite common among people of African or Asian ancestry, and in part is genetic. When lactose, or milk sugar, is not digested, it undergoes fermentation in the intestine. Symptoms include diarrhea, abdominal pain, bloating, and flatulence (gas formation).

Salmonella food poisoning is caused by bacteria in the genus *Salmonella*. These are part of the intestinal flora of animals, and animal foods such as meat and eggs may be sources of infection. These bacteria are not normal for people, and they cause the intestines to secrete large amounts of fluid. Symptoms include diarrhea, abdominal cramps, and vomiting and usually last only a few days. For elderly or debilitated people, however, salmonella food poisoning may be very serious or even fatal.

Diverticula are small outpouchings through weakened areas of the intestinal wall. They are more likely to occur in the colon than in the small intestine and may exist for years without causing any symptoms. The presence of diverticula is called **diverticulosis**. Inflammation of diverticula is called **diverticulitis**, which is usually the result of entrapment of feces and bacteria. Symptoms include abdominal pain and tenderness and fever. If uncomplicated, diverticulitis may be treated with antibiotics and modifications in diet. The most serious complication is perforation of diverticula, allowing fecal material into the abdominal cavity, causing peritonitis. A diet high in fiber is believed to be an important aspect of prevention, to provide bulk in the colon and prevent weakening of its wall.

LARGE INTESTINE

The **large intestine**, also called the **colon**, is approximately 2.5 inches (6.3 cm) in diameter and 5 feet (1.5 m) in length. It extends from the ileum of the small intestine to the anus, the terminal opening. The parts of the colon are shown in Fig. 16–9. The **cecum** is the first portion, and at its junction with the ileum is the **ileocecal valve**, which is not a sphincter but serves the same purpose. After undigested food (which is now mostly cellulose) and water pass from the ileum into the cecum, closure of the ileocecal valve prevents the backflow of fecal material.

Attached to the cecum is the **appendix**, a small, dead-end tube with abundant lymphatic tissue. The appendix seems to be a **vestigial organ**, that is, one whose size and function seem to be reduced. Although there is abundant lymphatic tissue in the wall of the appendix, the possibility that the appendix is concerned with immunity is not known with certainty. **Appendicitis** refers to inflammation of the appendix, which may occur if fecal material becomes impacted within it. This usually necessitates an **appendectomy**, the surgical removal of the appendix.

The remainder of the colon consists of the ascending, transverse, and descending colon, which encircle the small intestine; the sigmoid colon, which turns medially and downward; the rectum; and the anal canal. The rectum is about 6 inches long, and the anal canal is the last inch of the colon that surrounds the anus. Clinically, however, the terminal end of the colon is usually referred to as the rectum.

No digestion takes place in the colon. The only secretion of the colonic mucosa is mucus, which lubricates the passage of fecal material. The longitudinal smooth muscle layer of the colon is in three bands called **taeniae coli**. The rest of the colon is "gathered" to fit these bands. This gives the colon a puckered appearance; the puckers or pockets are called **haustra**, which provide for more surface area within the colon.

The functions of the colon are the absorption of water, minerals, and vitamins and the elimination of undigestible material. About 80% of the water that

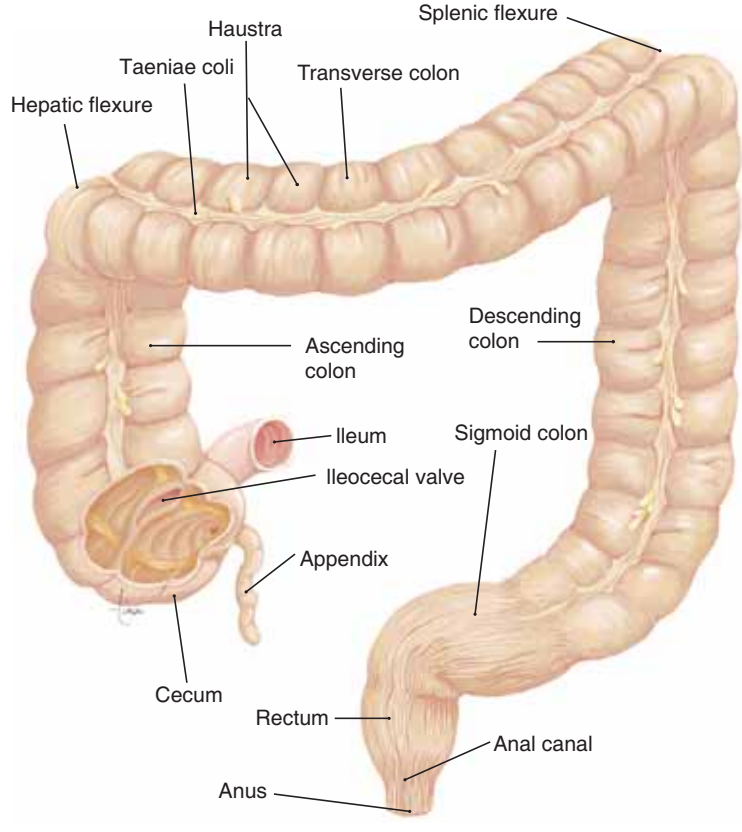


Figure 16–9. The large intestine shown in anterior view. The term *flexure* means a turn or bend.
QUESTION: What is the function of the ileocecal valve?

Box 16–4 INFANT BOTULISM

Botulism is most often acquired from food. When the spores of the botulism bacteria are in an anaerobic (without oxygen) environment such as a can of food, they germinate into active bacteria that produce a neurotoxin. If people ingest food containing this toxin, they will develop the paralysis that is characteristic of botulism.

For infants less than 1 year of age, however, ingestion of just the bacterial spores may be harmful. The infant's stomach does not produce much HCl, so ingested botulism spores may not be destroyed. Of equal importance, the infant's normal colon flora is not yet established. Without the normal population of colon bacteria to provide competition, spores of the botulism bacteria may germinate and produce their toxin.

An affected infant becomes lethargic and weak; paralysis may progress slowly or rapidly. Treatment (antitoxin) is available, but may be delayed if botulism is not suspected. Many cases of infant botulism have been traced to honey that was found to contain botulism spores. Such spores are not harmful to older children and adults, who have a normal colon flora that prevents the botulism bacteria from becoming established.

enters the colon is absorbed (400 to 800 mL per day). Positive and negative ions are also absorbed. The vitamins absorbed are those produced by the **normal flora**, the trillions of bacteria that live in the colon. Vitamin K is produced and absorbed in amounts usually sufficient to meet a person's daily need. Other vitamins produced in smaller amounts include riboflavin, thiamin, biotin, and folic acid. Everything absorbed by the colon circulates first to the liver by way of portal circulation. Yet another function of the normal colon flora is to inhibit the growth of pathogens (see Box 16–4: Infant Botulism).

ELIMINATION OF FECES

Feces consist of cellulose and other undigestible material, dead and living bacteria, and water. Elimination of feces is accomplished by the **defecation reflex**, a spinal cord reflex that may be controlled voluntarily. The rectum is usually empty until peristalsis of the colon pushes feces into it. These waves of peristalsis tend to occur after eating, especially when food enters the duodenum. The wall of the rectum is stretched by the entry of feces, and this is the stimulus for the defecation reflex.

Stretch receptors in the smooth muscle layer of the rectum generate sensory impulses that travel to the sacral spinal cord. The returning motor impulses cause the smooth muscle of the rectum to contract. Surrounding the anus is the **internal anal sphincter**, which is made of smooth muscle. As part of the reflex, this sphincter relaxes, permitting defecation to take place.

The **external anal sphincter** is made of skeletal muscle and surrounds the internal anal sphincter (Fig. 16–10). If defecation must be delayed, the external sphincter may be voluntarily contracted to close the anus. The awareness of the need to defecate passes as the stretch receptors of the rectum adapt. These receptors will be stimulated again when the next wave of peristalsis reaches the rectum (see Box 16–5: Fiber).

OTHER FUNCTIONS OF THE LIVER

The **liver** is a remarkable organ, and only the brain is capable of a greater variety of functions. The liver cells (hepatocytes) produce many enzymes that catalyze many different chemical reactions. These reactions are the functions of the liver. As blood flows through the sinusoids (capillaries) of the liver (see Fig. 16–6), materials are removed by the liver cells, and the products of the liver cells are secreted into the blood. Some of the liver functions will already be familiar to you. Others are mentioned again and discussed in more detail in the next chapter. Because the liver has such varied effects on so many body systems, we will use the categories below to summarize the liver functions.

1. **Carbohydrate metabolism**—As you know, the liver regulates the blood glucose level. Excess glucose is converted to glycogen (glycogenesis) when blood glucose is high; the hormones insulin and cortisol facilitate this process. During hypoglycemia or stress situations, glycogen is converted back to glucose (glycogenolysis) to raise the blood glucose level. Epinephrine and glucagon are the hormones that facilitate this process.

Box 16–5 FIBER

Fiber is a term we use to refer to the organic materials in the cell walls of plants. These are mainly cellulose and pectins. The role of dietary fiber and possible benefits that a high-fiber diet may provide are currently the focus of much research. It is important to differentiate what is known from what is, at present, merely speculation.

Many studies have shown that populations (large groups of people, especially those of different cultures) who consume high-fiber diets tend to have a lower frequency of certain diseases. These include diverticulitis, colon cancer, coronary artery disease, diabetes, and hypertension. Such diseases are much more common among populations whose diets are low in vegetables, fruits, and whole grains, and high in meat, dairy products, and processed foods. In contrast, a 2005 study showed no protective effect of fiber against colon cancer. What we can say for sure is that fiber may not be the only dietary or environmental factor involved.

Claims that high-fiber diets directly lower blood levels of cholesterol and fats are not supported by definitive clinical or experimental studies. One possible explanation may be that a person whose diet consists largely of high-fiber foods simply eats less of the foods high in cholesterol and fats, and this is the reason for that person's lower blood levels of fats and cholesterol.

Should people try to make great changes in their diets? Probably not, not if they are careful to limit fat intake and to include significant quantities of vegetables and fruits. Besides the possible benefits of fiber, unprocessed plant foods provide important amounts of vitamins and minerals.

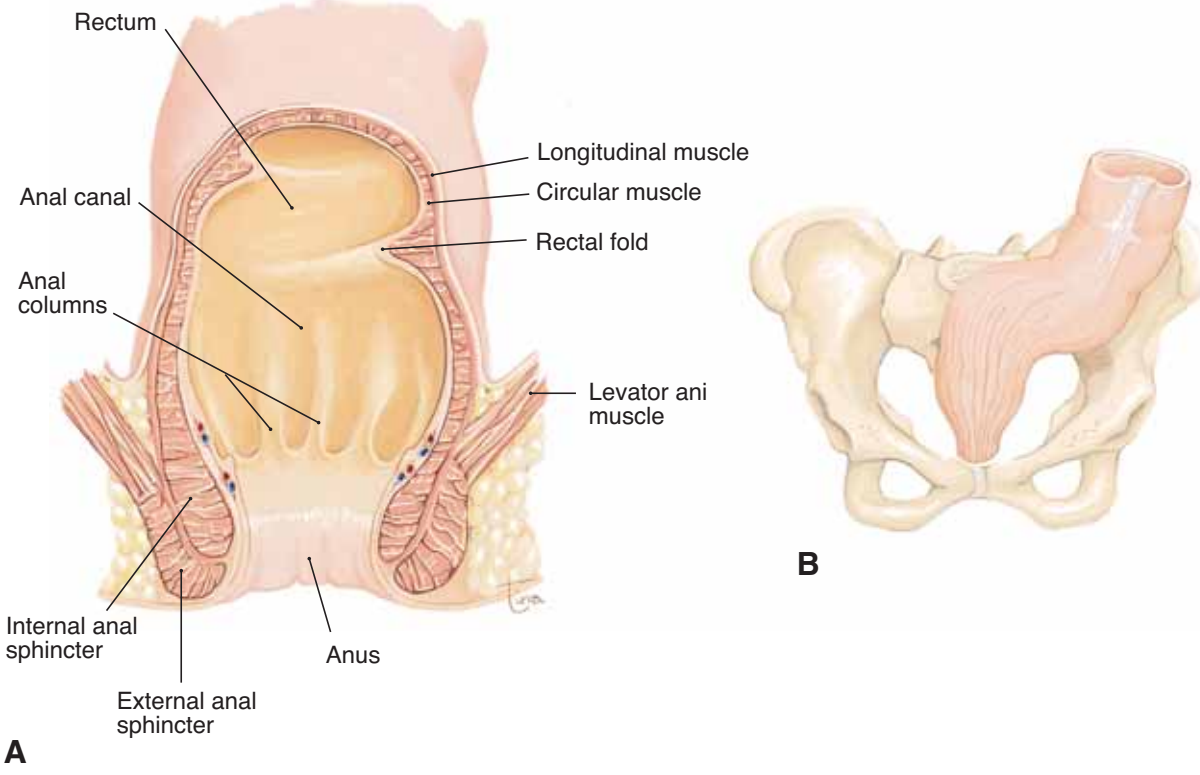


Figure 16–10. (**A**) Internal and external anal sphincters shown in a frontal section through the lower rectum and anal canal. (**B**) Position of rectum and anal canal relative to pelvic bone.
QUESTION: The internal anal sphincter is a continuation of which part of the rectum?

The liver also changes other monosaccharides to glucose. Fructose and galactose, for example, are end products of the digestion of sucrose and lactose. Because most cells, however, cannot readily use fructose and galactose as energy sources, they are converted by the liver to glucose, which is easily used by cells.

2. **Amino acid metabolism**—The liver regulates blood levels of amino acids based on tissue needs for protein synthesis. Of the 20 different amino acids needed for the production of human proteins, the liver is able to synthesize 12, called the **nonessential amino acids**. The chemical process by which this is done is called **transamination**, the transfer of an amino group (NH_2) from an amino acid present in excess to a free carbon chain that forms a complete, new amino acid molecule. The other eight amino acids, which the liver cannot synthesize, are called the **essential amino acids**. In this case, "essential" means that the amino acids must be supplied by our food, because the liver cannot manufacture them. Similarly, "non-essential" means that the amino acids do not have to be supplied in our food because the liver *can* make them. All 20 amino acids are required in order to make our body proteins.

   Excess amino acids, those not needed right away for protein synthesis, cannot be stored. However, they do serve another useful purpose. By the process of **deamination**, which also occurs in the liver, the NH_2 group is removed from an amino acid, and the remaining carbon chain may be converted to a simple carbohydrate molecule or to fat. Thus, excess amino acids are utilized for energy production: either for immediate energy or for the potential energy stored as fat in adipose tissue. The NH_2 groups that were detached from the original amino acids are combined to form urea, a waste product that will be removed from the blood by the kidneys and excreted in urine.
3. **Lipid metabolism**—The liver forms lipoproteins, which as their name tells us, are molecules of lipids and proteins, for the transport of fats in the blood to other tissues. The liver also synthesizes cholesterol and excretes excess cholesterol into bile to be eliminated in feces.

   Fatty acids are a potential source of energy, but in order to be used in cell respiration they must be broken down to smaller molecules. In the process of **beta-oxidation**, the long carbon chains of fatty acids are split into two-carbon molecules called acetyl groups, which are simple carbohydrates. These acetyl groups may be used by the liver cells to produce ATP or may be combined to form ketones to be transported in the blood to other cells. These other cells then use the ketones to produce ATP in cell respiration.
4. **Synthesis of plasma proteins**—This is a liver function that you will probably remember from Chapter 11. The liver synthesizes many of the proteins that circulate in the blood. **Albumin**, the most abundant plasma protein, helps maintain blood volume by pulling tissue fluid into capillaries.

   The **clotting factors** are also produced by the liver. These, as you recall, include prothrombin, fibrinogen, and Factor 8, which circulate in the blood until needed in the chemical clotting mechanism. The liver also synthesizes alpha and beta **globulins**, which are proteins that serve as carriers for other molecules, such as fats, in the blood.
5. **Formation of bilirubin**—This is another familiar function: The liver contains fixed macrophages that phagocytize old red blood cells (RBCs). Bilirubin is then formed from the heme portion of the hemoglobin. The liver also removes from the blood the bilirubin formed in the spleen and red bone marrow and excretes it into bile to be eliminated in feces.
6. **Phagocytosis by Kupffer cells**—The fixed macrophages of the liver are called **Kupffer cells** (or stellate reticuloendothelial cells). Besides destroying old RBCs, Kupffer cells phagocytize pathogens or other foreign material that circulate through the liver. Many of the bacteria that get to the liver come from the colon. These bacteria are part of the normal flora of the colon but would be very harmful elsewhere in the body. The bacteria that enter the blood with the water absorbed by the colon are carried to the liver by way of portal circulation. The Kupffer cells in the liver phagocytize and destroy these bacteria, removing them from the blood before the blood returns to the heart.
7. **Storage**—The liver stores the fat-soluble vitamins A, D, E, and K, and the water-soluble vitamin B_{12}. Up to a 6- to 12-month supply of vitamins A and D may be stored, and beef or chicken liver is an excellent dietary source of these vitamins.

   Also stored by the liver are the minerals iron and copper. You already know that iron is needed for hemoglobin and myoglobin and enables these pro-

teins to bond to oxygen. Copper (as well as iron) is part of some of the proteins needed for cell respiration, and is part of some of the enzymes necessary for hemoglobin synthesis.

8. **Detoxification**—The liver is capable of synthesizing enzymes that will detoxify harmful substances, that is, change them to less harmful ones. Alcohol, for example, is changed to acetate, which is a two-carbon molecule (an acetyl group) that can be used in cell respiration.

Medications are all potentially toxic, but the liver produces enzymes that break them down or change them. When given in a proper dosage, a medication exerts its therapeutic effect but is then changed to less active substances that are usually excreted by the kidneys. An overdose of a drug means that there is too much of it for the liver to detoxify in a given time, and the drug will remain in the body with possibly harmful effects. This is why alcohol should never be consumed when taking medication. Such a combination may cause the liver's detoxification ability to be overworked and ineffective, with the result that both the alcohol and the medication will remain toxic for a longer time. Barbiturates taken as sleeping pills after consumption of alcohol have too often proved fatal for just this reason.

Ammonia is a toxic substance produced by the bacteria in the colon. Because it is soluble in water, some ammonia is absorbed into the blood, but it is carried first to the liver by portal circulation. The liver converts ammonia to urea, a less toxic substance, before the ammonia can circulate and damage other organs, especially the brain. The urea formed is excreted by the kidneys (see Box 16–6: Hepatitis).

AGING AND THE DIGESTIVE SYSTEM

Many changes can be expected in the aging digestive system. The sense of taste becomes less acute, less saliva is produced, and there is greater likelihood of

Box 16–6 HEPATITIS

Hepatitis is inflammation of the liver caused by any of several viruses. The most common of these hepatitis viruses have been designated A, B, and C, although there are others. Symptoms of hepatitis include anorexia, nausea, fatigue, and possibly jaundice. Severity of disease ranges from very mild (even asymptomatic) to fatal. Hundreds of thousands of cases of hepatitis occur in the United States every year, and although liver inflammation is common to all of them, the three hepatitis viruses have different modes of transmission and different consequences for affected people.

Hepatitis A is an intestinal virus that is spread by the fecal–oral route. Food contaminated by the hands of people with mild cases is the usual vehicle of transmission, although shellfish harvested from water contaminated with human sewage are another possible source of this virus. Hepatitis A is most often mild, recovery provides lifelong immunity, and the carrier state is not known to occur. A vaccine is available, but people who have been exposed to hepatitis A may receive gamma globulin by injection to prevent the disease.

Hepatitis B is contracted by exposure to the body fluids of an infected person; these fluids include blood and semen. Hepatitis B may be severe or even fatal, and approximately 10% of those who recover become carriers of the virus. Possible consequences of the carrier state are chronic hepatitis progressing to cirrhosis or primary liver cancer. Of equal importance, carriers are sources of the virus for others, especially their sexual partners.

A vaccine is available for hepatitis B, and healthcare workers who have contact with blood, even *just* occasional contact, should receive it. Other potential recipients of the vaccine are the sexual partners of carriers. Pediatricians now consider this vaccine one of the standard ones for infants.

The **hepatitis C** virus is also present in body fluids and is spread by blood or mucous membrane contact. Most people develop chronic disease, but many may remain asymptomatic for years after being infected. With active disease the virus may cause liver failure. The only therapy then is a liver transplant.

It is important for healthcare personnel, and their patients, to know that these types of hepatitis are not spread by blood transfusions. Donated blood is tested for all three viruses.

periodontal disease and loss of teeth. Secretions are reduced throughout the digestive system, and the effectiveness of peristalsis diminishes. Indigestion may become more frequent, especially if the LES loses its tone, and there is a greater chance of esophageal damage. In the colon, diverticula may form; these are bubble-like outpouchings of the weakened wall of the colon that may be asymptomatic or become infected. Intestinal obstruction, of the large or small bowel, occurs with greater frequency among the elderly. Sluggish peristalsis contributes to constipation, which in turn may contribute to the formation of hemorrhoids. The risk of oral cancer or colon cancer also increases with age.

The liver usually continues to function adequately even well into old age, unless damaged by pathogens such as the hepatitis viruses or by toxins such as alcohol. There is a greater tendency for gallstones to form, perhaps necessitating removal of the gallbladder. Inflammation of the gallbladder (cholecystitis) is also more frequent in older adults. In the absence of specific diseases, the pancreas usually functions well, although acute pancreatitis of unknown cause is somewhat more likely in elderly people.

SUMMARY

The processes of the digestion of food and the absorption of nutrients enable the body to use complex food molecules for many purposes. Much of the food we eat literally becomes part of us. The body synthesizes proteins and lipids for the growth and repair of tissues and produces enzymes to catalyze all of the reactions that contribute to homeostasis. Some of our food provides the energy required for growth, repair, movement, sensation, and thinking. In the next chapter we will discuss the chemical basis of energy production from food and consider the relationship of energy production to the maintenance of body temperature.

STUDY OUTLINE

Function of the Digestive System—to break down food into simple chemicals that can be absorbed into the blood and lymph and utilized by cells

Divisions of the Digestive System

1. Alimentary tube—oral cavity, pharynx, esophagus, stomach, small intestine, large intestine. Digestion takes place in the oral cavity, stomach, and small intestine.
2. Accessory organs—salivary glands, teeth, tongue, liver, gallbladder, and pancreas. Each contributes to digestion.

Types of Digestion

1. Mechanical—breaks food into smaller pieces to increase the surface area for the action of enzymes.
2. Chemical—enzymes break down complex organics into simpler organics and inorganics; each enzyme is specific for the food it will digest.

End Products of Digestion

1. Carbohydrates are digested to monosaccharides.
2. Fats are digested to fatty acids and glycerol.
3. Proteins are digested to amino acids.
4. Other end products are vitamins, minerals, and water.

Oral Cavity—food enters by way of the mouth

1. Teeth and tongue break up food and mix it with saliva.
2. Tooth structure (see Fig. 16–2)—enamel covers the crown and provides a hard chewing surface; dentin is within the enamel and forms the roots; the pulp cavity contains blood vessels and endings of the trigeminal nerve; the periodontal membrane produces cement to anchor the tooth in the jawbone.
3. The tongue is skeletal muscle innervated by the hypoglossal nerves. Papillae on the upper surface contain taste buds (facial and glossopharyngeal nerves). Functions: taste, keeps food between the teeth when chewing, elevates to push food backward for swallowing.
4. Salivary glands—parotid, submandibular, and sublingual (see Fig. 16–3); ducts take saliva to the oral cavity.

5. Saliva—amylase digests starch to maltose; water dissolves food for tasting and moistens food for swallowing; lysozyme inhibits the growth of bacteria (see Tables 16–1 and 16–2).

Pharynx—food passageway from the oral cavity to the esophagus

1. No digestion takes place.
2. Contraction of pharyngeal muscles is part of swallowing reflex, regulated by the medulla.

Esophagus—food passageway from pharynx to stomach

1. No digestion takes place.
2. Lower esophageal sphincter (LES) at junction with stomach prevents backup of stomach contents.

Structural Layers of the Alimentary Tube (see Fig. 16–4)

1. Mucosa (lining)—made of epithelial tissue that produces the digestive secretions; lymph nodules contain macrophages to phagocytize pathogens that penetrate the mucosa; thin layer of smooth muscle to ripple the epithelium.
2. Submucosa—areolar connective tissue with blood vessels and lymphatic vessels; Meissner's plexus is a nerve network that innervates the mucosa, part of the enteric nervous system that extends the entire length of the alimentary tube.
3. External muscle layer—typically an inner circular layer and an outer longitudinal layer of smooth muscle; function is mechanical digestion and peristalsis; innervated by Auerbach's plexus, part of the enteric nervous system; sympathetic impulses decrease motility; parasympathetic impulses increase motility.
4. Serosa—outermost layer; above the diaphragm is fibrous connective tissue; below the diaphragm is the mesentery (serous). The peritoneum (serous) lines the abdominal cavity; serous fluid prevents friction between the serous layers.

Stomach—in upper left abdominal quadrant; a muscular sac that extends from the esophagus to the small intestine (see Fig. 16–5)

1. Reservoir for food; begins the digestion of protein.
2. Gastric juice is secreted by gastric pits (see Tables 16–1 and 16–2).
3. The pyloric sphincter at the junction with the duodenum prevents backup of intestinal contents.

Liver—consists of two lobes in the upper right and center of the abdominal cavity (see Figs. 16–1 and 16–6)

1. Functional unit is the hexagonal liver lobule: liver cells, sinusoids, branches of the hepatic artery and portal vein, and bile ducts.
2. The only digestive secretion is bile; the hepatic duct takes bile out of the liver and unites with the cystic duct of the gallbladder to form the common bile duct to the duodenum.
3. Bile salts emulsify fats, a type of mechanical digestion (see Table 16–1).
4. Excess cholesterol and bilirubin are excreted by the liver into bile.

Gallbladder—on undersurface of right lobe of liver (see Fig. 16–6)

1. Stores and concentrates bile until needed in the duodenum (see Table 16–2).
2. The cystic duct joins the hepatic duct to form the common bile duct.

Pancreas—in upper left abdominal quadrant between the duodenum and the spleen (see Fig. 16–1)

1. Pancreatic juice is secreted by acini, carried by pancreatic duct to the common bile duct to the duodenum (see Fig. 16–7).
2. Enzyme pancreatic juice contains enzymes for the digestion of all three food types (see Tables 16–1 and 16–2).
3. Bicarbonate pancreatic juice neutralizes HCl from the stomach in the duodenum.

Small Intestine—coiled within the center of the abdominal cavity (see Fig. 16–1); extends from stomach to colon

1. Duodenum—first 10 inches; the common bile duct brings in bile and pancreatic juice. Jejunum (8 feet) and ileum (11 feet).
2. Enzymes secreted by the intestinal glands complete digestion (see Tables 16–1 and 16–2). Surface area for absorption is increased by plica circulares, villi, and microvilli (see Fig. 16–8); microvilli are the brush border.
3. The villi contain capillary networks for the absorption of water-soluble nutrients: monosaccharides,

amino acids, vitamin C and the B vitamins, minerals, and water. Blood from the small intestine goes to the liver first by way of portal circulation.
4. The villi contain lacteals (lymph capillaries) for the absorption of fat-soluble nutrients: vitamins A, D, E, and K, fatty acids, and glycerol, which are combined to form chylomicrons. Lymph from the small intestine is carried back to the blood in the left subclavian vein.

Large Intestine (colon)—extends from the small intestine to the anus

1. Colon—parts (see Fig. 16–9): cecum, ascending colon, transverse colon, descending colon, sigmoid colon, rectum, anal canal.
2. Ileocecal valve—at the junction of the cecum and ileum; prevents backup of fecal material into the small intestine.
3. Colon—functions: absorption of water, minerals, vitamins; elimination of undigestible material.
4. Normal flora—the bacteria of the colon; produce vitamins, especially vitamin K, and inhibit the growth of pathogens.
5. Defecation reflex—stimulus: stretching of the rectum when peristalsis propels feces into it. Sensory impulses go to the sacral spinal cord, and motor impulses return to the smooth muscle of the rectum, which contracts. The internal anal sphincter relaxes to permit defecation. Voluntary control is provided by the external anal sphincter, made of skeletal muscle (see Fig. 16–10).

Liver—other functions

1. Carbohydrate metabolism—excess glucose is stored in the form of glycogen and converted back to glucose during hypoglycemia; fructose and galactose are changed to glucose.
2. Amino acid metabolism—the non-essential amino acids are synthesized by transamination; excess amino acids are changed to carbohydrates or fats by deamination; the amino groups are converted to urea and excreted by the kidneys.
3. Lipid metabolism—formation of lipoproteins for transport of fats in the blood; synthesis of cholesterol; excretion of excess cholesterol into bile; beta-oxidation of fatty acids to form two-carbon acetyl groups for energy use.
4. Synthesis of plasma proteins—albumin to help maintain blood volume; clotting factors for blood clotting; alpha and beta globulins as carrier molecules.
5. Formation of bilirubin—old RBCs are phagocytized, and bilirubin is formed from the heme and put into bile to be eliminated in feces.
6. Phagocytosis by Kupffer cells—fixed macrophages; phagocytize old RBCs and bacteria, especially bacteria absorbed by the colon.
7. Storage—vitamins: B_{12}, A, D, E, and K, and the minerals iron and copper.
8. Detoxification—liver enzymes change potential poisons to less harmful substances; examples of toxic substances are alcohol, medications, and ammonia absorbed by the colon.

REVIEW QUESTIONS

1. Name the organs of the alimentary tube, and describe the location of each. Name the accessory digestive organs, and describe the location of each. (pp. 370, 372, 373, 376, 378, 379, 385)
2. Explain the purpose of mechanical digestion, and give two examples. Explain the purpose of chemical digestion, and give two examples. (pp. 370, 374)
3. Name the end products of digestion, and explain how each is absorbed in the small intestine. (pp. 370, 384)
4. Explain the function of teeth and tongue, salivary amylase, enamel of teeth, lysozyme, and water of saliva. (pp. 370–372)
5. Describe the function of the pharynx, esophagus, and lower esophageal sphincter. (p. 373)
6. Name and describe the four layers of the alimentary tube. (pp. 373, 376)
7. State the two general functions of the stomach and the function of the pyloric sphincter. Explain the function of pepsin, HCl, and mucus. (pp. 376–378)
8. Describe the general functions of the small intestine, and name the three parts. Describe the structures that increase the surface area of the small intestine. (pp. 378, 383–384)
9. Explain how the liver, gallbladder, and pancreas contribute to digestion. (pp. 379, 381)

10. Describe the internal structure of a villus, and explain how its structure is related to absorption. (p. 384)
11. Name the parts of the large intestine, and describe the function of the ileocecal valve. (p. 385)
12. Describe the functions of the colon and of the normal flora of the colon. (pp. 385–386)
13. With respect to the defecation reflex, explain the stimulus, the part of the CNS directly involved, the effector muscle, the function of the internal anal sphincter, and the voluntary control possible. (p. 386)
14. Name the vitamins and minerals stored in the liver. Name the fixed macrophages of the liver, and explain their function. (p. 388)
15. Describe how the liver regulates blood glucose level. Explain the purpose of the processes of deamination and transamination. (pp. 386, 388)
16. Name the plasma proteins produced by the liver, and state the function of each. (p. 388)
17. Name the substances excreted by the liver into bile. (p. 388)

FOR FURTHER THOUGHT

1. Many people with GERD take proton-pump inhibitors, medications that reduce stomach acid. Why should these people be especially careful about what they eat or drink?
2. The colon does not have villi as part of its mucosa. Explain why villi are not necessary.
3. Food remains in the stomach for several hours. Passage of food through the small intestine also requires several hours. These two organs have very different shapes. Explain why they are able to retain food for so long, for efficient digestion and absorption.
4. Diarrhea can be unpleasant, but does have a purpose. Explain, and state the disadvantages as well.
5. Explain how a spinal cord transection at the level of T10 will affect the defecation reflex.
6. You have seen the word *enteric* (or *entero*) several times in this chapter. What does it mean? Define each of these: enteric bacilli, enterovirus, Enterococcus.
7. The word *symbiosis* indicates two different kinds of living things, and literally means "together-life." Our own alimentary tube is a perfect example. Explain, and state the advantages to each living thing.

K M C

CHAPTER 17

Chapter Outline

Body Temperature
Heat Production
Heat Loss
- Heat loss through the skin
- Heat loss through the respiratory tract
- Heat loss through the urinary and digestive tracts

Regulation of Body Temperature
- Mechanisms to increase heat loss
- Mechanisms to conserve heat

Fever
Metabolism
Cell Respiration
- Glycolysis
- Krebs citric acid cycle
- Cytochrome transport system
- Proteins and fats as energy sources
- Energy available from the three nutrient types

Synthesis Uses of Foods
- Glucose
- Amino acids
- Fatty acids and glycerol

Vitamins and Minerals
Metabolic Rate
Aging and Metabolism

Student Objectives

- State the normal range of human body temperature.
- Explain how cell respiration produces heat and the factors that affect heat production.
- Describe the pathways of heat loss through the skin and respiratory tract.
- Explain why the hypothalamus is called the "thermostat" of the body.
- Describe the mechanisms to increase heat loss.
- Describe the mechanisms to conserve heat.
- Explain how a fever is caused and its advantages and disadvantages.
- Define metabolism, anabolism, and catabolism.
- Describe what happens to a glucose molecule during the three stages of cell respiration.
- State what happens to each of the products of cell respiration.
- Explain how amino acids and fats may be used for energy production.
- Describe the synthesis uses for glucose, amino acids, and fats.
- Explain what is meant by metabolic rate and kilocalories.
- Describe the factors that affect a person's metabolic rate.

Body Temperature and Metabolism

New Terminology

Anabolism (an-**AB**-uh-lizm)
Catabolism (kuh-**TAB**-uh-lizm)
Coenzyme (ko-**EN**-zime)
Conduction (kon-**DUK**-shun)
Convection (kon-**VEK**-shun)
Cytochromes (**SIGH**-toh-krohms)
Endogenous pyrogen (en-**DOJ**-en-us **PYE**-roh-jen)
Fever (**FEE**-ver)
Glycolysis (gly-**KAHL**-ah-sis)
Kilocalorie (KILL-oh-**KAL**-oh-ree)
Krebs cycle (KREBS **SIGH**-kuhl)
Pyrogen (**PYE**-roh-jen)
Radiation (RAY-dee-**AY**-shun)
Vitamins (**VY**-tah-mins)

Related Clinical Terminology

Antipyretic (AN-tigh-pye-**RET**-ik)
Basal metabolic rate (**BAY**-zuhl met-ah-**BAHL**-ik RAYT)
Frostbite (**FRAWST**-bite)
Heat exhaustion (HEET eks-**ZAWS**-chun)
Heat stroke (HEET STROHK)
Hypothermia (HIGH-poh-**THER**-mee-ah)

*Terms that appear in **bold type** in the chapter text are defined in the glossary, which begins on page 547.*

During every moment of our lives, our cells are breaking down food molecules to obtain ATP (adenosine triphosphate) for energy-requiring cellular processes. Naturally, we are not aware of the process of cell respiration, but we may be aware of one of the products—energy in the form of heat. The human body is indeed warm, and its temperature is regulated very precisely. Though we cannot stand barefoot on the ice of Antarctica for months in winter, as penguins do, we can adapt to and survive a wide range of environmental temperatures.

This chapter discusses the regulation of body temperature and also discusses **metabolism**, which is the total of all reactions that take place within the body. These reactions include the energy-releasing ones of cell respiration and energy-requiring ones such as protein synthesis, or DNA synthesis for mitosis. As you will see, body temperature and metabolism are inseparable.

BODY TEMPERATURE

The normal range of human body temperature is 96.5° to 99.5°F (36° to 38°C), with an average oral temperature of 98.6°F (37°C). (A 1992 study suggested a slightly lower average oral temperature: 98.2° or 36.8°. But everyone seems to prefer the "traditional" average temperature.) Within a 24-hour period, an individual's temperature fluctuates 1° to 2°, with the lowest temperatures occurring during sleep.

At either end of the age spectrum, however, temperature regulation may not be as precise as it is in older children or younger adults. Infants have more surface area (skin) relative to volume and are likely to lose heat more rapidly. In the elderly, the mechanisms that maintain body temperature may not function as efficiently as they once did, and changes in environmental temperature may not be compensated for as quickly or effectively. This is especially important to remember when caring for patients who are very young or very old.

HEAT PRODUCTION

Cell respiration, the process that releases energy from food to produce ATP, also produces heat as one of its energy products. Although cell respiration takes place constantly, many factors influence the rate of this process:

1. The hormone **thyroxine** (and T_3), produced by the thyroid gland, increases the rate of cell respiration and heat production. The secretion of thyroxine is regulated by the body's rate of energy production, the metabolic rate itself. (See Chapter 10 for a discussion of the feedback mechanism involving the hypothalamus and anterior pituitary gland and Chapter 1 for an illustration.) When the metabolic rate decreases, the thyroid gland is stimulated to secrete more thyroxine. As thyroxine increases the rate of cell respiration, a negative feedback mechanism inhibits further secretion until metabolic rate decreases again. Thus, thyroxine is secreted whenever there is a need for increased cell respiration and is probably the most important regulator of day-to-day energy production.
2. In stress situations, **epinephrine** and norepinephrine are secreted by the adrenal medulla, and the **sympathetic** nervous system becomes more active. Epinephrine increases the rate of cell respiration, especially in organs such as the heart, skeletal muscles, and liver. Sympathetic stimulation also increases the activity of these organs. The increased production of ATP to meet the demands of the stress situation also means that more heat will be produced.
3. Organs that are normally active (producing ATP) are significant sources of heat when the body is at rest. The skeletal muscles, for example, are usually in a state of slight contraction called muscle tone. Because even slight contraction requires ATP, the muscles are also producing heat. This amounts to about 25% of the total body heat at rest and much more during exercise, when more ATP is produced.

   The liver is another organ that is continually active, producing ATP to supply energy for its many functions. As a result, the liver produces as much as 20% of the total body heat at rest. The heat produced by these active organs is dispersed throughout the body by the blood. As the relatively cooler blood flows through organs such as the muscles and liver, the heat they produce is transferred to the blood, warming it. The warmed blood circulates to other areas of the body, distributing this heat.
4. The intake of food also increases heat production, because the metabolic activity of the digestive tract is increased. Heat is generated as the digestive

organs produce ATP for peristalsis and for the synthesis of digestive enzymes.

5. Changes in body temperature also have an effect on metabolic rate and heat production. This becomes clinically important when a person has a **fever**, an abnormally high body temperature. The higher temperature increases the metabolic rate, which increases heat production and elevates body temperature further. Thus, a high fever may trigger a vicious cycle of ever-increasing heat production. Fever is discussed later in this chapter.

The factors that affect heat production are summarized in Table 17–1.

HEAT LOSS

The pathways of heat loss from the body are the skin, the respiratory tract, and, to a lesser extent, the urinary and digestive tracts.

Table 17–1 FACTORS THAT AFFECT HEAT PRODUCTION

Factor	Effect
Thyroxine	• The most important regulator of day-to-day metabolism; increases use of foods for ATP production, thereby increasing heat production
Epinephrine and sympathetic stimulation	• Important in stress situations; increases the metabolic activity of many organs; increases ATP and heat production
Skeletal muscles	• Normal muscle tone requires ATP; the heat produced is about 25% of the total body heat at rest
Liver	• Always metabolically active; produces as much as 20% of total body heat at rest
Food intake	• Increases activity of the GI tract; increases ATP and heat production
Higher body temperature	• Increases metabolic rate, which increases heat production, which further increases metabolic rate and heat production; may become detrimental during high fevers

Heat Loss through the Skin

Because the skin covers the body, most body heat is lost from the skin to the environment. When the environment is cooler than body temperature (as it usually is), heat loss is unavoidable. The amount of heat that is lost is determined by blood flow through the skin and by the activity of sweat glands.

Blood flow through the skin influences the amount of heat lost by the processes of radiation, conduction, and convection. **Radiation** means that heat from the body is transferred to cooler objects not touching the skin, much as a radiator warms the contents of a room (radiation starts to become less effective when the environmental temperature rises above 88°F). **Conduction** is the loss of heat to cooler air or objects, such as clothing, that touch the skin. **Convection** means that air currents move the warmer air away from the skin surface and facilitate the loss of heat; this is why a fan makes us feel cooler on hot days. Loss of heat by convection also gives us the "wind chill factor" we hear about in winter. A cold day that is windy will feel colder than a cold day when the air is still, because the wind blows the slightly warmer air surrounding the body away, replacing it with colder air.

As you may recall from Chapter 5, the temperature of the skin and the subsequent loss of heat are determined by blood flow through the skin. The arterioles in the dermis may constrict or dilate to decrease or increase blood flow. In a cold environment, **vasoconstriction** decreases blood flow through the dermis and thereby decreases heat loss. In a warm environment, **vasodilation** in the dermis increases blood flow to the body surface and loss of heat to the environment.

The other mechanism by which heat is lost from the skin is sweating. The **eccrine sweat glands** secrete sweat (water) onto the skin surface, and excess body heat evaporates the sweat. Think of running water into a hot frying pan; the pan is rapidly cooled as its heat vaporizes the water. Although sweating is not quite as dramatic (no visible formation of steam), the principle is just the same.

Sweating is most efficient when the humidity of the surrounding air is low. Humidity is the percentage of the maximum amount of water vapor the atmosphere can contain. A humidity reading of 90% means that the air is already 90% saturated with water vapor and can hold little more. In such a situation, sweat does not readily evaporate, but instead remains on the skin even as more sweat is secreted. If the humidity is 40%,

Box 17–1 HEAT-RELATED DISORDERS

Heat exhaustion is caused by excessive sweating with loss of water and salts, especially NaCl. The affected person feels very weak, and the skin is usually cool and clammy (moist). Body temperature is normal or slightly below normal, the pulse is often rapid and weak, and blood pressure may be low because of fluid loss. Other symptoms may include dizziness, vomiting, and muscle cramps. Treatment involves rest and consumption of salty fluids or fruit juices (in small amounts at frequent intervals).

Heat stroke is a life-threatening condition that may affect elderly or chronically ill people on hot, humid days, or otherwise healthy people who exercise too strenuously during such weather. High humidity makes sweating an ineffective mechanism of heat loss, but in high heat the sweating process continues. As fluid loss increases, sweating stops to preserve body fluid, and body temperature rises rapidly (over 105°F , possibly as high as 110°F).

The classic symptom of heat stroke is hot, dry skin. The affected person often loses consciousness, reflecting the destructive effect of such a high body temperature on the brain. Treatment should involve hospitalization so that IV fluids may be administered and body temperature lowered under medical supervision. A first-aid measure would be the application of cool (not ice cold) water to as much of the skin as possible. Fluids should never be forced on an unconscious person, because the fluid may be aspirated into the respiratory tract.

however, the air can hold a great deal more water vapor, and sweat evaporates quickly from the skin surface, removing excess body heat. In air that is completely dry, a person may tolerate a temperature of 200°F for nearly 1 hour.

Although sweating is a very effective mechanism of heat loss, it does have a disadvantage in that it requires the loss of water in order to also lose heat. Water loss during sweating may rapidly lead to dehydration, and the water lost must be replaced by drinking fluids (see Box 17–1: Heat-Related Disorders).

Small amounts of heat are also lost in what is called "insensible water loss." Because the skin is not like a plastic bag, but is somewhat permeable to water, a small amount of water diffuses through the skin and is evaporated by body heat. Compared to sweating, however, insensible water loss is a minor source of heat loss.

Heat Loss through the Respiratory Tract

Heat is lost from the respiratory tract as the warmth of the respiratory mucosa evaporates some water from the living epithelial surface. The water vapor formed is exhaled, and a small amount of heat is lost.

Animals such as dogs that do not have numerous sweat glands often pant in warm weather. Panting is the rapid movement of air into and out of the upper respiratory passages, where the warm surfaces evaporate large amounts of water. In this way the animal may lose large amounts of heat.

Heat Loss through the Urinary and Digestive Tracts

When excreted, urine and feces are at body temperature, and their elimination results in a very small amount of heat loss.

The pathways of heat loss are summarized in Table 17–2.

REGULATION OF BODY TEMPERATURE

The **hypothalamus** is responsible for the regulation of body temperature and is considered the "thermostat" of the body. As the thermostat, the hypothalamus maintains the "setting" of body temperature by balancing heat production and heat loss to keep the body at the set temperature.

To do this, the hypothalamus must receive information about the temperature within the body and about the environmental temperature. Specialized neurons of the hypothalamus detect changes in the temperature of the blood that flows through the brain. The temperature receptors in the skin provide information about the external temperature changes to which the body is exposed. The hypothalamus then integrates this sensory information and promotes the necessary responses to maintain body temperature within the normal range.

Mechanisms to Increase Heat Loss

In a warm environment or during exercise, the body temperature tends to rise, and greater heat loss is

Table 17–2 PATHWAYS OF HEAT LOSS

Pathway	Mechanism
Skin (major pathway)	• Radiation and conduction—heat is lost from the body to cooler air or objects. • Convection—air currents move warm air away from the skin. • Sweating—excess body heat evaporates sweat on the skin surface.
Respiratory tract (secondary pathway)	• Evaporation—body heat evaporates water from the respiratory mucosa, and water vapor is exhaled.
Urinary tract (minor pathway)	• Urination—urine is at body temperature when eliminated.
Digestive tract (minor pathway)	• Defecation—feces are at body temperature when eliminated.

needed. This is accomplished by vasodilation in the dermis and an increase in sweating. Vasodilation brings more warm blood close to the body surface, and heat is lost to the environment. However, if the environmental temperature is close to or higher than body temperature, this mechanism becomes ineffective. The second mechanism is increased sweating, in which excess body heat evaporates the sweat on the skin surface. As mentioned previously, sweating becomes inefficient when the atmospheric humidity is high.

On hot days, heat production may also be decreased by a decrease in muscle tone. This is why we may feel very sluggish on hot days; our muscles are even slightly less contracted than usual and are slower to respond.

Mechanisms to Conserve Heat

In a cold environment, heat loss from the body is unavoidable but may be reduced to some extent. Vasoconstriction in the dermis shunts blood away from the body surface, so that more heat is kept in the core of the body. Sweating decreases, and will stop completely if the temperature of the hypothalamus falls below about 98.6°F. (Remember that the internal temperature of the brain is higher than an oral temperature, and is less subject to any changes in environmental temperature.)

If these mechanisms are not sufficient to prevent the body temperature from dropping, more heat may be produced by increasing muscle tone. When this greater muscle tone becomes noticeable and rhythmic, it is called shivering and may increase heat production by as much as five times the normal.

People also have behavioral responses to cold, and these too are important to prevent heat loss. Such things as putting on a sweater or going indoors reflect our awareness of the discomfort of being cold. For people (we do not have thick fur as do some other mammals), these voluntary activities are of critical importance to the prevention of excessive heat loss when it is very cold (see Box 17–2: Cold-Related Disorders).

FEVER

A fever is an abnormally high body temperature and may accompany infectious diseases, extensive physical trauma, cancer, or damage to the CNS. The substances that may cause a fever are called **pyrogens**. Pyrogens include bacteria, foreign proteins, and chemicals released during inflammation. These inflammatory chemicals are called **endogenous pyrogens**. *Endogenous* means "generated from within." It is believed that pyrogens chemically affect the hypothalamus and "raise the setting" of the hypothalamic thermostat. The hypothalamus will then stimulate responses by the body to raise body temperature to this higher setting.

Let us use as a specific example a child who has a strep throat. The bacterial and endogenous pyrogens reset the hypothalamic thermostat upward, to 102°F. At first, the body is "colder" than the setting of the hypothalamus, and the heat conservation and production mechanisms are activated. The child feels cold and begins to shiver (chills). Eventually, sufficient heat is produced to raise the body temperature to the hypothalamic setting of 102°F. At this time, the child will feel neither too warm nor too cold, because the body temperature is what the hypothalamus wants.

As the effects of the pyrogens diminish, the hypothalamic setting decreases, perhaps close to normal again, 99°F. Now the child will feel warm, and the heat loss mechanisms will be activated. Vasodilation in the skin and sweating will occur until the body temperature drops to the new hypothalamic setting. This is sometimes referred to as the "crisis," but actually the crisis has passed, because sweating indicates that

Box 17–2 COLD-RELATED DISORDERS

Frostbite is the freezing of part of the body. Fingers, toes, the nose, and ears are most often affected by prolonged exposure to cold, because these areas have little volume in proportion to their surface.

At first the skin tingles, then becomes numb. If body fluids freeze, ice crystals may destroy capillaries and tissues (because water expands when it freezes), and blisters form. In the most severe cases gangrene develops; that is, tissue dies because of lack of oxygen.

Treatment of frostbite includes rewarming the affected area. If skin damage is apparent, it should be treated as if it were a burn injury.

Hypothermia is an abnormally low body temperature (below 95°F) that is most often the result of prolonged exposure to cold. Although the affected person certainly feels cold at first, this sensation may pass and be replaced by confusion, slurred speech, drowsiness, and lack of coordination. At this stage, people often do not realize the seriousness of their condition, and if outdoors (ice skating or skiing) may not seek a warmer environment. In progressive hypothermia, breathing and heart rate slow, and coma and death follow.

Other people at greater risk for hypothermia include the elderly, whose temperature-regulating mechanisms are no longer effective, and quadriplegics, who have no sensation of cold in the body. For both of these groups, heat production is or may be low because of inactivity of skeletal muscles.

Artificial hypothermia may be induced during some types of cardiovascular or neurologic surgery. This carefully controlled lowering of body temperature decreases the metabolic rate and need for oxygen and makes possible prolonged surgery without causing extensive tissue death in the patient.

the body temperature is returning to normal. The sequence of temperature changes during a fever is shown in Fig. 17–1.

You may be wondering if a fever serves a useful purpose. For low fevers that are the result of infection, the answer is yes. White blood cells increase their activity at moderately elevated temperatures, and the metabolism of some pathogens is inhibited. Thus, a fever may be beneficial in that it may shorten the duration of an infection by accelerating the destruction of the pathogen.

High fevers, however, may have serious consequences. A fever increases the metabolic rate, which increases heat production, which in turn raises body temperature even more. This is a positive feedback mechanism that will continue until an external event (such as aspirin or death of the pathogens) acts as a brake (see Fig. 1–3). When the body temperature rises above 106°F, the hypothalamus begins to lose its ability to regulate temperature. The proteins of cells, especially the enzymes, are also damaged by such high temperatures. Enzymes become denatured, that is, lose their shape and do not catalyze the reactions necessary within cells (see Fig. 2–9). As a result, cells begin to die. This is most serious in the brain, because neurons cannot be replaced, and cellular death is the cause of brain damage that may follow a prolonged high fever. The effects of changes in body temperature on the hypothalamus are shown in Fig. 17–2.

A medication such as aspirin is called an **antipyretic** because it lowers a fever, probably by affecting the hypothalamic thermostat. To help lower a high fever, the body may be cooled by sponging it with cool water. The excessive body heat will cause this external water to evaporate, thus reducing temperature. A very high fever requires medical attention.

METABOLISM

The term **metabolism** encompasses all of the reactions that take place in the body. Everything that happens within us is part of our metabolism. The reactions of metabolism may be divided into two major categories: anabolism and catabolism.

Anabolism means synthesis or "formation" reactions, the bonding together of smaller molecules to form larger ones. The synthesis of hemoglobin by cells of the red bone marrow, synthesis of glycogen by liver cells, and synthesis of fat to be stored in adipose tissue are all examples of anabolism. Such reactions require energy, usually in the form of ATP.

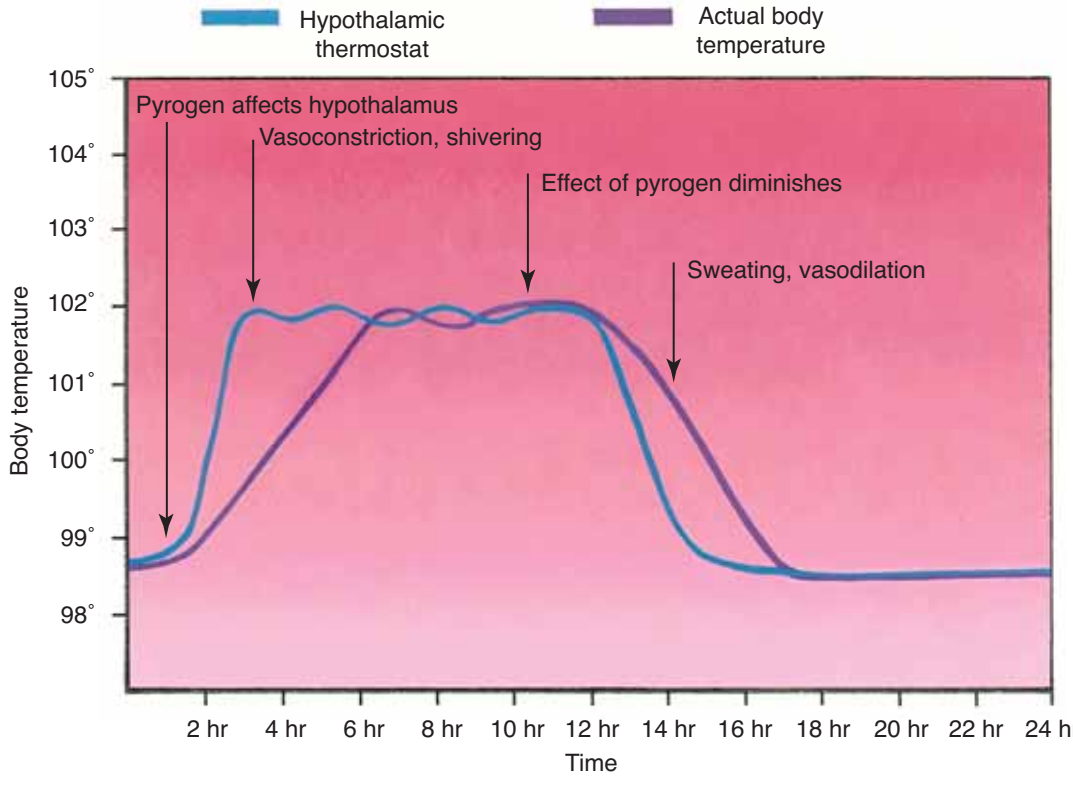


Figure 17–1. Changes in body temperature during an episode of fever. The body temperature changes (purple line) lag behind the changes in the hypothalamic thermostat (blue line) but eventually reach whatever the thermostat has called for.
QUESTION: In this cycle of fever, why do sweating and vasodilation occur when they do?

Catabolism means decomposition, the breaking of bonds of larger molecules to form smaller molecules. Cell respiration is a series of catabolic reactions that break down food molecules to carbon dioxide and water. During catabolism, energy is often released and used to synthesize ATP (the heat energy released was discussed in the previous section). The ATP formed during catabolism is then used for energy-requiring anabolic reactions.

Most of our anabolic and catabolic reactions are catalyzed by enzymes. Enzymes are proteins that enable reactions to take place rapidly at body temperature (see Chapter 2 to review the active site theory of enzyme functioning). The body has thousands of enzymes, and each is specific, that is, will catalyze only one type of reaction. As you read the discussions that follow, keep in mind the essential role of enzymes.

CELL RESPIRATION

You are already familiar with the summary reaction of cell respiration,

$$\underset{\text{(glucose)}}{C_6H_{12}O_6} + O_2 \rightarrow CO_2 + H_2O + ATP + \text{Heat},$$

the purpose of which is to produce ATP. Glucose contains potential energy, and when it is broken down to CO_2 and H_2O, this energy is released in the forms of ATP and heat. The oxygen that is required comes from breathing, and the CO_2 formed is circulated to the lungs to be exhaled. The water formed is called metabolic water, and helps to meet our daily need for water. Energy in the form of heat gives us a body temperature, and the ATP formed is used for energy-requiring reactions. Synthesis of ATP means that

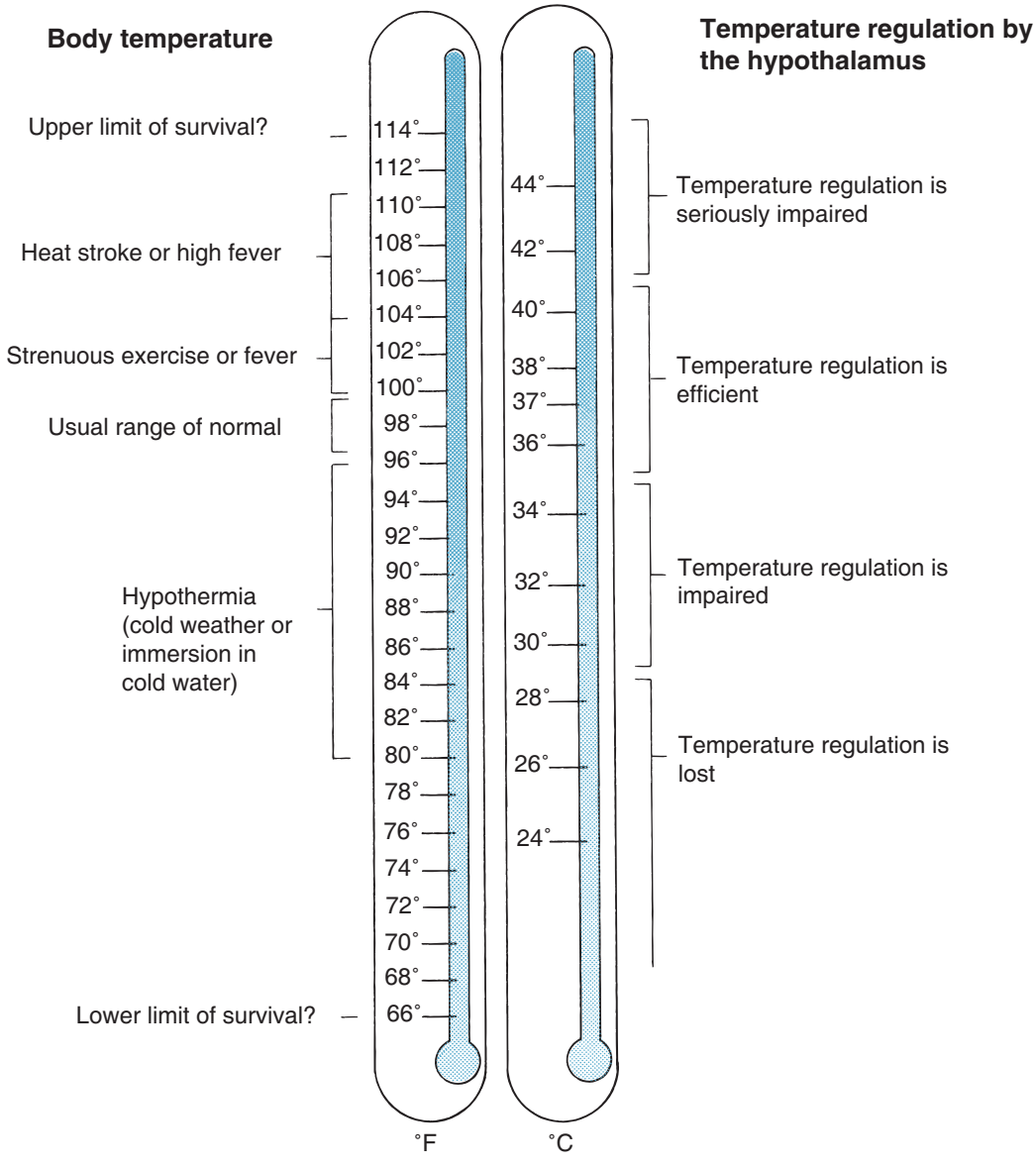


Figure 17–2. Effects of changes in body temperature on the temperature-regulating ability of the hypothalamus. Body temperature is shown in degrees Fahrenheit and degrees Celsius.
QUESTION: Give a range of temperature that an average person would probably survive.

energy is used to bond a free phosphate molecule to ADP (adenosine diphosphate). ADP and free phosphates are present in cells after ATP has been broken down for energy-requiring processes.

The breakdown of glucose summarized here is not quite that simple, however, and involves a complex series of reactions. Glucose is taken apart "piece by piece," with the removal of hydrogens and the splitting of carbon–carbon bonds. This releases the energy of glucose gradually, so that a significant portion (about 40%) is available to synthesize ATP.

Cell respiration of glucose involves three major stages: glycolysis, the Krebs citric acid cycle, and the cytochrome (or electron) transport system. Although

the details of each stage are beyond the scope of this book, we will summarize the most important aspects of each, and then relate to them the use of amino acids and fats for energy. This simple summary is depicted in Fig. 17–3.

Glycolysis

The enzymes for the reactions of **glycolysis** are found in the cytoplasm of cells, and oxygen is not required (glycolysis is an anaerobic process). Refer now to Fig. 17–3 as you read the following. In glycolysis, a six-carbon glucose molecule is broken down to two three-carbon molecules of pyruvic acid. Two molecules of ATP are necessary to start the process. The energy they supply is called energy of activation and is necessary to make glucose unstable enough to begin to break down. As a result of these reactions, enough energy is released to synthesize four molecules of ATP, for a net gain of two ATP molecules per glucose molecule. Also during glycolysis, two pairs of hydrogens are removed by NAD, a carrier molecule that contains the vitamin **niacin**. Two NAD molecules thus become $2NADH_2$, and these attached hydrogen pairs will be transported to the cytochrome transport system (stage 3).

If no oxygen is present in the cell, as may happen in muscle cells during exercise, pyruvic acid is converted to lactic acid, which causes muscle fatigue. If oxygen *is* present, however, pyruvic acid continues into the next stage, the Krebs citric acid cycle (or, more simply, the Krebs cycle).

Krebs Citric Acid Cycle

The enzymes for the **Krebs cycle** (or **citric acid cycle**) are located in the mitochondria of cells. This second stage of cell respiration is aerobic, meaning that oxygen is required. In a series of reactions, a pyruvic acid molecule is "taken apart," and its carbons are converted to CO_2. The first CO_2 molecule is removed by an enzyme that contains the vitamin **thiamine**. This leaves a two-carbon molecule called an acetyl group, which combines with a molecule called coenzyme A to form acetyl coenzyme A (acetyl CoA). As acetyl CoA continues in the Krebs cycle, two more carbons are removed as CO_2, and more pairs of hydrogens are picked up by NAD and FAD (another carrier molecule that contains the vitamin **riboflavin**). $NADH_2$ and $FADH_2$ will carry their hydrogens to the cytochrome transport system.

During the Krebs cycle, a small amount of energy is released, enough to synthesize one molecule of ATP (two per glucose). Notice also that a four-carbon molecule (oxaloacetic acid) is regenerated after the formation of CO_2. This molecule will react with the next acetyl CoA, which is what makes the Krebs cycle truly a self-perpetuating cycle. The results of the stages of cell respiration are listed in Table 17–3. Before you continue, you may wish to look at that table to see just where the process has gotten thus far.

Cytochrome Transport System

Cytochromes are proteins that contain either **iron** or **copper** and are found in the mitochondria of cells. The pairs of hydrogens that were once part of glucose are brought to the cytochromes by the carrier molecules NAD and FAD. Each hydrogen atom is then split into its proton (H^+ ion) and its electron. The electrons of the hydrogens are passed from one cytochrome to the next, and finally to oxygen. The reactions of the electrons with the cytochromes release most of the energy that was contained in the glucose molecule, enough to synthesize 34 molecules of ATP. As you can see, most of the ATP produced in cell respiration comes from this third stage.

Finally, and very importantly, each oxygen atom that has gained two electrons (from the cytochromes) reacts with two of the H^+ ions (protons) to form water. The formation of metabolic water contributes to the necessary intracellular fluid, and also prevents acidosis. If H^+ ions accumulated, they would rapidly lower the pH of the cell. This does not happen, however, because the H^+ ions react with oxygen to form water, and a decrease in pH is prevented.

The summary of the three stages of cell respiration in Table 17–3 also includes the vitamins and minerals that are essential for this process. An important overall concept is the relationship between eating and breathing. Eating provides us with a potential energy source (often glucose) and with necessary vitamins and minerals. However, to release the energy from food, we must breathe. This is *why* we breathe. The oxygen we inhale is essential for the completion of cell respiration, and the CO_2 produced is exhaled.

Proteins and Fats as Energy Sources

Although glucose is the preferred energy source for cells, proteins and fats also contain potential energy and are alternative energy sources in certain situations.

As you know, proteins are made of the smaller molecules called **amino acids**, and the primary use for the amino acids we obtain from food is the synthesis of

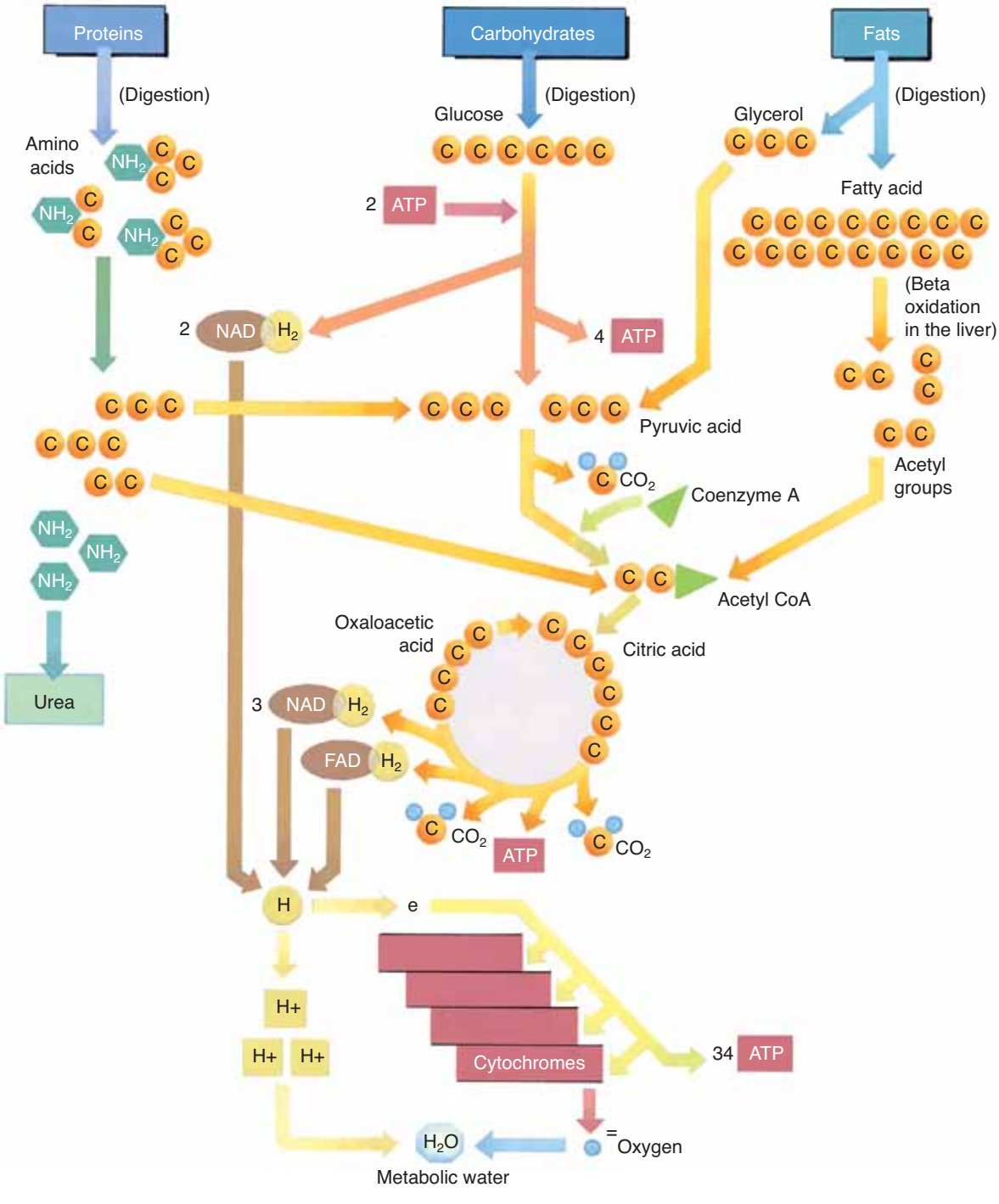


Figure 17–3. Schematic representation of cell respiration. The breakdown of glucose is shown in the center, amino acids on the left, and fatty acids and glycerol on the right. See text for description.

QUESTION: To which two molecules can all three food types be converted to enter the citric acid cycle?

Table 17–3 SUMMARY OF CELL RESPIRATION

Stage	Molecules That Enter the Process	Results	Vitamins or Minerals Needed
Glycolysis (cytoplasm)	Glucose—ATP needed as energy of activation	• 2 ATP (net) • 2 $NADH_2$ (to cytochrome transport system) • 2 pyruvic acid (aerobic: to Krebs cycle; anaerobic: lactic acid formation)	• Niacin (part of NAD)
Krebs citric acid cycle (mitochondria)	Pyruvic acid—from glucose or glycerol or excess amino acids *or* Acetyl CoA—from fatty acids or excess amino acids	• CO_2 (exhaled) • ATP (2 per glucose) • 3 $NADH_2$ and 1 $FADH_2$ (to cytochrome transport system) • A 4-carbon molecule is regenerated for the next cycle	• Thiamine (for removal of CO_2) • Niacin (part of NAD) • Riboflavin (part of FAD) • Pantothenic acid (part of coenzyme A)
Cytochrome transport system (mitochondria)	$NADH_2$ and $FADH_2$—from glycolysis or the Krebs cycle	• 34 ATP • Metabolic water	• Iron and copper (part of some cytochromes)

new proteins. Excess amino acids, however, those not needed immediately for protein synthesis, may be used for energy production. In the liver, excess amino acids are **deaminated**, that is, the amino group (NH_2) is removed. The remaining portion is converted to a molecule that will fit into the Krebs cycle. For example, a deaminated amino acid may be changed to a three-carbon pyruvic acid or to a two-carbon acetyl group. When these molecules enter the Krebs cycle, the results are just the same as if they had come from glucose. This is diagrammed in Fig. 17–3.

Fats are made of glycerol and fatty acids, which are the end products of fat digestion. These molecules may also be changed to ones that will take part in the Krebs cycle, and the reactions that change them usually take place in the liver. Glycerol is a three-carbon molecule that can be converted to the three-carbon pyruvic acid, which enters the Krebs cycle. In the process of beta-oxidation, the long carbon chains of fatty acids are split into two-carbon acetyl groups, which enter a later step in the Krebs cycle (see Fig. 17–3).

Both amino acids and fatty acids may be converted by the liver to **ketones**, which are two- or four-carbon molecules such as acetone and acetoacetic acid. Although body cells can use ketones in cell respiration, they do so slowly. In situations in which fats or amino acids have become the primary energy sources, a state called **ketosis** may develop; this is described in Box 17–3: Ketosis. Excess amino acids may also be converted to glucose; this is important to supply the brain when dietary intake of carbohydrates is low. The effects of hormones on the metabolism of food are summarized in Table 17–4.

Energy Available from the Three Nutrient Types

The potential energy in food is measured in units called **Calories** or **kilocalories**. A calorie (lowercase "c") is the amount of energy needed to raise the temperature of 1 gram of water 1°C. A kilocalorie or Calorie (capital "C") is 1000 times that amount of energy.

One gram of carbohydrate yields about 4 kilocalories. A gram of protein also yields about 4 kilocalories. A gram of fat, however, yields 9 kilocalories, and a gram of alcohol yields 7 kilocalories. This is why a diet high in fat is more likely to result in weight gain if the calories are not expended in energy-requiring activities.

You may have noticed that calorie content is part of the nutritional information on food labels. On such labels the term *calorie* actually means Calorie or kilocalories but is used for the sake of simplicity.

SYNTHESIS USES OF FOODS

Besides being available for energy production, each of the three food types is used in anabolic reactions to

Table 17–4 HORMONES THAT REGULATE METABOLISM

Hormone (Gland)	Effects
Thyroxine (thyroid gland)	• Increases use of all three food types for energy (glucose, fats, amino acids) • Increases protein synthesis
Growth hormone (anterior pituitary)	• Increases amino acid transport into cells • Increases protein synthesis • Increases use of fats for energy
Insulin (pancreas)	• Increases glucose transport into cells and use for energy • Increases conversion of glucose to glycogen in liver and muscles • Increases transport of amino acids and fatty acids into cells to be used for synthesis (*not* energy production)
Glucagon (pancreas)	• Increases conversion of glycogen to glucose • Increases use of amino acids and fats for energy
Cortisol (adrenal cortex)	• Increases conversion of glucose to glycogen in liver • Increases use of amino acids and fats for energy • Decreases protein synthesis except in liver and GI tract
Epinephrine (adrenal medulla)	• Increases conversion of glycogen to glucose • Increases use of fats for energy

synthesize necessary materials for cells and tissues. A simple summary of these reactions is shown in Fig. 17–4. The three food types and their end products of digestion are at the bottom of the picture, and the arrows going upward indicate synthesis and lead to the products formed. You may wish to refer to Fig. 17–4 as you read the next sections.

Glucose

Glucose is the raw material for the synthesis of another important monosaccharide, the **pentose sugars** that are part of nucleic acids. Deoxyribose is the five-carbon sugar found in DNA, and ribose is found in RNA. This function of glucose is very important, for without the pentose sugars our cells could neither produce new chromosomes for cell division nor carry out the process of protein synthesis.

Any glucose in excess of immediate energy needs or the need for pentose sugars is converted to **glycogen** in the liver and skeletal muscles. Glycogen is then an energy source during states of hypoglycemia or during exercise. If still more glucose is present, it will be changed to fat and stored in adipose tissue.

Box 17–3 KETOSIS

When fats and amino acids are to be used for energy, they are often converted by the liver to ketones. Ketones are organic molecules such as acetone that may be changed to acetyl CoA and enter the Krebs cycle. Other cells are able to use ketones as an energy source, but they do so slowly. When ketones are produced in small amounts, as they usually are between meals, the blood level does not rise sharply.

A state of **ketosis** exists when fats and proteins become the primary energy sources, and ketones accumulate in the blood faster than cells can utilize them. Because ketones are organic acids, they lower the pH of the blood. As the blood ketone level rises, the kidneys excrete ketones, but they must also excrete more water as a solvent, which leads to dehydration.

Ketosis is clinically important in diabetes mellitus, starvation, and eating disorders such as anorexia nervosa. Diabetics whose disease is poorly controlled may progress to **ketoacidosis**, a form of metabolic acidosis that may lead to confusion, coma, and death. Reversal of this state requires a carbohydrate energy source and the insulin necessary to utilize it.

Amino Acids

As mentioned previously, the primary uses for amino acids are the synthesis of the **non-essential amino acids** by the liver and the synthesis of new **proteins** in all tissues. By way of review, we can mention some proteins with which you are already familiar: keratin and melanin in the epidermis; collagen in the dermis, tendons, and ligaments; myosin, actin, and myoglobin in muscle cells; hemoglobin in RBCs; antibodies produced by WBCs; prothrombin and fibrinogen for

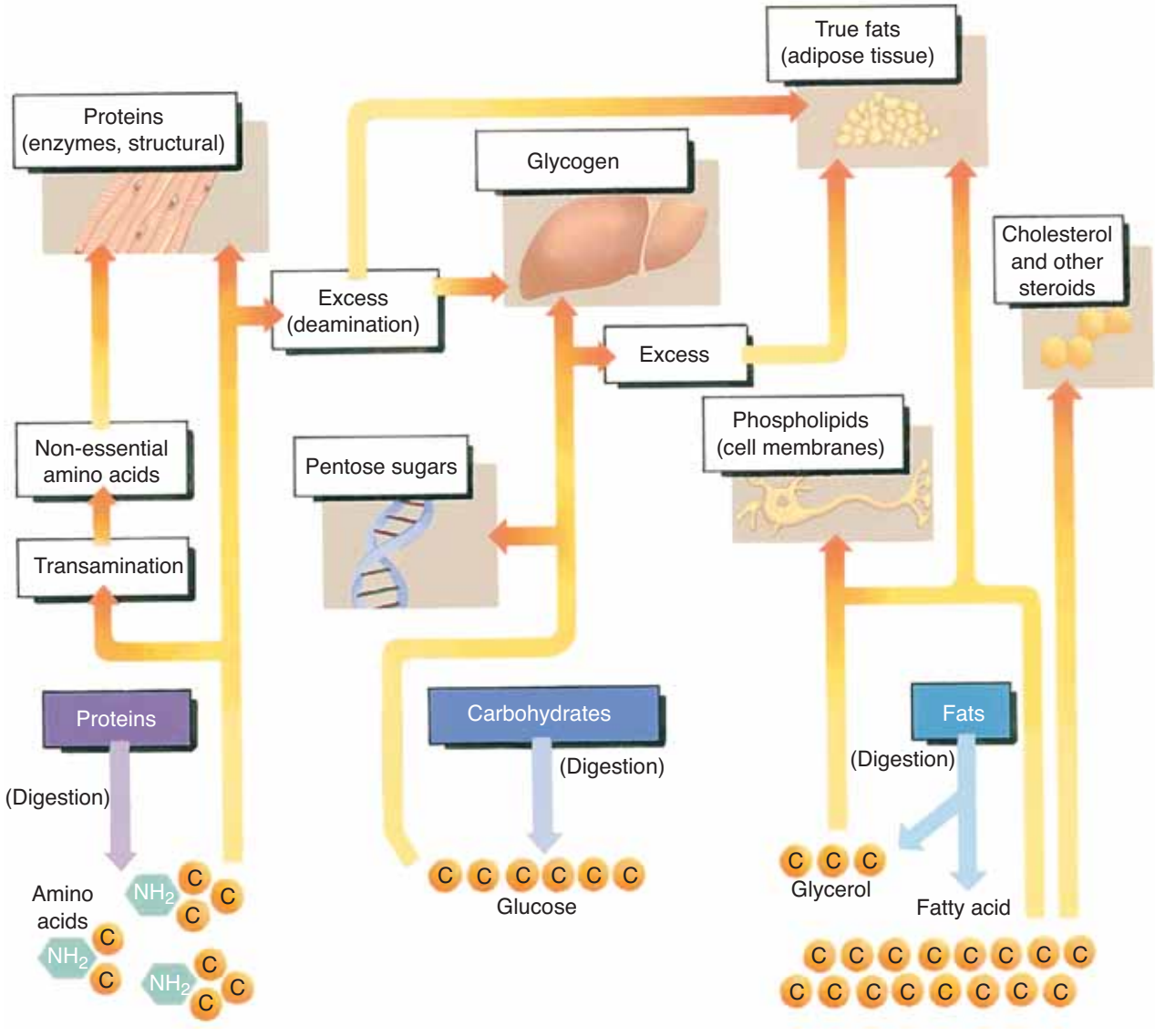


Figure 17–4. Synthesis uses of foods. See text for description.
QUESTION: Excess amino acids can be used to synthesize carbohydrates or fats. Can any other food be used to synthesize proteins?

clotting; albumin to maintain blood volume; pepsin and amylase for digestion; growth hormone and insulin; and the thousands of enzymes needed to catalyze reactions within the body.

The amino acids we obtain from the proteins in our food are used by our cells to synthesize all of these proteins in the amounts needed by the body. Only when the body's needs for new proteins have been met are amino acids used for energy production. But notice in Fig. 17–4 what happens to excess amino acids; they will be deaminated and converted to simple carbohydrates and contribute to glycogen storage or they may be changed to fat and stored in adipose tissue.

Fatty Acids and Glycerol

The end products of fat digestion that are not needed immediately for energy production may be stored as fat (triglycerides) in **adipose tissue**. Most adipose tissue is found subcutaneously and is potential energy for times when food intake decreases. Notice in Table 17–4 that insulin promotes fat synthesis and storage. One theory of weight gain proposes that a diet high in sugars and starches stimulates the secretion of so much insulin that fat can only be stored, not taken out of storage and used for energy.

Fatty acids and glycerol are also used for the synthesis of **phospholipids**, which are essential components of all cell membranes. Myelin, for example, is a phospholipid of the membranes of Schwann cells, which form the myelin sheath of peripheral neurons.

The liver can synthesize most of the fatty acids needed by the body. Two exceptions are linoleic acid and linolenic acid, which are **essential fatty acids** and must be obtained from the diet. Linoleic acid is part of lecithin, which in turn is part of all cell membranes. Vegetable oils are good sources of these essential fatty acids.

When fatty acids are broken down in the process of beta-oxidation, the resulting acetyl groups may also be used for the synthesis of **cholesterol**, a steroid. This takes place primarily in the liver, although all cells are capable of synthesizing cholesterol for their cell membranes. The liver uses cholesterol to synthesize bile salts for the emulsification of fats in digestion. The **steroid hormones** are also synthesized from cholesterol. Cortisol and aldosterone are produced by the adrenal cortex, estrogen and progesterone by the ovaries, and testosterone by the testes.

VITAMINS AND MINERALS

Vitamins are organic molecules needed in very small amounts for normal body functioning. Some vitamins are **coenzymes**; that is, they are necessary for the functioning of certain enzymes. Others are antioxidant vitamins, including vitamins C, E, and beta-carotene (a precursor for vitamin A). Antioxidants prevent damage from **free radicals**, which are molecules that contain an unpaired electron and are highly reactive. The reactions of free radicals can damage DNA, cell membranes, and the cell organelles. Free radicals are formed during some normal body reactions, but smoking and exposure to pollution will increase their formation. Antioxidant vitamins combine with free radicals before they can react with cellular components. Plant foods are good sources of these vitamins. Table 17–5 summarizes some important metabolic and nutritional aspects of the vitamins we need.

Deficiencies of vitamins often result in disease: vitamin C deficiency and scurvy, for example (see Box 4–2). Other deficiency diseases that have been known for decades include pellagra (lack of niacin), beri-beri (riboflavin), pernicious anemia (B_{12}), and rickets (D). More recently the importance of folic acid (folacin) for the development of the fetal central nervous system has been recognized. Adequate folic acid during pregnancy can significantly decrease the chance of spina bifida (open spinal column) and anencephaly (absence of the cerebrum, always fatal) in a fetus. All women should be aware of the need for extra (400 micrograms) folic acid during pregnancy.

Minerals are simple inorganic chemicals and have a variety of functions, many of which you are already familiar with. Table 17–6 lists some important aspects of minerals. We will return to the minerals as part of our study of fluid–electrolyte balance in Chapter 19.

METABOLIC RATE

Although the term **metabolism** is used to describe all of the chemical reactions that take place within the body, **metabolic rate** is usually expressed as an amount of heat production. This is because many body processes that utilize ATP also produce heat. These processes include the contraction of skeletal muscle, the pumping of the heart, and the normal breakdown of cellular components. Therefore, it is possible to quantify heat production as a measure of metabolic activity.

As mentioned previously, the energy available from food is measured in kilocalories (kcal). Kilocalories are also the units used to measure the energy expended by the body. During sleep, for example, energy expended by a 150-pound person is about 60 to 70 kcal per hour. Getting up and preparing breakfast increases energy expenditure to 80 to 90 kcal per hour. For mothers with several small children, this value may be significantly higher. Clearly, greater activity results in greater energy expenditure.

The energy required for merely living (lying quietly in bed) is the **basal metabolic rate** (BMR). See Box 17–4: Metabolic Rate for a formula to estimate

Table 17–5 VITAMINS

Vitamin	Functions	Food Sources	Comment
Water Soluble			
Thiamine (B_1)	• Conversion of pyruvic acid to acetyl CoA in cell respiration • Synthesis of pentose sugars • Synthesis of acetylcholine	• Meat, eggs, legumes, green leafy vegetables, grains	Rapidly destroyed by heat
Riboflavin (B_2)	• Part of FAD in cell respiration	• Meat, milk, cheese, grains	Small amounts produced by GI bacteria
Niacin (nicotinamide)	• Part of NAD in cell respiration • Metabolism of fat for energy	• Meat, fish, grains, legumes	
Pyridoxine (B_6)	• Part of enzymes needed for amino acid metabolism and protein synthesis, nucleic acid synthesis, synthesis of antibodies	• Meat, fish, grains, yeast, yogurt	Small amounts produced by GI bacteria
B_{12} (cyanocobalamin)	• Synthesis of DNA, especially in RBC production • Metabolism of amino acids for energy	• Liver, meat, fish, eggs, milk, cheese	Contains cobalt; intrinsic factor required for absorption
Biotin	• Synthesis of nucleic acids • Metabolism of fatty acids and amino acids	• Yeast, liver, eggs	Small amounts produced by GI bacteria
Folic acid (folacin)	• Synthesis of DNA, especially in blood cell production • Contributes to development of fetal CNS	• Liver, grains, legumes, leafy green vegetables	Small amounts produced by GI bacteria
Pantothenic acid	• Part of coenzyme A in cell respiration, use of amino acids and fats for energy	• Meat, fish, grains, legumes, vegetables	Small amounts produced by GI bacteria
Vitamin C (ascorbic acid)	• Synthesis of collagen, especially for wound healing • Metabolism of amino acids • Absorption of iron • An antioxidant—prevents cellular damage from free radicals	• Citrus fruits, tomatoes, potatoes	Rapidly destroyed by heat
Fat Soluble			
Vitamin A	• Synthesis of rhodopsin • Calcification of growing bones • Maintenance of epithelial tissues	• Yellow and green vegetables, liver, milk, eggs	Stored in liver; bile salts required for absorption
Vitamin D	• Absorption of calcium and phosphorus in the small intestine • Contributes to immune responses, action of insulin, and preservation of muscle mass and strength	• Fortified milk, egg yolks, fish liver oils	Produced in skin exposed to UV rays; stored in liver; bile salts required for absorption
Vitamin E	• An antioxidant—prevents destruction of cell membranes • Contributes to wound healing and detoxifying ability of the liver	• Nuts, wheat germ, seed oils	Stored in liver and adipose tissue; bile salts required for absorption
Vitamin K	• Synthesis of prothrombin and other clotting factors	• Liver, spinach, cabbage	Large amounts produced by GI bacteria; bile salts required for absorption; stored in liver

Table 17–6 MINERALS

Mineral	Functions	Food Sources	Comment
Calcium	• Formation of bones and teeth • Neuron and muscle functioning • Blood clotting	• Milk, cheese, yogurt, shellfish, leafy green vegetables	Vitamin D required for absorption; stored in bones
Phosphorus	• Formation of bones and teeth • Part of DNA, RNA, and ATP • Part of phosphate buffer system	• Milk, cheese, fish, meat	Vitamin D required for absorption; stored in bones
Sodium	• Contributes to osmotic pressure of body fluids • Nerve impulse transmission and muscle contraction • Part of bicarbonate buffer system	• Table salt, almost all foods	Most abundant cation (+) in extracellular fluid
Potassium	• Contributes to osmotic pressure of body fluids • Nerve impulse transmission and muscle contraction	• Virtually all foods	Most abundant cation (+) in intracellular fluid
Chlorine	• Contributes to osmotic pressure of body fluids • Part of HCl in gastric juice	• Table salt	Most abundant anion (−) in extracellular fluid
Iron	• Part of hemoglobin and myoglobin • Part of some cytochromes in cell respiration	• Meat, shellfish, dried apricots, legumes, eggs	Stored in liver
Iodine	• Part of thyroxine and T_3	• Iodized salt, seafood	
Sulfur	• Part of some amino acids • Part of thiamine and biotin	• Meat, eggs	Insulin and keratin require sulfur
Magnesium	• Formation of bone • Metabolism of ATP–ADP	• Green vegetables, legumes, seafood, milk	Part of chlorophyll in green plants
Manganese	• Formation of urea • Synthesis of fatty acids and cholesterol	• Legumes, grains, nuts, leafy green vegetables	Some stored in liver
Copper	• Synthesis of hemoglobin • Part of some cytochromes in cell respiration • Synthesis of melanin	• Liver, seafood, grains, nuts, legumes	Stored in liver
Cobalt	• Part of vitamin B_{12}	• Liver, meat, fish	Vitamin B_{12} stored in liver
Zinc	• Part of carbonic anhydrase needed for CO_2 transport • Part of peptidases needed for protein digestion • Necessary for normal taste sensation • Involved in wound healing	• Meat, seafood, grains, legumes	

your own metabolic rate. A number of factors affect the metabolic rate of an active person:

1. Exercise—Contraction of skeletal muscle increases energy expenditure and raises metabolic rate (see Box 17–5: Weight Loss).
2. Age—Metabolic rate is highest in young children and decreases with age. The energy requirements for growth and the greater heat loss by a smaller body contribute to the higher rate in children. After growth has stopped, metabolic rate decreases about 2% per decade. If a person

Box 17–4 METABOLIC RATE

To estimate your own basal metabolic rate (BMR), calculate kilocalories (kcal) used per hour as follows:

For women: use the factor of 0.9 kcal per kilogram (kg) of body weight
For men: use the factor of 1.0 kcal per kg of body weight
Then multiply kcal/hour by 24 hours to determine kcal per day.

Example: **A 120-pound woman**:

1. Change pounds to kilograms:
   120 lb at 2.2 lb/kg = 55 kg
2. Multiply kg weight by the BMR factor:
   55 kg x 0.9 kcal/kg/hr = 49.5 kcal/hr
3. Multiply kcal/hr by 24:
   49.5 kcal/hr x 24 = 1188 kcal/day
   (An approximate BMR, about 1200 kcal/day)

Example: **A 160-pound man**:

1. 160 lb at 2.2 lb/kg = 73 kg
2. 73 kg x 1.0 kcal/kg/hr = 73 kcal/hr
3. 73 kcal/hr x 24 = 1752 kcal/day

To approximate the amount of energy actually expended during an average day (24 hours), the following percentages may be used:

Sedentary activity: add 40% to 50% of the BMR to the BMR
Light activity: add 50% to 65% of the BMR to the BMR
Moderate activity: add 65% to 75% of the BMR to the BMR
Strenuous activity: add 75% to 100% of the BMR to the BMR

Using our example of the 120-pound woman with a BMR of 1200 kcal/day:

Sedentary: 1680 to 1800 kcal/day
Light: 1800 to 1980 kcal/day
Moderate: 1980 to 2100 kcal/day
Strenuous: 2100 to 2400 kcal/day

Box 17–5 WEIGHT LOSS

Although diet books are often found on the best-seller lists, there is no magic method that will result in weight loss. Losing weight depends on one simple fact: calorie expenditure in activity must exceed calorie intake in food (the term **calorie** here will be used to mean kilocalorie).

To lose 1 pound of body fat, which consists of fat, water, and protein, 3500 calories of energy must be expended. Although any form of exercise requires calories, the more strenuous the exercise, the more calories expended. Some examples are shown in the accompanying table.

Most food packaging contains nutritional information, including the calories per serving of the food. Keeping track of daily caloric intake is an important part of a decision to try to lose weight. It is also important to remember that sustained loss of fat usually does not exceed 1 to 2 pounds per week. In part this is so because as calorie intake decreases, the metabolic rate decreases. There will also be loss of some body protein so that amino acids can be converted to carbohydrates to supply the brain.

A sensible weight-loss diet will include carbohydrate to supply energy needs, will have sufficient protein (40 to 45 grams per day), and will be low in animal fat. Including vegetables and fruits will supply vitamins, minerals, and fiber.

Activity	Calories per 10 minutes *(average for a 150-lb person)*	Activity	Calories per 10 minutes *(average for a 150-lb person)*
Walking slowly	30	Running (8 mph)	120
Walking briskly	45	Cycling (10 mph)	70
Walking up stairs	170	Cycling (15 mph)	115
Dancing (slow)	40	Swimming	100
Dancing (fast)	65		

Box 17–6 LEPTIN AND BODY-MASS INDEX

K M C

The 1994 discovery of the hormone leptin was reported to the general public in 1995, along with speculation that leptin could become an anti-obesity medication, which it has not. Leptin is a protein produced by fat cells, and signals the hypothalamus to release a chemical that acts as an appetite suppressant. It seems to inform the brain of how much stored fat the body has, and is therefore involved in the regulation of body weight (along with many other chemicals, some still unknown).

Another likely role for leptin is as a contributor to the onset of puberty, especially in females. Girls who are very thin, with little body fat, tend to have a later first menstrual period than girls with average body fat, and a certain level of body fat is necessary for continued ovulation. Leptin may be the chemical mediator of this information.

The most recent research indicates that leptin directly decreases fat storage in cells, and improves the efficiency of the pancreatic cells that produce insulin. What was first believed to be a simple chemical signal has proved to be much more complex.

A good measure of leanness or fatness is the **body-mass index**.

To calculate: Multiple weight in pounds by 703.
Divide by height in inches.
Divide again by height in inches = body-mass index

Example: A person five foot six weighing 130 pounds.

130 x 703 = 91,390
91,390 ÷ 66 = 1385
1385 ÷ 66 = 20.98

The optimal body-mass index is considered to be 21. Any index over 25 is considered overweight.

becomes less active, the total decrease is almost 5% per decade.

3. Body configuration of adults—Tall, thin people usually have higher metabolic rates than do short, stocky people of the same weight. This is so because the tall, thin person has a larger surface area (proportional to weight) through which heat is continuously lost. The metabolic rate, therefore, is slightly higher to compensate for the greater heat loss. The variance of surface-to-weight ratios for different body configurations is illustrated in Fig. 17–5.
4. Sex hormones—Testosterone increases metabolic activity to a greater degree than does estrogen, giving men a slightly higher metabolic rate than women. Also, men tend to have more muscle, an active tissue, whereas women tend to have more fat, a relatively inactive tissue.
5. Sympathetic stimulation—In stress situations, the metabolism of many body cells is increased. Also contributing to this are the hormones epinephrine and norepinephrine. As a result, metabolic rate increases.
6. Decreased food intake—If the intake of food decreases for a prolonged period of time, metabolic rate also begins to decrease. It is as if the body's metabolism is "slowing down" to conserve whatever energy sources may still be available. (See also Box 17–6: Leptin and Body-Mass Index.)
7. Climate—People who live in cold climates may have metabolic rates 10% to 20% higher than people who live in tropical regions. This is believed to be due to the variations in the secretion of thyroxine, the hormone most responsible for regulation of metabolic rate. In a cold climate, the necessity for greater heat production brings about an

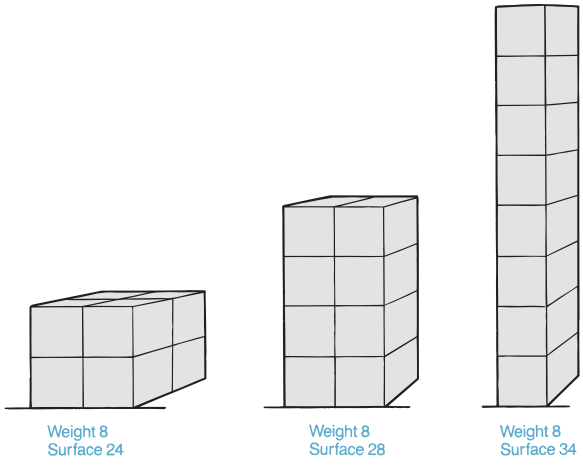


Figure 17–5. Surface-to-weight ratios. Imagine that the three shapes are people who all weigh the same amount. The "tall, thin person" on the right has about 50% more surface area than does the "short, stocky person" on the left. The more surface area (where heat is lost), the higher the metabolic rate.
QUESTION: Which of these ratios best represents an infant? (Rather than weight, think of inside-outside proportion.)

increased secretion of thyroxine and a higher metabolic rate.

AGING AND METABOLISM

As mentioned in the previous section, metabolic rate decreases with age. Elderly people who remain active, however, can easily maintain a metabolic rate (energy production) adequate for their needs as long as their general health is good. Some elderly people subject to physical or emotional disability, however, may be at risk for malnutrition. Caregivers may assess such a risk by asking how often the person eats every day; if appetite is good, fair, or poor; and how the food tastes. These simple questions may help ensure adequate nutrition.

Sensitivity to external temperature changes may decrease with age, and the regulation of body temperature is no longer as precise. Sweat glands are not as active, and prolonged high environmental temperatures are a real danger for elderly people. In August 2003, in Europe, an unusually long and severe heat wave was the cause of at least 25,000 deaths. Most of those who died were elderly.

SUMMARY

Food is needed for the synthesis of new cells and tissues, or is utilized to produce the energy required for such synthesis reactions. As a consequence of metabolism, heat energy is released to provide a constant body temperature and permit the continuation of metabolic activity. The metabolic pathways described in this chapter are only a small portion of the body's total metabolism. Even this simple presentation, however, suggests the great chemical complexity of the functioning human being.

STUDY OUTLINE

Body Temperature

1. Normal range is 96.5° to 99.5°F (36° to 38°C), with an average of 98.6°F (37°C).
2. Normal fluctuation in 24 hours is 1° to 2°F.
3. Temperature regulation in infants and the elderly is not as precise as it is at other ages.

Heat Production

Heat is one of the energy products of cell respiration. Many factors affect the total heat actually produced (see Table 17–1).

1. Thyroxine from the thyroid gland—the most important regulator of daily heat production. As metabolic rate decreases, more thyroxine is secreted to increase the rate of cell respiration.
2. Stress—sympathetic impulses and epinephrine and norepinephrine increase the metabolic activity of many organs, increasing the production of ATP and heat.
3. Active organs continuously produce heat. Skeletal muscle tone produces 25% of the total body heat at rest. The liver provides up to 20% of the resting body heat.
4. Food intake increases the activity of the digestive organs and increases heat production.
5. Changes in body temperature affect metabolic rate. A fever increases the metabolic rate, and more heat is produced; this may become detrimental during very high fevers.

Heat Loss (see Table 17–2)

1. Most heat is lost through the skin.
2. Blood flow through the dermis determines the amount of heat that is lost by radiation, conduction, and convection.
3. Vasodilation in the dermis increases blood flow and heat loss; radiation and conduction are effective only if the environment is cooler than the body.
4. Vasoconstriction in the dermis decreases blood flow and conserves heat in the core of the body.
5. Sweating is a very effective heat loss mechanism; excess body heat evaporates sweat on the skin surface; sweating is most effective when the atmospheric humidity is low.
6. Sweating also has a disadvantage in that water is lost and must be replaced to prevent serious dehydration.
7. Heat is lost from the respiratory tract by the evaporation of water from the warm respiratory mucosa; water vapor is part of exhaled air.
8. A very small amount of heat is lost as urine and feces are excreted at body temperature.

Regulation of Heat Loss

1. The hypothalamus is the thermostat of the body and regulates body temperature by balancing heat production and heat loss.
2. The hypothalamus receives information from its own neurons (blood temperature) and from the temperature receptors in the dermis.
3. Mechanisms to increase heat loss are vasodilation in the dermis and increased sweating. Decreased muscle tone will decrease heat production.
4. Mechanisms to conserve heat are vasoconstriction in the dermis and decreased sweating. Increased muscle tone (shivering) will increase heat production.

Fever—an abnormally elevated body temperature

1. Pyrogens are substances that cause a fever: bacteria, foreign proteins, or chemicals released during inflammation (endogenous pyrogens).
2. Pyrogens raise the setting of the hypothalamic thermostat; the person feels cold and begins to shiver to produce heat.
3. When the pyrogen has been eliminated, the hypothalamic setting returns to normal; the person feels warm, and sweating begins to lose heat to lower the body temperature.
4. A low fever may be beneficial because it increases the activity of WBCs and inhibits the activity of some pathogens.
5. A high fever may be detrimental because enzymes are denatured at high temperatures. This is most critical in the brain, where cells that die cannot be replaced.

Metabolism—all the reactions within the body

1. Anabolism—synthesis reactions that usually require energy in the form of ATP.
2. Catabolism—decomposition reactions that often release energy in the form of ATP.
3. Enzymes catalyze most anabolic and catabolic reactions.

Cell Respiration—the breakdown of food molecules to release their potential energy and synthesize ATP (Fig. 17–3)

1. Glucose + oxygen yields CO_2 + H_2O + ATP + heat.
2. The breakdown of glucose involves three stages: glycolysis, the Krebs cycle, and the cytochrome (electron) transport system (see also Table 17–3).
3. The oxygen necessary comes from breathing.
4. The water formed becomes part of intracellular fluid; CO_2 is exhaled; ATP is used for energy-requiring reactions; heat provides a body temperature.

Proteins and Fats—as energy sources (see Table 17–4 for hormonal regulation)

1. Excess amino acids are deaminated in the liver and converted to pyruvic acid or acetyl groups to enter the Krebs cycle. Amino acids may also be converted to glucose to supply the brain (Fig. 17–3).
2. Glycerol is converted to pyruvic acid to enter the Krebs cycle.
3. Fatty acids, in the process of beta-oxidation in the liver, are split into acetyl groups to enter the Krebs cycle; ketones are formed for transport to other cells (see Fig. 17–3).

Energy Available from Food

1. Energy is measured in kilocalories (Calories): kcal.
2. There are 4 kcal per gram of carbohydrate, 4 kcal per gram of protein, 9 kcal per gram of fat. With reference to food, kilocalories may be called calories.

Synthesis Uses of Foods (Fig. 17–4)

1. Glucose—used to synthesize the pentose sugars for DNA and RNA; used to synthesize glycogen to store energy in liver and muscles.
2. Amino acids—used to synthesize new proteins and the non-essential amino acids; essential amino acids must be obtained in the diet.
3. Fatty acids and glycerol—used to synthesize phospholipids for cell membranes, triglycerides for fat storage in adipose tissue, and cholesterol and other steroids; essential fatty acids must be obtained in the diet.
4. Any food eaten in excess will be changed to fat and stored.
5. Vitamins and minerals—see Tables 17–5 and 17–6.

Metabolic Rate—heat production by the body; measured in kcal

1. Basal metabolic rate (BMR) is the energy required to maintain life (see Box 17–4); several factors influence the metabolic rate of an active person.

2. Age—metabolic rate is highest in young children and decreases with age.
3. Body configuration—more surface area proportional to weight (tall and thin) means a higher metabolic rate.
4. Sex hormones—men usually have a higher metabolic rate than do women; men have more muscle proportional to fat than do women.
5. Sympathetic stimulation—metabolic activity increases in stress situations.
6. Decreased food intake—metabolic rate decreases to conserve available energy sources.
7. Climate—people who live in cold climates usually have higher metabolic rates because of a greater need for heat production.

REVIEW QUESTIONS

1. State the normal range of human body temperature in °F and °C. (p. 396)
2. State the summary equation of cell respiration, and state what happens to (or the purpose of) each of the products. (p. 401)
3. Describe the role of each in heat production: thyroxine, skeletal muscles, stress situations, and the liver. (p. 396)
4. Describe the two mechanisms of heat loss through the skin, and explain the role of blood flow. Describe how heat is lost through the respiratory tract. (pp. 397–398)
5. Explain the circumstances that exist when sweating and vasodilation in the dermis are not effective mechanisms of heat loss. (p. 397)
6. Name the part of the brain that regulates body temperature, and explain what is meant by a thermostat. (p. 398)
7. Describe the responses by the body to a warm environment and to a cold environment. (pp. 399)
8. Explain how pyrogens are believed to cause a fever, and give two examples of pyrogens. (p. 399)
9. Define metabolism, anabolism, catabolism, kilocalorie, and metabolic rate. (pp. 400, 401, 405, 408)
10. Name the three stages of the cell respiration of glucose and state where in the cell each takes place and whether or not oxygen is required. (pp. 403)
11. For each, state the molecules that enter the process and the results of the process: glycolysis, Krebs cycle, and cytochrome transport system. (pp. 403–405)
12. Explain how fatty acids, glycerol, and excess amino acids are used for energy production in cell respiration. (pp. 403, 405)
13. Describe the synthesis uses for glucose, amino acids, and fatty acids. (pp. 406–408)
14. Describe four factors that affect the metabolic rate of an active person. (pp. 410, 412)
15. If lunch consists of 60 grams of carbohydrate, 15 grams of protein, and 10 grams of fat, how many kilocalories are provided by this meal? (p. 405)

FOR FURTHER THOUGHT

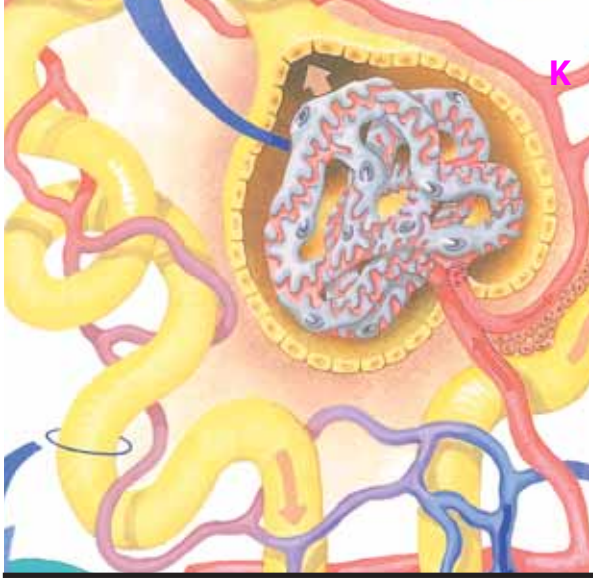
1. For many people, iceberg lettuce is the vegetable eaten most often. What does lettuce provide? What does lettuce lack, compared to vegetables such as broccoli?
2. Fourteen-year-old Donna has just decided that eating meat is "gross," and that she will be a vegetarian. What difficulties are there with such a diet; that is, what nutrients may be lacking? How may they be obtained?
3. Studies with animals have shown that caloric restriction may prolong life by protecting the brain from some effects of aging. The animals' diet was about half the usual calories they would consume. For people, 1250 to 1500 calories per day would be

restrictive (compared to the 2000 calories or more that many of us in North America consume). Would it be worth it for a life span of 110 years? Describe the problems with such a diet.

4. Every summer small children are left alone in cars "just for a few minutes," while a parent does an errand. The result may be tragic—severe brain damage or death of the child from heat stroke. Explain why small children are so susceptible to heat.
5. Remember the *Titanic*, which sank in April of 1912? There were not enough lifeboats for everyone, and many people were in the water of the North Atlantic. They did have life jackets, and did not drown, but many were dead within half an hour. Explain why.
6. An elderly person and a quadriplegic person may each have difficulties during cold weather. Explain how the problem is a little different for each.

CHAPTER 18

The Urinary System



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CHAPTER 18

Chapter Outline

Student Objectives

- Describe the location and general function of each organ of the urinary system.
- Name the parts of a nephron and the important blood vessels associated with them.
- Explain how the following are involved in urine formation: glomerular filtration, tubular reabsorption, tubular secretion, and blood flow through the kidney.
- Describe the mechanisms of tubular reabsorption, and explain the importance of tubular secretion.
- Describe how the kidneys help maintain normal blood volume and blood pressure.
- Name and state the functions of the hormones that affect the kidneys.
- Describe how the kidneys help maintain normal pH of blood and tissue fluid.
- Describe the urination reflex, and explain how voluntary control is possible.
- Describe the characteristics of normal urine.

The Urinary System

New Terminology

Bowman's capsule (**BOW**-manz **KAP**-suhl)
Detrusor muscle (de-**TROO**-ser)
External urethral sphincter (yoo-**REE**-thruhl **SFINK**-ter)
Glomerular filtration rate (gloh-**MER**-yoo-ler fill-**TRAY**-shun RAYT)
Glomerulus (gloh-**MER**-yoo-lus)
Internal urethral sphincter (yoo-**REE**-thruhl **SFINK**-ter)
Juxtaglomerular cells (JUKS-tah-gloh-**MER**-yoo-ler SELLS)
Micturition (MIK-tyoo-**RISH**-un)
Nephron (**NEFF**-ron)
Nitrogenous wastes (nigh-**TRAH**-jen-us)
Peritubular capillaries (PER-ee-**TOO**-byoo-ler)
Renal corpuscle (**REE**-nuhl **KOR**-pus'l)
Renal filtrate (**REE**-nuhl **FILL**-trayt)
Renal tubule (**REE**-nuhl **TOO**-byoo'l)
Retroperitoneal (RE-troh-PER-i-toh-**NEE**-uhl)
Specific gravity (spe-**SIF**-ik **GRA**-vi-tee)
Threshold level (**THRESH**-hold **LE**-vuhl)
Trigone (**TRY**-gohn)
Ureter (**YOOR**-uh-ter)
Urethra (yoo-**REE**-thrah)
Urinary bladder (**YOOR**-i-NAR-ee **BLA**-der)

Related Clinical Terminology

Cystitis (sis-**TIGH**-tis)
Dysuria (dis-**YOO**-ree-ah)
Hemodialysis (HEE-moh-dye-**AL**-i-sis)
Nephritis (ne-**FRY**-tis)
Oliguria (AH-li-**GYOO**-ree-ah)
Polyuria (PAH-li-**YOO**-ree-ah)
Renal calculi (**REE**-nuhl **KAL**-kew-lye)
Renal failure (**REE**-nuhl **FAYL**-yer)
Uremia (yoo-**REE**-me-ah)

*Terms that appear in **bold type** in the chapter text are defined in the glossary, which begins on page 547.*

The first successful human organ transplant was a kidney transplant performed in 1953. Because the donor and recipient were identical twins, rejection was not a problem. Thousands of kidney transplants have been performed since then, and the development of immunosuppressive medications has permitted many people to live normal lives with donated kidneys. Although a person usually has two kidneys, one kidney is sufficient to carry out the complex work required to maintain homeostasis of the body fluids.

The **urinary system** consists of two kidneys, two ureters, the urinary bladder, and the urethra (Fig. 18–1). The formation of urine is the function of the kidneys, and the rest of the system is responsible for eliminating the urine.

Body cells produce waste products such as urea,

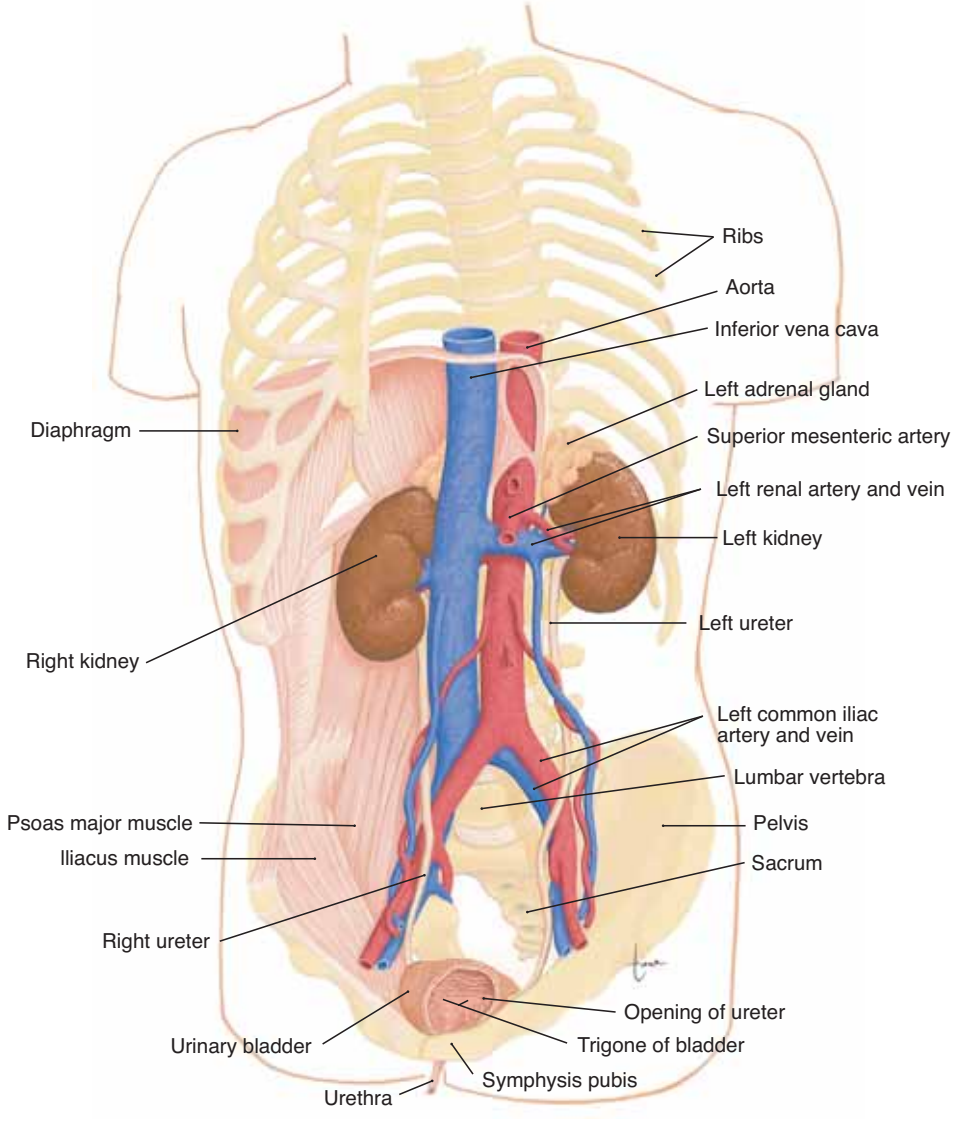


Figure 18–1. The urinary system shown in anterior view.
QUESTION: Why is blood pressure relatively high in the kidneys? What do you see that would suggest this?

creatinine, and ammonia, which must be removed from the blood before they accumulate to toxic levels. As the kidneys form urine to excrete these waste products, they also accomplish several other important functions:

1. Regulation of the volume of blood by excretion or conservation of water
2. Regulation of the electrolyte content of the blood by the excretion or conservation of minerals
3. Regulation of the acid–base balance of the blood by excretion or conservation of ions such as H^+ ions or HCO_3^- ions
4. Regulation of all of the above in tissue fluid

The process of urine formation, therefore, helps maintain the normal composition, volume, and pH of both blood and tissue fluid by removing those substances that would upset the normal constancy and balance of these extracellular fluids.

KIDNEYS

The two **kidneys** are located in the upper abdominal cavity on either side of the vertebral column, behind the peritoneum (**retroperitoneal**). The upper portions of the kidneys rest on the lower surface of the diaphragm and are enclosed and protected by the lower rib cage (see Fig. 18–1). The kidneys are embedded in adipose tissue that acts as a cushion and is in turn covered by a fibrous connective tissue membrane called the **renal fascia**, which helps hold the kidneys in place (see Box 18–1: Floating Kidney).

Each kidney has an indentation called the **hilus** on its medial side. At the hilus, the renal artery enters the kidney, and the renal vein and ureter emerge. The renal artery is a branch of the abdominal aorta, and the renal vein returns blood to the inferior vena cava (see Fig. 18–1). The ureter carries urine from the kidney to the urinary bladder.

Box 18–1 FLOATING KIDNEY

A floating kidney is one that has moved out of its normal position. This may happen in very thin people whose renal cushion of adipose tissue is thin, or it may be the result of a sharp blow to the back that dislodges a kidney.

A kidney can function in any position; the problem with a floating kidney is that the ureter may become twisted or kinked. If urine cannot flow through the ureter, the urine backs up and collects in the renal pelvis. Incoming urine from the renal tubules then backs up as well. If the renal filtrate cannot flow out of Bowman's capsules, the pressure within Bowman's capsules increases, opposing the blood pressure in the glomeruli. Glomerular filtration then cannot take place efficiently. If uncorrected, this may lead to permanent kidney damage.

INTERNAL STRUCTURE OF THE KIDNEY

In a coronal or frontal section of the kidney, three areas can be distinguished (Fig. 18–2). The lateral and middle areas are tissue layers, and the medial area at the hilus is a cavity. The outer tissue layer is called the **renal cortex**; it is made of renal corpuscles and convoluted tubules. These are parts of the nephron and are described in the next section. The inner tissue layer is the **renal medulla**, which is made of loops of Henle and collecting tubules (also parts of the nephron). The renal medulla consists of wedge-shaped pieces called **renal pyramids**. The tip of each pyramid is its apex or papilla.

The third area is the **renal pelvis**; this is not a layer of tissues, but rather a cavity formed by the expansion of the ureter within the kidney at the hilus. Funnel-shaped extensions of the renal pelvis, called **calyces** (singular: **calyx**), enclose the papillae of the renal pyramids. Urine flows from the renal pyramids into the calyces, then to the renal pelvis and out into the ureter.

THE NEPHRON

The **nephron** is the structural and functional unit of the kidney. Each kidney contains approximately 1 million nephrons. It is in the nephrons, with their associated blood vessels, that urine is formed. Each nephron has two major portions: a renal corpuscle and a renal tubule. Each of these major parts has further subdivisions, which are shown with their blood vessels in Fig. 18–3.

Renal Corpuscle

A **renal corpuscle** consists of a glomerulus surrounded by a Bowman's capsule. The **glomerulus** is a capillary network that arises from an **afferent arteriole** and empties into an **efferent arteriole**. The diameter

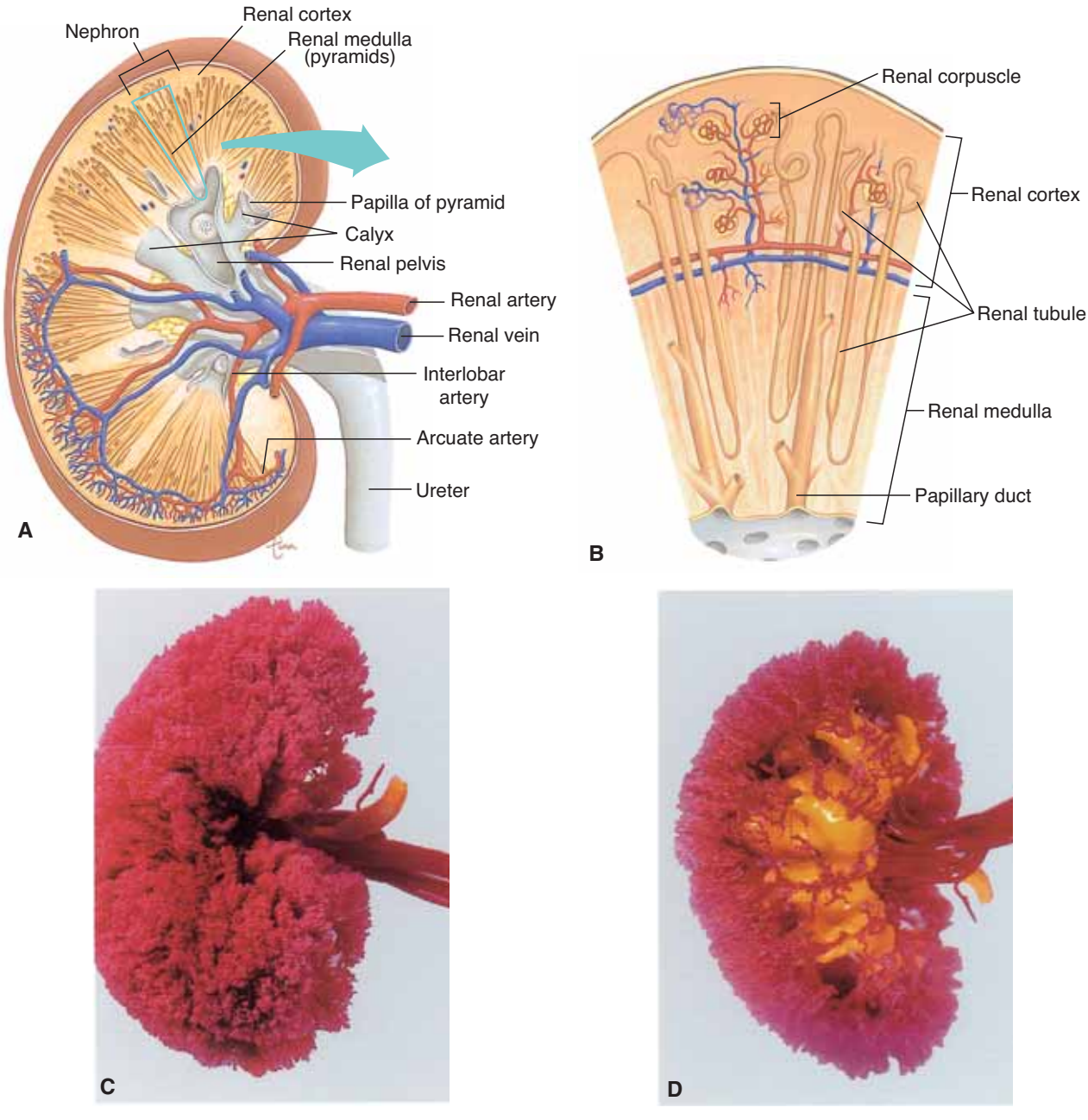


Figure 18–2. (**A**) Frontal section of the right kidney showing internal structure and blood vessels. (**B**) The magnified section of the kidney shows several nephrons. (**C**) Vascular cast of a kidney in lateral view. Red plastic fills the blood vessels. (**D**) Vascular cast in medial view. Blood vessels have been removed; yellow plastic fills the renal pelvis. (Photographs C and D by Dan Kaufman.)

QUESTION: Which main parts of a nephron are found in the renal cortex? Which areas of a kidney have many blood vessels?

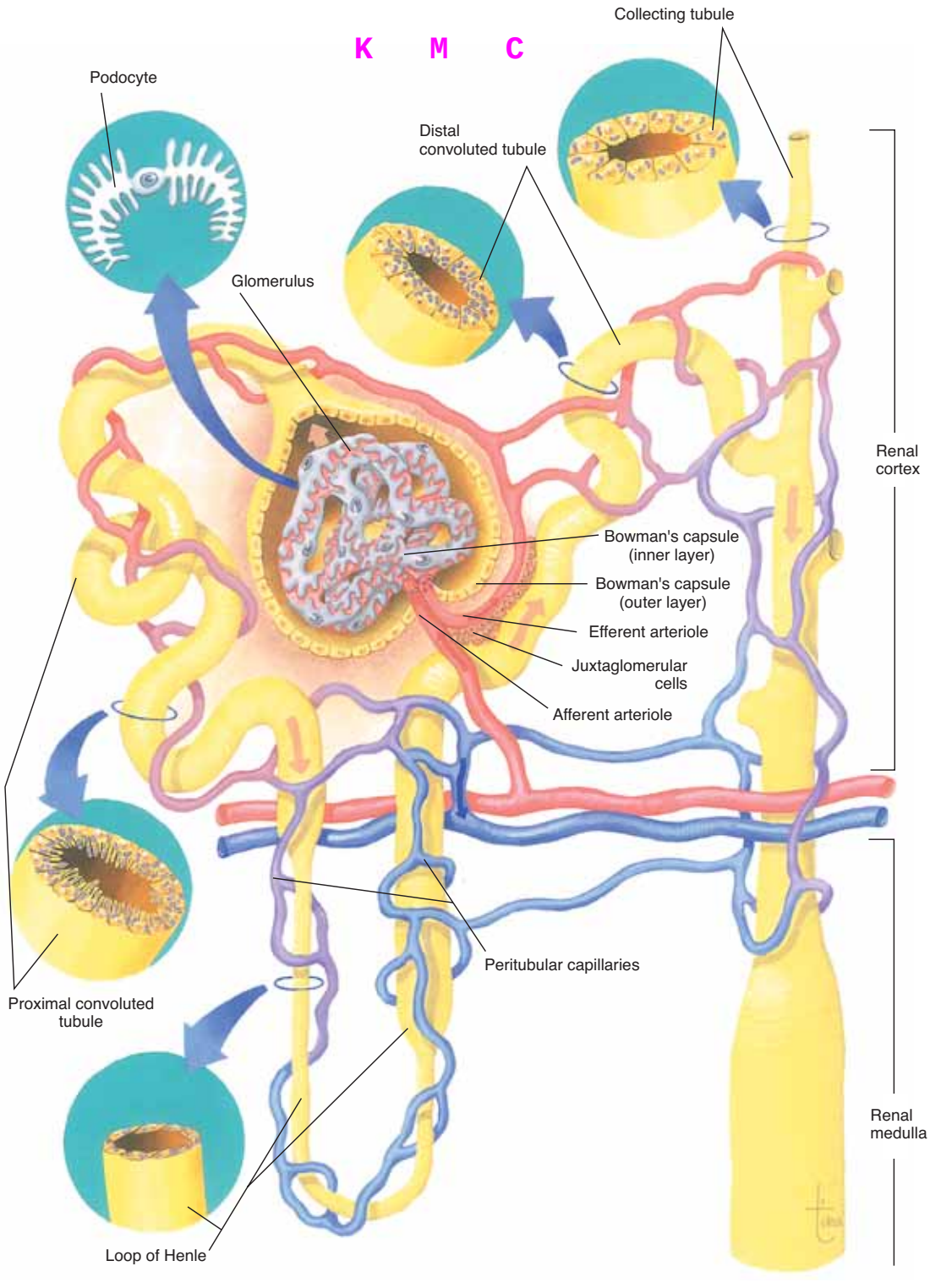


Figure 18–3. A nephron with its associated blood vessels. Portions of the nephron have been magnified. The arrows indicate the direction of blood flow and flow of renal filtrate. See text for description.

QUESTION: How does the shape of a podocyte contribute to its function? How is the lining of the proximal convoluted tubule specialized?

of the efferent arteriole is smaller than that of the afferent arteriole, which helps maintain a fairly high blood pressure in the glomerulus.

Bowman's capsule (or glomerular capsule) is the expanded end of a renal tubule; it encloses the glomerulus. The inner layer of Bowman's capsule is made of **podocytes**; the name means "foot cells," and the "feet" of the podocytes are on the surface of the glomerular capillaries. The arrangement of podocytes creates pores, spaces between adjacent "feet," which make this layer very permeable. The outer layer of Bowman's capsule has no pores and is not permeable. The space between the inner and outer layers of Bowman's capsule contains renal filtrate, the fluid that is formed from the blood in the glomerulus and will eventually become urine.

Renal Tubule

The **renal tubule** continues from Bowman's capsule and consists of the following parts: **proximal convoluted tubule** (in the renal cortex), **loop of Henle** (or loop of the nephron, in the renal medulla), and **distal convoluted tubule** (in the renal cortex). The distal convoluted tubules from several nephrons empty into a **collecting tubule**. Several collecting tubules then unite to form a papillary duct that empties urine into a calyx of the renal pelvis.

Cross-sections of the parts of the renal tubule are shown in Fig. 18–3. Notice how thin the walls of the tubule are, and also the microvilli in the proximal convoluted tubule. These anatomic characteristics provide for efficient exchanges of materials, as you will see.

All parts of the renal tubule are surrounded by **peritubular capillaries**, which arise from the efferent arteriole. The peritubular capillaries will receive the materials reabsorbed by the renal tubules; this is described in the section on urine formation.

BLOOD VESSELS OF THE KIDNEY

The pathway of blood flow through the kidney is an essential part of the process of urine formation. Blood from the abdominal aorta enters the **renal artery**, which branches extensively within the kidney into smaller arteries (see Fig. 18–2). The smallest arteries give rise to afferent arterioles in the renal cortex (see Fig. 18–3). From the afferent arterioles, blood flows into the glomeruli (capillaries), to efferent arterioles, to peritubular capillaries, to veins within the kidney, to the **renal vein**, and finally to the inferior vena cava. Notice that in this pathway there are two sets of capillaries, and recall that it is in capillaries that exchanges take place between the blood and surrounding tissues. Therefore, in the kidneys there are two sites of exchange. The exchanges that take place between the nephrons and the capillaries of the kidneys will form urine from blood plasma.

Figure 18–2 shows two views of a vascular cast of a kidney; the shape of the blood vessels has been preserved in red plastic. You can see how dense the vasculature of a kidney is, and most of these vessels are capillaries.

FORMATION OF URINE

The formation of urine involves three major processes. The first is glomerular filtration, which takes place in the renal corpuscles. The second and third are tubular reabsorption and tubular secretion, which take place in the renal tubules.

GLOMERULAR FILTRATION

You may recall that filtration is the process in which blood pressure forces plasma and dissolved material out of capillaries. In **glomerular filtration**, blood pressure forces plasma, dissolved substances, and small proteins out of the glomeruli and into Bowman's capsules. This fluid is no longer plasma but is called **renal filtrate**.

The blood pressure in the glomeruli, compared with that in other capillaries, is relatively high, about 60 mmHg. The pressure in Bowman's capsule is very low, and its inner, podocyte layer is very permeable, so that approximately 20% to 25% of the blood that enters glomeruli becomes renal filtrate in Bowman's capsules. The blood cells and larger proteins are too large to be forced out of the glomeruli, so they remain in the blood. Waste products are dissolved in blood plasma, so they pass into the renal filtrate. Useful materials such as nutrients and minerals are also dissolved in plasma and are also present in renal filtrate. Filtration is not selective with respect to usefulness; it is selective only with respect to size. Therefore, renal filtrate is very much like blood plasma, except that there is far less protein and no blood cells are present.

The **glomerular filtration rate** (GFR) is the amount of renal filtrate formed by the kidneys in 1 minute, and averages 100 to 125 mL per minute. GFR

Box 18–2 RENAL FAILURE AND HEMODIALYSIS

Renal failure, the inability of the kidneys to function properly, may be the result of three general causes, which may be called prerenal, intrinsic renal, and postrenal.

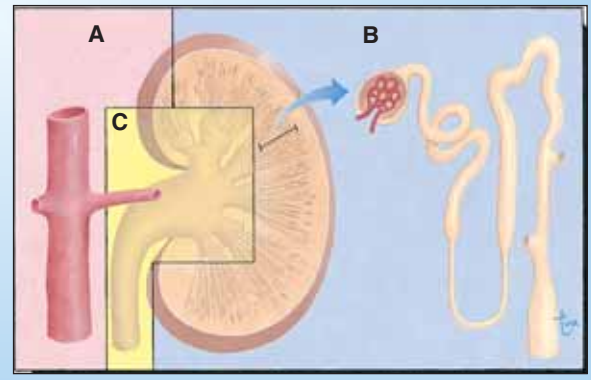
"Prerenal" means that the problem is "before" the kidneys, that is, in the blood flow to the kidneys. Any condition that decreases blood flow to the kidneys may result in renal damage and failure. Examples are severe hemorrhage or very low blood pressure following a heart attack (MI).

"Intrinsic renal" means that the problem is in the kidneys themselves. Diabetes and hypertension damage the blood vessels of the kidneys, and are the causes of 70% of all cases of end-stage renal failure. Bacterial infections of the kidneys or exposure to chemicals (certain antibiotics) may cause damage to the nephrons. Polycystic kidney disease is a genetic disorder in which the kidney tubules dilate and become nonfunctional. Severe damage may not be apparent until age 40 to 60 years but may then progress to renal failure.

"Postrenal" means that the problem is "after" the kidneys, somewhere in the rest of the urinary tract. Obstruction of urine flow may be caused by kidney stones, a twisted ureter, or prostatic hypertrophy.

Treatment of renal failure involves correcting the specific cause, if possible. If not possible, and kidney damage is permanent, the person is said to have chronic renal failure. **Hemodialysis** is the use of an artificial kidney machine to do what the patient's nephrons can no longer do. The patient's blood is passed through minute tubes surrounded by fluid (dialysate) with the same chemical composition as plasma. Waste products and excess minerals diffuse out of the patient's blood into the fluid of the machine.

Although hemodialysis does prolong life for those with chronic renal failure, it does not fully take the place of functioning kidneys. The increasing success rate of kidney transplants, however, does indeed provide the possibility of a normal life for people with chronic renal failure.



Box Figure 18–A Causes of renal failure. (**A**) Prerenal. (**B**) Intrinsic renal. (**C**) Postrenal.

may be altered if the rate of blood flow through the kidney changes. If blood flow increases, the GFR increases, and more filtrate is formed. If blood flow decreases (as may happen following a severe hemorrhage), the GFR decreases, less filtrate is formed, and urinary output decreases (see Box 18–2: Renal Failure and Hemodialysis).

TUBULAR REABSORPTION

Tubular reabsorption takes place from the renal tubules into the peritubular capillaries. In a 24-hour period, the kidneys form 150 to 180 liters of filtrate, and normal urinary output in that time is 1 to 2 liters. Therefore, it becomes apparent that most of the renal filtrate does not become urine. Approximately 99% of the filtrate is reabsorbed back into the blood in the peritubular capillaries. Only about 1% of the filtrate will enter the renal pelvis as urine.

Most reabsorption and secretion (about 65%) take place in the proximal convoluted tubules, whose cells have **microvilli** that greatly increase their surface area. The distal convoluted tubules and collecting tubules are also important sites for the reabsorption of water (Fig. 18–4).

Mechanisms of Reabsorption

1. **Active transport**—the cells of the renal tubule use ATP to transport most of the useful materials from the filtrate to the blood. These useful materials include glucose, amino acids, vitamins, and positive ions.

   For many of these substances, the renal tubules have a **threshold level** of reabsorption. This means that there is a limit to how much the tubules can remove from the filtrate. For example, if the filtrate level of glucose is normal (reflecting a normal

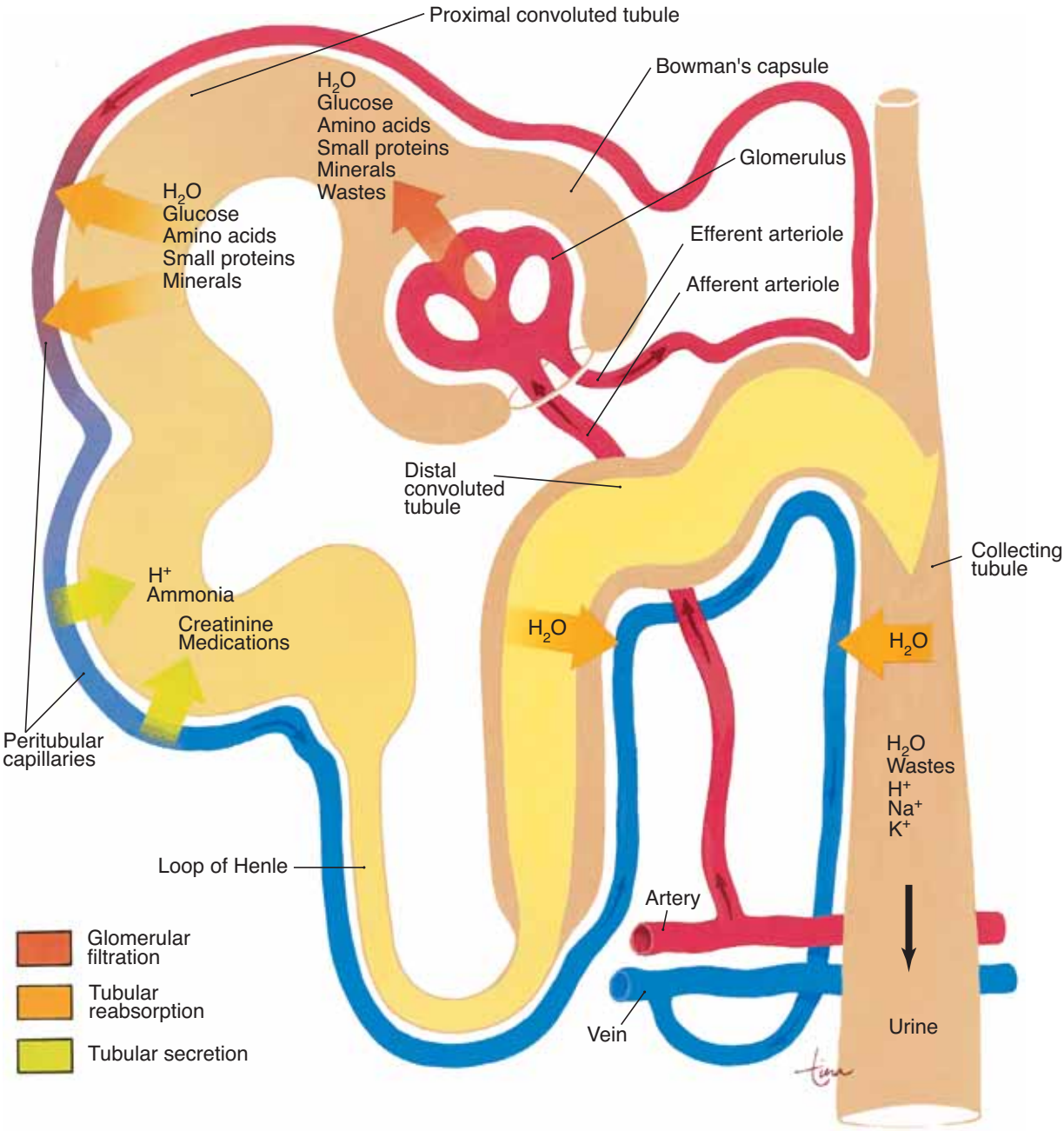


Figure 18–4. Schematic representation of glomerular filtration, tubular reabsorption, and tubular secretion. The renal tubule has been uncoiled, and the peritubular capillaries are shown adjacent to the tubule.

QUESTION: Describe tubular secretion; that is, it goes from where to where? What substances may be secreted?

blood glucose level), the tubules will reabsorb all of the glucose, and none will be found in the urine. What happens is this: The number of glucose transporter molecules in the membranes of the tubule cells is sufficient to take in the number of glucose molecules passing by in the filtrate. If, however, the blood glucose level is above normal, the amount of glucose in the filtrate will also be above normal and will exceed the threshold level of reabsorption. The number of glucose molecules to be reabsorbed is more than the number of the transporter molecules available to do so. In this situation, therefore, some glucose will remain in the filtrate and be present in urine.

The reabsorption of Ca^{+2} ions is increased by parathyroid hormone (PTH). The parathyroid glands secrete PTH when the blood calcium level decreases. The reabsorption of Ca^{+2} ions by the kidneys is one of the mechanisms by which the blood calcium level is raised back to normal.

The hormone aldosterone, secreted by the adrenal cortex, increases the reabsorption of Na^+ ions and the excretion of K^+ ions. Besides regulating the blood levels of sodium and potassium, aldosterone also affects the volume of blood.

2. **Passive transport**—many of the negative ions that are returned to the blood are reabsorbed following the reabsorption of positive ions, because unlike charges attract.
3. **Osmosis**—the reabsorption of water follows the reabsorption of minerals, especially sodium ions. The hormones that affect reabsorption of water are discussed in the next section.
4. **Pinocytosis**—small proteins are too large to be reabsorbed by active transport. They become adsorbed to the membranes of the cells of the proximal convoluted tubules. The cell membrane then sinks inward and folds around the protein to take it in (see Fig. 3–3 for depictions of this and the other transport mechanisms). Normally all proteins in the filtrate are reabsorbed; none is found in urine.

TUBULAR SECRETION

This mechanism also changes the composition of urine. In **tubular secretion**, substances are actively secreted from the blood in the peritubular capillaries into the filtrate in the renal tubules. Waste products, such as ammonia and some creatinine, and the metabolic products of medications may be secreted into the filtrate to be eliminated in urine. Hydrogen ions (H^+) may be secreted by the tubule cells to help maintain the normal pH of blood.

HORMONES THAT INFLUENCE REABSORPTION OF WATER

Aldosterone is secreted by the adrenal cortex in response to a high blood potassium level, to a low blood sodium level, or to a decrease in blood pressure. When aldosterone stimulates the reabsorption of Na^+ ions, water follows from the filtrate back to the blood. This helps maintain normal blood volume and blood pressure.

You may recall that the antagonist to aldosterone is **atrial natriuretic peptide** (ANP), which is secreted by the atria of the heart when the atrial walls are stretched by high blood pressure or greater blood volume. ANP decreases the reabsorption of Na^+ ions by the kidneys; these remain in the filtrate, as does water, and are excreted. By increasing the elimination of sodium and water, ANP lowers blood volume and blood pressure.

Antidiuretic hormone (ADH) is released by the posterior pituitary gland when the amount of water in the body decreases. Under the influence of ADH, the distal convoluted tubules and collecting tubules are able to reabsorb more water from the renal filtrate. This helps maintain normal blood volume and blood pressure, and also permits the kidneys to produce urine that is more concentrated than body fluids. Producing a concentrated urine is essential to prevent excessive water loss while still excreting all the substances that must be eliminated.

If the amount of water in the body increases, however, the secretion of ADH diminishes, and the kidneys will reabsorb less water. Urine then becomes dilute, and water is eliminated until its concentration in the body returns to normal. This may occur following ingestion of excessive quantities of fluids.

SUMMARY OF URINE FORMATION

1. The kidneys form urine from blood plasma. Blood flow through the kidneys is a major factor in determining urinary output.
2. Glomerular filtration is the first step in urine formation. Filtration is not selective in terms of usefulness of materials; it is selective only in terms of size. High blood pressure in the glomeruli forces

plasma, dissolved materials, and small proteins into Bowman's capsules; the fluid is now called renal filtrate.

3. Tubular reabsorption is selective in terms of usefulness. Nutrients such as glucose, amino acids, and vitamins are reabsorbed by active transport and may have renal threshold levels. Positive ions are reabsorbed by active transport and negative ions are reabsorbed most often by passive transport. Water is reabsorbed by osmosis, and small proteins are reabsorbed by pinocytosis.

   Reabsorption takes place from the filtrate in the renal tubules to the blood in the peritubular capillaries.
4. Tubular secretion takes place from the blood in the peritubular capillaries to the filtrate in the renal tubules and can ensure that wastes such as creatinine or excess H^+ ions are actively put into the filtrate to be excreted.
5. Hormones such as aldosterone, ANP, and ADH influence the reabsorption of water and help maintain normal blood volume and blood pressure. The secretion of ADH determines whether a concentrated or dilute urine will be formed.
6. Waste products remain in the renal filtrate and are excreted in urine. The effects of hormones on the kidneys are summarized in Table 18–1 and illustrated in Fig. 18–5.

THE KIDNEYS AND ACID–BASE BALANCE

The kidneys are the organs most responsible for maintaining the pH of blood and tissue fluid within normal ranges. They have the greatest ability to compensate for the pH changes that are a normal part of body metabolism or the result of disease, and to make the necessary corrections.

This regulatory function of the kidneys is complex, but at its simplest it may be described as follows. If body fluids are becoming too acidic, the kidneys will secrete more H^+ ions into the renal filtrate and will return more HCO_3^- ions to the blood. This will help raise the pH of the blood back to normal. The reactions involved in such a mechanism are shown in Fig. 18–6, to which we will return later. First, however, let us briefly consider how the kidneys will compensate for body fluids that are becoming too alkaline. You might expect the kidneys to do just the opposite of what was just described, and that is just what happens. The kidneys will return H^+ ions to the blood and excrete HCO_3^- ions in urine. This will help lower the pH of the blood back to normal.

Because the natural tendency is for body fluids to become more acidic, let us look at the pH-raising mechanism in more detail (see Fig. 18–6). The cells of the renal tubules can secrete H^+ ions or ammonia in exchange for Na^+ ions and, by doing so, influence the reabsorption of other ions. Hydrogen ions are obtained from the reaction of CO_2 and water (or other processes). An amine group from an amino acid is combined with an H^+ ion to form ammonia.

The tubule cell secretes the H^+ ion and the ammonia into the renal filtrate, and two Na^+ ions are reabsorbed in exchange. In the filtrate, the H^+ ion and ammonia form NH_4^+ (an ammonium radical), which reacts with a chloride ion (Cl^-) to form NH_4Cl (ammonium chloride) that is excreted in urine.

As the Na^+ ions are returned to the blood in the

Table 18–1 EFFECTS OF HORMONES ON THE KIDNEYS

Hormone (gland)	Function
Antidiuretic hormone (ADH) (posterior pituitary)	• Increases reabsorption of water from the filtrate to the blood.
Parathyroid hormone (PTH) (parathyroid glands)	• Increases reabsorption of Ca^{+2} ions from filtrate to the blood and excretion of phosphate ions into the filtrate.
Aldosterone (adrenal cortex)	• Increases reabsorption of Na^+ ions from the filtrate to the blood and excretion of K^+ ions into the filtrate. Water is reabsorbed following the reabsorption of sodium.
Atrial natriuretic peptide (ANP) (atria of heart)	• Decreases reabsorption of Na^+ ions, which remain in the filtrate. More sodium and water are eliminated in urine.

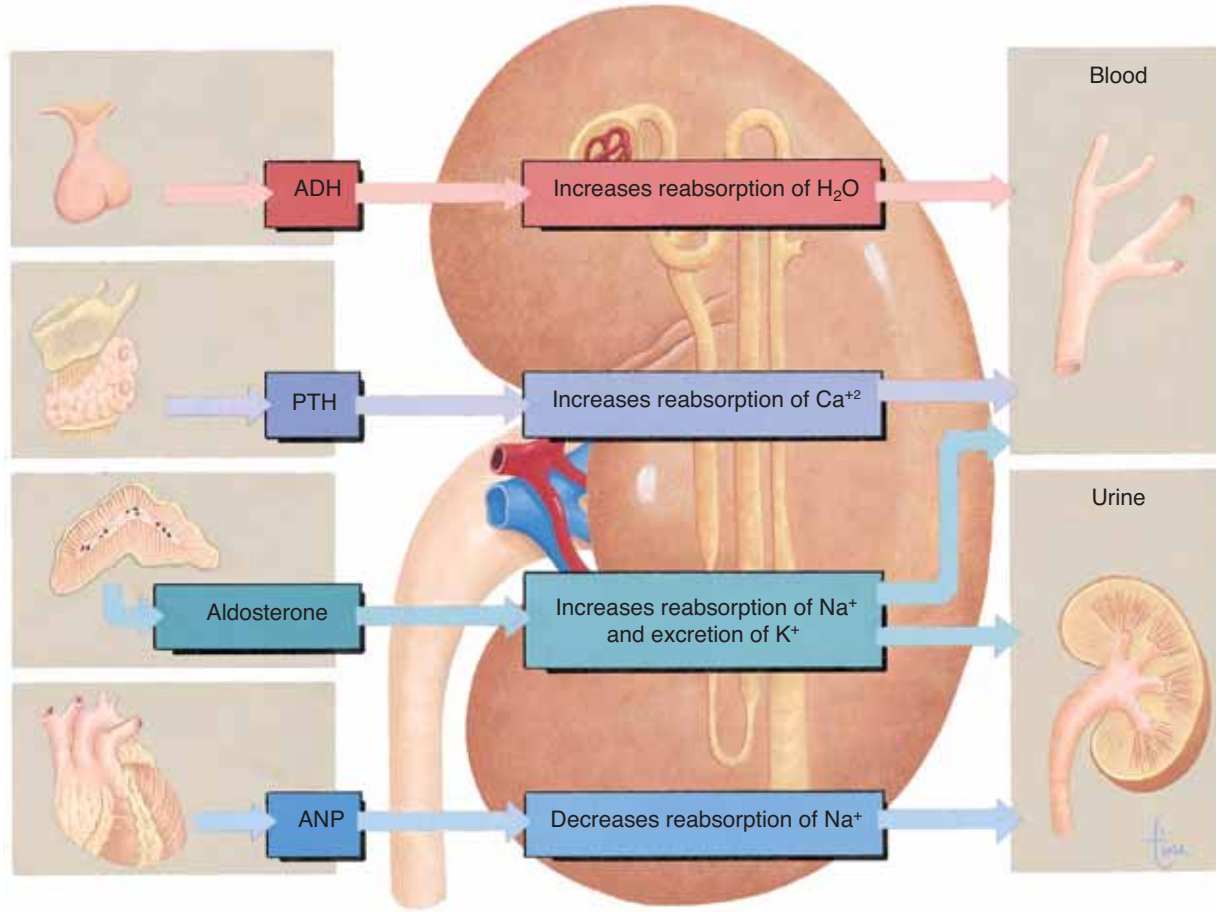


Figure 18–5. Effects of hormones on the kidneys.
QUESTION: Do any of these hormones affect both reabsorption and secretion? If so, how?

peritubular capillaries, HCO_3^- ions follow. Notice what has happened: Two H^+ ions have been excreted in urine, and two Na^+ ions and two HCO_3^- ions have been returned to the blood. As reactions like these take place, the body fluids are prevented from becoming too acidic.

Another mechanism used by the cells of the kidney tubules to regulate pH is the phosphate buffer system, which is described in Chapter 19.

OTHER FUNCTIONS OF THE KIDNEYS

In addition to the functions described thus far, the kidneys have other functions, some of which are not directly related to the formation of urine. These functions are secretion of renin (which does influence urine formation), production of erythropoietin, and activation of vitamin D.

1. **Secretion of renin**—When blood pressure decreases, the **juxtaglomerular** (*juxta* means "next to") **cells** in the walls of the afferent arterioles secrete the enzyme **renin**. Renin then initiates the renin-angiotensin mechanism to raise blood pressure. This was first described in Chapter 13, and the sequence of events is presented in Table 18–2. The end product of this mechanism is **angiotensin II**, which causes vasoconstriction and increases the secretion of aldosterone, both of which help raise blood pressure.

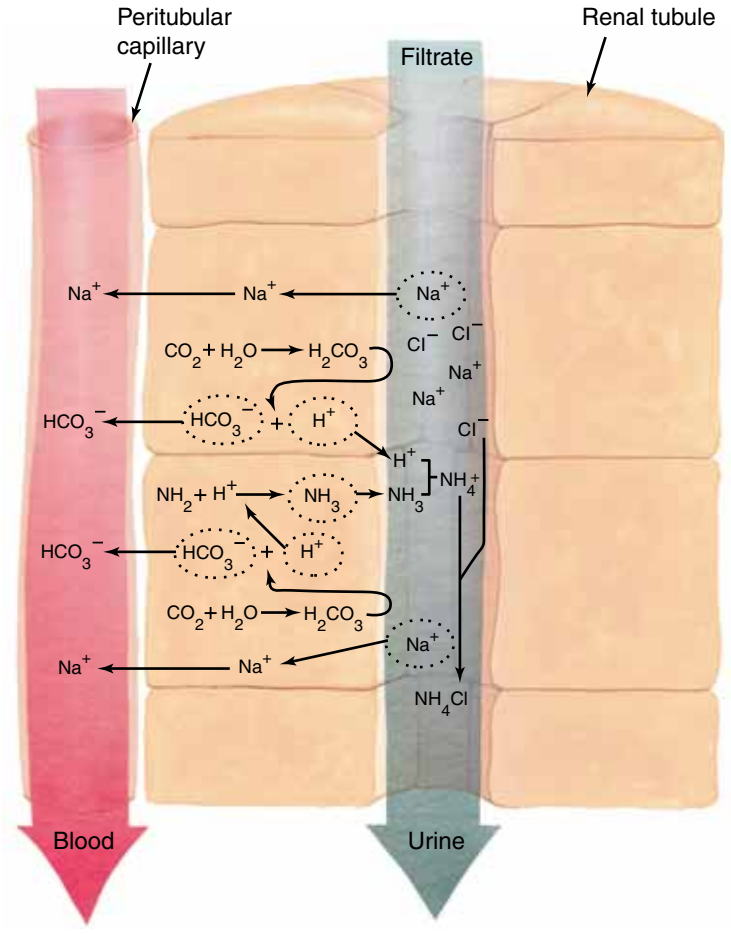


Figure 18–6. Renal regulation of acid–base balance. The cells of the renal tubule secrete H^+ ions and ammonia into the filtrate and return Na^+ ions and HCO_3^- ions to the blood in the peritubular capillaries. See text for further description.
QUESTION: The cells of the renal tubule make good use of CO_2. What do the cells use CO_2 for?

A normal blood pressure is essential to normal body functioning. Perhaps the most serious change is a sudden, drastic decrease in blood pressure, such as would follow a severe hemorrhage. In response to such a decrease, the kidneys will decrease filtration and urinary output and will initiate the formation of angiotensin II. In these ways the kidneys help ensure that the heart has enough blood to pump to maintain cardiac output and blood pressure.

2. **Secretion of erythropoietin**—This hormone is secreted whenever the blood oxygen level decreases (a state of hypoxia). Erythropoietin stimulates the red bone marrow to increase the rate of RBC production. With more RBCs in circulation, the oxygen-carrying capacity of the blood is greater, and the hypoxic state may be corrected (see also Box 18–3: Erythropoietin).
3. **Activation of vitamin D**—This vitamin exists in several structural forms that are converted to **calcitriol** (D_2) by the kidneys. Calcitriol is the most active form of vitamin D, which increases the absorption of calcium and phosphate in the small intestine.

Table 18–2 THE RENIN-ANGIOTENSIN MECHANISM

Sequence
1. Decreased blood pressure stimulates the kidneys to secrete renin.
2. Renin splits the plasma protein angiotensinogen (synthesized by the liver) to angiotensin I.
3. Angiotensin I is converted to angiotensin II by an enzyme found in lung tissue and vascular endothelium.
4. Angiotensin II causes vasoconstriction and stimulates the adrenal cortex to secrete aldosterone.

Box 18–3 ERYTHROPOIETIN

Anemia is one of the most debilitating consequences of renal failure, one that hemodialysis cannot reverse. Diseased kidneys stop producing erythropoietin, a natural stimulus for RBC production. Erythropoietin can be produced by genetic engineering and is available for hemodialysis patients. In the past, their anemia could only be treated with transfusions, which exposed these patients to possible immunologic complications of repeated exposure to donated blood or to viral diseases. The synthetic erythropoietin eliminates such risks. Others who benefit from this medication are cancer patients and AIDS patients with severe anemia.

ELIMINATION OF URINE

The ureters, urinary bladder, and urethra do not change the composition or amount of urine, but are responsible for the periodic elimination of urine.

URETERS

Each **ureter** extends from the hilus of a kidney to the lower, posterior side of the urinary bladder (see Fig. 18–1). Like the kidneys, the ureters are retroperitoneal, that is, behind the peritoneum of the dorsal abdominal cavity.

The smooth muscle in the wall of the ureter contracts in peristaltic waves to propel urine toward the urinary bladder. As the bladder fills, it expands and compresses the lower ends of the ureters to prevent backflow of urine.

URINARY BLADDER

The **urinary bladder** is a muscular sac below the peritoneum and behind the pubic bones. In women, the bladder is inferior to the uterus; in men, the bladder is superior to the prostate gland. The bladder is a reservoir for accumulating urine, and it contracts to eliminate urine.

The mucosa of the bladder is **transitional epithelium**, which permits expansion without tearing the lining. When the bladder is empty, the mucosa appears wrinkled; these folds are **rugae**, which also permit expansion. On the floor of the bladder is a triangular area called the **trigone**, which has no rugae and does not expand. The points of the triangle are the openings of the two ureters and that of the urethra (Fig. 18–7).

The smooth muscle layer in the wall of the bladder is called the **detrusor muscle**. It is a muscle in the form of a sphere; when it contracts it becomes a smaller sphere, and its volume diminishes. Around the opening of the urethra the muscle fibers of the detrusor form the **internal urethral sphincter** (or sphincter of the bladder), which is involuntary.

URETHRA

The **urethra** (see Fig. 18–7) carries urine from the bladder to the exterior. The **external urethral sphincter** is made of the surrounding skeletal muscle of the pelvic floor, and is under voluntary control.

In women, the urethra is 1 to 1.5 inches (2.5 to 4 cm) long and is anterior to the vagina. In men, the urethra is 7 to 8 inches (17 to 20 cm) long. The first part just outside the bladder is called the prostatic urethra because it is surrounded by the prostate gland. The next inch is the membranous urethra, around which is the external urethral sphincter. The longest portion is the cavernous urethra (or spongy or penile urethra), which passes through the cavernous (or erectile) tissue of the penis. The male urethra carries semen as well as urine.

THE URINATION REFLEX

Urination may also be called **micturition** or **voiding**. This reflex is a spinal cord reflex over which voluntary control may be exerted. The stimulus for the reflex is stretching of the detrusor muscle of the bladder. The bladder can hold as much as 800 mL of urine, or even more, but the reflex is activated long before the maximum is reached.

When urine volume reaches 200 to 400 mL, the stretching is sufficient to generate sensory impulses that travel to the sacral spinal cord. Motor impulses return along parasympathetic nerves to the detrusor muscle, causing contraction. At the same time, the internal urethral sphincter relaxes. If the external urethral sphincter is voluntarily relaxed, urine flows into the urethra, and the bladder is emptied.

Urination can be prevented by voluntary contraction of the external urethral sphincter. However, if the bladder continues to fill and be stretched, voluntary control is eventually no longer possible.

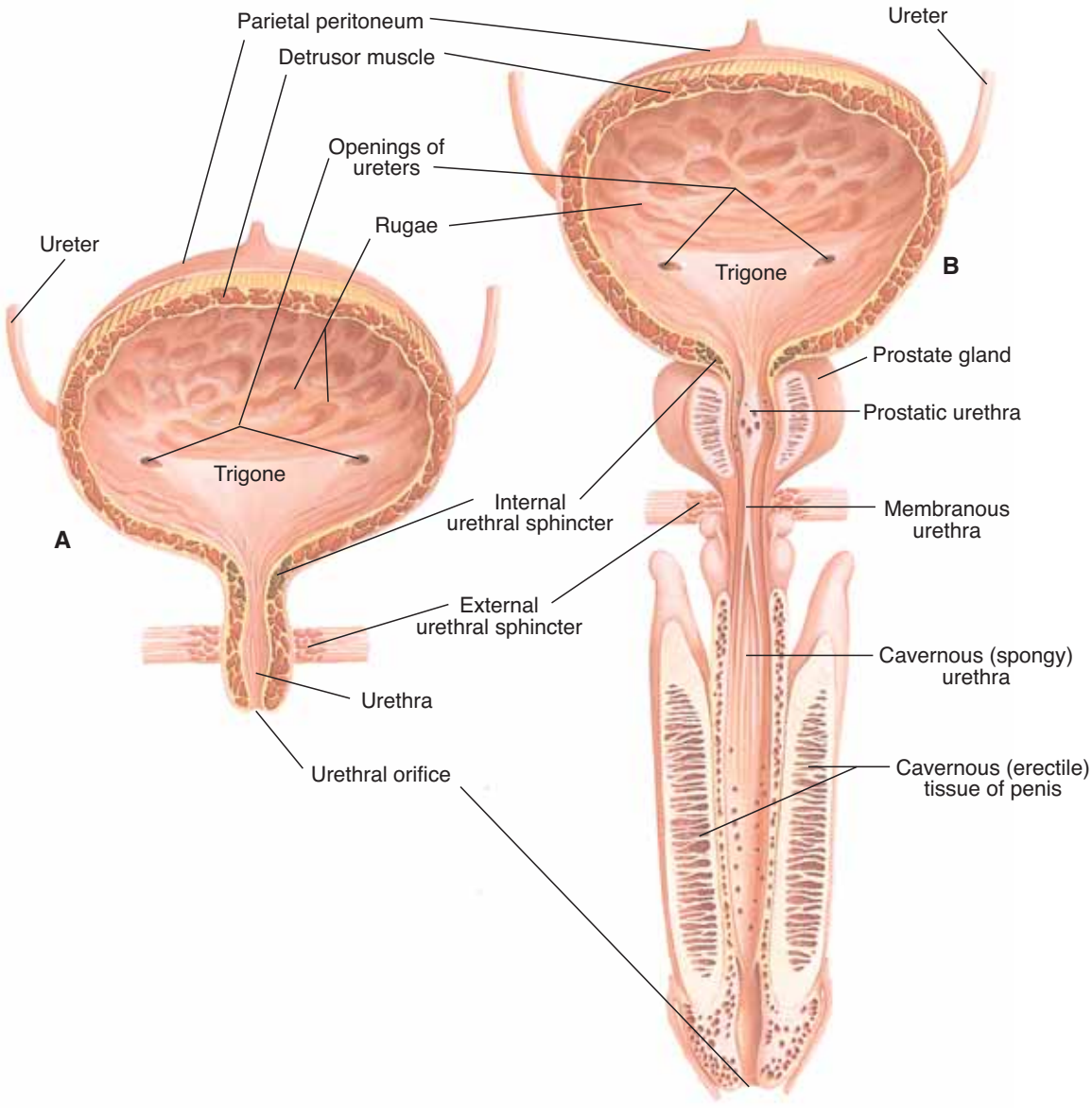


Figure 18–7. (**A**) Frontal section of female urinary bladder and urethra. (**B**) Frontal section of male urinary bladder and urethra.
QUESTION: Name the sphincters of the urinary system and state whether each is voluntary or involuntary.

CHARACTERISTICS OF URINE

The characteristics of urine include the physical and chemical aspects that are often evaluated as part of a urinalysis. Some of these are described in this section, and others are included in Appendix D: Normal Values for Some Commonly Used Urine Tests.

Amount—normal urinary output per 24 hours is 1 to 2 liters. Many factors can significantly change output. Excessive sweating or loss of fluid through

diarrhea will decrease urinary output (**oliguria**) to conserve body water. Excessive fluid intake will increase urinary output (**polyuria**). Consumption of alcohol will also increase output because alcohol inhibits the secretion of ADH, and the kidneys will reabsorb less water.

Color—the typical yellow color of urine (from urochrome, a breakdown product of bile) is often referred to as "straw" or "amber." Concentrated urine is a deeper yellow (amber) than is dilute urine. Freshly voided urine is also clear rather than cloudy.

Specific gravity—the normal range is 1.010 to 1.025; this is a measure of the dissolved materials in urine. The specific gravity of distilled water is 1.000, meaning that there are no solutes present. Therefore, the higher the specific gravity number, the more dissolved material is present. Someone who has been exercising strenuously and has lost body water in sweat will usually produce less urine, which will be more concentrated and have a higher specific gravity.

The specific gravity of the urine is an indicator of the concentrating ability of the kidneys: The kidneys must excrete the waste products that are constantly formed in as little water as possible.

pH—the pH range of urine is between 4.6 and 8.0, with an average value of 6.0. Diet has the greatest influence on urine pH. A vegetarian diet will result in a more alkaline urine, whereas a high-protein diet will result in a more acidic urine.

Constituents—urine is approximately 95% water, which is the solvent for waste products and salts. Salts are not considered true waste products because they may well be utilized by the body when needed, but excess amounts will be excreted in urine (see Box 18–4: Kidney Stones).

Nitrogenous wastes—as their name indicates, all of these wastes contain nitrogen. Urea is formed by liver cells when excess amino acids are deaminated to be used for energy production. Creatinine comes from the metabolism of creatine phosphate, an energy source in muscles. Uric acid comes from the metabolism of nucleic acids, that is, the breakdown of DNA and RNA. Although these are waste products, there is always a certain amount of each in the blood. Box 18–5: Blood Tests and Kidney Function describes the relationship between blood levels of these waste products and kidney function.

Other non-nitrogenous waste products include small amounts of urobilin from the hemoglobin of old RBCs (see Fig. 11–4), and may include the metabolic products of medications. Table 18–3 summarizes the characteristics of urine.

When a substance not normally found in urine does appear there, there is a reason for it. The reason may be quite specific or more general. Table 18–4 lists some abnormal constituents of urine and possible reasons for each (see also Box 18–6: Urinary Tract Infections).

AGING AND THE URINARY SYSTEM

With age, the number of nephrons in the kidneys decreases, often to half the original number by the age of 70 to 80, and the kidneys lose some of their con-

Box 18–4 KIDNEY STONES

Kidney stones, or **renal calculi**, are crystals of the salts that are normally present in urine. A very high concentration of salts in urine may trigger precipitation of the salt and formation of crystals, which can range in size from microscopic to 10 to 20 mm in diameter. The most common type of kidney stone is made of calcium salts; a less common type is made of uric acid.

Kidney stones are most likely to form in the renal pelvis. Predisposing factors include decreased fluid intake or overingestion of minerals (as in mineral supplements), both of which lead to the formation of a very concentrated urine.

The entry of a kidney stone into a ureter may cause intense pain (renal colic) and bleeding. Obstruction of a ureter by a stone may cause backup of urine and possible kidney damage. Treatments include surgery to remove the stone, or lithotripsy, the use of shock waves to crush the stone into pieces small enough to be eliminated without damage to the urinary tract. A recent study links lithotripsy with an increased risk of diabetes or hypertension later in life, though the mechanisms that would bring about these conditions have not yet been discovered.

Box 18–5 BLOOD TESTS AND KIDNEY FUNCTION

Waste products are normally present in the blood, and the concentration of each varies within a normal range. As part of the standard lab work called blood chemistry, the levels of the three nitrogenous waste products are determined (urea, creatinine, and uric acid).

If blood levels of these three substances are within normal ranges, it may be concluded that the kidneys are excreting these wastes at normal rates. If, however, these blood levels are elevated, one possible cause is that kidney function has been impaired. Of the three, the creatinine level is probably the most reliable indicator of kidney functioning. Blood urea nitrogen (BUN) may vary considerably in certain situations not directly related to the kidneys. For example, BUN may be elevated as a consequence of a high-protein diet or of starvation when body protein is being broken down at a faster rate than normal. Uric acid levels may also vary according to diet. However, elevated blood levels of all three nitrogenous wastes usually indicate impaired glomerular filtration.

Table 18–3 CHARACTERISTICS OF NORMAL URINE

Characteristic	Description
Amount	1–2 liters per 24 hours; highly variable depending on fluid intake and water loss through the skin and GI tract
Color	Straw or amber; darker means more concentrated; should be clear, not cloudy
Specific gravity	1.010–1.025; a measure of the dissolved material in urine; the lower the value, the more dilute the urine
pH	Average 6; range 4.6–8.0; diet has the greatest effect on urine pH
Composition	95% water; 5% salts and waste products
Nitrogenous wastes	Urea—from amino acid metabolism Creatinine—from muscle metabolism Uric acid—from nucleic acid metabolism

Table 18–4 ABNORMAL CONSTITUENTS IN URINE

Characteristic	Reason(s)
Glycosuria (presence of glucose)	As long as blood glucose levels are within normal limits, filtrate levels will also be normal and will not exceed the threshold level for reabsorption. In an untreated diabetic, for example, blood glucose is too high; therefore the filtrate glucose level is too high. The kidneys reabsorb glucose up to their threshold level, but the excess remains in the filtrate and is excreted in urine.
Proteinuria (presence of protein)	Most plasma proteins are too large to be forced out of the glomeruli, and the small proteins that enter the filtrate are reabsorbed by pinocytosis. The presence of protein in the urine indicates that the glomeruli have become too permeable, as occurs in some types of kidney disease.
Hematuria (presence of blood—RBCs)	The presence of RBCs in urine may also indicate that the glomeruli have become too permeable. Another possible cause might be bleeding somewhere in the urinary tract. Pinpointing the site of bleeding would require specific diagnostic tests.
Bacteriuria (presence of bacteria)	Bacteria give urine a cloudy rather than clear appearance; WBCs may be present also. The presence of bacteria means that there is an infection somewhere in the urinary tract. Further diagnostic tests would be needed to determine the precise location.
Ketonuria (presence of ketones)	Ketones are formed from fats and proteins that are used for energy production. A trace of ketones in urine is normal. Higher levels of ketones indicate an increased use of fats and proteins for energy. This may be the result of malfunctioning carbohydrate metabolism (as in diabetes mellitus) or simply the result of a high-protein diet.

Box 18–6 URINARY TRACT INFECTIONS

Infections may occur anywhere in the urinary tract and are most often caused by the microbial agents of sexually transmitted diseases (see Chapter 20) or by the bacteria that are part of the normal flora of the colon. In women especially, the urinary and anal openings are in close proximity, and colon bacteria on the skin of the perineum may invade the urinary tract. The use of urinary catheters in hospitalized or bedridden patients may also be a factor if sterile technique is not carefully followed.

Cystitis is inflammation of the urinary bladder. Symptoms include frequency of urination, painful voiding, and low back pain. **Nephritis** (or pyelonephritis) is inflammation of the kidneys. Although this may be the result of a systemic bacterial infection, nephritis is a common complication of untreated lower urinary tract infections such as cystitis. Possible symptoms are fever and flank pain (in the area of the kidneys). Untreated nephritis may result in severe damage to nephrons and progress to renal failure.

centrating ability. The glomerular filtration rate also decreases, partly as a consequence of arteriosclerosis and diminished renal blood flow. Despite these changes, excretion of nitrogenous wastes usually remains adequate.

The urinary bladder decreases in size, and the tone of the detrusor muscle decreases. These changes may lead to a need to urinate more frequently. Urinary incontinence (the inability to control voiding) is *not* an inevitable consequence of aging, and can be prevented or minimized. Elderly people are, however, more at risk for infections of the urinary tract, especially if voiding leaves residual urine in the bladder.

SUMMARY

The kidneys are the principal regulators of the internal environment of the body. The composition of all body fluids is either directly or indirectly regulated by the kidneys as they form urine from blood plasma. The kidneys are also of great importance in the regulation of the pH of the body fluids. These topics are the subject of the next chapter.

STUDY OUTLINE

The urinary system consists of two kidneys, two ureters, the urinary bladder, and the urethra.

1. The kidneys form urine to excrete waste products and to regulate the volume, electrolytes, and pH of blood and tissue fluid.
2. The other organs of the system are concerned with elimination of urine.

Kidneys (see Fig. 18–1)

1. Retroperitoneal on either side of the backbone in the upper abdominal cavity; partially protected by the lower rib cage.
2. Adipose tissue and the renal fascia cushion the kidneys and help hold them in place.
3. Hilus—an indentation on the medial side; renal artery enters, renal vein and ureter emerge.

Kidney—internal structure (see Fig. 18–2)

1. Renal cortex—outer tissue layer, made of renal corpuscles and convoluted tubules.
2. Renal medulla (pyramids)—inner tissue layer, made of loops of Henle and collecting tubules.
3. Renal pelvis—a cavity formed by the expanded end of the ureter within the kidney at the hilus; extensions around the papillae of the pyramids are called calyces, which collect urine.

The Nephron—the functional unit of the kidney (see Fig. 18–3); 1 million per kidney

1. Renal corpuscle—consists of a glomerulus surrounded by a Bowman's capsule.
   - Glomerulus—a capillary network between an afferent arteriole and an efferent arteriole.
   - Bowman's capsule—the expanded end of a renal

tubule that encloses the glomerulus; inner layer is made of podocytes, has pores, and is very permeable; contains renal filtrate (potential urine).

2. Renal tubule—consists of the proximal convoluted tubule, loop of Henle, distal convoluted tubule, and collecting tubule. Collecting tubules unite to form papillary ducts that empty urine into the calyces of the renal pelvis.
   - Peritubular capillaries—arise from the efferent arteriole and surround all parts of the renal tubule.

Blood Vessels of the Kidney (see Figs. 18–1, 18–2, and 18–3)

1. Pathway: abdominal aorta → renal artery → small arteries in the kidney → afferent arterioles → glomeruli → efferent arterioles → peritubular capillaries → small veins in the kidney → renal vein → inferior vena cava.
2. Two sets of capillaries provide for two sites of exchanges between the blood and tissues in the process of urine formation.

Formation of Urine (see Fig. 18–4)

1. Glomerular filtration—takes place from the glomerulus to Bowman's capsule. High blood pressure (60 mmHg) in the glomerulus forces plasma, dissolved materials, and small proteins out of the blood and into Bowman's capsule. The fluid is now called filtrate. Filtration is selective only in terms of size; blood cells and large proteins remain in the blood.
2. GFR is 100 to 125 mL per minute. Increased blood flow to the kidney increases GFR; decreased blood flow decreases GFR.
3. Tubular reabsorption—takes place from the filtrate in the renal tubule to the blood in the peritubular capillaries; 99% of the filtrate is reabsorbed; only 1% becomes urine.
   - Active transport—reabsorption of glucose, amino acids, vitamins, and positive ions; threshold level is a limit to the quantity that can be reabsorbed.
   - Passive transport—most negative ions follow the reabsorption of positive ions.
   - Osmosis—water follows the reabsorption of minerals, especially sodium.
   - Pinocytosis—small proteins are engulfed by proximal tubule cells.
4. Tubular secretion—takes place from the blood in the peritubular capillaries to the filtrate in the renal tubule; creatinine and other waste products may be secreted into the filtrate to be excreted in urine; secretion of H^+ ions helps maintain pH of blood.
5. Hormones that affect reabsorption—aldosterone, atrial natriuretic peptide, antidiuretic hormone, and parathyroid hormone—see Table 18–1 and Fig. 18–5.

The Kidneys and Acid–Base Balance

1. The kidneys have the greatest capacity to compensate for normal and abnormal pH changes.
2. If the body fluids are becoming too acidic, the kidneys excrete H^+ ions and return HCO_3^- ions to the blood (see Fig. 18–6).
3. If the body fluids are becoming too alkaline, the kidneys return H^+ ions to the blood and excrete HCO_3^- ions.

Other Functions of the Kidneys

1. Secretion of renin by juxtaglomerular cells when blood pressure decreases (see Table 18–2). Angiotensin II causes vasoconstriction and increases secretion of aldosterone.
2. Secretion of erythropoietin in response to hypoxia; stimulates red bone marrow to increase rate of RBC production.
3. Activation of vitamin D—conversion of inactive forms to the active form.

Elimination of Urine—the function of the ureters, urinary bladder, and urethra

Ureters (see Figs. 18–1 and 18–7)

1. Each extends from the hilus of a kidney to the lower posterior side of the urinary bladder.
2. Peristalsis of smooth muscle layer propels urine toward bladder.

Urinary Bladder (see Figs. 18–1 and 18–7)

1. A muscular sac below the peritoneum and behind the pubic bones; in women, below the uterus; in men, above the prostate gland.
2. Mucosa—transitional epithelial tissue folded into rugae; permit expansion without tearing.
3. Trigone—triangular area on bladder floor; no rugae, does not expand; bounded by openings of ureters and urethra.

K M C

4. Detrusor muscle—the smooth muscle layer, a spherical muscle; contracts to expel urine (reflex).
5. Internal urethral sphincter—involuntary; formed by detrusor muscle fibers around the opening of the urethra.

Urethra—takes urine from the bladder to the exterior (see Fig. 18–7)

1. In women—1 to 1.5 inches long; anterior to vagina.
2. In men—7 to 8 inches long; passes through the prostate gland and penis.
3. Has the external urethral sphincter: skeletal muscle of pelvic floor (voluntary).

The Urination Reflex—also called micturition or voiding

1. Stimulus: stretching of the detrusor muscle by accumulating urine.
2. Sensory impulses to spinal cord, motor impulses (parasympathetic) return to detrusor muscle, which contracts; internal urethral sphincter relaxes.
3. The external urethral sphincter provides voluntary control.

Characteristics of Urine (see Table 18–3)

Abnormal Constituents of Urine (see Table 18–4)

REVIEW QUESTIONS

1. Describe the location of the kidneys, ureters, urinary bladder, and urethra. (pp. 421, 431)
2. Name the three areas of the kidney, and state what each consists of. (p. 421)
3. Name the two major parts of a nephron. State the general function of nephrons. (p. 421)
4. Name the parts of a renal corpuscle. What process takes place here? Name the parts of a renal tubule. What processes take place here? (pp. 421, 424)
5. State the mechanism of tubular reabsorption of each of the following: (pp. 425, 427)
   a. Water
   b. Glucose
   c. Small proteins
   d. Positive ions
   e. Negative ions
   f. Amino acids
   g. Vitamins

   Also explain what is meant by a threshold level of reabsorption.
6. Explain the importance of tubular secretion. (p. 427)
7. Describe the pathway of blood flow through the kidney from the abdominal aorta to the inferior vena cava. (p. 424)
8. Name the two sets of capillaries in the kidney, and state the processes that take place in each. (pp. 424, 425)
9. Name the hormone that has each of these effects on the kidneys: (pp. 428–429)
   a. Promotes reabsorption of Na^+ ions
   b. Promotes direct reabsorption of water
   c. Promotes reabsorption of Ca^{+2} ions
   d. Promotes excretion of K^+ ions
   e. Decreases reabsorption of Na^+ ions
10. In what circumstances will the kidneys excrete H^+ ions? What ions will be returned to the blood? How will this affect the pH of blood? (p. 428)
11. In what circumstances do the kidneys secrete renin, and what is its purpose? (p. 429)
12. In what circumstances do the kidneys secrete erythropoietin, and what is its purpose? (p. 430)
13. Describe the function of the ureters and that of the urethra. (p. 431)
14. With respect to the urinary bladder, describe the function of rugae and the detrusor muscle. (p. 431)
15. Describe the urination reflex in terms of stimulus, part of the CNS involved, effector muscle, internal urethral sphincter, and voluntary control. (pp. 431)
16. Describe the characteristics of normal urine in terms of appearance, amount, pH, specific gravity, and composition. (pp. 432–433)
17. State the source of each of the nitrogenous waste products: creatinine, uric acid, and urea. (p. 433)

FOR FURTHER THOUGHT

1. The functioning of the kidneys may be likened to cleaning your room by throwing everything out the window, then going outside to retrieve what you wish to keep, such as jammies and slippers. Imagine the contents of a room, liken them to the materials in the blood (you yourself are a kidney), and describe what happens to each, and why.
2. Explain why fatty acids are not found in urine. Under what circumstances are water-soluble vitamins (such as vitamin C) found in urine?
3. Explain how a spinal cord transection at the level of T11 will affect the urination reflex.
4. As part of his yearly physical for the college football team, 20-year-old Patrick has a urinalysis, which shows a high level of ketones. He is not diabetic, and is not ill. What might cause the high urine level of ketones? What blood chemistry test (for nitrogenous wastes) would help confirm this?
5. A patient being evaluated for food poisoning has a blood pH of 7.33, a urine pH of 4.5, and a respiratory rate of 28 per minute. What kind of pH imbalance is this? Explain your reasoning step by step.
6. Erythropoietin, called EPO, has become a drug used illegally by some athletes. Which athletes use EPO, that is, in what kind of sports? What benefits are they hoping for? What part of a CBC would indicate that an athlete is taking EPO? Explain.
7. After a 4-hour workout on a hot June day, the high school track coach tells her group to keep drinking plenty of water. The girls assure their coach that they will know just how to determine if they are sufficiently hydrated that evening, that they have their color scheme memorized. What do they mean?