

# 4 Tissues

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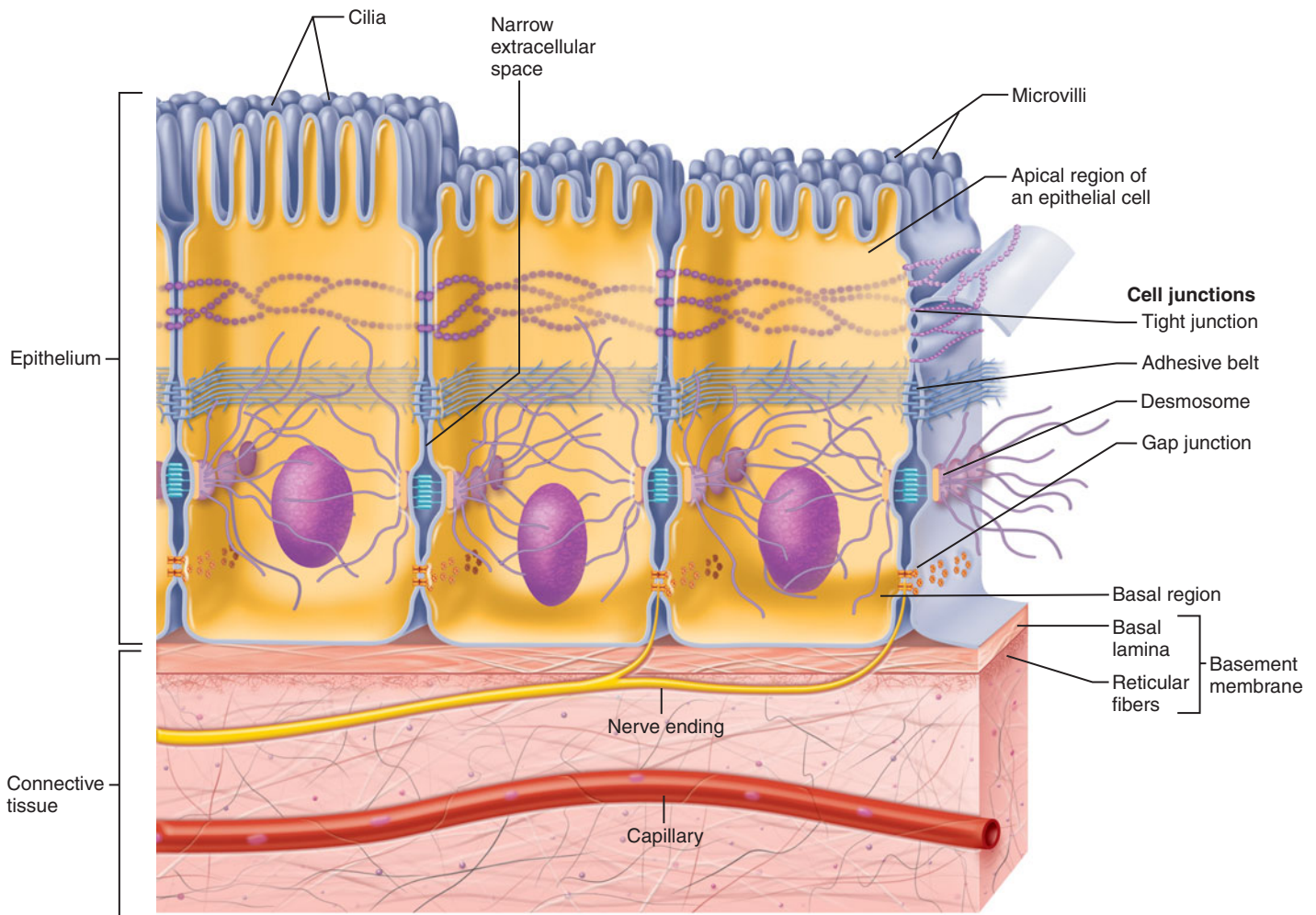
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## The Tissues Throughout Life 95

**T**he cells of the human body do not operate independently of one another. Instead, related cells live and work together in cell communities called **tissues**. A tissue is defined as *a group of cells of similar structure that perform a common function*. However, tissues do not consist entirely of cells: Between the cells is a nonliving material, the *extracellular matrix*.

The word *tissue* derives from the Old French word meaning “to weave,” reflecting the fact that the different tissues are woven together to form the “fabric” of the human body. The four basic types of tissue are **epithelium**, **connective tissue**, **muscle tissue**, and





**FIGURE 4.1 Special characteristics of epithelium.** A sheet of closely joined epithelial cells rests on connective tissue proper. Epithelia contain nerve endings but no blood vessels. Note the special features on the epithelial cell surfaces: cilia, microvilli, cell junctions, and basal lamina.

**nervous tissue.** If a single, broad functional term were assigned to each basic tissue, the terms would be *covering* (epithelium), *support* (connective), *movement* (muscle), and *control* (nervous). However, these terms reflect only a fraction of the functions that each tissue performs.

Tissues are the building blocks of the body's organs. Because most organs contain all four tissue types, learning about the structure and functions of tissues will provide a strong foundation for your understanding of the structure and functions of the organs discussed in the remaining chapters of this book.

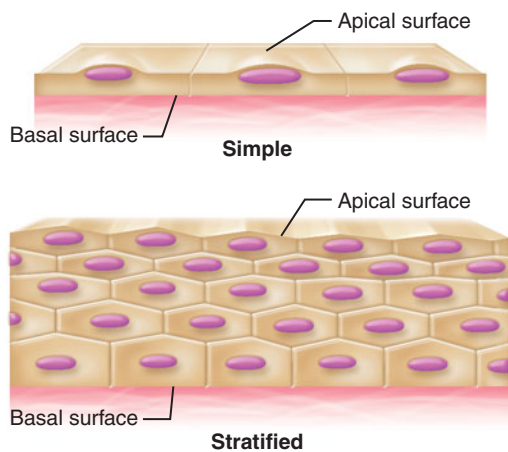
## I. EPITHELIA

- List several functional and structural characteristics of epithelial tissue.
- Classify the different epithelia of the body based on the number of cell layers and the shape of the cells.
- Define exocrine and endocrine glands.
- Explain how multicellular exocrine glands are classified.

An **epithelium** (ep"i-the'le-um; "covering") is a sheet of cells that covers a body surface or lines a body cavity (**Figure 4.1**). With minor exceptions, all of the outer and inner surfaces of the body are covered by epithelia. Examples include the outer layer of the skin; the inner lining of all hollow viscera, such as the stomach and respiratory tubes; the lining of the peritoneal cavity; and the lining of all blood vessels. Epithelia also form most of the body's glands.

Epithelia occur at the interfaces between two different environments. The epidermis of the skin, for example, lies between the inside and outside of the body. Therefore, all functions of epithelia reflect their role as interface tissues and boundary layers: New stimuli, including harmful ones, are experienced at body interfaces, so epithelia both *protect* the underlying tissues and contain nerve endings for *sensory reception*. Nearly all substances that are received or given off by the body must pass across an epithelium, so epithelia function in *diffusion* (the movement of molecules down their concentration gradient), *secretion* (the release of molecules from cells), *absorption* (bringing small molecules into the body), and *ion*





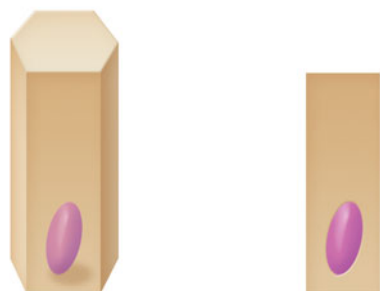
(a) Classification based on number of cell layers



Squamous



Cuboidal



Columnar

(b) Classification based on cell shape

**FIGURE 4.2** Classification of epithelia.

*transport* (moving ions across the interface). Furthermore, body fluids can be *filtered* across thin epithelia, and some epithelia form *slippery surfaces* along which substances move (food glides along the intestinal lining, for example).

## Special Characteristics of Epithelia

Epithelial tissues have many characteristics that distinguish them from other tissue types (Figure 4.1):

1. **Cellularity.** Epithelia are composed almost entirely of cells. These cells are separated by a minimal amount of extracellular material, mainly projections of their integral membrane proteins into the narrow spaces between the cells.

2. **Specialized contacts.** Adjacent epithelial cells are directly joined at many points by special cell junctions.
3. **Polarity.** All epithelia have a free upper (apical) surface and a lower (basal) surface. They exhibit polarity, a term meaning that the cell regions near the apical surface differ from those near the basal surface. As shown in Figure 4.1, the basal surface of an epithelium lies on a thin sheet called a *basal lamina*, which is part of a *basement membrane*. This is explained further on p. 76. The free apical surface abuts the open space of a cavity, tubule, gland, or hollow organ.
4. **Support by connective tissue.** All epithelial sheets in the body are supported by an underlying layer of connective tissue.
5. **Avascular but innervated.** Whereas most tissues in the body are *vascular* (contain blood vessels), epithelium is *avascular* (a-vas'ku-lar), meaning it lacks blood vessels. Epithelial cells receive their nutrients from capillaries in the underlying connective tissue. Although blood vessels do not penetrate epithelial sheets, nerve endings do; that is, epithelium is *innervated*.
6. **Regeneration.** Epithelial tissue has a high regenerative capacity. Some epithelia are exposed to friction, and their surface cells rub off. Others are destroyed by hostile substances in the external environment such as bacteria, acids, and smoke. As long as epithelial cells receive adequate nutrition, they can replace lost cells quickly by cell division.

## Classification of Epithelia

Many kinds of epithelia exist in the body. To classify them, each epithelium is given two names. The first name indicates the number of cell layers in the epithelium, and the last name describes the shape of the cells (Figure 4.2). In classification by cell layers, an epithelium is called **simple** if it has just one cell layer or **stratified** if it has more than one layer. In classification by cell shape, the cells are called squamous, cuboidal, or columnar. **Squamous** (sqwa'mus; "platelike") cells are flat cells; **cuboidal** cells are shaped like cubes; and **columnar** cells are taller than they are wide, like columns. In each case, the shape of the nucleus conforms to that of the cell: The nucleus of a squamous cell is disc-shaped, that of a cuboidal cell is spherical, and that of a columnar cell is an oval elongated from top to bottom. The shape of the nucleus is an important feature to keep in mind when distinguishing epithelial types.

Simple epithelia are easy to classify by cell shape because all cells in the layer usually have the same shape. In stratified epithelia, however, the cell shapes usually differ among the different cell layers. To avoid ambiguity, stratified epithelia are named according to the shape of the cells in the *apical* layer. This naming system will become clearer as you explore the specific epithelial types.

It is useful to keep in mind how tissue structure reflects tissue function (Table 4.1). Stratified epithelial tissues function to protect. Multiple layers of cells protect underlying connective tissues in areas where abrasion is common. For

**TABLE 4.1** Function of Epithelial Tissue Related to Tissue Type

| Cell Shape                             | Number of Layers                                                                  |                                                                           |
|----------------------------------------|-----------------------------------------------------------------------------------|---------------------------------------------------------------------------|
|                                        | One Layer: Simple Epithelial Tissues                                              | More Than One Layer: Stratified Epithelial Tissues                        |
| <b>Squamous</b>                        | Diffusion and filtration<br>Secretion in serous membranes                         | Protection                                                                |
| <b>Cuboidal</b><br><br><b>Columnar</b> | Secretion and absorption;<br>ciliated types propel mucus or<br>reproductive cells | Protection; these tissue types are rare in<br>humans (see pp. 70–71)      |
| <b>Transitional</b>                    |                                                                                   | Protection; stretching to accommodate<br>distension of urinary structures |

simple epithelia, the shape of the cells is indicative of tissue function. Squamous cells are found where diffusion or filtration are important, because these are distance-dependent processes; the thinner the layer, the more quickly the process occurs. Columnar and cuboidal cells are found in tissues involved in secretion and absorption. Larger cells are necessary for the additional cellular machinery needed to produce and package secretions and to produce the necessary energy for these processes. Ciliated epithelia function to propel material, for example, mucus. Keep these generalizations in mind as you study each type of epithelial tissue in detail.

As you read about the types of epithelium, refer to **Figure 4.3**. Using the photomicrographs, try to pick out the individual cells within each epithelium. This is not always easy, because the boundaries between epithelial cells often are indistinct. Furthermore, the nucleus of a particular cell may or may not be visible, depending on the plane of the cut made to prepare the tissue slides. To better understand this, think about slicing a pear in transverse sections; slices from the top of the pear will not contain any seeds, but slices from the middle region will. The same is true for sections through tissues: Some cells may be sliced through the nucleus, whereas others may not.

### Simple Epithelia

**Simple Squamous Epithelium (FIGURE 4.3a)** A simple squamous epithelium is a single layer of flat cells. When viewed from above, the closely fitting cells resemble a tiled floor. When viewed in lateral section, they resemble fried eggs seen from the side. Thin and often permeable, this type of epithelium occurs wherever small molecules pass through a membrane quickly, by processes of diffusion or filtration. The walls of capillaries consist exclusively of this epithelium, whose exceptional thinness encourages efficient exchange of nutrients and wastes between the bloodstream and surrounding tissue cells. In the lungs, this epithelium forms the thin walls of the air sacs, where gas exchange occurs.

**Simple Cuboidal Epithelium (FIGURE 4.3b)** Simple cuboidal epithelium consists of a single layer of cube-shaped cells. This epithelium forms the secretory cells of many glands, the walls of the smallest ducts of glands, and of many tubules in the kidney. Its functions are the same as those of simple columnar epithelium.

**Simple Columnar Epithelium (FIGURE 4.3c)** Simple columnar epithelium is a single layer of tall cells aligned like soldiers in a row. It lines the digestive tube from the stomach to the anal canal. It functions in the active movement of molecules, namely in absorption, secretion, and ion transport. The structure of simple columnar epithelium is ideal for these functions: It is thin enough to allow large numbers of molecules to pass through it quickly, yet thick enough to house the cellular machinery needed to perform the complex processes of molecular transport.

Some simple columnar epithelia bear *cilia* (sil'e-ah; “eyelashes”), whiplike bristles on the apex of epithelial cells that beat rhythmically to move substances across certain body surfaces (see Figure 4.1). A simple ciliated columnar epithelium lines the inside of the uterine tube. Its cilia help move the ovum to the uterus, a journey traced in Chapter 3. Cilia are considered in detail later in this chapter.

**Pseudostratified Columnar Epithelium (FIGURE 4.3d)** The cells of pseudostratified (soo-do-strat'ĭ-fĭd) columnar epithelium are varied in height. All of its cells rest on the basement membrane, but only the tall cells reach the apical surface of the epithelium. The short cells are undifferentiated and continuously give rise to the tall cells. The cell nuclei lie at several different levels, giving the false impression that this epithelium is stratified (*pseudo* = false).

Pseudostratified columnar epithelium, like simple columnar epithelium, functions in secretion or absorption. A ciliated type lines the interior of the respiratory tubes. Here, the cilia propel sheets of dust-trapping mucus out of the lungs.

(Text continues on page 72.)

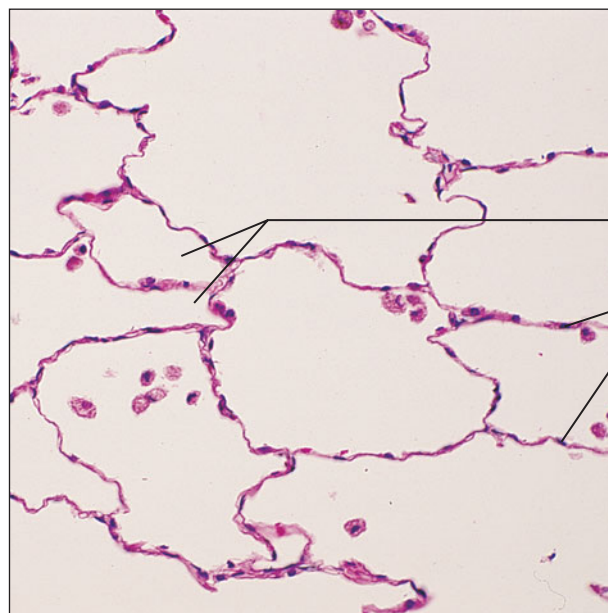
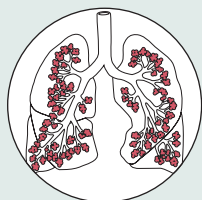
**(a) Simple squamous epithelium**

**Description:** Single layer of flattened cells with disc-shaped central nuclei and sparse cytoplasm; the simplest of the epithelia.



**Function:** Allows passage of materials by diffusion and filtration in sites where protection is not important; secretes lubricating substances in serosae.

**Location:** Kidney glomeruli; air sacs of lungs; lining of heart, blood vessels, and lymphatic vessels; lining of ventral body cavity (serosae).



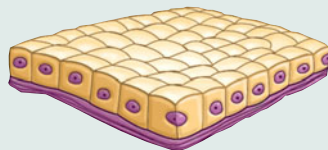
Air sacs of lung tissue

Nuclei of squamous epithelial cells

**Photomicrograph:** Simple squamous epithelium forming part of the alveolar (air sac) walls (200 $\times$ ).

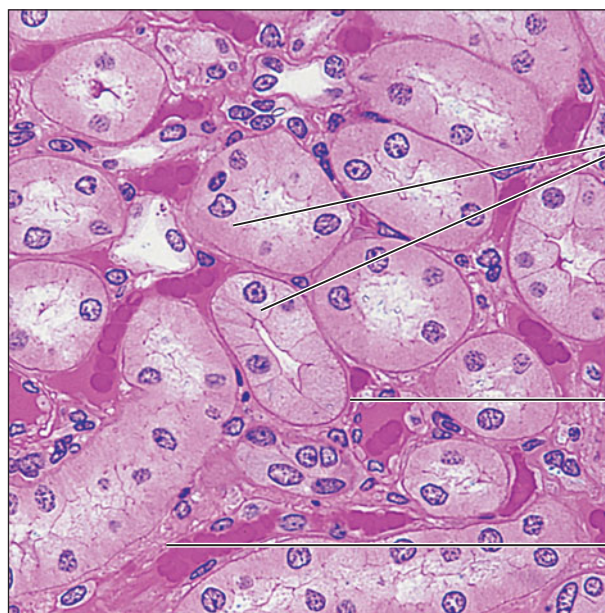
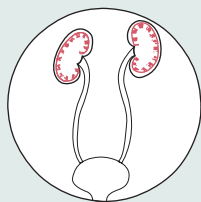
**(b) Simple cuboidal epithelium**

**Description:** Single layer of cubelike cells with large, spherical central nuclei.



**Function:** Secretion and absorption.

**Location:** Kidney tubules; ducts and secretory portions of small glands; ovary surface.



Simple cuboidal epithelial cells

Basement membrane

Connective tissue

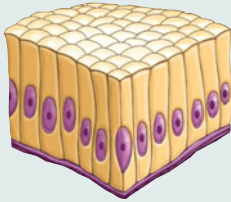
**Photomicrograph:** Simple cuboidal epithelium in kidney tubules (430 $\times$ ).

**FIGURE 4.3 Epithelial tissues.** (See *A Brief Atlas of the Human Body*, Second Edition, Plates 2 and 3.)



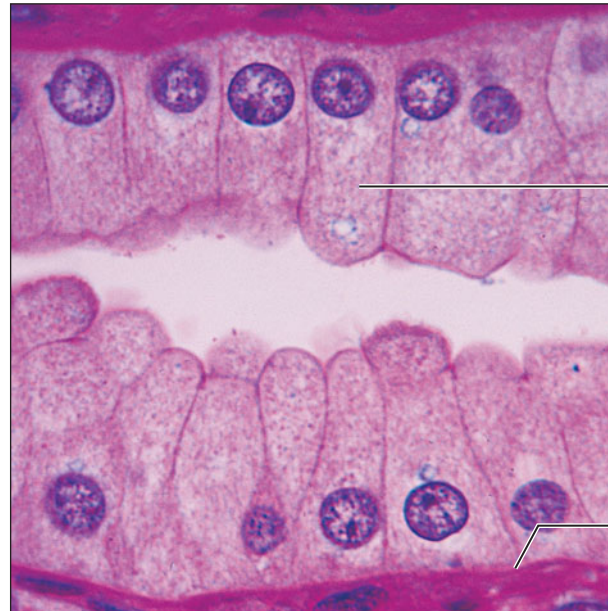
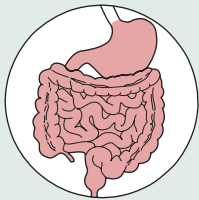
**(c) Simple columnar epithelium**

**Description:** Single layer of tall cells with round to oval nuclei; some cells bear cilia; layer may contain mucus-secreting unicellular glands (goblet cells).



**Function:** Absorption; secretion of mucus, enzymes, and other substances; ciliated type propels mucus (or reproductive cells) by ciliary action.

**Location:** Nonciliated type lines most of the digestive tract (stomach to anal canal), gallbladder, and excretory ducts of some glands; ciliated variety lines small bronchi, uterine tubes, and some regions of the uterus.



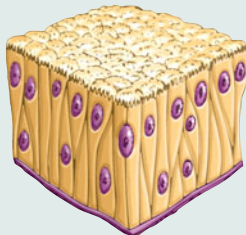
Simple columnar epithelial cell

Basement membrane

**Photomicrograph:** Simple columnar epithelium of the stomach mucosa (1150 $\times$ ).

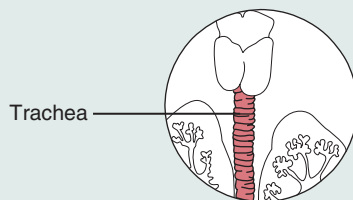
**(d) Pseudostratified columnar epithelium**

**Description:** Single layer of cells of differing heights, some not reaching the free surface; nuclei seen at different levels; may contain mucus-secreting goblet cells and bear cilia.

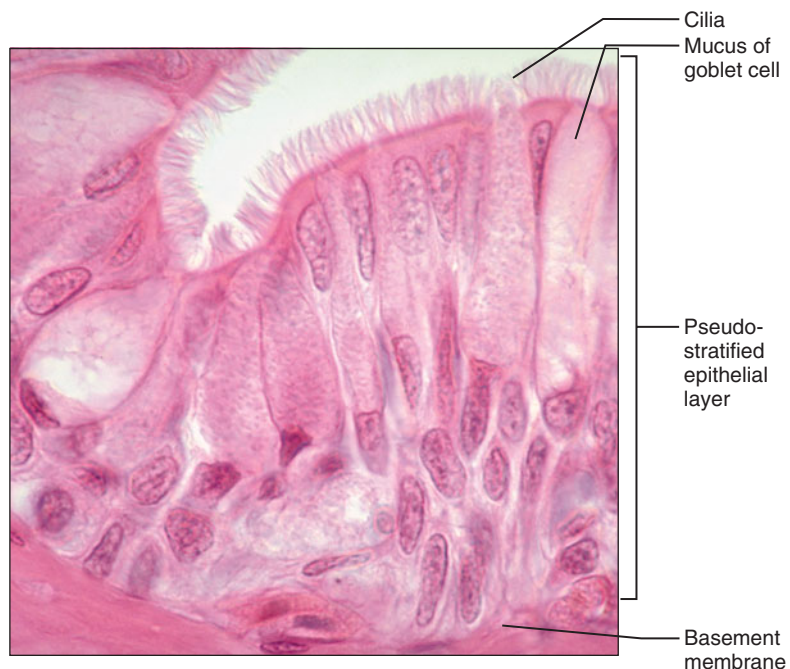


**Function:** Secretion, particularly of mucus; propulsion of mucus by ciliary action.

**Location:** Nonciliated type in male's sperm-carrying ducts and ducts of large glands; ciliated variety lines the trachea, most of the upper respiratory tract.



Trachea



Cilia  
Mucus of goblet cell

Pseudostratified epithelial layer

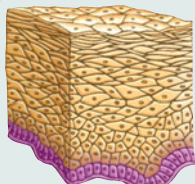
Basement membrane

**Photomicrograph:** Pseudostratified ciliated columnar epithelium lining the human trachea (780 $\times$ ).

**FIGURE 4.3 Epithelial tissues, continued.** (See *A Brief Atlas of the Human Body*, Second Edition, Plates 4–6.)

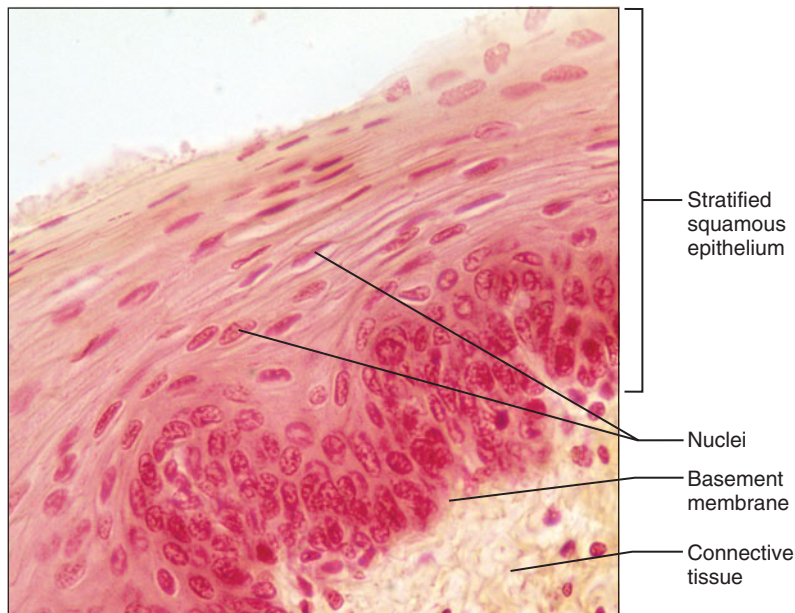
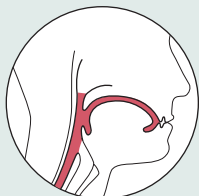
**(e) Stratified squamous epithelium**

**Description:** Thick membrane composed of several cell layers; basal cells are cuboidal or columnar and metabolically active; surface cells are flattened (squamous); in the keratinized type, the surface cells are full of keratin and dead; basal cells are active in mitosis and produce the cells of the more superficial layers.



**Function:** Protects underlying tissues in areas subjected to abrasion.

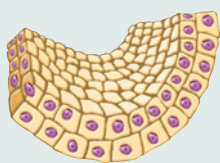
**Location:** Nonkeratinized type forms the moist linings of the esophagus, mouth, and vagina; keratinized variety forms the epidermis of the skin, a dry membrane.



**Photomicrograph:** Stratified squamous epithelium lining the esophagus (430 $\times$ ).

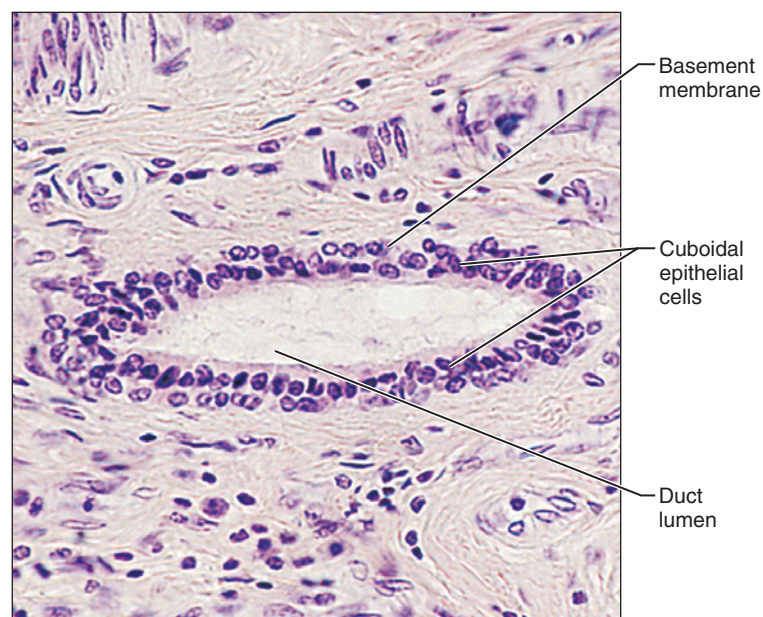
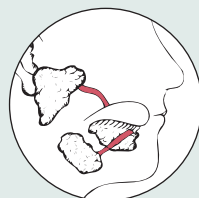
**(f) Stratified cuboidal epithelium**

**Description:** Generally two layers of cubelike cells.



**Function:** Protection

**Location:** Largest ducts of sweat glands, mammary glands, and salivary glands.



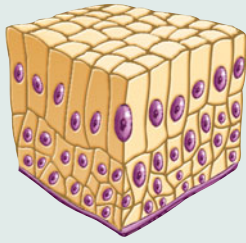
**Photomicrograph:** Stratified cuboidal epithelium forming a salivary gland duct (285 $\times$ ).

**FIGURE 4.3 Epithelial tissues, continued.** (See *A Brief Atlas of the Human Body*, Second Edition, Plates 7 and 8.)



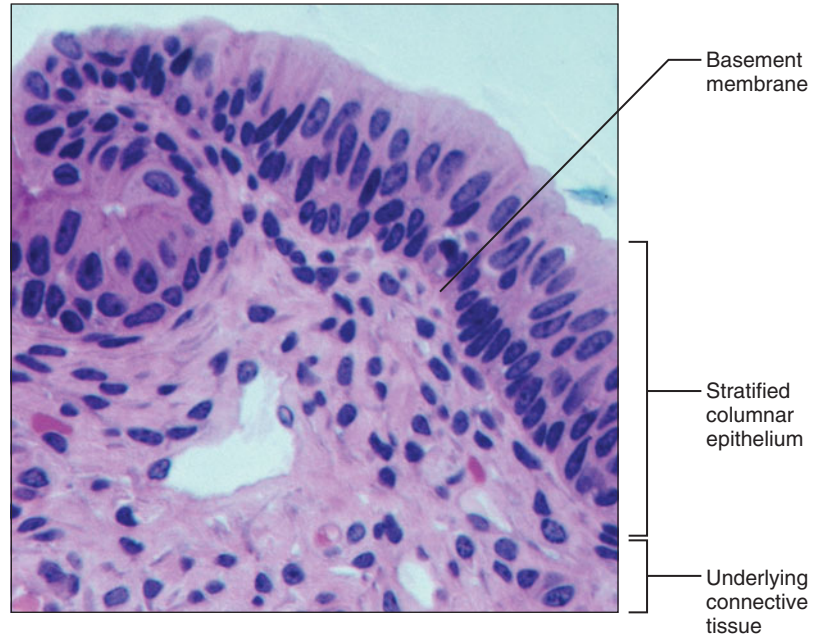
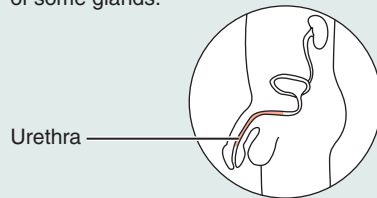
**(g) Stratified columnar epithelium**

**Description:** Several cell layers; basal cells usually cuboidal; superficial cells elongated and columnar.



**Function:** Protection; secretion.

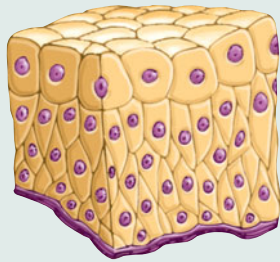
**Location:** Rare in the body; small amounts in male urethra and in large ducts of some glands.



**Photomicrograph:** Stratified columnar epithelium lining of the male urethra (315 $\times$ ).

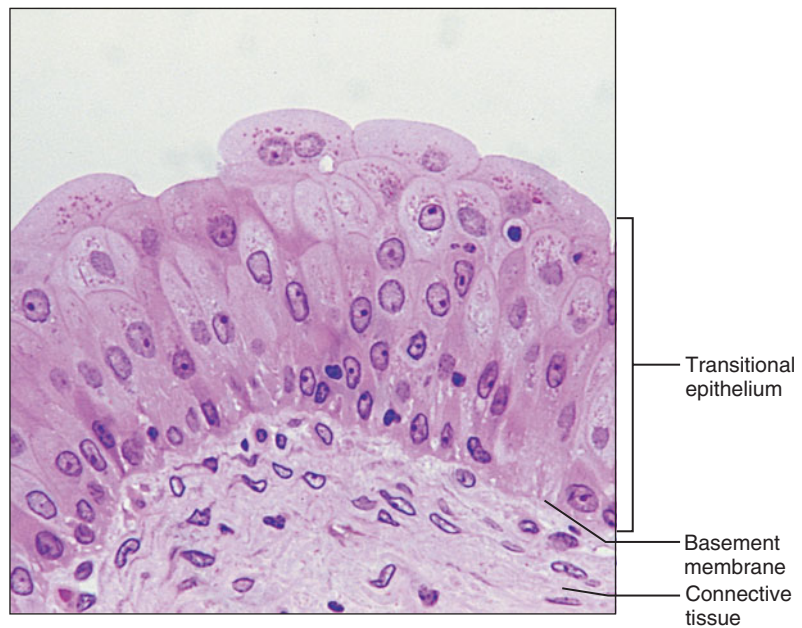
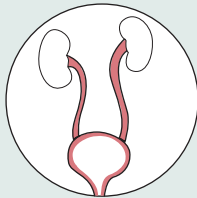
**(h) Transitional epithelium**

**Description:** Resembles both stratified squamous and stratified cuboidal; basal cells cuboidal or columnar; surface cells dome shaped or squamous-like, depending on degree of organ stretch.



**Function:** Stretches readily and permits distension of urinary organ by contained urine.

**Location:** Lines the ureters, bladder, and part of the urethra.



**Photomicrograph:** Transitional epithelium lining the bladder, relaxed state (390 $\times$ ); note the bulbous, or rounded, appearance of the cells at the surface; these cells flatten and become elongated when the bladder is filled with urine.

**FIGURE 4.3 Epithelial tissues, continued.** (See *A Brief Atlas of the Human Body*, Second Edition, Plates 9 and 10.)

Source: Part (g) Kessel and Kardon/Visuals Unlimited.



## Stratified Epithelia

Stratified epithelia contain two or more layers of cells. They regenerate from below; that is, the basal cells divide and push apically to replace the older surface cells. Stratified epithelia are more durable than simple epithelia, and their major (but not only) role is protection.

**Stratified Squamous Epithelium (FIGURE 4.3e)** As you might expect, stratified squamous epithelium consists of many cell layers whose surface cells are squamous. In the deeper layers, the cells are cuboidal or columnar. Of all the epithelial types, this is the thickest and best adapted for protection. It covers the often-abraded surfaces of our body, forming the epidermis of the skin and the inner lining of the mouth, esophagus, and vagina. To avoid memorizing all its locations, simply remember that this epithelium forms the outermost layer of the skin and extends a certain distance into every body opening that is directly continuous with the skin.

The epidermis of the skin is *keratinized*, meaning that its surface cells contain an especially tough protective protein called *keratin*. The other stratified squamous epithelia of the body lack keratin and are *nonkeratinized*. Keratin is explained in detail in Chapter 5 (p. 103).

**Stratified Cuboidal and Columnar Epithelia (FIGURE 4.3f AND g)** Stratified cuboidal and stratified columnar epithelia are rare types of tissue, located in the large ducts of some glands, for example sweat glands, mammary glands, and salivary glands. Stratified columnar epithelium is also found in small amounts in the male urethra.

**Transitional Epithelium (FIGURE 4.3h)** Transitional epithelium lines the inside of the hollow urinary organs. Such organs (the urinary bladder, for example) stretch as they fill with urine. As the transitional epithelium stretches, it thins from about six cell layers to three, and its apical cells unfold and flatten. When relaxed, portions of the apical surface invaginate into the cell, giving this surface a scalloped appearance. Thus, this epithelium undergoes “transitions” in shape. It also forms an impermeable barrier that keeps urine from passing through the wall of the bladder.

## check your understanding

1. In each of the epithelial tissues shown in Figure 4.3a–h, identify the apical region of the tissue.
2. Why are cuboidal or columnar cells found in epithelia that function in secretion and absorption? List three locations of cuboidal epithelium.
3. Why is columnar epithelium *not* found in locations where diffusion occurs? What type of epithelium is found in these locations?

For answers, see Appendix B.

## Glands

Epithelial cells that make and secrete a product form **glands**. The products of glands are aqueous (water-based) fluids that

usually contain proteins. *Secretion* is the process whereby gland cells obtain needed substances from the blood and transform them chemically into a product that is then discharged from the cell. More specifically, the protein product is made in the rough endoplasmic reticulum (ER), then packaged into secretory granules by the Golgi apparatus and ultimately released from the cell by exocytosis (see p. 28 and Figure 2.8). These organelles are well developed in most gland cells that secrete proteins.

Glands are classified as **endocrine** (en'do-krin; “internal secretion”) or **exocrine** (ek'so-krin; “external secretion”), depending on where they release their product, and as **unicellular** (“one-celled”) or **multicellular** (“many-celled”) on the basis of cell number. Unicellular glands are scattered within epithelial sheets, whereas most multicellular glands develop by invagination of an epithelial sheet into the underlying connective tissue.

### Endocrine Glands

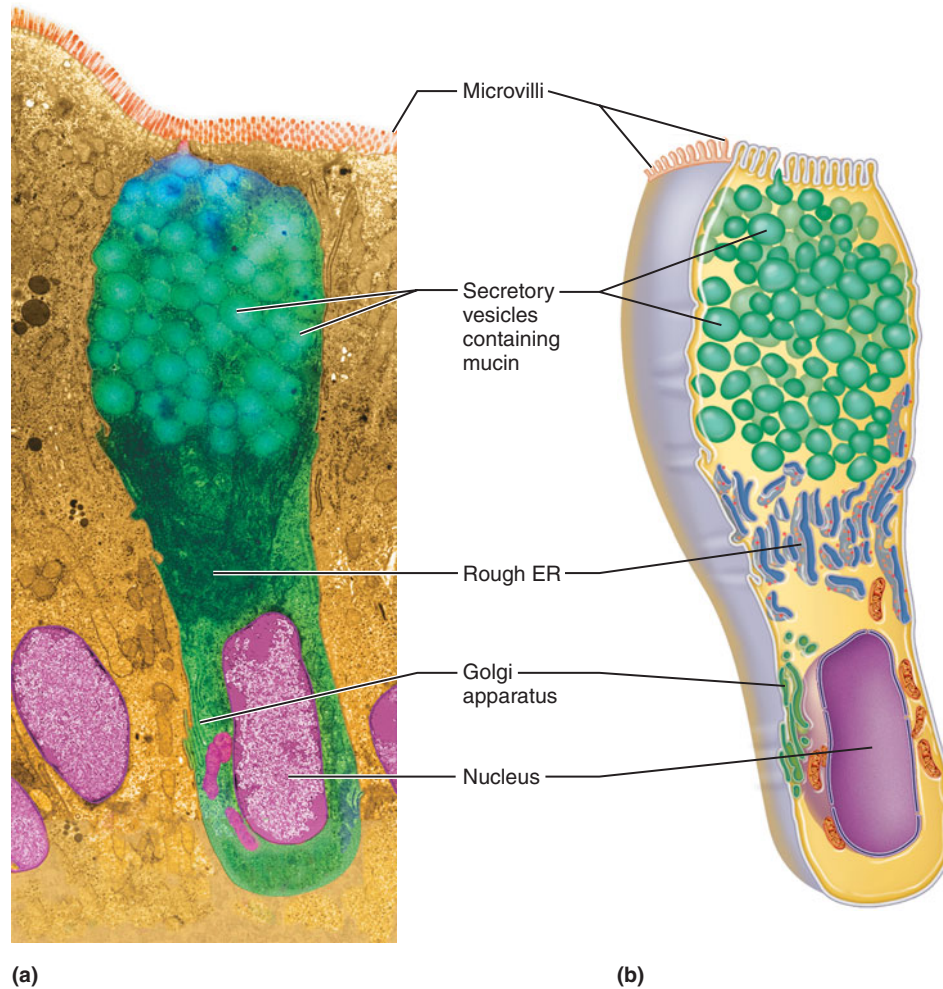
Endocrine glands lack ducts, so they are often referred to as *ductless glands*. They secrete directly into the tissue fluid that surrounds them. More specifically, endocrine glands produce messenger molecules called **hormones** (hor'mōnz; “exciters”), which they release into the extracellular space. These hormones then enter nearby capillaries and travel through the bloodstream to specific *target organs*, which are commonly far removed from the endocrine gland that produces the hormone. Each hormone signals its target organs to respond in some characteristic way. For example, endocrine cells in the intestine secrete a hormone that signals for the pancreas to release the enzymes that help digest a meal.

Although most endocrine glands derive from epithelia, some derive from other tissues. The endocrine system is discussed in detail in Chapter 17.

### Exocrine Glands

Exocrine glands are numerous, and many of their products are familiar ones. All exocrine glands secrete their products onto body surfaces (skin) or into body cavities (like the digestive tube), and multicellular exocrine glands have **ducts** that carry their product to the epithelial surfaces. The activity of an exocrine secretion is local, that is, the secretion acts near the area where it is released. Exocrine glands are a diverse group: They include many types of mucus-secreting glands, the sweat glands and oil glands of the skin, salivary glands of the mouth, the liver (which secretes bile), the pancreas (which secretes digestive enzymes), mammary glands (which secrete milk), and many others.

**Unicellular Exocrine Glands** The only important example of a one-celled exocrine gland is the **goblet cell** (Figure 4.4). True to its name, a goblet cell is indeed shaped like a goblet, a drinking glass with a stem. Goblet cells are scattered within the epithelial lining of the intestines and respiratory tubes, between columnar cells with other functions. They produce **mucin** (mu'sin), a glycoprotein (sugar protein)



**FIGURE 4.4 Goblet cell (unicellular exocrine gland).** (a) Photomicrograph of a mucus-secreting goblet cell in the simple columnar epithelium that lines the small intestine (1585 $\times$ ). (b) Diagram of a goblet cell. Note the secretory vesicles and the well-developed rough ER and Golgi apparatus.

that dissolves in water when secreted. The resulting complex of mucin and water is viscous, slimy **mucus**. Mucus covers, protects, and lubricates many internal body surfaces.

**Multicellular Exocrine Glands** Each multicellular exocrine gland has two basic parts: an epithelium-walled *duct* and a *secretory unit* consisting of the secretory epithelium (Figure 4.5). Also, in all but the simplest glands, a supportive connective tissue surrounds the secretory unit, carrying with it blood vessels and nerve fibers. Often, the connective tissue forms a *fibrous capsule* that extends into the gland proper and partitions the gland into subdivisions called *lobes* (not illustrated).

Multicellular glands are classified by the structure of their ducts (Figure 4.5). **Simple** glands have an unbranched duct, whereas **compound** glands have a branched duct. The glands are further categorized by their secretory units: They are **tubular** if their secretory cells form tubes and **alveolar** (al-ve' o-lar) if the secretory cells form spherical sacs (*alveolus* =

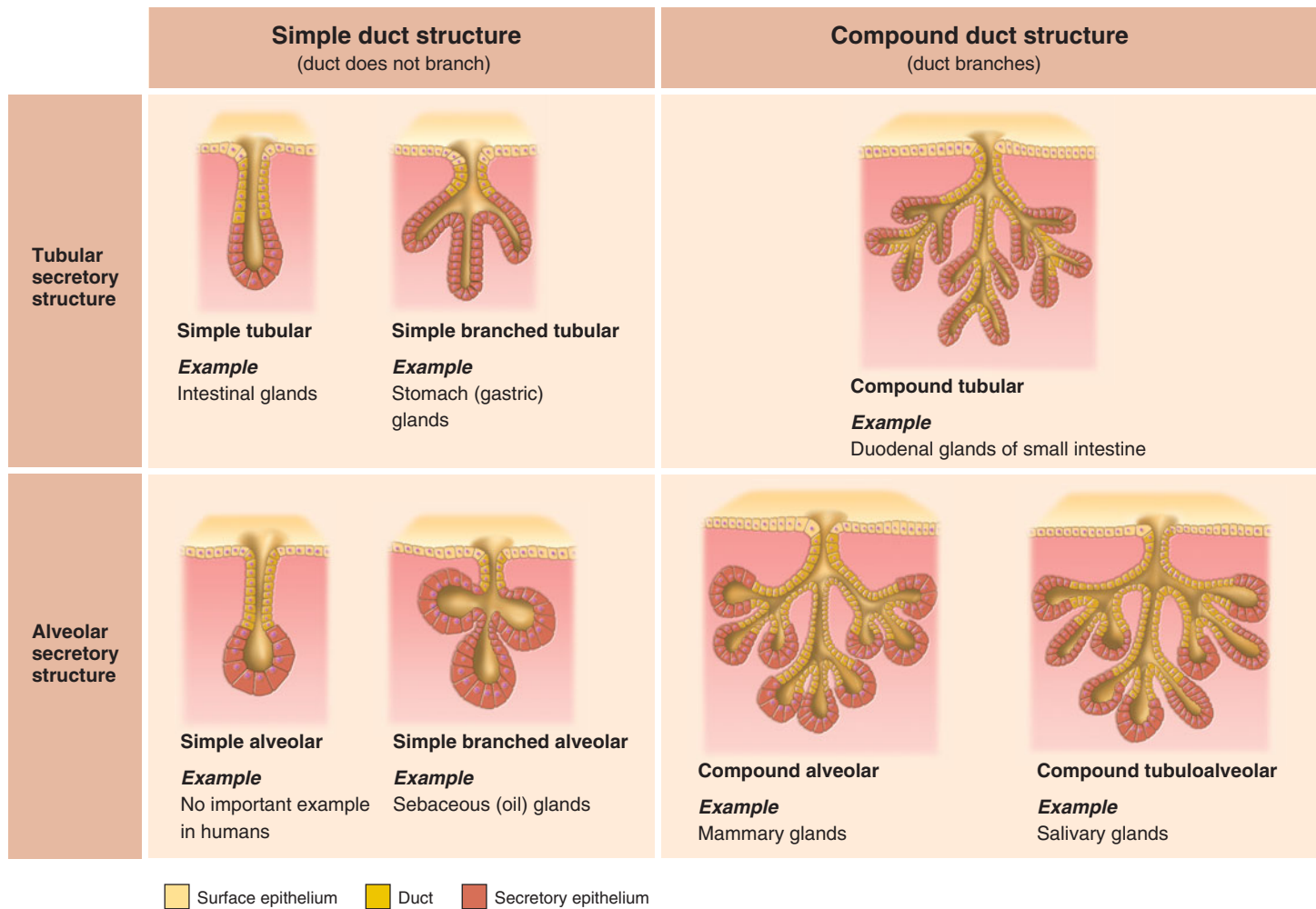
a small, hollow cavity). Furthermore, some glands are **tubuloalveolar**; that is, they contain both tubular and alveolar units. Another word for *alveolar* is *acinar* (as'i-nar; *acinus* = grape or berry).

### check your understanding

4. What type of gland are goblet cells? What do they secrete?
5. An \_\_\_\_\_ gland secretes into the tissue fluid, and its secretion is carried to a target organ by the bloodstream.
6. What feature distinguishes a simple exocrine gland from a compound exocrine gland?

For answers, see Appendix B.





**FIGURE 4.5 Types of multicellular exocrine glands.** Multicellular glands are classified according to the structure of their ducts (simple or compound) and the structure of their secretory units (tubular, alveolar, tubuloalveolar).

## Epithelial Surface Features

- Describe apical, lateral, and basal surface features of epithelia and epithelial cells.

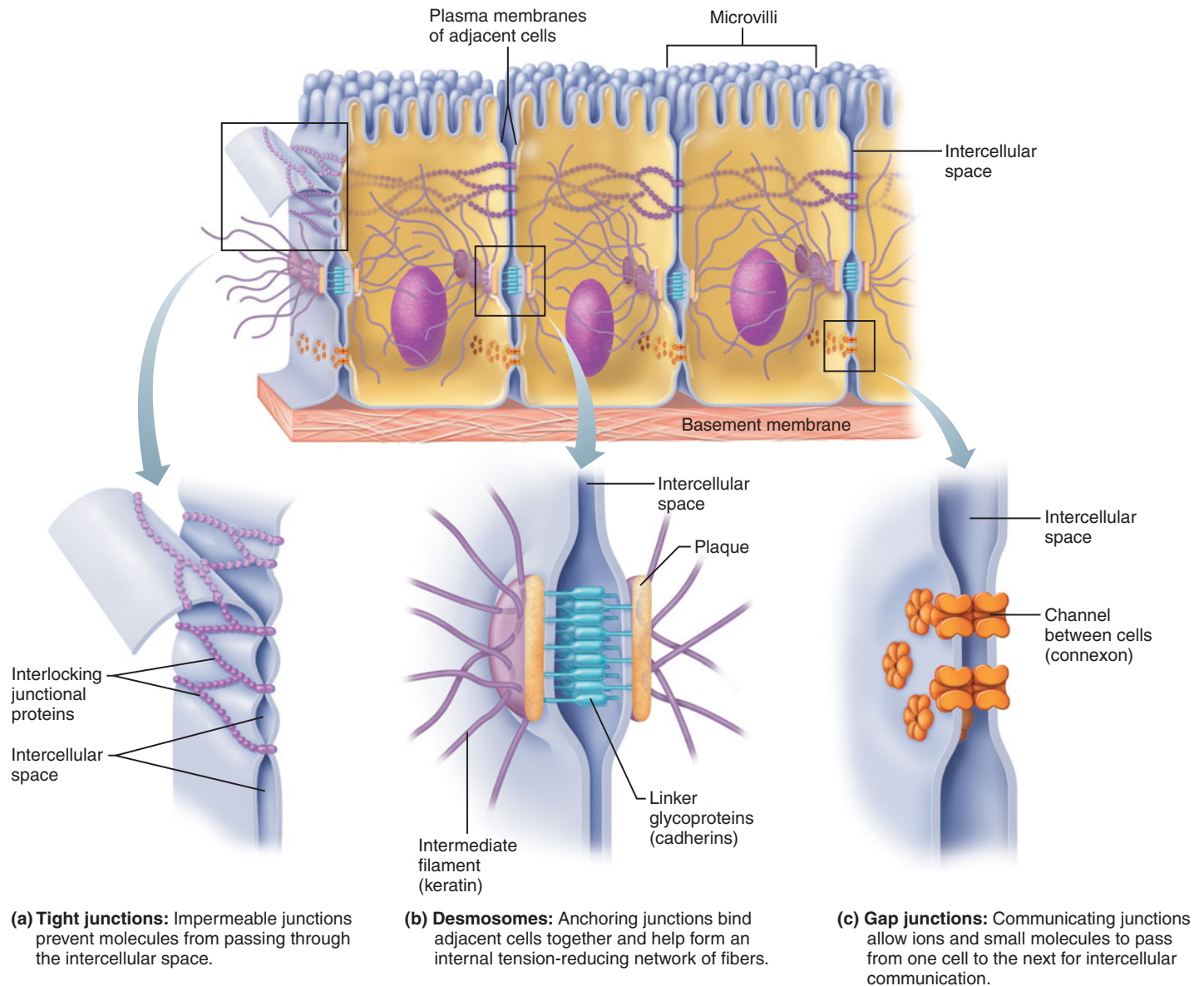
As previously described, epithelial tissues are composed of many cells closely joined together by special cell junctions along their lateral walls. Epithelial tissues also have distinct apical and basal regions. The basal region sits on a specialized boundary with the underlying connective tissue; the apical region of certain epithelia has modifications associated with specific functions. These special features are described next.

### Lateral Surface Features: Cell Junctions

Three factors act to bind epithelial cells to one another: (1) *adhesion proteins* in the plasma membranes of the adjacent cells link together in the narrow extracellular space; (2) the wavy contours of the membranes of adjacent cells join in a tongue-and-groove fashion; and (3) there are special cell junctions (**Figure 4.6**). **Cell junctions**, the most important of the factors, are characteristic of epithelial tissue but are found in other tissue types as well.

**Tight Junctions** In the apical region of most epithelial tissues, a beltlike junction extends around the periphery of each cell (**Figure 4.6a**). This is a **tight junction**, or a *zonula occludens* (zōn'u-lah o-klood'enz; “belt that shuts off”). At tight junctions, the adjacent cells are so close that some proteins in their plasma membranes are fused. This fusion forms a seal that closes off the extracellular space; thus tight junctions prevent molecules from passing between the cells of epithelial tissue. For example, the tight junctions in the epithelium lining the digestive tract keep digestive enzymes, ions, and microorganisms in the intestine from seeping into the bloodstream. Tight junctions need not be entirely impermeable; some are more leaky than others and may let certain types of ions through.

**Adhesive Belt Junctions** Just below the tight junctions in epithelial tissues are **adhesive belt junctions**, or *zonula adherens* (zōn'u-lah ad-hir-ens), a type of anchoring junction (**Figure 4.1**). Transmembrane linker proteins attach to the actin microfilaments of the cytoskeleton and bind adjacent cells. This junction reinforces the tight junctions, particularly



**FIGURE 4.6 Cell junctions.** An epithelial cell shown joined to adjacent cells by three common types of cell junction.

when the tissues are stretched. Together with tight junctions, these form the tight junctional complex around the apical lateral borders of epithelial tissues.

**Desmosomes** The main junctions for binding cells together are called **desmosomes** (dez'mo-sōmz; "binding bodies"), or **anchoring junctions**. These adhesive spots are scattered along the abutting sides of adjacent cells (Figure 4.6b). Desmosomes have a complex structure: On the cytoplasmic face of each plasma membrane is a circular plaque. The plaques of neighboring cells are joined by linker proteins. These project from both cell membranes and interdigitate like the teeth of a zipper in the extracellular space. In addition, intermediate filaments (the cytoskeletal elements that resist tension) insert into each plaque from its inner, cytoplasmic side. Bundles of these filaments extend across the cytoplasm and anchor at other desmosomes on the opposite side of the same cell. Overall, this arrangement not only

holds adjacent cells together but also interconnects intermediate filaments of the entire epithelium into one continuous network of strong guy-wires. The epithelium is thus less likely to tear when pulled on, because the pulling forces are distributed evenly throughout the sheet.

Desmosomes are found in cardiac muscle tissue as well as in epithelial tissues. In general, these junctions are common in tissues that experience great mechanical stress.

**Gap Junctions** A **gap junction**, or *nexus* (nek'sus; "bond"), is a tunnel-like junction that can occur anywhere along the lateral membranes of adjacent cells (Figure 4.6c). Gap junctions function in intercellular communication by allowing small molecules to move directly between neighboring cells. At such junctions, the adjacent plasma membranes are very close, and the cells are connected by hollow cylinders of protein (connexons). Ions, simple sugars, and other small molecules pass through these cylinders from one cell to



the next. Gap junctions are common in embryonic tissues and in many adult tissues, including connective tissues. They are also prevalent in smooth and cardiac muscle, where the passage of ions through gap junctions synchronizes contraction.

### Basal Feature: The Basal Lamina

At the border between the epithelium and the connective tissue deep to it is a supporting sheet called the **basal lamina** (lam'ī-nah; "sheet"), shown in Figure 4.1. This thin, noncellular sheet consists of proteins secreted by the epithelial cells. Functionally, the basal lamina acts as a selective filter; that is, it determines which molecules from capillaries in the underlying connective tissue are allowed to enter the epithelium. The basal lamina also acts as scaffolding along which regenerating epithelial cells can migrate. Luckily, infections and toxins that destroy epithelial cells usually leave the basal lamina in place, for without this lamina, epithelial regeneration is more difficult.

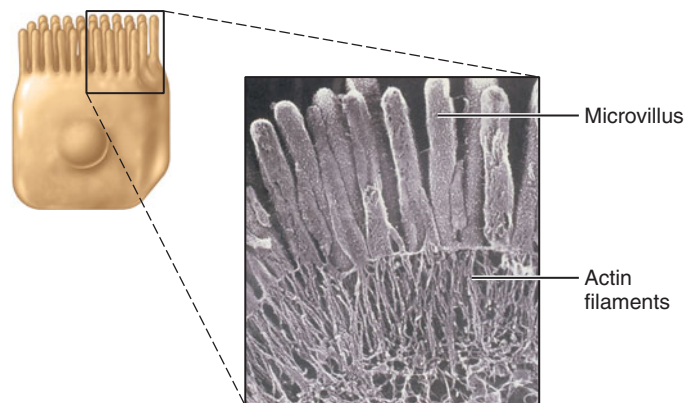
Directly deep to the basal lamina is a layer of reticular fibers (defined shortly) belonging to the underlying connective tissue. Together, these reticular fibers plus the basal lamina form the **basement membrane** (see Figure 4.1). The thin basal lamina can be seen only by electron microscopy, but the thicker basement membrane is visible by light microscopy (see Figure 4.3). Although this text distinguishes between *basal lamina* and *basement membrane*, many scientists use these two terms interchangeably.

**BASEMENT MEMBRANES AND DIABETES** In untreated cases of diabetes mellitus, the basement membranes associated with the endothelium of capillaries thicken over time, perhaps because they take on sugar (glucose), which is present in high concentrations in diabetics. Thickening is especially evident in the capillaries in the kidneys and retina of the eye, which can become nonfunctional. For this reason, kidney failure and blindness are major symptoms of advanced diabetes.



### Apical Surface Features: Microvilli and Cilia

**Microvilli** (mi"cro-vī'li; "little shaggy hairs") are fingerlike extensions of the plasma membrane of apical epithelial cells (Figure 4.7). Each microvillus contains a core of actin filaments that extend into the actin microfilaments of the cytoskeleton and function to stiffen the microvillus. Microvilli occur on almost every moist epithelium in the body but are longest and most abundant on epithelia that absorb nutrients (in the small intestine) or transport ions (in the kidney). In such epithelia, microvilli maximize the surface area across which small molecules enter or leave cells. Microvilli are also abundant on epithelia that secrete mucus, where they help anchor the mucous sheets to the epithelial surface.



**FIGURE 4.7 Microvilli.**

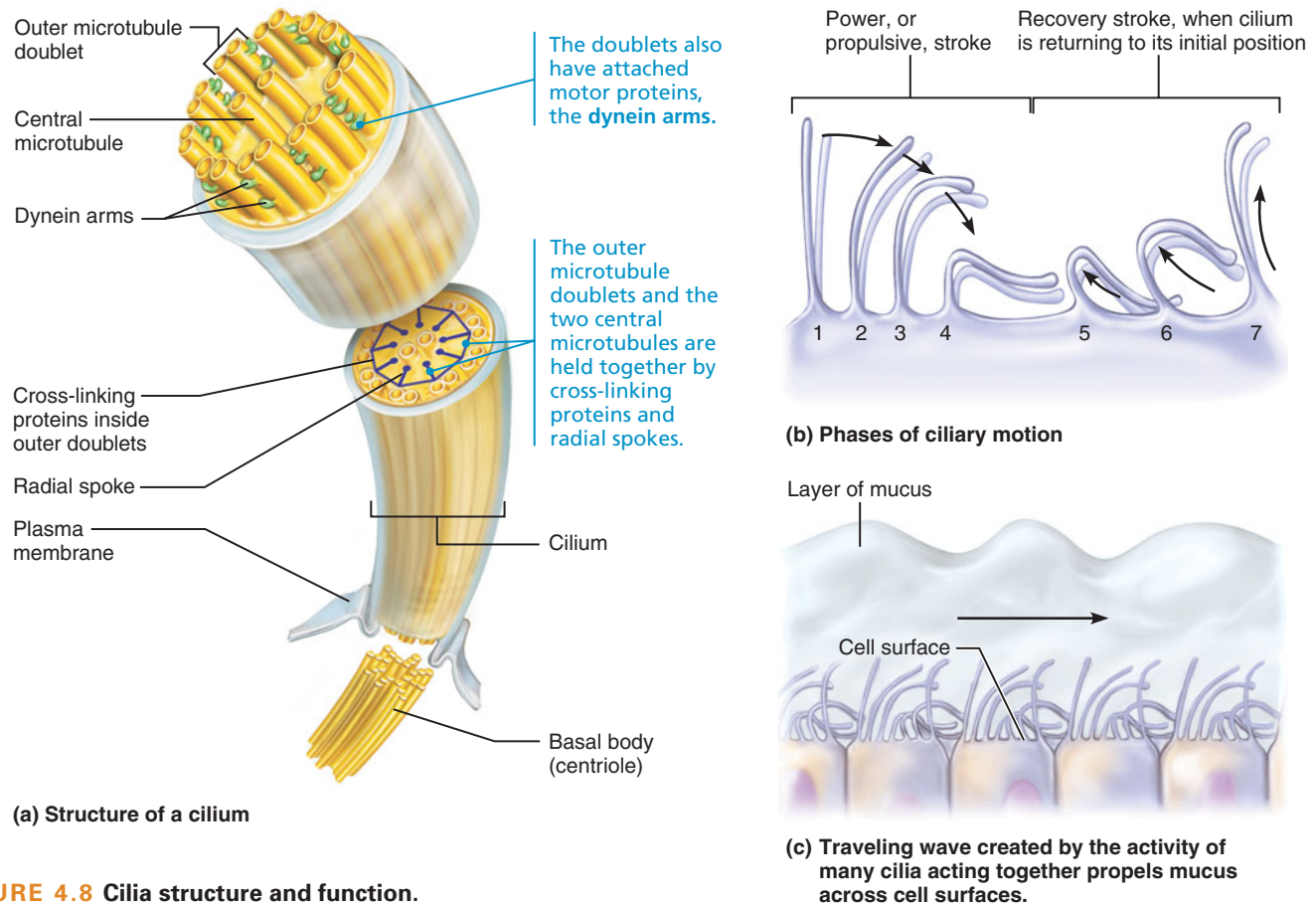
**Cilia** are whiplike, highly motile extensions of the apical surface membranes of certain epithelial cells (see Figure 4.1). Each cilium contains a core of microtubules held together by cross-linking and radial proteins (Figure 4.8). The microtubules are arranged in pairs, called *doublers*, with nine outer doublers encircling one central pair. Ciliary movement is generated when adjacent doublers grip one another with side arms made of the motor protein dynein (p. 35) and these arms start to oscillate. This causes the doublers to slide along the length of each other, like centipedes trying to run over each other's backs. As a result, the cilium bends.

The microtubules in cilia are arranged in much the same way as in the cytoplasmic organelles called centrioles (p. 35). Indeed, cilia originate as their microtubules assemble around centrioles that have migrated from the centrosome to the apical plasma membrane. The centriole at the base of each cilium is called a **basal body** (Figure 4.8a).

The cilia on an epithelium bend and move in coordinated waves, like waves across a field of grass on a windy day. These waves push mucus and other substances over the epithelial surface (Figure 4.8c). Each cilium executes a propulsive *power stroke*, followed by a nonpropulsive *recovery stroke* similar to feathering an oar or a canoe paddle (Figure 4.8b). This sequence ensures that fluid is moved in one direction only. An extremely long, isolated cilium is called a *flagellum* (flah-jel'um; "whip"). The only flagellated cells in the human body are sperm, which use their flagella to swim through the female reproductive tract.

**KARTAGENER'S SYNDROME** A type of *immotile cilia syndrome*, Kartagener's syndrome is an inherited disease in which the dynein arms within the cilia fail to form. This condition leads to frequent respiratory infections because the nonfunctional cilia cannot sweep inhaled bacteria out of the respiratory tubes.





**FIGURE 4.8** Cilia structure and function.

### check your understanding

- How do cilia differ from microvilli?
- How do the intermediate filaments within epithelial cells function to bind together the entire sheet of epithelia?
- In addition to epithelial tissue, what other types of tissues contain gap junctions?

For answers, see Appendix B.

## II. CONNECTIVE TISSUE

- Describe the features that are common to all connective tissues.
- Identify the four main classes of connective tissue.

The second of the four basic types of tissue is **connective tissue**, the most diverse and abundant type of tissue. There are four main classes of connective tissue and many subclasses. The main classes are (1) *connective tissue proper*, familiar examples of which are fat tissue and the fibrous tissue of ligaments; (2) *cartilage*; (3) *bone tissue*; and (4) *blood*. Connective tissues do far more than just connect the tissues and organs of the body together. They also form the basis of the skeleton (bone and cartilage), store and carry nutrients

(fat tissue and blood), surround all the blood vessels and nerves of the body (connective tissue proper), and lead the body's fight against infection.

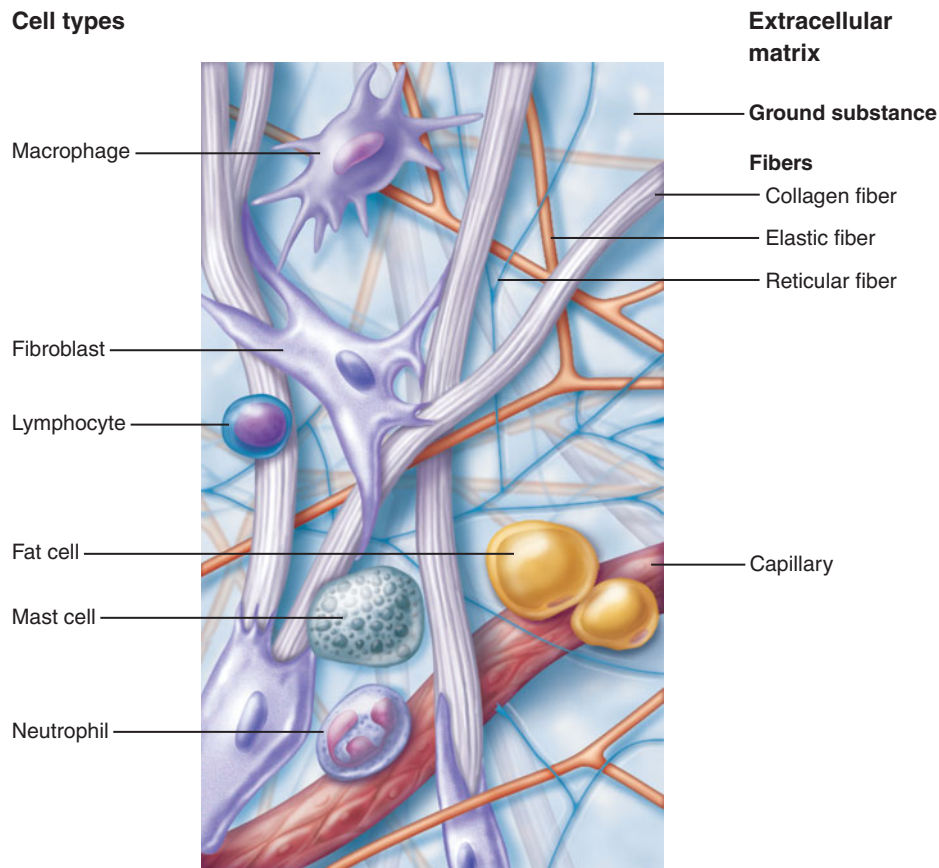
In this section, we will first discuss the special characteristics of connective tissues and then describe the structural elements found in connective tissues. Finally, we will review the structure, function, and location of the specific types of connective tissues.

### Special Characteristics of Connective Tissues

As different as they are, fat, bone, and blood are all connective tissues. All connective tissues share the same simple structural plan (**Figure 4.9**).

- Relatively few cells, lots of extracellular matrix.** The cells of connective tissues are separated from one another by a large amount of extracellular material called the **extracellular matrix** (ma'triks; "womb"). This differs markedly from epithelial tissue, whose cells crowd closely together.
- Extracellular matrix composed of ground substance and fibers.** The extracellular matrix is produced by the cells of the connective tissue. It is composed of some type





**FIGURE 4.9** Areolar connective tissue: A model connective tissue.

of **ground substance** embedded with protein **fibers**. The ground substance varies for each class of connective tissue. In many, it is a soft, gel-like substance that holds tissue fluid. In bone, it is hard—calcified by inorganic calcium salts. The fibrous portion of the matrix provides support for the connective tissue. Three types of protein fibers are found in connective tissues: *collagen fibers*, *reticular fibers*, and *elastic fibers*. The types, density, and distribution of the fibers are distinctive for each type of connective tissue. **Table 4.2** compares these features for the four main classes of connective tissue. The differences among the physical properties and functions of each type of connective tissue are due to differences in the composition of the extracellular matrix. The details of the matrix structure will be discussed with each type of connective tissue.

3. **Embryonic origin.** Another feature common to connective tissues is that they all originate from the embryonic tissue called **mesenchyme** (p. 51). Mesenchyme is shown in **Figure 4.10**.

## Structural Elements of Connective Tissues

Connective tissues are composed of cells and a significant amount of extracellular matrix. Although connective tissues differ in their structural properties because of differences in the types of cells and the composition of the extracellular

matrix, they all share similar structural elements. As we describe the structural features of connective tissues, we will use loose areolar connective tissue as a model to illustrate these features (See Figure 4.9).

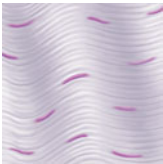
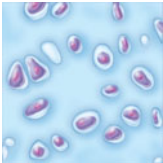
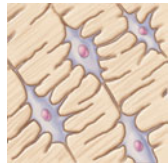
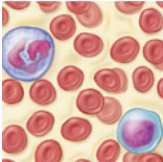
### Cells

In most connective tissues, the primary cell type produces the extracellular matrix (see Table 4.2). In connective tissue proper, these cells are called **fibroblasts** (literally, “fiber buds” or “fiber formers”). Fibroblasts make the protein subunits of fibers, which then assemble into fibers when the fibroblast secretes them. Fibroblasts also secrete the molecules that form the ground substance of the matrix. In cartilage tissue, the cells that secrete the matrix are **chondroblasts** (kon’dro-blasts; “cartilage formers”), and in bone they are **osteoblasts** (os’tē-o-blasts; “bone formers”). Once these tissue-forming cells are not actively secreting new matrix, they are termed **fibrocytes**, **chondrocytes**, and **osteocytes** (*cyte* = cell). They function to maintain the tissue matrix and keep the tissue healthy.

The cells found in blood are an exception. These cells do not produce the plasma matrix of blood. The cellular components of blood function to carry respiratory gases (red blood cells), to fight infections (white blood cells), and to aid in blood clotting (platelets).

Additional cell types are found in many connective tissues, as shown in Figure 4.9. For example, fat cells store energy; various white blood cells (neutrophils, lymphocytes,

TABLE 4.2 Comparison of Classes of Connective Tissues

| Tissue Class and Example                                                                                                                                       | Subclasses                                                                                                                                                                                                                                                    | Components                                               |                                                                                  | General Features                                                                                                                             |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------|----------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|
|                                                                                                                                                                |                                                                                                                                                                                                                                                               | Cells                                                    | Matrix                                                                           |                                                                                                                                              |
| <b>Connective Tissue Proper</b><br><br><i>Dense regular connective tissue</i> | 1. Loose connective tissue <ul style="list-style-type: none"> <li>• Areolar</li> <li>• Adipose</li> <li>• Reticular</li> </ul> 2. Dense connective tissue <ul style="list-style-type: none"> <li>• Regular</li> <li>• Irregular</li> <li>• Elastic</li> </ul> | Fibroblasts<br>Fibrocytes<br>Defense cells<br>Fat cells  | Gel-like ground substance<br>All three fiber types: collagen, reticular, elastic | Six different types; vary in density and types of fibers<br>Functions as a binding tissue<br>Resists mechanical stress, particularly tension |
| <b>Cartilage</b><br><br><i>Hyaline cartilage</i>                              | 1. Hyaline cartilage<br>2. Elastic cartilage<br>3. Fibrocartilage                                                                                                                                                                                             | Chondroblasts found in growing cartilage<br>Chondrocytes | Gel-like ground substance<br>Fibers: collagen, elastic fibers in some            | Resists compression because of the large amounts of water held in the matrix<br>Functions to cushion and support body structures             |
| <b>Bone Tissue</b><br><br><i>Compact bone</i>                               | 1. Compact bone<br>2. Spongy bone                                                                                                                                                                                                                             | Osteoblasts<br>Osteocytes                                | Gel-like ground substance calcified with inorganic salts<br>Fibers: collagen     | Hard tissue that resists both compression and tension<br>Functions in support                                                                |
| <b>Blood</b><br>                                                            | Blood cell formation and differentiation are quite complex<br>Details are provided in Chapter 18                                                                                                                                                              | Erythrocytes (RBCs)<br>Leukocytes (WBCs)<br>Platelets    | Plasma<br>No fibers                                                              | A fluid tissue<br>Functions to carry O <sub>2</sub> , CO <sub>2</sub> , nutrients, wastes, and other substances (hormones, for example)      |

and macrophages) respond to and protect against infectious agents; and mast cells release signaling molecules that mediate the inflammation reaction and promote healing.

### Fibers

The extracellular matrix of a connective tissue is composed of fibers and ground substance (Figure 4.9). Three types of fibers are found in connective tissues: *collagen fibers*, *reticular fibers*, and *elastic fibers*. In general, the fibers function in

support, yet each type of fiber contributes unique properties to the connective tissue.

**Collagen fibers**, the thick whitish gray fibers in Figure 4.9, are the strongest and most abundant type of fiber in connective tissues. Collagen fibers resist tension (pulling forces) and contribute strength to a connective tissue. Pulling tests show that collagen fibers are stronger than steel fibers of the same size! The thick collagen fibers that one sees with the light microscope are bundles of thinner collagen fibrils,



which consist of still thinner strands that are strongly cross-linked to one another. This cross-linking is the source of collagen's great tensile strength.

**Reticular** (re-tik'u-lar) **fibers**, the thin blue fibers shown in Figure 4.9, are bundles of a special type of collagen fibril. These short fibers cluster into a meshlike network (*reticulum* = network) that covers and supports the structures bordering the connective tissue. For example, capillaries are coated with fuzzy nets of reticular fibers, and these fibers form part of the basement membrane of epithelia. Individual reticular fibers glide freely across one another when the network is pulled, so they allow more give than collagen fibers do.

The last fiber type found in certain connective tissues is **elastic fibers**, illustrated as gold fibers in Figure 4.9. Elastic fibers contain the rubberlike protein **elastin** (e-last'in), which allows them to function like rubber bands. While we typically think of rubber bands as being stretchy, the defining feature of an elastic material is its ability to recoil back to its original form after being stretched. Connective tissue can stretch only so much before its thick, ropelike collagen fibers become taut. When the tension is released, the elastic fibers recoil, and the stretched tissue resumes its original shape.

**SCURVY** Vitamin C, which is abundant in citrus fruits such as oranges and lemons, is necessary for the proper cross-linking of the molecules that make up collagen fibers. A deficiency of this vitamin in the diet can lead to **scurvy**, a weakening of collagen and connective tissue throughout the body. Strong collagen is necessary for holding teeth in their sockets, reinforcing the walls of blood vessels, healing wounds, and forming scar tissue. Common signs of scurvy include loss of teeth, blood vessel rupture, and poor healing.



## Ground Substance

The other component of the matrix of connective tissue is the ground substance (Figure 4.9). The molecules that compose the ground substance are produced and secreted by the primary cell type of the connective tissue (fibroblasts, chondroblasts, or osteoblasts). The ground substance in most connective tissues is a gel-like material that consists of large sugar and sugar-protein molecules (proteoglycans and glycosaminoglycans). These molecules soak up fluid like a sponge. The fluid-filled ground substance functions to cushion and protect body structures (connective tissue proper), to withstand compressive stresses (cartilage), or to hold the tissue fluid that bathes all the cells in our body (areolar connective tissue). In bone tissue, the secreted ground substance is embedded with calcified mineral salts, which make the matrix hard and contribute to its function in supporting the body.

Here again, blood is an exception. The ground substance of blood, plasma, is not produced by the blood cells. Blood plasma is composed of water (about 90%) and various dissolved proteins, nutrients, ions, gases, and other molecules. These molecules are either produced by cells in other organs

and then secreted into blood (for example, plasma proteins and hormones) or transported into blood from an external source (water, air, and nutrients).

## check your understanding

- How do epithelial tissues differ from connective tissues in the arrangement of the cells in each tissue?
- Distinguish the matrix of a connective tissue from the ground substance.
- Which structural element of connective tissue resists tension? Which resists compression? Which allows for recoil?

For answers, see Appendix B.

## Classification of Connective Tissues

- Differentiate the different types of connective tissues in reference to the types of cells located within the tissue, the structure and composition of the extracellular matrix, and the main function of each.

### Connective Tissue Proper—Loose Connective Tissues

Connective tissue proper has two subclasses: **loose connective tissue** (areolar, adipose, and reticular) and **dense connective tissue** (dense irregular, dense regular, and elastic). These subclasses are distinguished by the density of fibers: In loose connective tissues, the fibers are distributed throughout the tissue but are separated from each other by ground substance.

**Areolar Connective Tissue** (FIGURE 4.9 AND FIGURE 4.10b) Loose areolar connective tissue is the most widespread type of connective tissue proper. This tissue underlies almost all the epithelia of the body and surrounds almost all the small nerves and blood vessels, including the capillaries. The structure of this tissue reflects its basic functions, which are common to many other types of connective tissues: (1) supporting and binding other tissues, (2) holding body fluids, (3) defending the body against infection, and (4) storing nutrients as fat.

The fibers of areolar connective tissue provide support. Areolar connective tissue has all three types of fibers in its extracellular matrix: collagen fibers, reticular fibers, and elastic fibers (although the reticular fibers do not show up when the common histological stains hematoxylin and eosin are used).

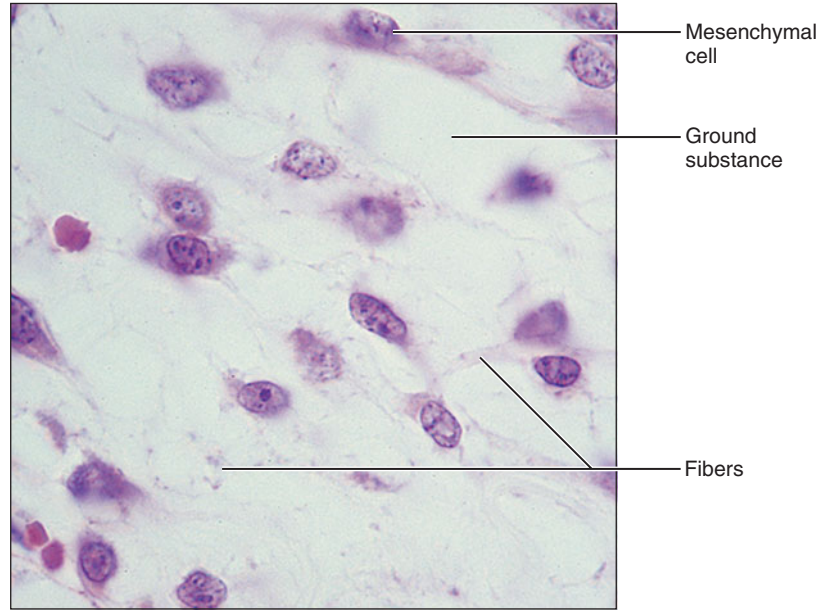
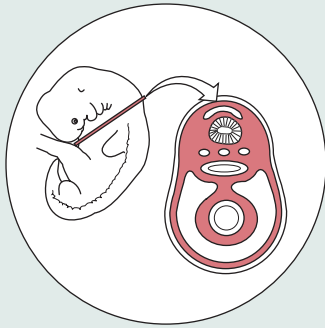
The ground substance of areolar connective tissue holds fluid. All the cells of the body are bathed in tissue fluid, or **interstitial fluid**. This fluid is derived from leakage of fluid and small molecules from the blood as it travels through the capillaries. Nutrients and oxygen are delivered to cells and waste molecules are carried away from cells via diffusion through this fluid. Areolar connective tissue lies between the capillaries and all other cells and tissues in the body. It soaks up this tissue fluid, much like a sponge. Thus it keeps the body's cells surrounded by fluid and facilitates the passage of nutrients, gases, waste products, and other molecules to and from the cells.

## (a) Embryonic connective tissue: mesenchyme

**Description:** Embryonic connective tissue; gel-like ground substance containing fibers; star-shaped mesenchymal cells.

**Function:** Gives rise to all other connective tissue types.

**Location:** Primarily in embryo.



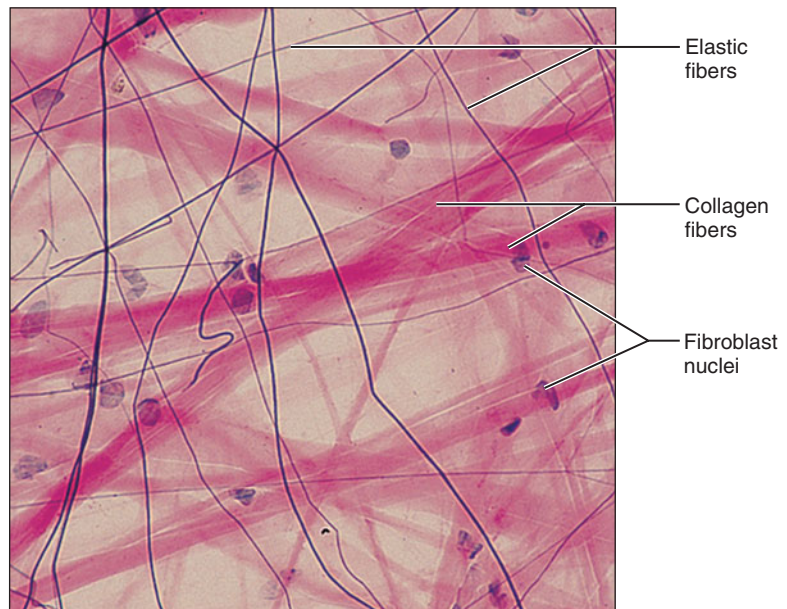
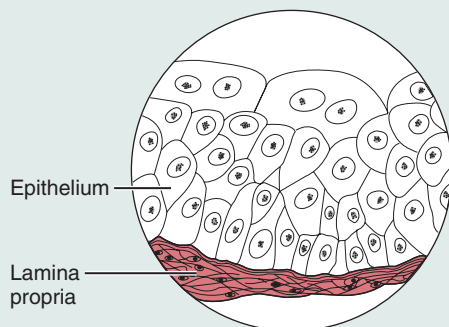
**Photomicrograph:** Mesenchymal tissue, an embryonic connective tissue (600 $\times$ ); the clear-appearing background is the fluid ground substance of the matrix; notice the fine, sparse fibers.

## (b) Connective tissue proper: loose connective tissue, areolar

**Description:** Gel-like matrix with all three fiber types; cells: fibroblasts, macrophages, mast cells, and some white blood cells.

**Function:** Wraps and cushions organs; its macrophages phagocytize bacteria; plays important role in inflammation; holds and conveys tissue fluid.

**Location:** Widely distributed under epithelia of body, e.g., forms lamina propria of mucous membranes; packages organs; surrounds capillaries.



**Photomicrograph:** Areolar connective tissue, a soft packaging tissue of the body (360 $\times$ ).

**FIGURE 4.10 Connective tissues.** (See *A Brief Atlas of the Human Body*, Second Edition, Plate 11.)

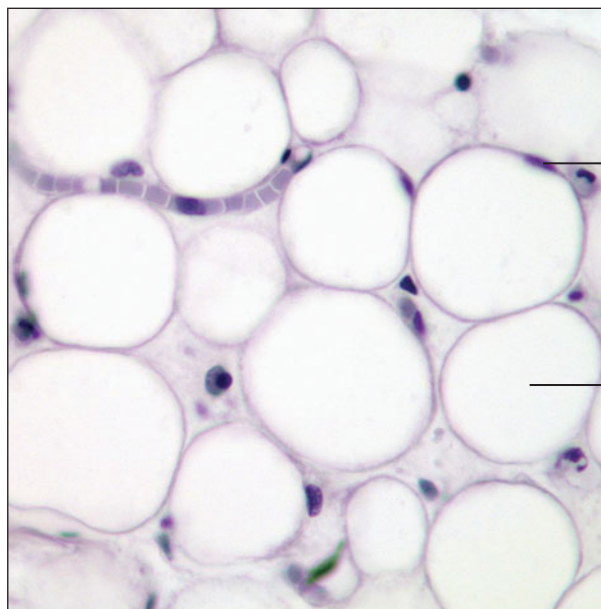
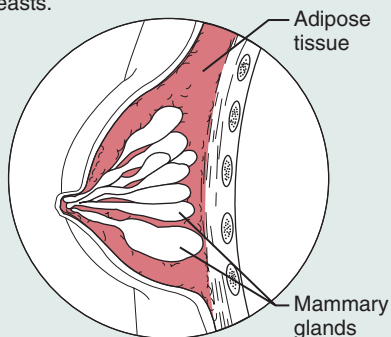


## (c) Connective tissue proper: loose connective tissue, adipose

**Description:** Matrix as in areolar, but very sparse; closely packed adipocytes, or fat cells, have nucleus pushed to the side by large fat droplet.

**Function:** Provides reserve food fuel; insulates against heat loss; supports and protects organs.

**Location:** Under skin in the hypodermis; around kidneys and eyeballs; within abdomen; in breasts.



Nucleus of fat cell

Vacuole containing fat droplet

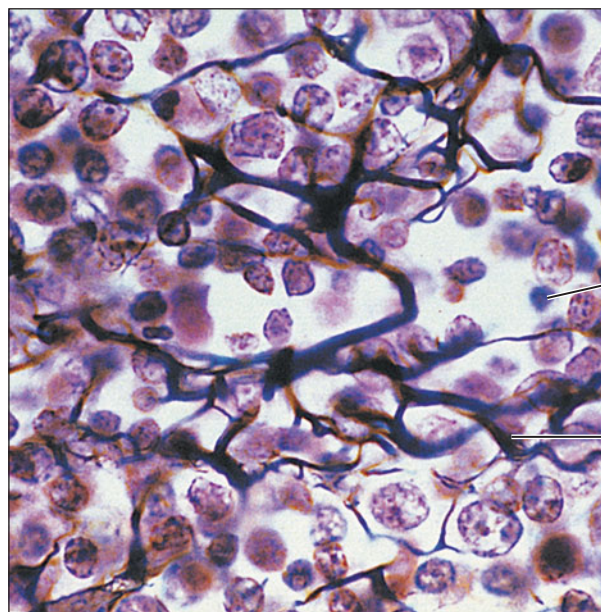
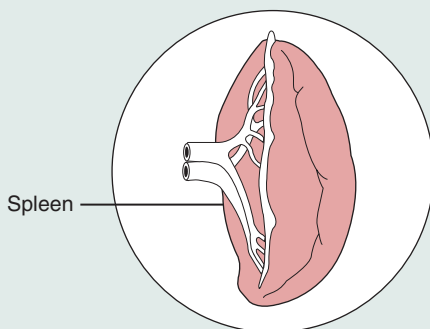
**Photomicrograph:** Adipose tissue from the subcutaneous layer under the skin (500 $\times$ ).

## (d) Connective tissue proper: loose connective tissue, reticular

**Description:** Network of reticular fibers in a typical loose ground substance; reticular cells lie on the network.

**Function:** Fibers form a soft internal skeleton (stroma) that supports other cell types including white blood cells, mast cells, and macrophages.

**Location:** Lymphoid organs (lymph nodes, bone marrow, and spleen).



White blood cell (lymphocyte)

Reticular fibers

**Photomicrograph:** Dark-staining network of reticular connective tissue fibers forming the internal skeleton of the spleen (555 $\times$ ).

**FIGURE 4.10** Connective tissues, continued. (See *A Brief Atlas of the Human Body*, Second Edition, Plates 12 and 13.)

Areolar connective tissue is the body's first line of defense against invading microorganisms, such as bacteria, viruses, fungi, and parasites. Lying just deep to the epithelial tissues that line the body surfaces and surrounding capillaries, it is in an ideal location to destroy microorganisms at their entry site—before they enter the capillaries and use the vascular system to spread to other locations. Areolar connective tissue contains a variety of defense cells, as shown in Figure 4.9, which respond in specific ways to destroy infectious agents.

Cellular defenses are not the only means by which areolar connective tissue fights infection. The viscous ground substance and the dense networks of collagen fibers in the extracellular matrix slow the progress of invading microorganisms. Some bacteria, however, secrete enzymes that rapidly break down ground substance or collagen. Such matrix-degrading bacteria are highly invasive; that is, they spread rapidly through the connective tissues and are especially difficult for the body's defenses to control. An example of such a bacterium is the *Streptococcus* strain responsible for strep throat.

A minor function of areolar connective tissue is to store energy reserves as fat. The large, fat-storing cells are **fat cells**, also called *adipose* (ad'ĭ-pōs) *cells*, and *adipocytes* (see Figure 4.9). Fat cells are egg-shaped, and their cytoplasm is dominated by a single, giant lipid droplet that flattens the nucleus and cytoplasm at one end of the cell. Mature fat cells are among the largest cells in the body and cannot divide. In areolar connective tissue, fat cells occur singly or in small groups.

**Adipose Tissue (FIGURE 4.10c)** **Adipose tissue** is similar to areolar connective tissue in structure and function, but its nutrient-storing function is much greater. Correspondingly, adipose tissue is crowded with fat cells, which account for 90% of its mass. These fat cells are grouped into large clusters called lobules. Adipose tissue is richly vascularized, reflecting its high metabolic activity. It removes lipids from the bloodstream after meals and later releases them into the blood, as needed. Without the fat stores in our adipose tissue, we could not live for more than a few days without eating.

Much of the body's adipose tissue occurs in the layer beneath the skin called the *hypodermis*. Adipose tissue also is abundant in the mesenteries, which are sheets of serous membranes that hold the stomach and intestines in place. Fat in this location is called *visceral fat*. Additionally, fat forms cushioning pads around the kidneys and behind the eyeballs in the orbits.

Whereas the abundant fat beneath the skin serves the general nutrient needs of the entire body, smaller depots of fat serve the local nutrient needs of highly active organs. Such depots occur around the hard-working heart and around lymph nodes (where cells of the immune system are furiously fighting infection), within some muscles, and as individual fat cells in the bone marrow (where new blood cells are produced at a frantic rate). Many of these local depots offer special lipids that are highly enriched.

The typical, nutrient-storing fat is *white adipose tissue* or *white fat*. Another type, called **brown adipose tissue**, produces heat and is a nutrient consumer. Brown fat, thought

to occur only in babies to aid in thermoregulation, has also been identified in adults. It is located in the hypodermis between the two scapulae (shoulder blades) in the center of the back, on the side of the anterior neck, and on the anterior abdominal wall. It is even more richly vascularized than white fat. Each brown-fat cell contains many lipid droplets and numerous mitochondria, which use the lipid fuel to heat the bloodstream rather than to produce ATP molecules.

**Reticular Connective Tissue (FIGURE 4.10d)** **Reticular connective tissue** resembles areolar tissue, but the only fibers in its matrix are reticular fibers. These fine fibers form a broad, three-dimensional network like the frame of a house. The spaces in the framework create a labyrinth of caverns that hold many free cells. The bone marrow, spleen, and lymph nodes, which house many free blood cells outside their capillaries, consist largely of reticular connective tissue. Fibroblasts called **reticular cells** lie along the reticular network of this tissue. Reticular tissue is discussed further in Chapters 18 and 21.

### Connective Tissue Proper—Dense Connective Tissue

**Dense connective tissue**, or *fibrous connective tissue*, contains more collagen than areolar connective tissue does. With its thick collagen fibers, it can resist extremely strong pulling (tensile) forces. There are three types of dense connective tissue: *irregular*, *regular*, and *elastic*.

**Dense Irregular Connective Tissue (FIGURE 4.10e)** **Dense irregular connective tissue** is similar to areolar tissue, but its collagen fibers are much thicker. These fibers run in different planes, allowing this tissue to resist strong tensions from different directions. This tissue dominates the leathery dermis of the skin, which is commonly stretched, pulled, and hit from various angles. This tissue also makes up the *fibrous capsules* that surround certain organs in the body, such as kidneys, lymph nodes, and bones. Its cellular and matrix elements are the same as in areolar connective tissue.

Dense irregular connective tissue is confusing, even for experts. The dermis obviously fits the name because its fibers run randomly, as one would expect for a tissue called “irregular.” However, the fibrous capsules of organs consist of two layers, with all the fibers in a layer running parallel to each other but perpendicular to the fibers in the other layer. That is, two perpendicular “regular” layers can make the tissue “irregular.”

**Dense Regular Connective Tissue (FIGURE 4.10f)** All collagen fibers in **dense regular connective tissue** usually run in the same direction, parallel to the direction of pull. Crowded between the collagen fibers are rows of fibroblasts, which continuously manufacture the fibers and a scant ground substance. When this tissue is not under tension, its collagen fibers are slightly wavy. Unlike areolar connective tissue, dense regular connective tissue is poorly vascularized and contains no fat cells or defense cells.

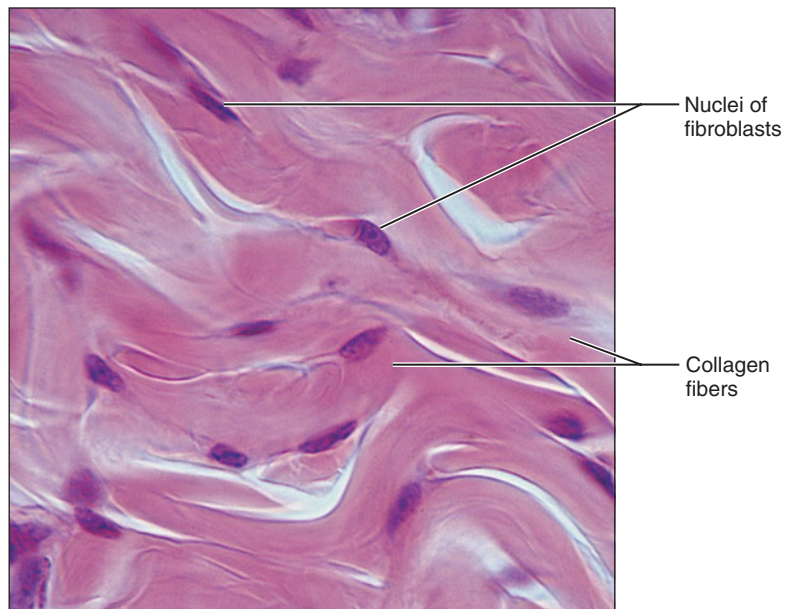
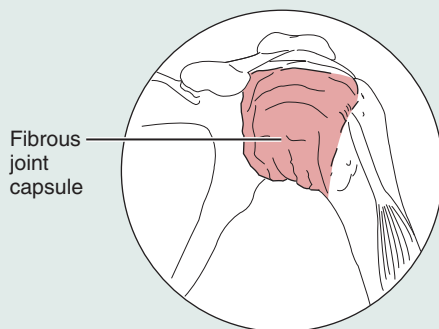
With its enormous tensile strength, dense regular connective tissue is the main component of *ligaments*, bands or sheets that bind bones to one another. It also is the main tissue in *tendons*, which are cords that attach muscles to bones, and *aponeuroses* (ap'o-nu-ro'sēs), which are sheetlike tendons.

## (e) Connective tissue proper: dense connective tissue, dense irregular

**Description:** Primarily irregularly arranged collagen fibers; some elastic fibers; major cell type is the fibroblast.

**Function:** Able to withstand tension exerted in many directions; provides structural strength.

**Location:** Fibrous capsules of organs and of joints; dermis of the skin; submucosa of digestive tract.



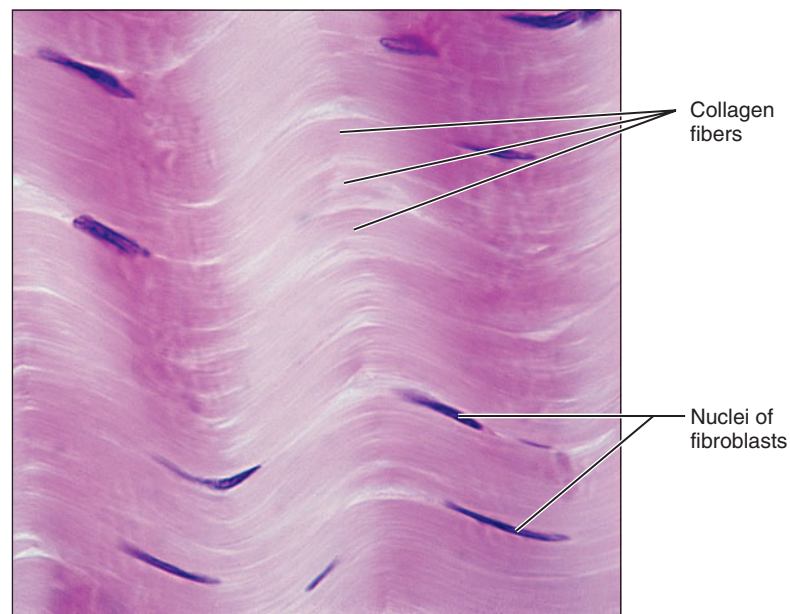
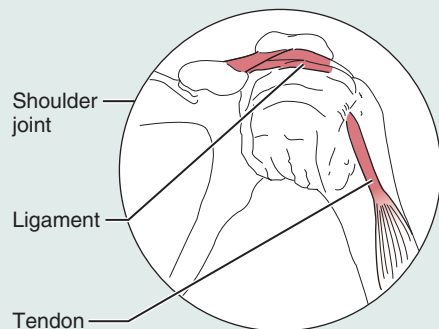
**Photomicrograph:** Dense irregular connective tissue from the dermis of the skin (600 $\times$ ).

## (f) Connective tissue proper: dense connective tissue, dense regular

**Description:** Primarily parallel collagen fibers; a few elastic fibers; major cell type is the fibroblast.

**Function:** Attaches muscles to bones or to muscles; attaches bones to bones; withstands great tensile stress when pulling force is applied in one direction.

**Location:** Tendons, most ligaments, aponeuroses.



**Photomicrograph:** Dense regular connective tissue from a tendon (270 $\times$ ).

**FIGURE 4.10 Connective tissues, continued.** (See *A Brief Atlas of the Human Body*, Second Edition, Plates 14 and 15.)

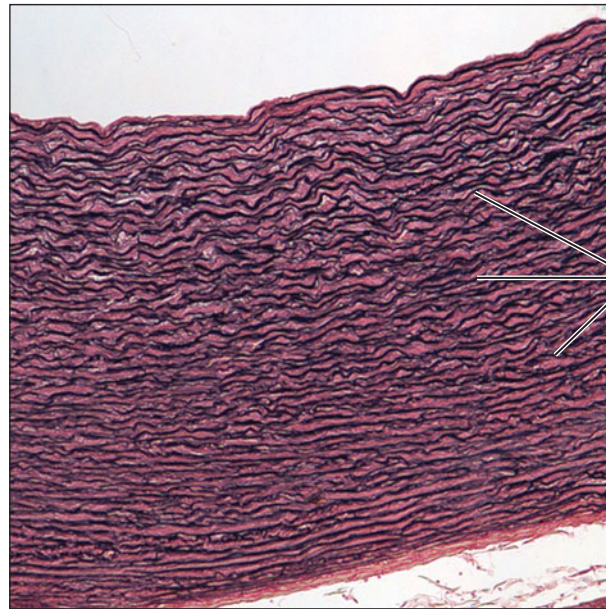
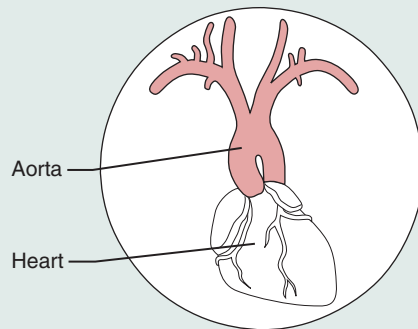


## (g) Connective tissue proper: dense connective tissue, elastic

**Description:** Dense regular connective tissue containing a high proportion of elastic fibers.

**Function:** Allows recoil of tissue following stretching; maintains pulsatile flow of blood through arteries; aids passive recoil of lungs following inspiration.

**Location:** Walls of large arteries; within certain ligaments associated with the vertebral column; within the walls of the bronchial tubes.



**Photomicrograph:** Elastic connective tissue in the wall of the aorta (85 $\times$ ).

**FIGURE 4.10 Connective tissues, continued.** (See *A Brief Atlas of the Human Body*, Second Edition, Plates 16.)

Dense regular connective tissue also forms **fascia** (fash'-e-ah; "a band"), a fibrous membrane that wraps around muscles, muscle groups, large vessels, and nerves. Many sheets of fascia occur throughout the body, binding structures together like plastic sandwich wrap. When the word *fascia* is used alone, it is understood to mean *deep fascia*. *Superficial fascia*, something else entirely, is the fatty hypodermis below the skin.

**Elastic Connective Tissue (FIGURE 4.10g)** In **elastic connective tissue**, elastic fibers are the predominant type of fiber, and bundles of elastic fibers outnumber the bundles of collagen fibers. This tissue is located in structures where recoil from stretching is important: within the walls of arteries, in certain ligaments (*ligamentum nuchae* and *ligamentum flavum*, which connect successive vertebrae), and surrounding the bronchial tubes in the lungs.

### check your understanding

- How does loose connective tissue differ from dense connective tissue?
- Which type of connective tissue forms the following structures: ligaments and tendons; the hypodermis of the skin; the tissue that underlies epithelia; lymph nodes?

For answers, see Appendix B.

### Cartilage

As you have seen, connective tissue proper has the ability to resist tension (pulling). Cartilage and bone are the firm connective tissues that resist *compression* (pressing) as well as tension. Like all connective tissues, they consist of cells separated by a matrix containing fibers, ground substance, and tissue fluid. However, these skeletal tissues exaggerate the supportive functions of connective tissue and play no role in fat storage or defense against disease.

**Cartilage** (Figure 4.10h–j), a firm but flexible tissue, occurs in several parts of the skeleton. For example, it forms the supporting rings of the trachea (windpipe) and gives shape to the nose and ears. Like nearly all connective tissues, cartilage consists of cells separated by an abundant extracellular matrix (Figure 4.10h). This matrix contains thin collagen fibrils, a ground substance, and an exceptional quantity of tissue fluid; in fact, cartilage consists of up to 80% water! The arrangement of water in its matrix enables cartilage to spring back from compression, as explained in Chapter 6, p. 124.

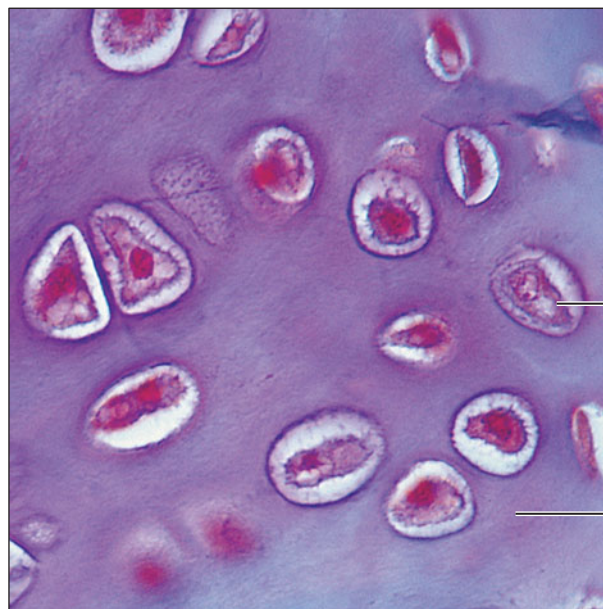
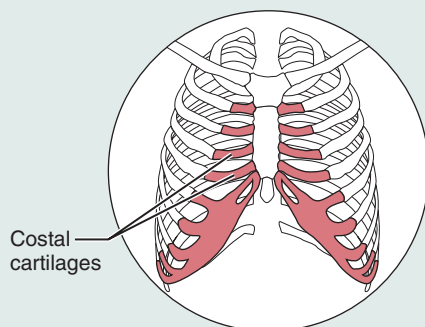
Cartilage is simpler than other connective tissues: It contains no blood vessels or nerves and just one kind of cell, the **chondrocyte**. Each chondrocyte resides within a cavity in the matrix called a **lacuna**. Immature chondrocytes are *chondroblasts*, cells that actively secrete the matrix during cartilage growth. Cartilage is found in three varieties, each dominated by a particular fiber type: hyaline cartilage,

**(h) Cartilage: hyaline**

**Description:** Amorphous but firm matrix; collagen fibers form an imperceptible network; chondroblasts produce the matrix and when mature (chondrocytes) lie in lacunae.

**Function:** Supports and reinforces; has resilient cushioning properties; resists compressive stress.

**Location:** Forms most of the embryonic skeleton; covers the ends of long bones in joint cavities; forms costal cartilages of the ribs; cartilages of the nose, trachea, and larynx.



Chondrocyte  
in lacuna

Matrix

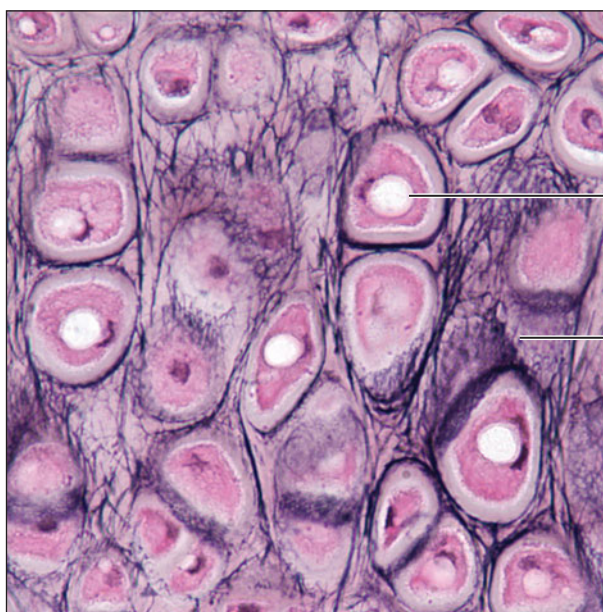
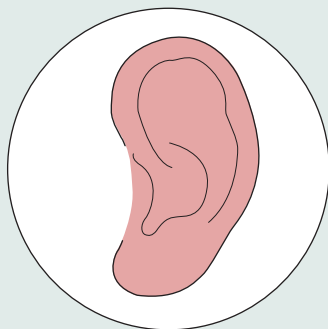
**Photomicrograph:** Hyaline cartilage from the trachea (720 $\times$ ).

**(i) Cartilage: elastic**

**Description:** Similar to hyaline cartilage, but more elastic fibers in matrix.

**Function:** Maintains the shape of a structure while allowing great flexibility.

**Location:** Supports the external ear (pinna); epiglottis.



Chondrocyte  
in lacuna

Matrix

**Photomicrograph:** Elastic cartilage from the human ear pinna; forms the flexible skeleton of the ear (980 $\times$ ).

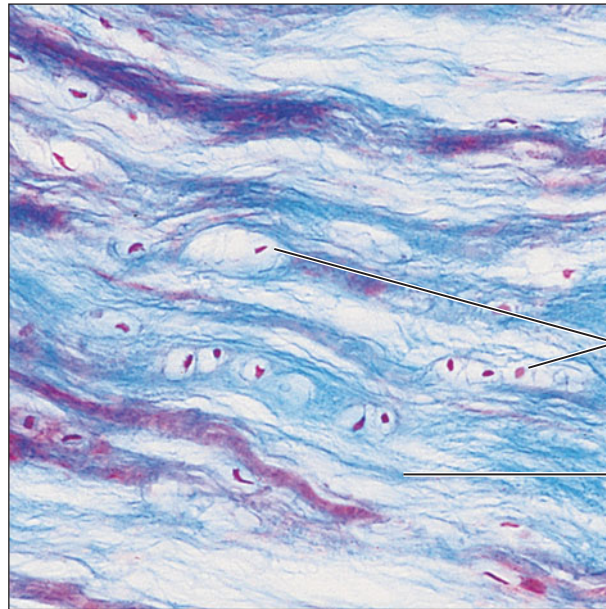
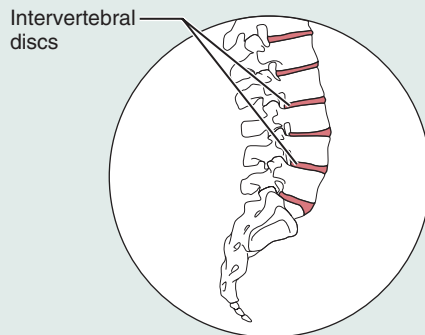


**(j) Cartilage: fibrocartilage**

**Description:** Matrix similar to but less firm than that in hyaline cartilage; thick collagen fibers predominate.

**Function:** Tensile strength with the ability to absorb compressive shock.

**Location:** Intervertebral discs; pubic symphysis; discs of knee joint.



Chondrocytes  
in lacunae

Collagen  
fiber

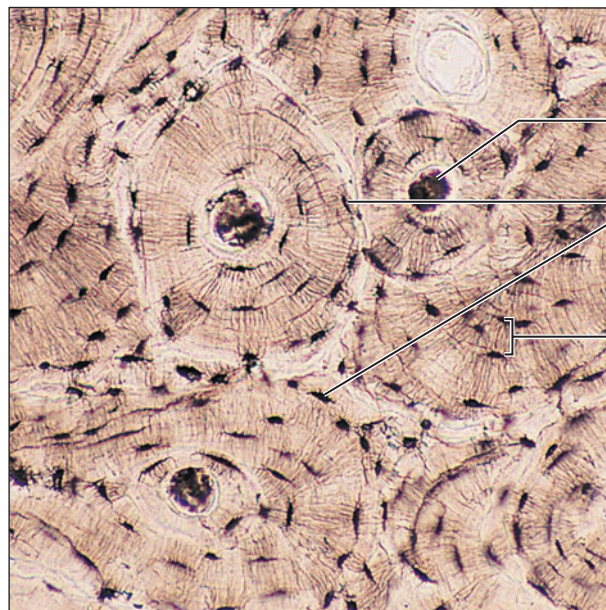
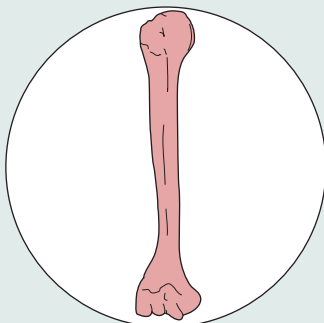
**Photomicrograph:** Fibrocartilage of an intervertebral disc (180 $\times$ ). Special staining produced the blue color seen.

**(k) Others: bone (osseous tissue)**

**Description:** Hard, calcified matrix containing many collagen fibers; osteocytes lie in lacunae. Very well vascularized.

**Function:** Bone supports and protects (by enclosing); provides levers for the muscles to act on; stores calcium and other minerals and fat; marrow inside bones is the site for blood cell formation (hematopoiesis).

**Location:** Bones



Central  
canal

Lacunae

Lamella

**Photomicrograph:** Cross-sectional view of bone (190 $\times$ ).

**FIGURE 4.10** **Connective tissues**, continued. (See *A Brief Atlas of the Human Body*, Second Edition, Plates 19 and 20.)

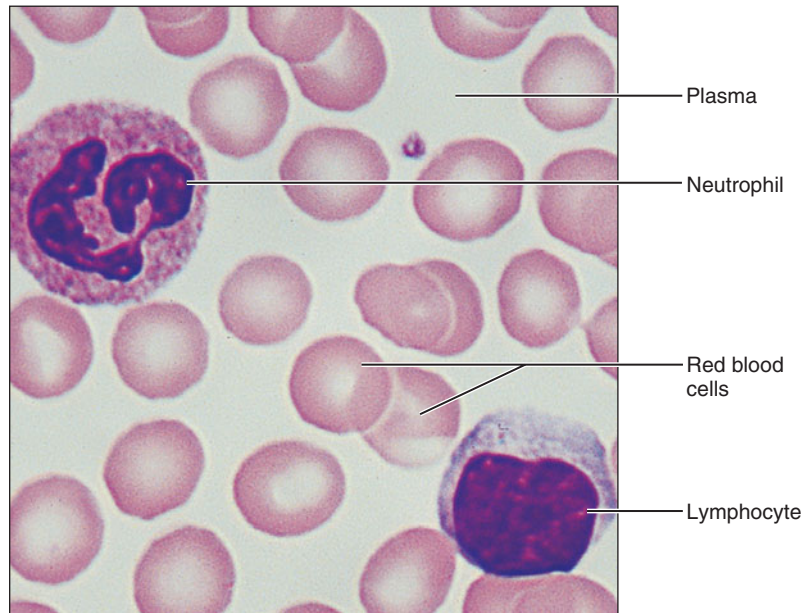
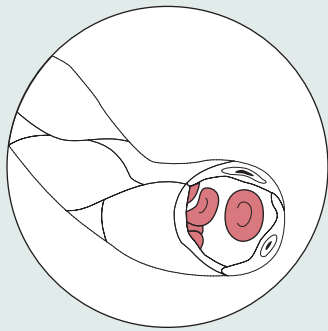


## (I) Others: blood

**Description:** Red and white blood cells in a fluid matrix (plasma).

**Function:** Transport of respiratory gases, nutrients, wastes, and other substances.

**Location:** Contained within blood vessels.



**Photomicrograph:** Smear of human blood (1785 $\times$ ); two white blood cells (neutrophil and lymphocyte) are seen surrounded by red blood cells.

**FIGURE 4.10** **Connective tissues, continued.** (See *A Brief Atlas of the Human Body*, Second Edition, Plates 22–27.)

elastic cartilage, and fibrocartilage. These are introduced in Figure 4.10h–j and discussed in Chapter 6, pp. 123–126.

### Bone

Because of its rocklike hardness, **bone tissue** has a tremendous ability to support and protect body structures. Bone matrix contains inorganic calcium salts (bone salts), which enable bone to resist compression, and an abundance of collagen fibers, which allow bone to withstand strong tension (Figure 4.10k, p. 87).

Immature bone cells, called **osteoblasts**, secrete the collagen fibers and ground substance of the matrix. Then bone salts precipitate on and between the collagen fibers, hardening the matrix. The mature bone cells, called **osteocytes**, inhabit cavities (*lacunae*) in this hardened matrix. Bone is a living and dynamic tissue, well supplied with blood vessels. It is discussed further in Chapter 6.

### Blood

**Blood** (Figure 4.10l), the fluid in the blood vessels, is the most atypical connective tissue. It does not bind things together or give mechanical support. It is classified as a connective tissue because it develops from mesenchyme and consists of blood *cells* surrounded by a nonliving matrix, the liquid blood *plasma*. Its cells and matrix are very different from those in other connective tissues. Blood functions as the transport vehicle for the cardiovascular system, carrying defense cells, nutrients, wastes, respiratory gases, and many

other substances throughout the body. Blood is discussed in detail in Chapter 18.

### check your understanding

15. Which connective tissues contain collagen fibers?
16. In which connective tissues are the cells located in lacunae?
17. Which component of cartilage tissue functions to resist compressive forces?

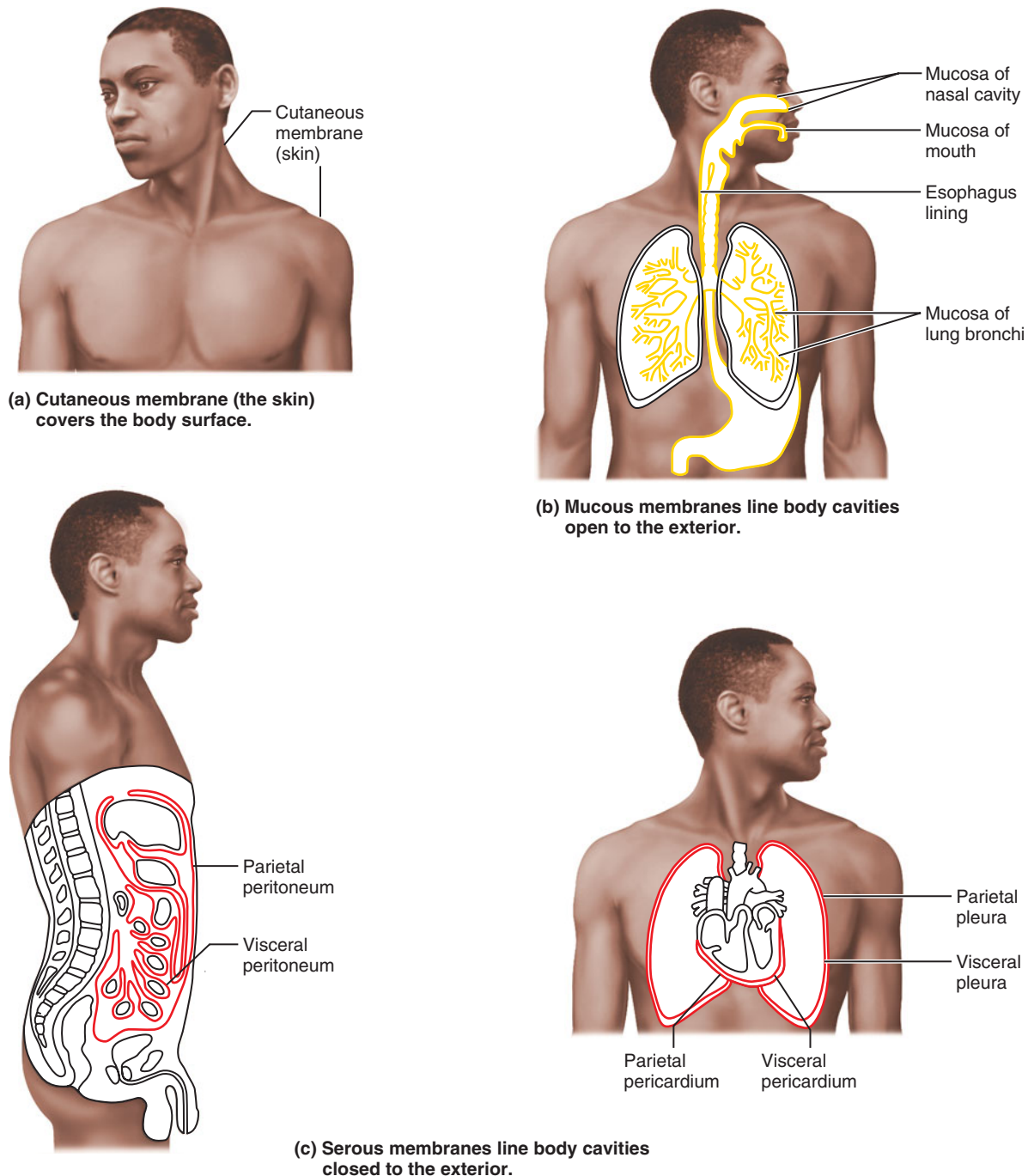
For answers, see Appendix B.

## Covering and Lining Membranes

- Discuss the structure and function of mucous, serous, and cutaneous membranes.

Now that you have learned about connective and epithelial tissues, you can consider the **covering** and **lining membranes** that combine these two tissue types (Figure 4.11). These membranes, which cover broad areas within the body, consist of an epithelial sheet plus the underlying layer of connective tissue proper. These membranes are of three types: cutaneous, mucous, and serous.

The **cutaneous membrane** (ku-ta'ne-us; “skin”) is the skin, covering the outer surface of the body (Figure 4.11a). Its outer epithelium is the thick epidermis, and its inner connective



**FIGURE 4.11** Types of membranes.

tissue is the dense dermis. It is a dry membrane. The skin is discussed further in Chapter 5.

A **mucous membrane**, or **mucosa** (mu-ko'sah), lines the inside of every hollow internal organ that opens to the outside of the body. More specifically, mucous membranes line the tubes of the respiratory, digestive, reproductive, and urinary systems (Figure 4.11b). Although different mucous membranes vary widely in the types of epithelia they contain, all are wet or moist. As their name implies, many mucous membranes secrete mucus. Not all of them do so, however.

All mucous membranes consist of an epithelial sheet directly underlain by a layer of loose areolar connective tissue called the *lamina propria* (lam'i-nah pro'pre-ah; "one's own layer"). In the mucous membranes of the digestive system, the lamina propria rests on a layer of smooth muscle cells. Later chapters discuss the specific mucous membranes of the body.

**Serous membranes**, or **serosae**, introduced in Chapter 1, are the slippery membranes that line the closed pleural, pericardial, and peritoneal cavities (Figures 4.11c and 1.7).

A serous membrane consists of a simple squamous epithelium, called **mesothelium**, lying on a thin layer of areolar connective tissue. This membrane produces a slippery *serous fluid*, beginning as a filtrate of the blood in capillaries in the connective tissue, with the addition of lubricating molecules by the mesothelium.

### III. MUSCLE TISSUE

► Briefly describe the three types of muscle tissue.

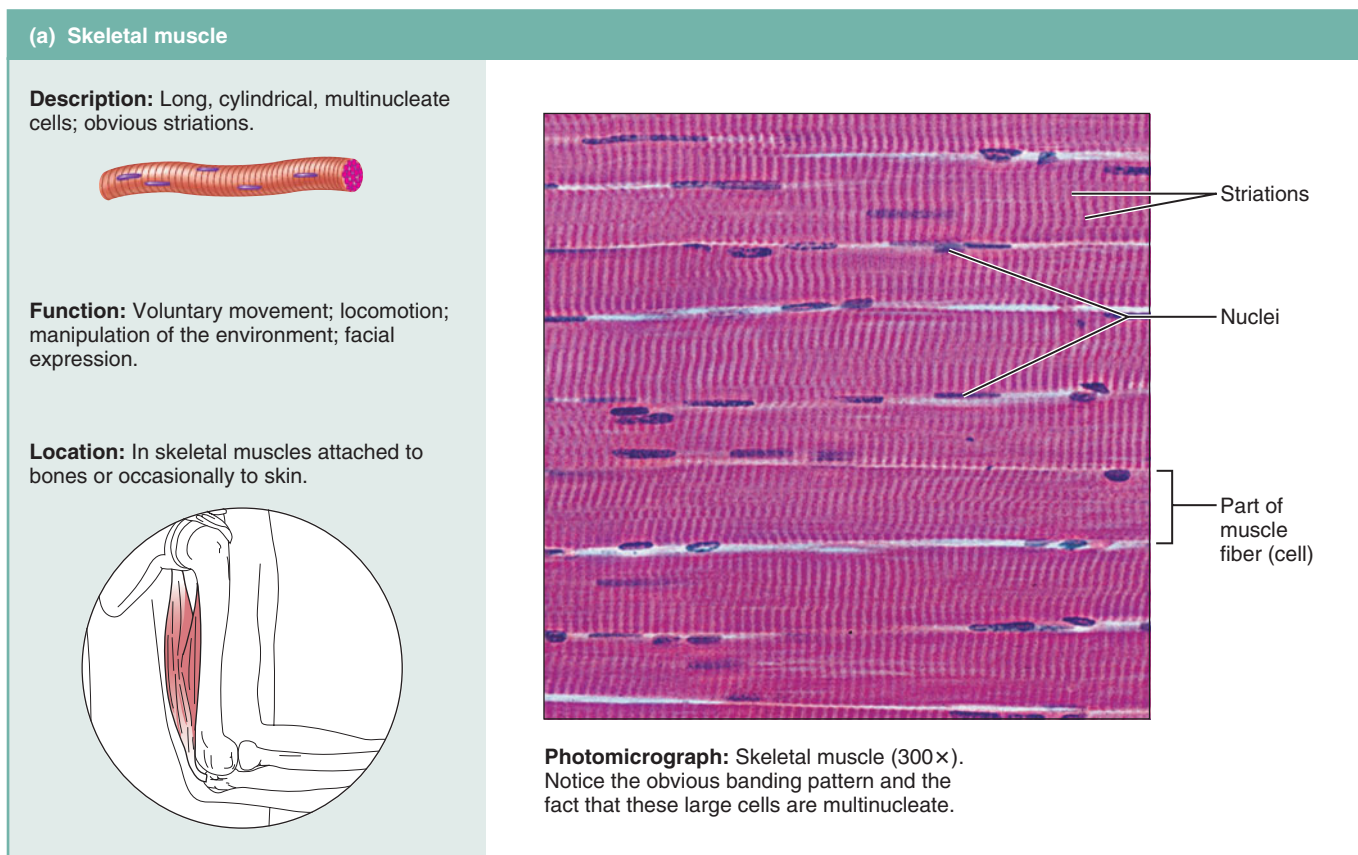
The two remaining tissue types are muscle and nervous tissues. These are sometimes called *composite tissues* because, along with their own muscle or nerve cells, they contain small amounts of areolar connective tissue. (Areolar connective tissue surrounds all blood vessels, and both muscle and nervous tissue are richly vascularized.)

**Muscle tissues** (Figure 4.12) bring about most kinds of body movements. Most muscle cells are called **muscle fibers**. They have an elongated shape and contract forcefully as they shorten. These cells contain many myofilaments (mi"o-fil'ah-ments; "muscle filaments"), cellular organelles filled with the actin and myosin filaments that bring about contraction in all cell types (p. 34). There are three kinds of muscle tissue: skeletal, cardiac, and smooth.

**Skeletal muscle tissue** (Figure 4.12a) is the major component of organs called skeletal muscles, which pull on bones to cause body movements. Skeletal muscle cells are long, large cylinders that contain many nuclei. Their obvious striated, or banded, appearance reflects a highly organized arrangement of their myofilaments. Skeletal muscle tissue is described in detail in Chapter 10.

**Cardiac muscle tissue** (Figure 4.12b) occurs in the wall of the heart. It contracts to propel blood through the blood vessels. Like skeletal muscle cells, cardiac muscle cells are striated. However, they differ in two ways: (1) Each cardiac cell has just one nucleus, and (2) cardiac cells branch and join at special cellular junctions called *intercalated* (in-ter'kah-la"ted) *discs*. The details of cardiac muscle tissue are discussed in Chapter 19.

**Smooth muscle tissue** (Figure 4.12c) is so named because there are no visible striations in its cells. These cells are elongated with tapered ends and contain one centrally located nucleus. Smooth muscle primarily occurs in the walls of hollow viscera such as the digestive and urinary organs, uterus, and blood vessels. It generally acts to squeeze substances through these organs by alternately contracting and relaxing. Smooth muscle tissue is described in detail in Chapter 23.

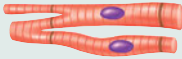


**FIGURE 4.12 Muscle tissues.** (See *A Brief Atlas of the Human Body*, Second Edition, Plate 28.)



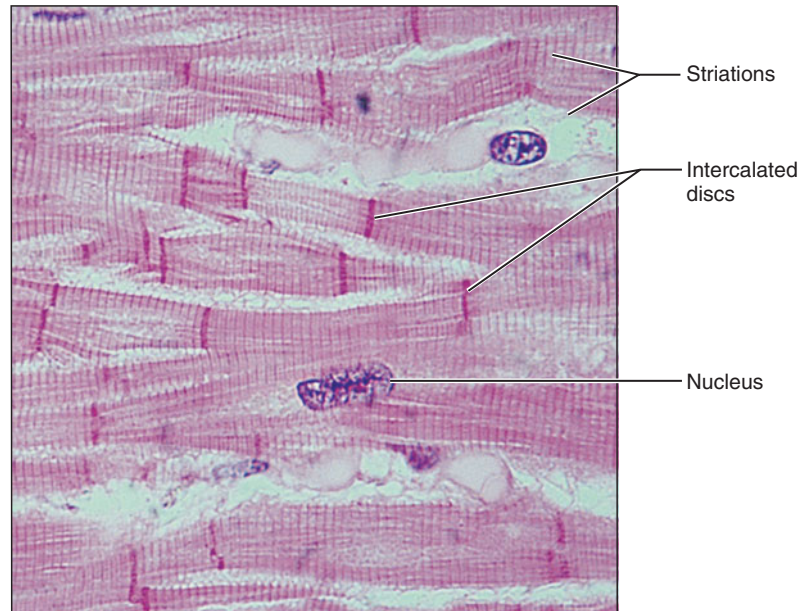
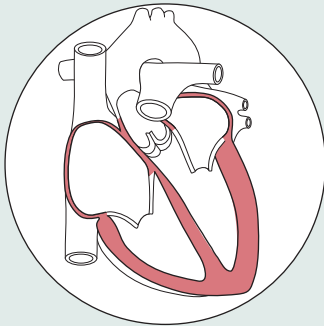
**(b) Cardiac muscle**

**Description:** Branching, striated, generally uninucleate cells that interdigitate at specialized junctions (intercalated discs).



**Function:** As it contracts, it propels blood into the circulation; involuntary control.

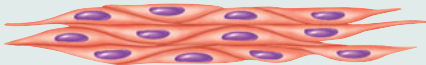
**Location:** The walls of the heart.



**Photomicrograph:** Cardiac muscle (600 $\times$ ); notice the striations, branching of cells, and the intercalated discs.

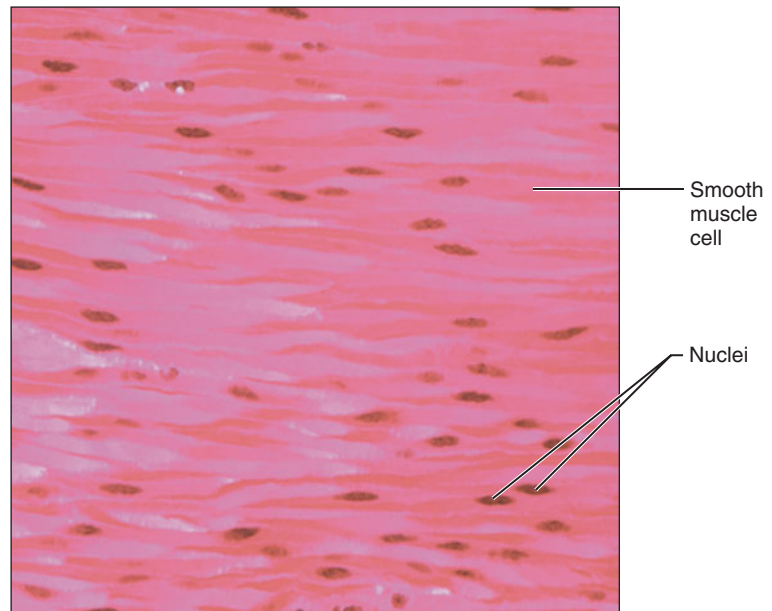
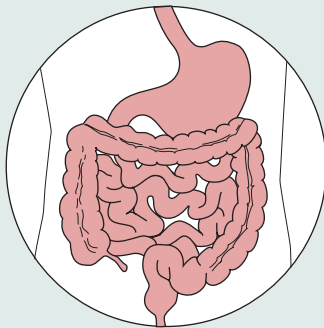
**(c) Smooth muscle**

**Description:** Spindle-shaped cells with central nuclei; no striations; cells arranged closely to form sheets.



**Function:** Propels substances or objects (foodstuffs, urine, a baby) along internal passageways; involuntary control.

**Location:** Mostly in the walls of hollow organs.

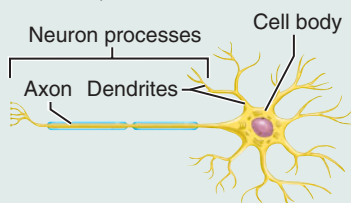


**Photomicrograph:** Sheet of smooth muscle (220 $\times$ ).

**FIGURE 4.12 Muscle tissues, continued.** (See *A Brief Atlas of the Human Body*, Second Edition, Plates 31 and 32.)

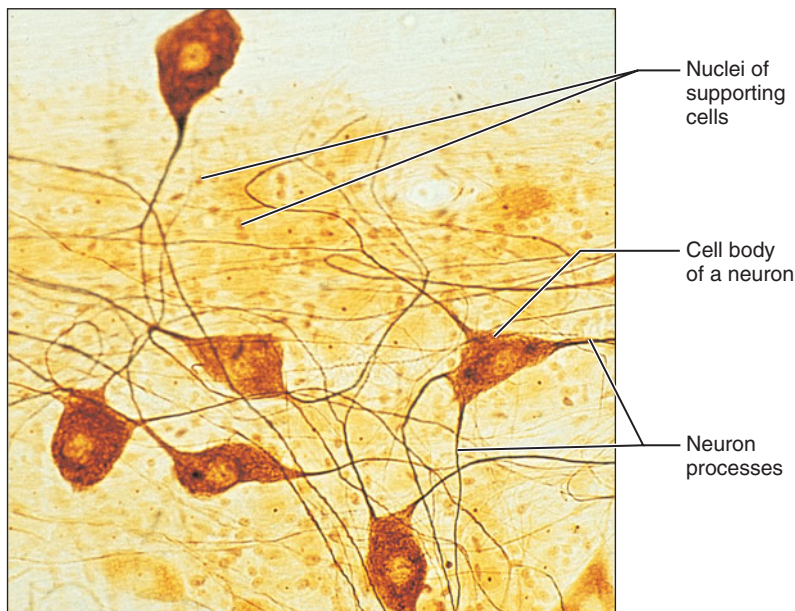
## Nervous tissue

**Description:** Neurons are branching cells; cell processes that may be quite long extend from the nucleus-containing cell body; also contributing to nervous tissue are nonirritable supporting cells (not illustrated).



**Function:** Transmit electrical signals from sensory receptors and to effectors (muscles and glands) which control their activity.

**Location:** Brain, spinal cord, and nerves.



**Photomicrograph:** Neurons (200×)

**FIGURE 4.13 Nervous tissue.** (See *A Brief Atlas of the Human Body*, Second Edition, Plate 33.)

## IV. NERVOUS TISSUE

- Distinguish the cell types found in nervous tissue.

**Nervous tissue** is the main component of the nervous organs—the brain, spinal cord, and nerves—which regulate and control body functions. It contains two types of cells, neurons and supporting cells. **Neurons** are the highly specialized nerve cells (**Figure 4.13**) that generate and conduct electrical impulses. They have extensions, or processes, that allow them to transmit impulses over substantial distances within the body. **Dendrites** are cell processes that extend from the cell body of a neuron like branches of a tree. The dendrites, the receptive region of the neuron, transmit signals toward the cell body. A neuron also has a singular, long cell process extending from its cell body, the **axon**, that generates nerve impulses and transmits them away from the cell body. The supporting cells, called **neuroglia**, are nonconducting cells that nourish, insulate, and protect the delicate neurons. A more complete discussion of nervous tissue appears in Chapter 12.

### check your understanding

- Look at Figure 4.10c. How can you tell this tissue is *not* stratified squamous epithelium?
- Which nerve cells function to transmit electrical impulses?
- Which muscle tissues are striated?

For answers, see Appendix B.

## TISSUE RESPONSE TO INJURY

- Describe the inflammatory and repair processes by which tissues recover from injury.

The body has many mechanisms for protecting itself from injury and invading microorganisms. Intact epithelia act as a physical barrier, but once that barrier has been penetrated, protective responses are activated in the underlying connective

tissue proper. These are the *inflammatory* and *immune responses*. Inflammation is a nonspecific, local response that develops quickly and limits the damage to the injury site. The immune response, by contrast, takes longer to develop and is highly specific. It destroys particular infectious microorganisms and foreign molecules at the site of infection and throughout the body. This section concentrates on inflammation; the immune response is discussed in Chapter 21.

## Inflammation

Almost every injury or infection leads to an inflammatory response. For example, assume your skin is cut by a dirty piece of glass, crushed by a blow in football, or has an infected pimple. As short-term, or acute, inflammation develops in the connective tissue, it produces four symptoms: *heat, redness, swelling, and pain*. You can trace the source of each symptom.

The initial insult induces the release of *inflammatory chemicals* into the nearby tissue fluid. Injured tissue cells, macrophages, mast cells, and proteins from blood all serve as sources of these inflammatory mediators. These chemicals signal nearby blood vessels to dilate (widen), thus increasing the flow of blood to the injury site. The increase in blood flow is the source of the *heat and redness* of inflammation. Certain inflammatory chemicals, such as histamine, increase the permeability of the capillaries, causing large amounts of tissue fluid to leave the bloodstream. The resulting accumulation of fluid in the connective tissue, called **edema** (ĕ-de'mah; "swelling"), causes the *swelling* of inflammation. The excess fluid presses on nerve endings, contributing to the sensation of *pain*. Some of the inflammatory chemicals also cause pain by affecting the nerve endings directly.

At first glance, inflammatory edema seems detrimental, but it is actually beneficial. The entry of blood-derived fluid into the injured connective tissue (1) helps to dilute toxins secreted by bacteria, (2) brings in oxygen and nutrients from the blood, necessary for tissue repair, and (3) brings in antibodies from the blood to fight infection. In very severe infections and in all wounds that sever blood vessels, the fluid leaking from the capillaries contains *clotting* proteins. In these cases, clotting occurs in the connective tissue matrix. The fibrous clot isolates the injured area and "walls in" the infectious microorganisms, preventing their spread.

The next stage in inflammation is *stasis* ("standing"). This is the slowdown in local blood flow that necessarily follows a massive exit of fluid from the capillaries. At this stage, white blood cells begin to leave the small vessels. First to appear at the infection site are neutrophils, then macrophages. These cells devour the infectious microorganisms and the damaged tissue cells as well.

## Repair

Even as inflammation proceeds, repair begins. Tissue repair can occur in two major ways: by regeneration and by fibrosis.

**Regeneration** is the replacement of a destroyed tissue by new tissue of the same kind, whereas **fibrosis** involves the proliferation of a fibrous connective tissue called **scar tissue**. Tissue repair in a skin wound involves both regeneration and fibrosis. After the blood within the cut has clotted, the surface part of the clot dries to form a scab (Figure 4.14, ①). At this point, the repair begins with a step called organization.

**Organization** is the process by which the clot is replaced by granulation tissue (Figure 4.14, ②). **Granulation tissue** is a delicate pink tissue made of several elements. It contains capillaries that grow in from nearby areas, as well as proliferating fibroblasts that produce new collagen fibers to bridge the gash. Some of its fibroblasts have contractile properties that pull the margins of the wound together. As organization proceeds, macrophages digest the original clot, and the deposit of collagen continues. As more collagen is made, the granulation tissue gradually transforms into fibrous scar tissue (Figure 4.14, ③).

During organization, the surface epithelium begins to *regenerate*, growing under the scab until the scab falls away. The end result is a fully regenerated epithelium and an underlying area of scar.

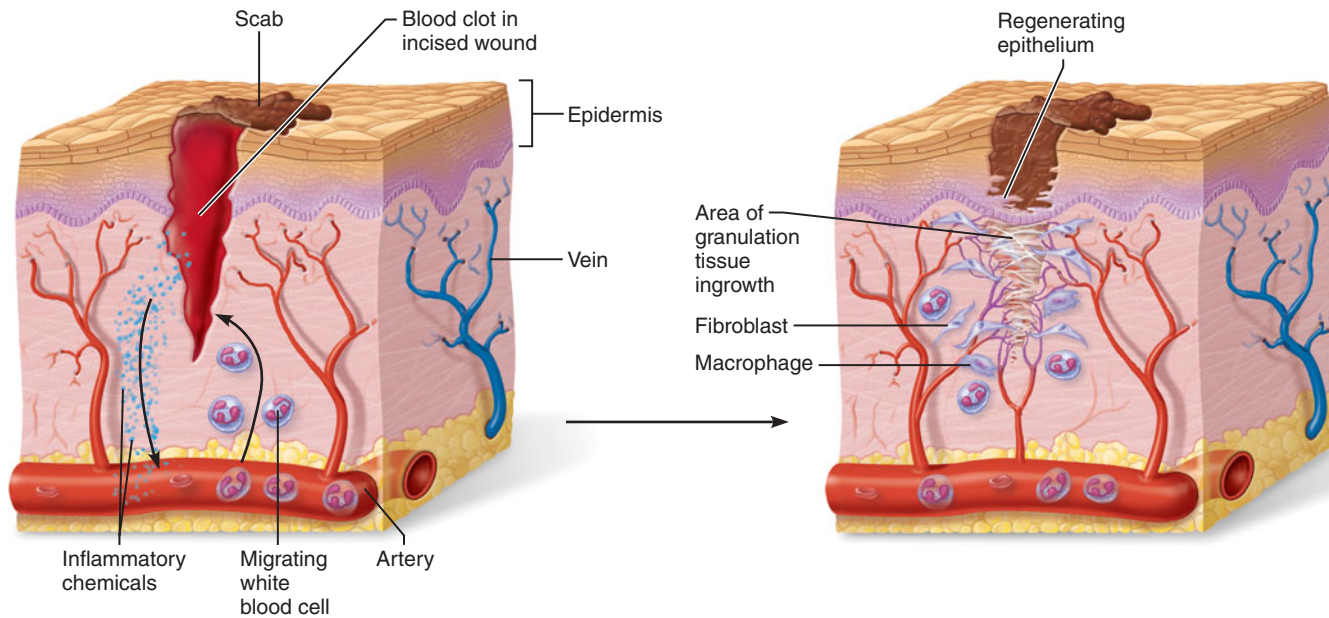
The process we have just outlined describes the healing of a wound such as a cut, scrape, or puncture. In pure *infections* (a pimple or sore throat), by contrast, there is usually no clot formation or scarring. Only severe infections lead to scarring.

The capacity for regeneration varies widely among the different tissues. Epithelia regenerate extremely well, as do bone, areolar connective tissue, dense irregular connective tissue, and blood-forming tissue. Smooth muscle and dense regular connective tissue have a moderate capacity for regeneration, but skeletal muscle and cartilage have only a weak capacity. Cardiac muscle and the nervous tissue in the brain and spinal cord have no functional regenerative capacity. However, recent studies have shown that some unexpected cellular division occurs in both these tissues after damage, and efforts are under way to coax them to regenerate better.

In nonregenerating tissues and in exceptionally severe wounds, fibrosis totally replaces the lost tissue. The resulting scar appears as a pale, often shiny area and shrinks during the months after it first forms. A scar consists mostly of collagen fibers and contains few cells or capillaries. Although it is very strong, it lacks the flexibility and elasticity of most normal tissues, and it is unable to perform the normal functions of the tissue it has replaced.

Irritation of visceral organs can cause them to adhere to one another or to the body wall as they scar. Such **adhesions** can prevent the normal churning actions of loops of the intestine, dangerously halting the movement of food through the digestive tube. They can also restrict the movement of the heart and lungs and immobilize the joints. After almost all





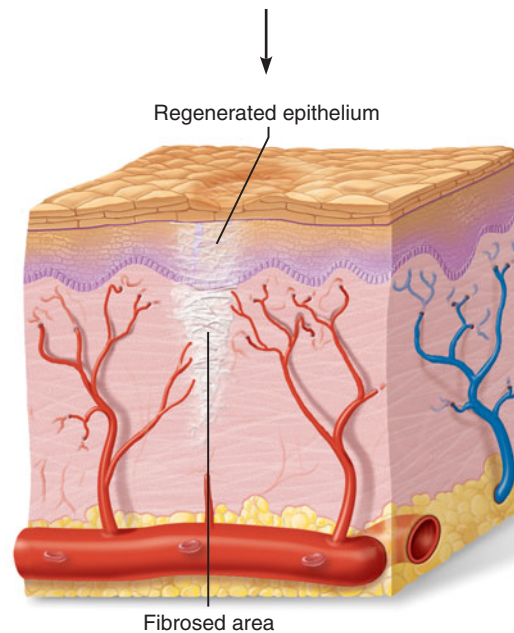
### ① Inflammation sets the stage:

- Severed blood vessels bleed.
- Inflammatory chemicals are released.
- Local blood vessels become more permeable, allowing white blood cells, fluid, clotting proteins, and other plasma proteins to seep into the injured area.
- Clotting occurs; surface dries and forms a scab.

### ② Organization restores the blood supply:

- The clot is replaced by granulation tissue, which restores the vascular supply.
- Fibroblasts produce collagen fibers that bridge the gap.
- Macrophages phagocytize cell debris.
- Surface epithelial cells multiply and migrate over the granulation tissue.

**FIGURE 4.14** Tissue repair of a skin wound.



### ③ Regeneration and fibrosis effect permanent repair:

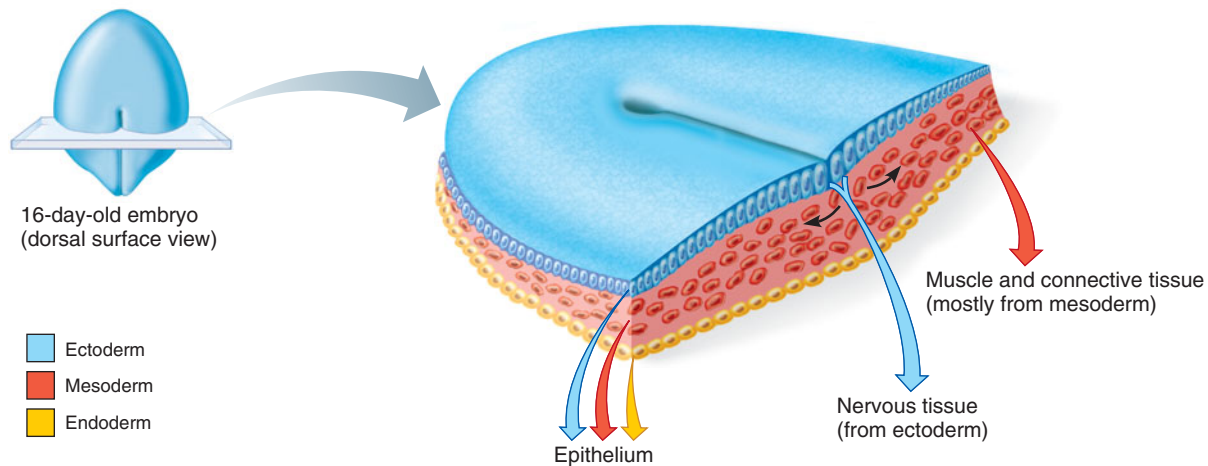
- The fibrosed area matures and contracts; the epithelium thickens.
- A fully regenerated epithelium with an underlying area of scar tissue results.

abdominal surgeries, adhesions form between the body wall and the abdominal viscera, making subsequent surgery in that region more difficult.

### check your understanding

21. Which tissues regenerate easily? Which tissues do not regenerate?
22. Is the scar tissue that creates a "scar" located in the epithelium or in the underlying connective tissue?
23. What causes the heat and swelling in an infected tissue?

For answers, see Appendix B.



**FIGURE 4.15** Embryonic germ layers and the primary tissue types they produce.

## THE TISSUES THROUGHOUT LIFE

- Indicate the embryonic derivation of each tissue class.
- Briefly describe changes that occur in tissues with age.

The embryonic derivations of the four basic tissues are as follows (**Figure 4.15**): Connective and muscle tissues derive from mesenchyme, mostly of the mesoderm germ layer. Most epithelial tissues develop from embryonic epithelium of the ectoderm and endoderm layers. A few epithelia, however, derive from mesodermal mesenchyme, namely the epithelium lining the vessels and the mesothelium lining the ventral body cavity. The nervous tissue in the brain and spinal cord derives from ectodermal epithelium (recall Chapter 3, p. 56).

By the end of the second month of development, the four primary tissues have formed, and all major organs are in place. In virtually all tissues, the cells continue to divide throughout the prenatal period, providing the rapid body growth that occurs before birth. The division of *nerve* cells, however, stops or nearly stops during the fetal period. After birth, the cells of most other tissues continue to divide until adult body size is reached. In adulthood, only the epithelial tissues and blood cell-forming tissues are highly mitotic. Cellular division in other tissues slows greatly, although many tissues retain a regenerative capacity.

Some tissues that regenerate throughout life do so through the division of their mature, differentiated cells. This is common in epithelial tissues. The new differentiated cells replace older cells within the tissue. Abnormalities in this process can result in pathological conditions. Cancer is a disease in which tissue cells divide uncontrollably and expand beyond the normal tissue boundaries. The most common types of cancers in humans are carcinomas, cancer arising from epithelia. Cancer is discussed in **A Closer Look** on p. 96.

Many tissues contain populations of **stem cells**, relatively undifferentiated cells that renew themselves continually and divide to produce new tissue cells as needed. Stem cells have long been known to exist in the rapidly replacing tissues, such as the epidermis, the lining of the digestive tube, some connective tissues, and blood-forming tissue. Now, however, they have been found elsewhere: in the brain, adipose tissue, and probably the liver and pancreas.

Given good nutrition, good circulation, and relatively infrequent wounds and infections, the tissues normally function well through youth and middle age. The importance of nutrition for tissue health cannot be overemphasized. For example, vitamin A is needed for the normal regeneration of epithelium (liver and carrots are rich in this vitamin). Because proteins are the structural material of the body, an adequate intake of protein is essential for the tissues to retain their structural integrity.

With increasing age, the epithelia thin and are more easily breached. The amount of collagen in the body declines, making tissue repair less efficient. Wounds do not heal as fast as in youth. Bone, muscle, and nervous tissues begin to atrophy. These events are due in part to a decrease in circulatory efficiency, which reduces the delivery of nutrients to the tissues, but in some cases diet is a contributing factor. A diet low in protein and vitamins can negatively affect tissue health.

### check your understanding

24. Which embryonic layer or layers form epithelium?
25. How do cancerous cells differ from other highly mitotic cell types?

For answers, see Appendix B.

# a closer look

## Cancer—The Intimate Enemy

Although once perceived as disorganized cell growth, cancer is now known to be a logical, coordinated process in which a precise sequence of tiny alterations changes a normal cell into a killer. Let's take a closer look at what cancer really is.

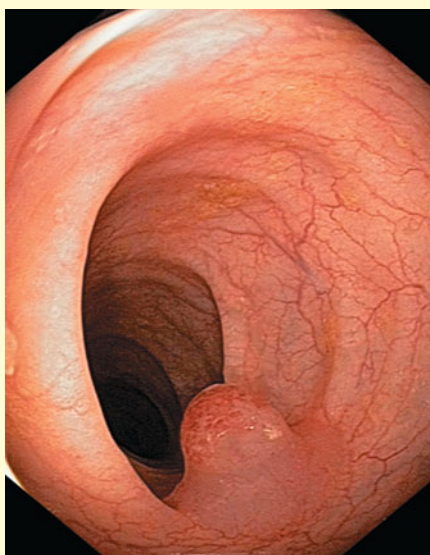
When cells fail to honor normal controls of cell division and multiply excessively, an abnormal mass of proliferating cells called a **neoplasm** (ne'o-plazm, "new growth") results. Neoplasms are classified as benign ("kindly") or malignant ("bad"). A **benign neoplasm**, commonly called a **tumor**, is strictly a local affair. Its cells remain compacted, are often encapsulated, tend to grow slowly, and seldom kill their hosts if they are removed before they compress vital organs.

In contrast, **cancers** are **malignant neoplasms**, nonencapsulated masses that grow relentlessly. Their cells resemble immature cells, and they invade their surroundings rather than pushing them aside, as reflected in the name *cancer*, from the Latin word for "crab." Malignant cells can also break away from the parent mass, the primary tumor, and travel via blood or lymph to other body organs, where they form secondary cancer masses.

This capability of traveling to other parts of the body is called **metastasis** (mē-tas'tah-sis). Metastasis and invasiveness distinguish cancer cells from the cells of benign neoplasms. Cancer cells consume an exceptional amount of the body's nutrients, leading to weight loss and tissue wasting that contribute to death.

### Mechanisms of Carcinogenesis

Physical factors (radiation, mechanical trauma), certain viral infections, and many chemicals (tobacco tars, saccharin, some natural food chemicals) can act as **carcinogens** (cancer-causers). These factors all cause mutations—changes in DNA that alter the expression of certain genes. However, not all carcinogens do damage; most are eliminated by peroxisomal or lysosomal enzymes or



Endoscopic view of a colon polyp.

by the immune system. Furthermore, one mutation usually isn't enough; it takes several genetic changes to transform a normal cell into a cancerous cell.

Cancer can result from two types of genetic mutations. **Oncogenes** (onco = tumor) result from mutations in normal genes that regulate cell division, differentiation, and growth. When mutated, these genes are abnormally activated, causing abnormal growth and cell division, which can lead to cancer. A second group of genes, **tumor-suppressor genes**, function in normal cells to halt cell division, repair damaged DNA, and initiate programmed cell death (called *apoptosis*), when the cellular DNA is severely damaged. Mutations in tumor-suppressor genes lead to inactivation of these cellular controls and in turn to uncontrolled cell division. Mutations in tumor-suppressor genes are implicated in many types of cancer.

Colorectal cancer, one of the best-understood human cancers, involves mutations in both of these genetic pathways. As with most cancers, a metastasis develops gradually. One of the first signs is a polyp, a small benign growth consisting of apparently normal

mucosa cells (see the photo). As cell division continues, the growth enlarges, becoming an adenoma. As various tumor-suppressor genes are inactivated and an oncogene is activated, the mutations pile up, and the adenoma becomes increasingly abnormal. The final consequence is colon carcinoma, a form of cancer that metastasizes quickly.

Cancer can arise from almost any cell type but most commonly originates in the epithelial tissues of the skin, lung, colon, breast, and prostate gland. Epithelia are particularly susceptible because these tissues normally experience high rates of mitosis. Mutation of the many genes controlling mitosis can lead to uncontrolled cell division and, potentially, cancer.

### Diagnosis and Treatment

Screening procedures are vital for early detection. Unfortunately, most cancers are diagnosed only after symptoms have already appeared. In this case the diagnostic method is usually a **biopsy**: removing a tissue sample surgically and examining it microscopically for malignant cells.

Most cancers are removed surgically, if possible. To destroy metastasized cells, radiation therapy and chemotherapy commonly follow surgery. Anticancer drugs have unpleasant side effects—nausea, vomiting, hair loss—because they kill all rapidly dividing cells, including normal tissues and cells. Radiation also has side effects because it can destroy healthy tissue as well as cancer cells.

Promising new therapies act by 1) delivering drugs more precisely to the cancer while sparing normal tissue through the use of tiny drug-coated metal beads, which are guided to the tumor by a powerful magnet, and 2) starving cancer cells by cutting off their blood supply.

Other experimental treatments seek to repair defective tumor-suppressor genes and oncogenes, destroy cancer cells with viruses, or signal cancer cells to commit suicide by apoptosis.



## RELATED CLINICAL TERMS

**ADENOMA** (ad-ě-no'mah) (*aden* = gland; *oma* = tumor) Any neoplasm of glandular epithelium, benign or malignant. The malignant type is more specifically called *adenocarcinoma*.

**CARCINOMA** (kar'sī-no'mah) (*karkinos* = crab, cancer) Cancer arising in an epithelium. Ninety percent of all human cancers are of this type: lung, breast, prostate, colon, and others.

**EPITHELIAL-CONNECTIVE TISSUE INTERACTIONS** An exchange of chemical signals between epithelia and the underlying connective tissues, especially in the control of the events of embryonic development and in the generation of cancer as epithelial tumor cells gain

the ability to metastasize. These exchanges are also called epithelial-stromal interactions or, in embryos, epithelial-mesenchymal interactions. This is currently a very active area of research.

**LESION** (le'zhun; "wound") Any injury, wound, or infection that affects tissue over an area of a definite size, as opposed to being widely spread throughout the body.

**SARCOMA** (sar-ko'mah) (*sarkos* = flesh; *oma* = tumor) Cancer arising in the mesenchyme-derived tissues; that is, in connective tissues and muscle.

## CHAPTER SUMMARY

You can use the following media study tool for additional help when you review specific key topics in Chapter 4.

**PAL** = Practice Anatomy Lab™

1. Tissues are collections of structurally similar cells with related functions. They also contain nonliving material between their cells. The four primary tissues are epithelium, connective tissue, muscle, and nervous tissue.

### I. Epithelia (pp. 65–77)

2. Epithelia are sheets of cells that cover body surfaces and line body cavities. Their functions include protection, sensory reception, diffusion, absorption, ion transport, and filtration. Glandular epithelia function in secretion.

#### Special Characteristics of Epithelia (p. 66)

3. Epithelia exhibit a high degree of cellularity, little extracellular material, specialized cell junctions, polarity, avascularity, and the ability to regenerate. They are underlain by loose connective tissue.

#### Classification of Epithelia (pp. 66–72)

4. Epithelia are classified by cell shape as squamous, cuboidal, or columnar, and by the number of cell layers as simple (one layer) or stratified (more than one layer). Stratified epithelia are named according to the shape of their apical cells.
5. Simple squamous epithelium is a single layer of flat cells. Its thinness allows molecules to pass through it rapidly by passive diffusion. It lines the air sacs of the lungs, the interior of blood vessels (endothelium), and the ventral body cavity (mesothelium).
6. Simple cuboidal epithelium occurs in kidney tubules, the secretory cells of many glands, and the small ducts of glands.
7. Simple columnar epithelium lines the stomach and intestines, and a ciliated version lines the uterine tubes. Like simple cuboidal epithelium, it is active in secretion, absorption, and ion transport.
8. Pseudostratified columnar epithelium is a simple epithelium that contains both short and tall cells. A ciliated version lines most of the respiratory passages.
9. Stratified squamous epithelium is multilayered and thick. Its apical cells are flat, and it resists abrasion. Examples are the epidermis and the lining of the mouth, esophagus, and vagina.
10. Stratified cuboidal and stratified columnar epithelium, while rare, line the large ducts of some glands.

11. Transitional epithelium is a stratified epithelium that thins when it stretches. It lines the hollow urinary organs.

#### Glands (pp. 72–74)

12. A gland is one or more cells specialized to secrete a product. Most glandular products are proteins released by exocytosis.
13. Exocrine glands secrete their products onto body surfaces or into body cavities. Mucus-secreting goblet cells are unicellular exocrine glands. Multicellular exocrine glands are classified by the structure of their ducts as simple or compound and by the structure of their secretory units as tubular, alveolar (acinar), or tubuloalveolar.
14. Endocrine (ductless) glands secrete hormones, which enter the circulatory vessels and travel to target organs, from which they signal a response.

#### Epithelial Surface Features (pp. 74–77)

15. Features of lateral epithelial cell surfaces: The main types of cell junctions are tight junctions that close off the extracellular spaces, adhesive belt junctions and desmosomes that bind cells together, and gap junctions through which small molecules pass from cell to cell.
16. Feature on the basal epithelial surface: Epithelial cells lie on a protein sheet called the basal lamina. This acts as a filter and a scaffolding on which regenerating epithelial cells can grow. The basal lamina, plus some underlying reticular fibers, form the thicker basement membrane.
17. Features of apical epithelial surfaces: Microvilli occur on most moist epithelia. They increase the epithelial surface area and may anchor sheets of mucus. Cilia are whiplike projections that beat to move fluid (usually mucus). Microtubules in the cores of cilia generate ciliary movement.

#### **PAL** Histology/Epithelial Tissue

### II. Connective Tissue (pp. 77–90)

18. Connective tissue is the most diverse and abundant class of tissues. Its four basic classes are connective tissue proper (loose and dense), cartilage, bone, and blood.

#### Special Characteristics of Connective Tissues (pp. 77–78)

19. Despite the diversity of connective tissues, all consist of cells separated by abundant extracellular matrix. In all connective tissues except blood, the matrix consists of ground substance, fibers, and

tissue fluid. All connective tissues are derived from embryonic mesenchyme.

### Structural Elements of Connective Tissue (pp. 78–80)

20. The primary cell type in connective tissue produces the fibers and the ground substance of the extracellular matrix: fibroblasts in connective tissue proper; chondroblasts in cartilage; osteoblasts in bone. Once the tissue is formed, these cells are called fibrocytes, chondrocytes, and osteocytes, and they function to maintain the tissue matrix. Additional cell types that respond to infectious agents are found in many connective tissues.
21. Three types of fibers are found in connective tissues: Collagen fibers function to resist tension, reticular fibers provide structural support, and elastic fibers enable recoil of stretched tissues.
22. The ground substance is a gel-like material that functions to hold fluid. The matrix of bone is hardened with calcified mineral salts.

### Classification of Connective Tissues (pp. 80–88)

23. *Loose areolar connective tissue* surrounds capillaries and underlies most epithelia. Its main functions are to (1) support and bind other tissues with its fibers (collagen, reticular, elastic), (2) hold tissue fluid in its jellylike ground substance, (3) fight infection with its many blood-derived defense cells (macrophages, plasma cells, neutrophils, etc.), and (4) store nutrients in fat cells.
24. *Adipose connective tissue* is similar to areolar connective tissue but is dominated by nutrient-storing fat cells. This white fat is plentiful in the hypodermis below the skin. Babies also have brown fat that heats their blood and body.
25. *Reticular connective tissue* resembles areolar tissue, except that its only fibers are reticular fibers. These form networks of caverns that hold free blood cells. Reticular tissue occurs in bone marrow, lymph nodes, and the spleen.
26. Dense connective tissue contains exceptionally thick collagen fibers and resists tremendous pulling forces. In *dense irregular connective tissue*, the collagen fibers run in various directions. This tissue occurs in the dermis and in organ capsules.
27. *Dense regular connective tissue* contains bundles of collagen fibers that all run in the same direction and are separated by rows of fibroblasts. This tissue, which is subject to high tension from a single direction, is the main tissue in tendons, ligaments, and fascia.
28. *Elastic connective tissue* has a high proportion of elastic fibers. This tissue is located in the walls of arteries, around the bronchial tubes, and within certain ligaments.
29. Cartilage and bone have the basic structure of connective tissue (cells and matrix), but their stiff matrix allows them to resist compression. Cartilage is springy and avascular. Its matrix contains mostly water.
30. Bone tissue has a hard, collagen-rich matrix embedded with calcium salts. This mineral gives bone compressive strength.
31. Blood consists of red and white blood cells in a fluid matrix called plasma. It is the most atypical connective tissue.

### Covering and Lining Membranes (pp. 88–90)

32. Membranes, each consisting of an epithelium plus an underlying layer of connective tissue, cover broad surfaces in the body. The

cutaneous membrane (skin), which is dry, covers the body surface. Mucous membranes, which are moist, line the hollow internal organs that open to the body exterior. Serous membranes, which are slippery, line the pleural, pericardial, and peritoneal cavities.

### PAL Histology/Connective Tissue

### III. Muscle Tissue (pp. 90–91)

33. Muscle tissue consists of long muscle cells that are specialized to contract and generate movement. A scant extracellular matrix separates the muscle cells. There are three types of muscle tissue:

*Skeletal muscle* is in the muscles that move the skeleton. Its cells are cylindrical and striated.

*Cardiac muscle* is in the wall of the heart, and it pumps blood. Its cells branch and have striations.

*Smooth muscle* is in the walls of hollow organs, and it usually propels substances through these organs. Its cells are elongated with tapered ends and lack striations.

### PAL Histology/Muscular Tissue

### IV. Nervous Tissue (p. 92)

34. Nervous tissue, the main tissue of the nervous system, is composed of neurons and supporting cells called neuroglia. Nervous tissue regulates body functions. *Neurons* are branching cells that receive and transmit electrical impulses. *Neuroglia* nourish, insulate, and protect neurons.

### PAL Histology/Nervous Tissue

### Tissue Response to Injury (pp. 92–94)

#### Inflammation (p. 93)

35. Inflammation is a response to tissue injury and infection. It is localized to the connective tissue and the vessels of the injury site. The inflammatory response begins with dilation of blood vessels (causing redness and heat), followed by edema (causing swelling and pain). Stasis results, and white blood cells migrate into the injured tissue.

#### Repair (pp. 93–94)

36. Tissue repair begins during inflammation and may involve tissue regeneration, fibrosis (scarring), or both. Repair of a cut begins with organization, during which the clot is replaced with granulation tissue. Collagen deposition replaces granulation tissue with scar tissue.
37. Certain tissues, such as cardiac muscle and most nervous tissue, do not regenerate naturally and are replaced by scar tissue.

### The Tissues Throughout Life (pp. 95–96)

38. Epithelial tissue forms from all three embryonic layers: ectoderm, mesoderm, and endoderm. Nervous tissue is derived from ectoderm, and muscle and connective tissues are derived from mesenchyme, primarily from the mesoderm germ layer.
39. Tissue function declines with age. The decrease in mass and viability seen in most tissues during old age partially reflects circulatory deficits or poor nutrition.

## REVIEW QUESTIONS

### Multiple Choice/Matching Questions

For answers, see Appendix B.

- Use the key to match each basic tissue type with a description below.

**Key:**

- (a) connective tissue      (b) epithelium  
(c) muscle tissue      (d) nervous tissue

- (1) composed largely of nonliving extracellular matrix; important in protection, support, defense, and holding tissue fluid  
— (2) the tissue immediately responsible for body movement  
— (3) the tissue that provides an awareness of the external environment and enables us to react to it  
— (4) the tissue that lines body cavities and covers surfaces  
— (5) the tissue that includes most glands

- An epithelium that has several cell layers, with flat cells in the apical layer, is called (choose all that apply): (a) ciliated, (b) columnar, (c) stratified, (d) simple, (e) squamous.
- Match the epithelial type named in column B with the appropriate location in column A.

**Column A**

- (1) lines inside of stomach and most of intestines  
— (2) lines inside of mouth  
— (3) lines much of respiratory tract (including the trachea)  
— (4) mesothelium  
— (5) lines inside of urinary bladder

**Column B**

- (a) pseudostratified ciliated columnar  
(b) simple columnar  
(c) simple cuboidal  
(d) simple squamous  
(e) stratified columnar  
(f) stratified squamous  
(g) transitional

- The type of gland that secretes products such as milk, saliva, bile, or sweat through a duct is (a) an endocrine gland, (b) an exocrine gland, (c) a goblet cell.
- In connective tissue proper, the cell type that secretes the fibers and ground substance is the (a) fibroblast, (b) plasma cell, (c) mast cell, (d) macrophage, (e) chondrocyte.
- Identify the cell surface features described below.
  - whiplike extensions that move fluids across epithelial surfaces
  - little “fingers” on apical epithelial surfaces that increase cell surface area and anchor mucus
  - the cell junction that holds cells together by linking the intermediate filaments of adjacent cells
  - a cell junction that closes off the extracellular space
  - of the basement membrane and the basal lamina, the one that can be seen by light microscopy
- Match each epithelial tissue in column B with its function listed in column A.

**Column A**

- (1) functions in diffusion and filtration  
— (2) functions in protection  
— (3) functions in secretion and absorption  
— (4) changes shape as the tissue stretches  
— (5) produces movement of material

**Column B**

- (a) stratified epithelium  
(b) simple columnar epithelium  
(c) transitional epithelium  
(d) ciliated epithelium  
(e) simple squamous epithelium

- For each connective tissue listed, indicate the predominant type or types of fibers found in the extracellular matrix by choosing responses from the following: (a) collagen fibers, (b) elastic fibers, (c) reticular fibers.
  - bone
  - loose areolar connective tissue
  - dense irregular connective tissue
  - reticular connective tissue
  - fibrocartilage
- The muscle tissue that is striated is (a) skeletal muscle, (b) cardiac muscle, (c) smooth muscle, (d) cardiac and skeletal muscle, (e) all three types of muscle tissue.
- Neuroglia (a) conduct electrical impulses, (b) are nerve stem cells, (c) are support cells that aid neurons, (d) are an abnormal growth of neural tissue.
- Which of the following cells are not found in a connective tissue? (a) fibroblasts, (b) goblet cells, (c) macrophages, (d) mast cells, (d) chondrocytes.
- The ground substance in connective tissue proper functions to (a) support and strengthen the tissue, (b) hold tissue fluid, (c) fight infection, (d) store nutrients, (e) resist tension.
- What embryonic layer (ectoderm, mesoderm, or endoderm) primarily forms each of the following major tissues? (a) connective tissue, (b) muscle tissue, (c) nervous tissue.

### Short Answer Essay Questions

- Define tissue.
- Explain the classification of multicellular exocrine glands, and supply an example of each class.
- Name the specific type of connective tissue being described:
  - around the capillaries
  - in the ligamentum flavum between vertebrae
  - the original, embryonic connective tissue
  - hard tissue of the skull
  - main tissue in ligaments
  - dominates the dermis
  - dominates the hypodermis



17. Name four functions of areolar connective tissue, and relate each function to a specific structural part of this tissue.
18. (a) Where does tissue fluid come from? (b) What is the function of tissue fluid?
19. Name the four classic symptoms of inflammation, and explain what each symptom represents in terms of changes in the injured tissue.
20. (a) Define endocrine gland. (b) What is a hormone?
21. Name two specific tissues that regenerate well and two that regenerate poorly.
22. Of the four basic tissue types, which two develop from mesenchyme?
23. What is fascia?
24. A fourth-grade teacher told his science class that “the body consists entirely of cells.” Hearing this, a pupil raised her hand and said her mother (an anatomist) told her the body does *not* entirely consist of cells, and, in fact, a noncellular material probably makes up more of the body than the cells do. What is this noncellular material?
25. What are the differences between a mucous membrane and a serous membrane?
26. What is the main type of tissue in the following structures? (a) a ligament or tendon; (b) a bone of the leg; (c) a muscle such as the biceps of the arm; (d) the brain; (e) the flexible skeleton in the outer ear; (f) the contractile wall of the heart; (g) kidney tubules.
27. Indicate the name and location of an epithelial tissue formed from each of the embryonic layers: ectoderm, mesoderm, and endoderm.

## CRITICAL REASONING & CLINICAL APPLICATION QUESTIONS

1. Systemic lupus erythematosus, or lupus, is a condition that sometimes affects young women. It is a chronic (persistent) inflammation that affects all or most of the connective tissue proper in the body. Suzy is told by her doctor that she has lupus, and she asks whether it will have widespread or merely localized effects within the body. What would the physician answer?
2. Sailors who made long ocean journeys in the time of Christopher Columbus ate only bread, water, and salted meat on their journeys. They often suffered from scurvy. Eventually the problem was solved, and ocean sailors no longer developed scurvy. Try to deduce how the problem was solved. (Hint: It was not by inventing faster boats!)
3. Three patients in an intensive care unit have sustained damage and widespread tissue death in three different organs. One patient has brain damage from a stroke, another had a heart attack that destroyed cardiac muscle, and the third injured much of her liver (a gland) in a crushing car accident. All three patients have stabilized and will survive, but only one will gain full functional recovery through tissue regeneration. Which one, and why?
4. In adults, over 90% of all cancers are either adenomas (adenocarcinomas) or carcinomas. In fact, cancers of the skin, lung, colon, breast, and prostate are all in these categories. Which one of the four basic tissue types gives rise to most cancers? Why might this type of tissue be so susceptible to cancer?
5. A patch of scar tissue that forms in the wall of the urinary bladder, the heart, or another hollow organ may severely hamper the function of that organ. Considering the properties of scar tissue, why do you think this is so?
6. Ciliated epithelium is located in the bronchial tubes and in the uterine tubes. What functional similarity do these structures share that is accomplished by ciliated epithelium?



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