4

Tissue: The Living Fabric

Unicellular (one-cell) organisms are rugged individualists. Each cell alone obtains and digests its food, ejects its wastes, and carries out all the other activities necessary to keep itself alive and "buzzin' around on all cylinders." But in the multicellular human body, cells do not operate independently. Instead, they form tight cell communities that live and work together.

Individual body cells are specialized, with each type performing specific functions that help maintain homeostasis and benefit the body as a whole. Cell specialization is obvious: Muscle cells look and act differently from skin cells, which in turn are easy to distinguish from brain cells. Cell specialization allows the body to function in sophisticated ways, but division of labor has certain hazards. When a particular group of cells is indispensable, its injury or loss can disable or even destroy the body.

Tissues (*tissu* = woven) are groups of cells that are similar in structure and perform a common or related function. Four primary tissue types interweave to form

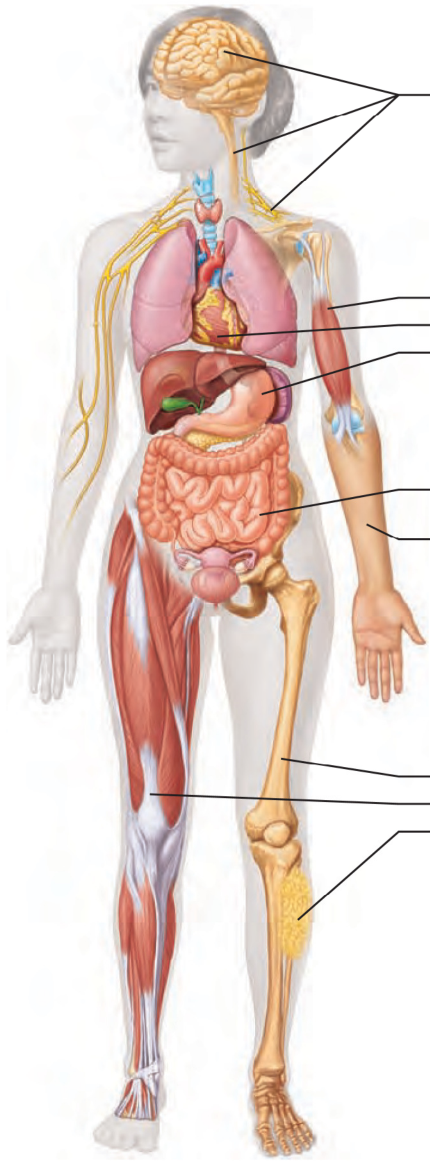


Figure 4.1 Overview of four basic tissue types: epithelial, connective, muscle, and nervous tissues.

the "fabric" of the body. These basic tissues are epithelial, connective, nervous, and muscle tissue.

If we summarized the role of each primary tissue in a single word, we could say that epithelial tissue *covers*, connective tissue *supports*, nervous tissue *controls*, and muscle tissue *produces movement*. However, these words reveal only a fraction of what each tissue does **(Figure 4.1)**.

As we explained in Chapter 1, tissues are organized into organs such as the kidneys and heart. Most organs contain all four tissue types, and their arrangement determines the organ's structure and capabilities. The study of tissues, or **histology**, complements the study of gross anatomy. Together they provide the structural basis for understanding organ physiology.

Preparing Human Tissue for Microscopy

✓ List the steps involved in preparing animal tissue for microscopic viewing.

Microscopy allows us to study tissue structure. Before a specimen can be viewed through a microscope, it must be **fixed** (preserved) and then cut into **sections** (slices) thin enough to transmit light or electrons. Finally, the specimen must be **stained** to enhance contrast.

The stains used in light microscopy are beautifully colored organic dyes, most of which were originally developed by clothing manufacturers in the mid-1800s. Many dyes consist of negatively charged molecules (acidic stains) or positively charged molecules (basic stains) that bind within the tissue to macromolecules of the opposite charge. Different parts of cells and tissues take up different dyes, distinguishing different anatomical structures.

For transmission electron microscopy (TEM), tissue sections are "stained" with heavy metal salts. These metals deflect electrons in the beam to different extents, providing contrast. Electron-microscope images are in shades of gray because color is a property of light, not of electron waves, but the image may be artificially colored to enhance contrast. Another kind of electron microscopy, scanning electron microscopy (SEM), provides three-dimensional pictures of an unsectioned tissue surface.

Preserved tissue we see under the microscope has been exposed to many procedures that alter its original condition and introduce minor distortions called **artifacts**. For this reason, most microscopic structures we view are not exactly like those in living tissue.

Check Your Understanding

1. What is the purpose of fixing tissue for microscopic viewing?
2. What types of stains are used to stain tissues to be viewed with an electron microscope?

For answers, see Appendix H.

Epithelial Tissue

✓ List several structural and functional characteristics of epithelial tissue.

✓ Name, classify, and describe the various types of epithelia, and indicate their chief function(s) and location(s).

Epithelial tissue (ep″ĭ-the′le-ul), or an **epithelium** (plural: epithelia), is a sheet of cells that covers a body surface or lines a body cavity (*epithe* = laid on, covering). Two forms occur in the body:

- *Covering and lining epithelium*, which forms the outer layer of the skin; dips into and lines the open cavities of the urogenital, digestive, and respiratory systems; and covers the walls and organs of the closed ventral body cavity
- *Glandular epithelium*, which fashions the glands of the body

Epithelia form boundaries between different environments, and nearly all substances received or given off by the body must pass through an epithelium. For example, the epidermis of the skin lies between the inside and the outside of the body. Epithelium lining the urinary bladder separates underlying cells of the bladder wall from urine.

In its role as an interface tissue, epithelium accomplishes many functions, including (1) protection, (2) absorption, (3) filtration, (4) excretion, (5) secretion, and (6) sensory reception, all of which will be touched upon later in this chapter.

Special Characteristics of Epithelium

Epithelial tissues have five distinguishing characteristics: polarity, specialized contacts, supported by connective tissues, being avascular but innervated, and having the ability to regenerate.

Polarity

All epithelia have an **apical surface**, an upper free surface exposed to the body exterior or the cavity of an internal organ, and a lower attached **basal surface**. The two surfaces differ in both structure and function. For this reason, we say that epithelia exhibit *apical-basal polarity*.

Although some apical surfaces are smooth and slick, most have **microvilli**, fingerlike extensions of the plasma membrane. Microvilli tremendously increase the exposed surface area. In epithelia that absorb or secrete (export) substances (those lining the intestine or kidney tubules, for instance), the microvilli are often so dense that the cell apices have a fuzzy appearance called a *brush border*. Some epithelia, such as that lining the trachea (windpipe), have motile **cilia** (tiny hairlike projections) that propel substances along their free surface.

Adjacent to the basal surface of an epithelium is a thin supporting sheet called the **basal lamina** (lam′ĭ-nah; "sheet"). This noncellular, adhesive sheet consists largely of glycoproteins secreted by the epithelial cells plus some fine collagen fibers. The basal lamina acts as a selective filter that determines which molecules diffusing from the underlying connective tissue are allowed to enter the epithelium. The basal lamina also acts as scaffolding along which epithelial cells can migrate to repair a wound.

Specialized Contacts

Except for glandular epithelia (discussed on pp. 124–125), epithelial cells fit closely together to form continuous sheets. Lateral contacts, including *tight junctions* and *desmosomes*, bind adjacent cells together at many points (these junctions are described in Chapter 3). The tight junctions help keep proteins in the apical region of the plasma membrane from diffusing into the basal region, and thus help to maintain epithelial polarity.

Supported by Connective Tissue

All epithelial sheets rest upon and are supported by connective tissue. Just deep to the basal lamina is the **reticular lamina**, a layer of extracellular material containing a fine network of collagen protein fibers that "belongs to" the underlying connective tissue. The two laminae form the **basement membrane**, which reinforces the epithelial sheet, helps it resist stretching and tearing, and defines the epithelial boundary.

Homeostatic Imbalance 4.1

An important characteristic of cancerous epithelial cells is their failure to respect the basement membrane boundary, which they penetrate to invade the tissues beneath. ✚

Avascular but Innervated

Although epithelium is *avascular* (contains no blood vessels), it is *innervated* (supplied by nerve fibers). Epithelial cells are nourished by substances diffusing from blood vessels in the underlying connective tissue.

Regeneration

Epithelium has a high regenerative capacity. Some epithelia are exposed to friction and their surface cells rub off. Others are damaged by hostile substances in the external environment (bacteria, acids, smoke). If and when their apical-basal polarity and lateral contacts are destroyed, epithelial cells begin to reproduce themselves rapidly. As long as epithelial cells receive adequate nutrition, they can replace lost cells by cell division.

☑ Check Your Understanding

3. Epithelial tissue is the only tissue type that has polarity, that is, an apical and a basal surface. Why is this important?
4. Which of the following properties apply to epithelial tissue? Has blood vessels, can repair itself (regenerate), cells joined by lateral contacts.

For answers, see Appendix H.

Classification of Epithelia

Each epithelium has two names. The first name indicates the number of cell layers present, and the second describes the shape of its cells. Based on the number of cell layers, there are simple and stratified epithelia **(Figure 4.2a)**.

- **Simple epithelia** consist of a single cell layer. They are typically found where absorption, secretion, and filtration occur and a thin epithelial barrier is desirable.
- **Stratified epithelia**, composed of two or more cell layers stacked on top of each other, are common in high-abrasion areas where protection is important, such as the skin surface and the lining of the mouth.

In cross section, all epithelial cells have six (somewhat irregular) sides, and an apical surface view of an epithelial sheet looks like a honeycomb. This polyhedral shape allows the cells to be closely packed. However, epithelial cells vary in height, and on that basis, there are three common shapes of epithelial cells (Figure 4.2b):

- **Squamous cells** (skwa′mus) are flattened and scalelike (*squam* = scale).
- **Cuboidal cells** (ku-boi′dahl) are boxlike, approximately as tall as they are wide.
- **Columnar cells** (kŏ-lum′nar) are tall and column shaped.

In each case, the shape of the nucleus conforms to that of the cell. The nucleus of a squamous cell is a flattened disc; that of a cuboidal cell is spherical; and a columnar cell nucleus is elongated from top to bottom and usually located closer to the cell base. Keep nuclear shape in mind when you attempt to identify epithelial types.

Simple epithelia are easy to classify by cell shape because the cells usually have the same shape. In stratified epithelia, however, cell shape differs in the different 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 we explore the specific epithelial types.

As you read about the epithelial classes, study **Figure 4.3**. 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.

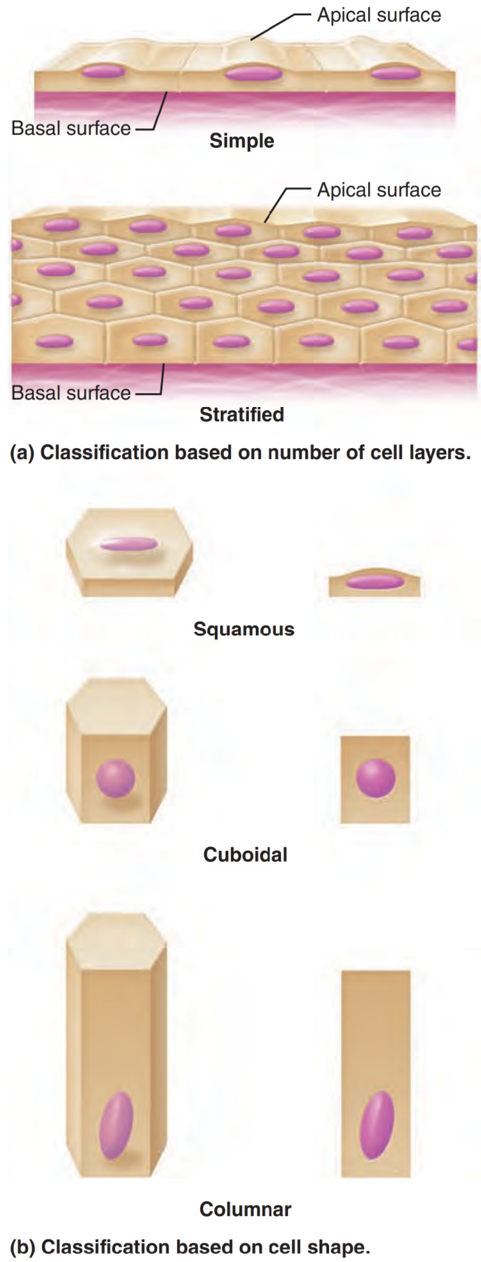


Figure 4.2 Classification of epithelia. Note that cell shape influences the shape of the nucleus.

Simple Epithelia

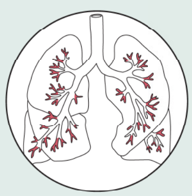
The simple epithelia are most concerned with absorption, secretion, and filtration. Because they consist of a single cell layer and are usually very thin, protection is not one of their specialties.

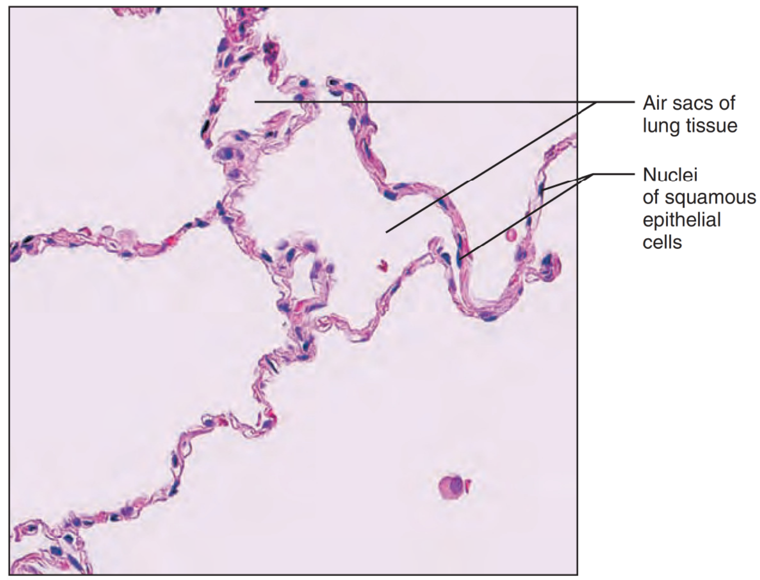
(a) Simple squamous epithelium

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

Function: Allows materials to pass 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).





Photomicrograph: Simple squamous epithelium forming part of the alveolar (air sac) walls (140×).

Figure 4.3 Epithelial tissues. (a) Simple epithelium. (For related images, see *A Brief Atlas of the Human Body*, Plates 1 and 2.)

Simple Squamous Epithelium The cells of a **simple squamous epithelium** are flattened laterally, and their cytoplasm is sparse (Figure 4.3a). In a surface view, the close-fitting cells resemble a tiled floor. When the cells are cut perpendicular to their free surface, they resemble fried eggs seen from the side, with their cytoplasm wisping out from the slightly bulging nucleus.

Thin and often permeable, simple squamous epithelium is found where filtration or the exchange of substances by rapid diffusion is a priority. In the kidneys, it forms part of the filtration membrane. In the lungs, it forms the walls of the air sacs across which gas exchange occurs (Figure 4.3a).

Two simple squamous epithelia in the body have special names that reflect their location.

- **Endothelium** (en″do-the′le-um; "inner covering") provides a slick, friction-reducing lining in lymphatic vessels and in all hollow organs of the cardiovascular system—blood vessels and the heart. Capillaries consist exclusively of endothelium, and its exceptional thinness encourages the efficient exchange of nutrients and wastes between the bloodstream and surrounding tissue cells.
- **Mesothelium** (mez″o-the′le-um; "middle covering") is the epithelium found in serous membranes, the membranes lining the ventral body cavity and covering its organs.

Simple Cuboidal Epithelium **Simple cuboidal epithelium** consists of a single layer of cells as tall as they are wide (Figure 4.3b). The spherical nuclei stain darkly, causing the cell layer to look like a string of beads when viewed microscopically. Important functions of simple cuboidal epithelium are secretion and absorption. This epithelium forms the walls of the smallest ducts of glands and of many kidney tubules.

Simple Columnar Epithelium **Simple columnar epithelium** is a single layer of tall, closely packed cells, aligned like soldiers in a row (Figure 4.3c). It lines the digestive tract from the stomach through the rectum. Columnar cells are mostly associated with absorption and secretion, and the digestive tract lining has two distinct modifications that make it ideal for that dual function:

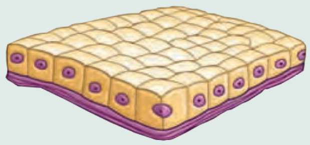
- Dense microvilli on the apical surface of absorptive cells
- Tubular glands made primarily of cells that secrete mucus-containing intestinal juice

Additionally, some simple columnar epithelia display cilia on their free surfaces, which help move substances or cells through an internal passageway.

Pseudostratified Columnar Epithelium The cells of **pseudostratified columnar epithelium** (soo″do-stră′tĭ-fīd) vary in height (Figure 4.3d). All of its cells rest on the basement membrane, but only the tallest reach the free surface of the epithelium. Because the cell nuclei lie at different levels above the basement membrane, the tissue gives the false (pseudo) impression that

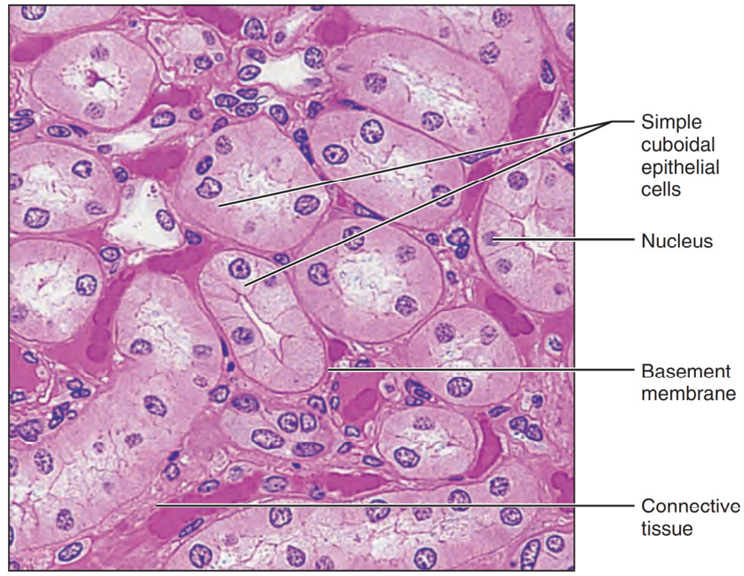
(b) Simple cuboidal epithelium

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



Function: Secretion and absorption.

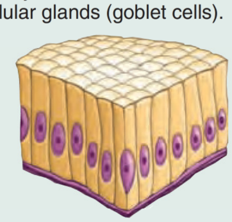
Location: Kidney tubules; ducts and secretory portions of small glands; ovary surface.



Photomicrograph: Simple cuboidal epithelium in kidney tubules (430×).

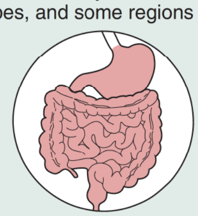
(c) Simple columnar epithelium

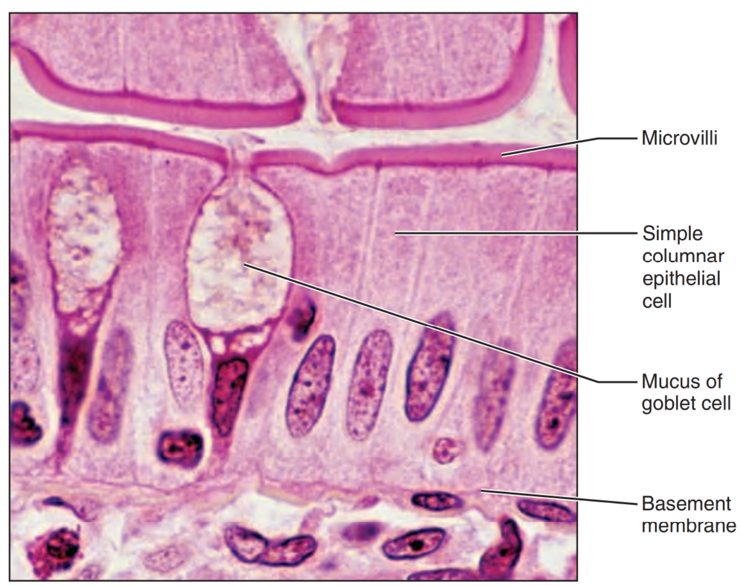
Description: Single layer of tall cells with *round* to *oval* nuclei; some cells bear cilia; layer may contain mucus-secreting unicellular glands (goblet cells).



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 rectum), gallbladder, and excretory ducts of some glands; ciliated variety lines small bronchi, uterine tubes, and some regions of the uterus.



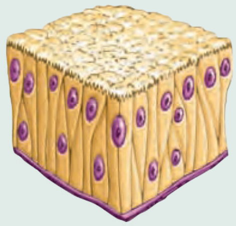


Photomicrograph: Simple columnar epithelium of the small intestine mucosa (660×).

Figure 4.3 *(continued)* **(b)** and **(c)** Simple epithelium. (For related images, see *A Brief Atlas of the Human Body*, Plates 3, 4, and 5.)

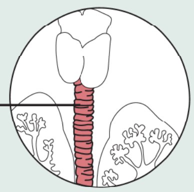
(d) Pseudostratified columnar epithelium

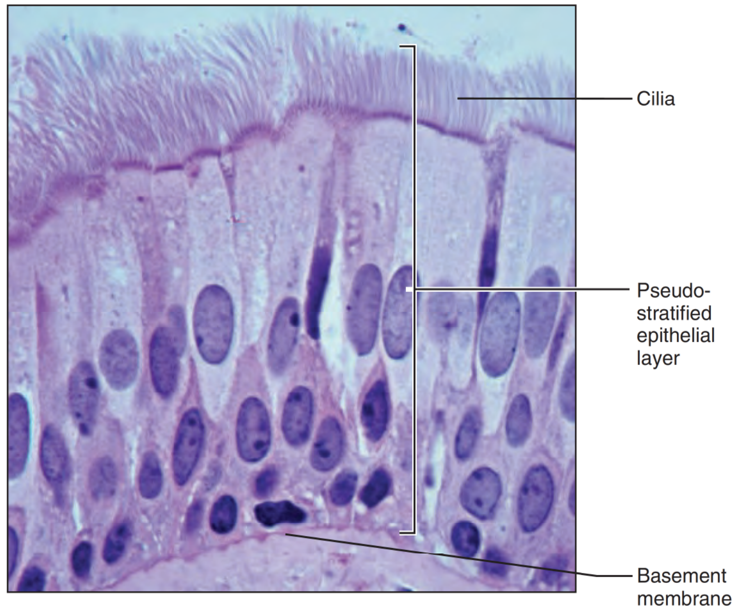
Description: Single layer of cells of differing heights, some not reaching the free surface; nuclei seen at different levels; may contain mucus-secreting cells and bear cilia.



Function: Secrete substances, particularly 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.





Photomicrograph: Pseudostratified ciliated columnar epithelium lining the human trachea (800×).

Figure 4.3 *(continued)* **Epithelial tissues. (d)** Simple epithelium. (For a related image, see *A Brief Atlas of the Human Body*, Plate 6.)

several cell layers are present; hence "pseudostratified." The short cells are relatively unspecialized and give rise to the taller cells. This epithelium, like the simple columnar variety, secretes or absorbs substances. A ciliated version containing mucus-secreting cells lines most of the respiratory tract. Here the motile cilia propel sheets of dust-trapping mucus superiorly away from the lungs.

Stratified Epithelia

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

Stratified Squamous Epithelium **Stratified squamous epithelium** is the most widespread of the stratified epithelia (Figure 4.3e). Composed of several layers, it is thick and well suited for its protective role in the body. Its free surface cells are squamous, and cells of the deeper layers are cuboidal or columnar. This epithelium is found in areas subjected to wear and tear, and its surface cells are constantly being rubbed away and replaced by division of its basal cells. Because epithelium depends on nutrients diffusing from deeper connective tissue, the epithelial cells farther from the basement membrane are less viable and those at the apical surface are often flattened and atrophied.

To avoid memorizing all its locations, simply remember that this epithelium forms the external part of the skin and extends a short distance into every body opening that is directly continuous with the skin. The outer layer, or epidermis, of the skin is *keratinized* (ker′ah-tin″īzd), meaning its surface cells contain *keratin*, a tough protective protein. (We discuss the epidermis in Chapter 5.) The other stratified squamous epithelia of the body are *nonkeratinized*.

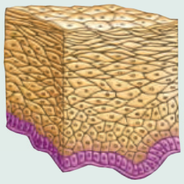
Stratified Cuboidal and Columnar Epithelia **Stratified cuboidal epithelium** is quite rare in the body, mostly found in the ducts of some of the larger glands (sweat glands, mammary glands). It typically has two layers of cuboidal cells.

Stratified columnar epithelium also has a limited distribution in the body. Small amounts are found in the pharynx, the male urethra, and lining some glandular ducts. This epithelium also occurs at transition areas or junctions between two other types of epithelia. Only its apical layer of cells is columnar. Because of their relative scarcity in the body, Figure 4.3 does not illustrate these two stratified epithelia (but see *A Brief Atlas of the Human Body*, Plates 8 and 9).

Transitional Epithelium **Transitional epithelium** forms the lining of hollow urinary organs, which stretch as they fill with urine (Figure 4.3f). Cells of its basal layer are cuboidal or columnar. The apical cells vary in appearance, depending on the degree of distension (stretching) of the organ. When the organ is distended with urine, the transitional epithelium thins from about six cell layers to three, and its domelike apical cells flatten

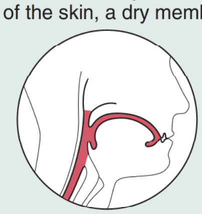
(e) Stratified squamous epithelium

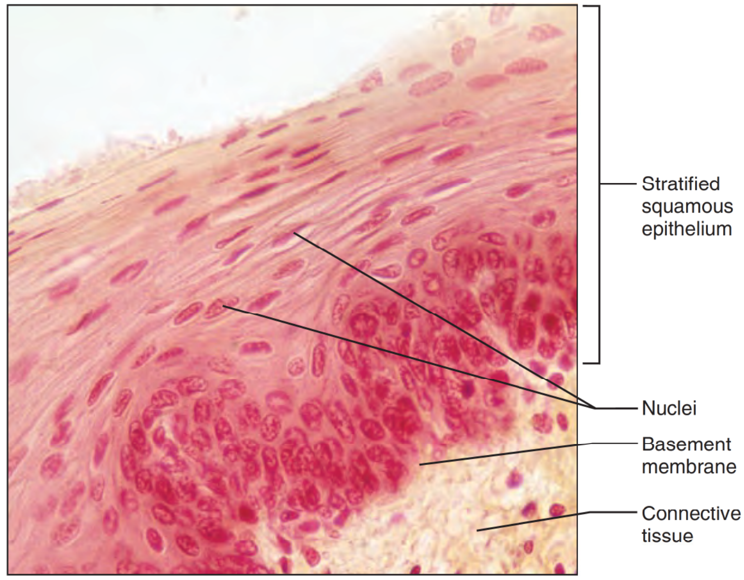
Description: Thick membrane composed of several cell layers; basal cells are cuboidal or columnar and metabolically active; surface cells are flattened (squamous); in the keratinized type, the surface cells are full of keratin and dead; basal cells are active in mitosis and produce the cells of the more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

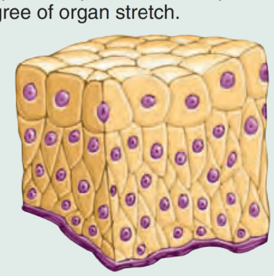




Photomicrograph: Stratified squamous epithelium lining the esophagus (285×).

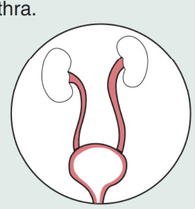
(f) Transitional epithelium

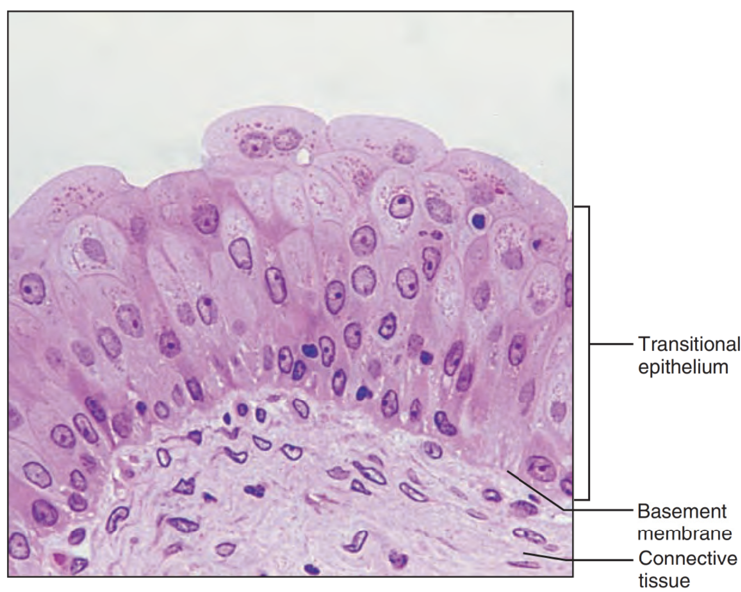
Description: Resembles both stratified squamous and stratified cuboidal; basal cells cuboidal or columnar; surface cells dome shaped or squamouslike, depending on degree of organ stretch.



Function: Stretches readily, permits stored urine to distend urinary organ.

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





Photomicrograph: Transitional epithelium lining the bladder, relaxed state (360×); note the bulbous, or rounded, appearance of the cells at the surface; these cells flatten and elongate when the bladder fills with urine.

Figure 4.3 *(continued)* **(e)** and **(f)** Stratified epithelium. (For related images, see *A Brief Atlas of the Human Body*, Plates 7 and 10.)

and become squamouslike. The ability of transitional cells to change their shape (undergo "transitions") allows a greater volume of urine to flow through a tubelike organ. In the bladder, it allows more urine to be stored.

Check Your Understanding

5. Stratified epithelia are "built" for protection or to resist abrasion. What are the simple epithelia better at?
6. Some epithelia are pseudostratified. What does this mean?
7. Where is transitional epithelium found and what is its importance at those sites?

For answers, see Appendix H.

Glandular Epithelia

- ✓ Define gland.
- ✓ Differentiate between exocrine and endocrine glands, and between multicellular and unicellular glands.
- ✓ Describe how multicellular exocrine glands are classified structurally and functionally.

A **gland** consists of one or more cells that make and secrete a particular product. This product, called a **secretion**, is an aqueous (water-based) fluid that usually contains proteins, but there is variation. For example, some glands release a lipid- or steroid-rich secretion.

Secretion is an active process. Glandular cells obtain needed substances from the blood and transform them chemically into a product that is then discharged from the cell. Notice that the term *secretion* can refer to both the gland's *product* and the *process* of making and releasing that product.

Glands are classified according to two sets of traits:

- Where they release their product—glands may be *endocrine* ("internally secreting") or *exocrine* ("externally secreting")
- Relative cell number—glands may be *unicellular* ("one-celled") or *multicellular* ("many-celled")

Unicellular glands are scattered within epithelial sheets. By contrast, most multicellular epithelial glands form by invagination (inward growth) of an epithelial sheet into the underlying connective tissue. At least initially, most have *ducts*, tubelike connections to the epithelial sheets.

Endocrine Glands

Because **endocrine glands** eventually lose their ducts, they are often called *ductless glands*. They produce **hormones**, messenger chemicals that they secrete by exocytosis directly into the extracellular space. From there the hormones enter the blood or lymphatic fluid and travel to specific target organs. Each hormone prompts its target organ(s) to respond in some characteristic way. For example, hormones produced by certain intestinal cells cause the pancreas to release enzymes that help digest food in the digestive tract.

Endocrine glands are structurally diverse, so one description does not fit all. Most are compact multicellular organs, but some individual hormone-producing cells are scattered in the digestive tract lining (mucosa) and in the brain, giving rise to their collective description as the *diffuse endocrine system*. Endocrine secretions are also varied, ranging from modified amino acids to peptides, glycoproteins, and steroids. Since not all endocrine glands are epithelial derivatives, we defer consideration of their structure and function to Chapter 16.

Exocrine Glands

All **exocrine glands** secrete their products onto body surfaces (skin) or into body cavities. The unicellular glands do so directly (by exocytosis), whereas the multicellular glands do so via an epithelium-walled duct that transports the secretion to the epithelial surface. Exocrine glands are a diverse lot and many of their products are familiar. They include mucous, sweat, oil, and salivary glands, the liver (which secretes bile), the pancreas (which synthesizes digestive enzymes), and many others.

Unicellular Exocrine Glands The only important examples of **unicellular** (or one-celled) glands are *mucous cells* and *goblet cells*. Unicellular glands are sprinkled in the epithelial linings of the intestinal and respiratory tracts amid columnar cells with other functions (see Figure 4.3c).

In humans, all such glands produce **mucin** (mu′sin), a complex glycoprotein that dissolves in water when secreted. Once dissolved, mucin forms mucus, a slimy coating that protects and lubricates surfaces. In **goblet cells** the cuplike accumulation of mucin distends the top of the cell, making the cells look like a glass with a stem (thus "goblet" cell, **Figure 4.4**). This distortion does not occur in **mucous cells**.

Multicellular Exocrine Glands Compared to the unicellular glands, **multicellular exocrine glands** are structurally more complex. They have two basic parts: an epithelium-derived *duct* and a *secretory unit* (*acinus*) consisting of secretory cells. In all but the simplest glands, *supportive connective tissue* surrounds the secretory unit and supplies it with blood vessels and nerve fibers, and forms a *fibrous capsule* that extends into the gland and divides it into *lobes*.

Multicellular exocrine glands can be classified by structure and by type of secretion.

- **Structural classification.** On the basis of their duct structures, multicellular exocrine glands are either simple or compound **(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 as (1) **tubular** if the secretory cells form tubes; (2) **alveolar** (al-ve′o-lar) if the secretory cells form small, flasklike sacs (*alveolus* = "small hollow cavity"); or (3) **tubuloalveolar** if they have both types of secretory units. Note that the term **acinar** (as′ĭ-nar; "berrylike") is used interchangeably with alveolar.
- **Modes of secretion.** Multicellular exocrine glands secrete their products in different ways, so they can also be

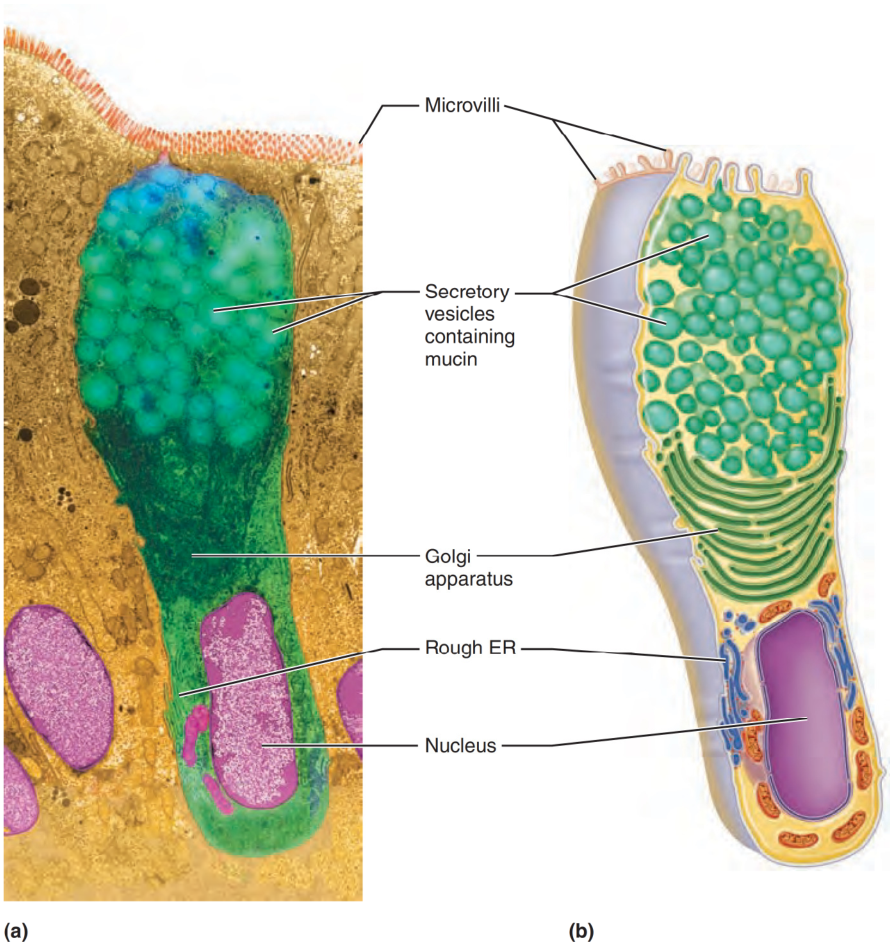


Figure 4.4 Goblet cell (unicellular exocrine gland). (a) Photomicrograph of a goblet cell in the simple columnar epithelium lining the small intestine (1640×). **(b)** Corresponding diagram. Notice the secretory vesicles and well-developed rough ER and Golgi apparatus.

described functionally as *merocrine*, *holocrine*, or *apocrine* glands. Most are **merocrine glands** (mer′o-krin), which secrete their products by exocytosis as they are produced. The secretory cells are not altered in any way (so think "merely secrete" to remember their mode of secretion). The pancreas, most sweat glands, and salivary glands belong to this class **(Figure 4.6a)**.

Secretory cells of **holocrine glands** (hol′o-krin) accumulate their products within them until they rupture. (They are replaced by the division of underlying cells.) Because holocrine gland secretions include the synthesized product plus dead cell fragments (*holo* = whole, all), you could say that their cells "die for their cause." Sebaceous (oil) glands of the skin are the only true example of holocrine glands (Figure 4.6b).

Although *apocrine glands* (ap′o-krin) are present in other animals, there is some controversy over whether humans have this third gland type. Like holocrine glands, apocrine glands accumulate their products, but in this case only just beneath the free surface. Eventually, the apex of the cell pinches off (*apo* = from, off), releasing the secretory granules and a small amount of cytoplasm. The cell repairs its damage and the process repeats again and again. The best possibility in humans is the release of lipid droplets by lactating mammary glands, but most histologists classify mammary glands as merocrine glands because this is the means by which milk proteins are secreted.

Check Your Understanding

8. What common secretion do all unicellular exocrine glands produce?
9. How are multicellular exocrine glands classified?
10. Which gland type—merocrine or holocrine—would you expect to have the highest rate of cell division? Why?

For answers, see Appendix H.

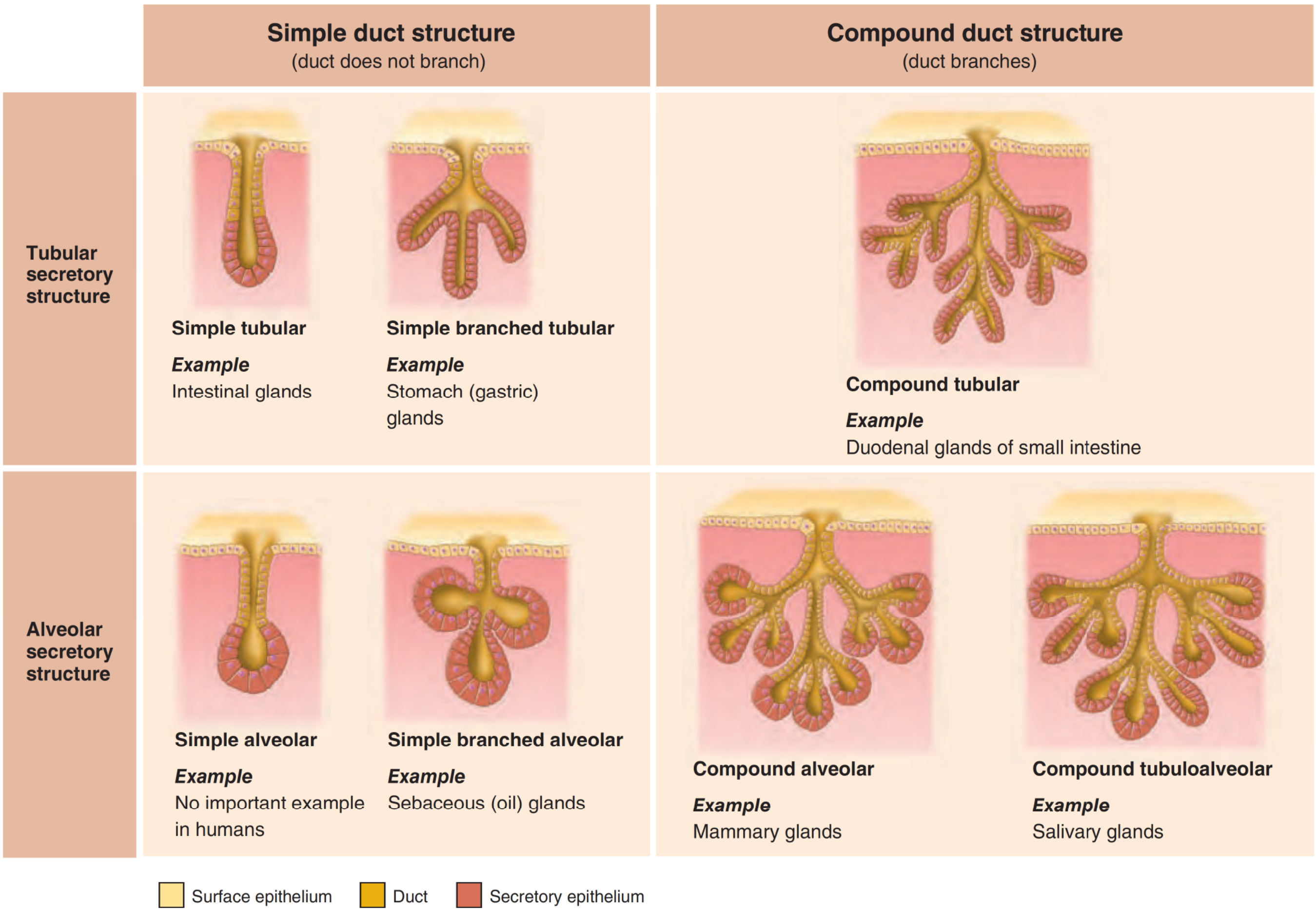


Figure 4.5 Types of multicellular exocrine glands. Multicellular glands are classified according to duct type (simple or compound) and the structure of their secretory units (tubular, alveolar, or tubuloalveolar).

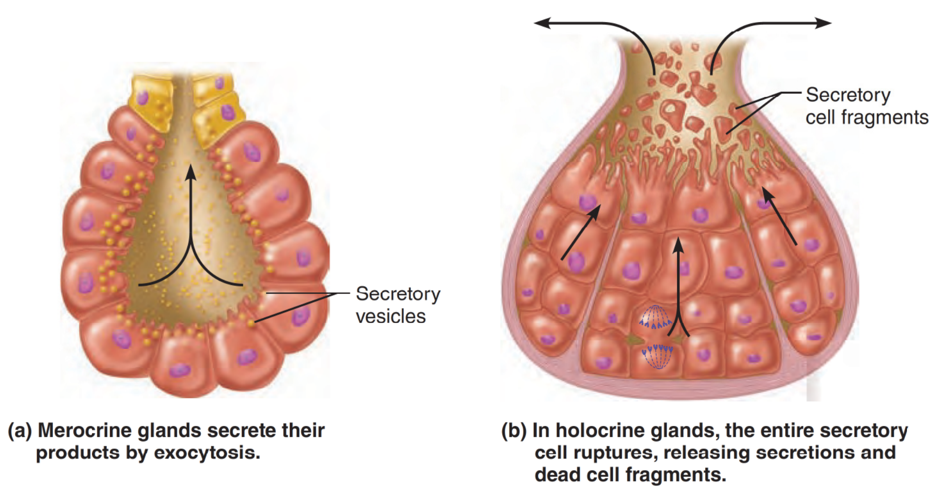


Figure 4.6 Chief modes of secretion in human exocrine glands.

Connective Tissue

✓ Indicate common characteristics of connective tissue, and list and describe its structural elements.

Connective tissue is the most abundant and widely distributed of the primary tissues, but its amount in particular organs varies. For example, skin consists primarily of connective tissue, while the brain contains very little.

There are four main classes of connective tissue and several subclasses (**Table 4.1** on p. 129). The main classes are (1) *connective tissue proper* (which includes fat and the fibrous tissue of ligaments), (2) *cartilage*, (3) *bone*, and (4) *blood*.

Connective tissue does much more than just *connect* body parts. Its major functions include (1) *binding and supporting*, (2) *protecting*, (3) *insulating*, (4) *storing* reserve fuel, and (5) *transporting* substances within the body. For example, bone and cartilage support and protect body organs by providing the hard underpinnings of the skeleton. Fat insulates and protects body organs and provides a fuel reserve. Blood transports substances inside the body.

Common Characteristics of Connective Tissue

Connective tissues share three characteristics that set them apart from other primary tissues:

- **Common origin.** All connective tissues arise from *mesenchyme* (an embryonic tissue).
- **Degrees of vascularity.** Connective tissues run the gamut of vascularity. Cartilage is avascular. Dense connective tissue is poorly vascularized, and the other types of connective tissue have a rich supply of blood vessels.
- **Extracellular matrix.** All other primary tissues are composed mainly of cells, but connective tissues are largely nonliving **extracellular matrix** (ma′triks; "womb"), which separates, often widely, the living cells of the tissue. Because of its matrix, connective tissue can bear weight, withstand great tension, and endure abuses, such as physical trauma and abrasion that no other tissue can tolerate.

Structural Elements of Connective Tissue

Connective tissues have three main elements: *ground substance*, *fibers*, and *cells* (Table 4.1). Together ground substance and fibers make up the extracellular matrix. (Note that some authors use the term *matrix* to indicate the ground substance only.)

The composition and arrangement of these three elements vary tremendously. The result is an amazing diversity of connective tissues, each adapted to perform a specific function in the body. For example, the matrix can be delicate and fragile to form a soft "packing" around an organ, or it can form "ropes" (tendons and ligaments) of incredible strength. Nonetheless, connective tissues have a common structural plan, and we use *areolar connective tissue* (ah-re′o-lar) as our *prototype*, or model (**Figure 4.7** and Figure 4.8a). All other subclasses are simply variants of this plan.

Ground Substance

Ground substance is the unstructured material that fills the space between the cells and contains the fibers. It is composed of *interstitial* (*tissue*) *fluid, cell adhesion proteins*, and *proteoglycans* (pro″te-o-gli′kanz). Cell adhesion proteins (*fibronectin*, *laminin*, and others) serve mainly as a connective tissue glue that allows connective tissue cells to attach to matrix elements. The proteoglycans consist of a protein core to which *glycosaminoglycans* (GAGs) (gli″kos-ah-me″no-gli′kanz) are attached. The strandlike GAGs, most importantly *chondroitin sulfate* and *hyaluronic acid* (hi″ah-lu-ron′ik), are large, negatively charged polysaccharides that stick out from the core protein like the fibers of a bottle brush. The proteoglycans tend to form huge aggregates in which the GAGs intertwine and trap water, forming a substance that varies from a fluid to a viscous gel. The higher the GAG content, the more viscous the ground substance.

The ground substance consists of large amounts of fluid and functions as a molecular sieve, or medium, through which nutrients and other dissolved substances can diffuse between the blood capillaries and the cells. The fibers embedded in the ground substance make it less pliable and hinder diffusion somewhat.

Connective Tissue Fibers

The fibers of connective tissue provide support. Three types of fibers are found in connective tissue matrix: collagen, elastic, and reticular fibers. Of these, collagen fibers are by far the strongest and most abundant.

Collagen fibers are constructed primarily of the fibrous protein *collagen*. Collagen molecules are secreted into the extracellular space, where they assemble spontaneously into cross-linked fibrils, which in turn are bundled together into the thick collagen fibers seen with a microscope. Because their fibrils cross-link, collagen fibers are extremely tough and provide high tensile strength (that is, the ability to resist being pulled apart) to the matrix. Indeed, stress tests show that collagen fibers are stronger than steel fibers of the same size!

Elastic fibers are long, thin fibers that form branching networks in the extracellular matrix. These fibers contain a rubberlike protein, *elastin*, that allows them to stretch and recoil like rubber bands. Connective tissue can stretch only so much before its thick, ropelike collagen fibers become taut. Then, when the tension lets up, elastic fibers snap the connective tissue back to its normal length and shape. Elastic fibers are found where greater elasticity is needed, for example, in the skin, lungs, and blood vessel walls.

Reticular fibers are short, fine, collagenous fibers with a slightly different chemistry and form. They are continuous with collagen fibers, and they branch extensively, forming delicate networks (*reticul* = network) that surround small blood vessels and support the soft tissue of organs. They are particularly abundant where connective tissue abuts other tissue types, for example, in the basement membrane of epithelial tissues, and around capillaries, where they form fuzzy "nets" that allow more "give" than the larger collagen fibers.

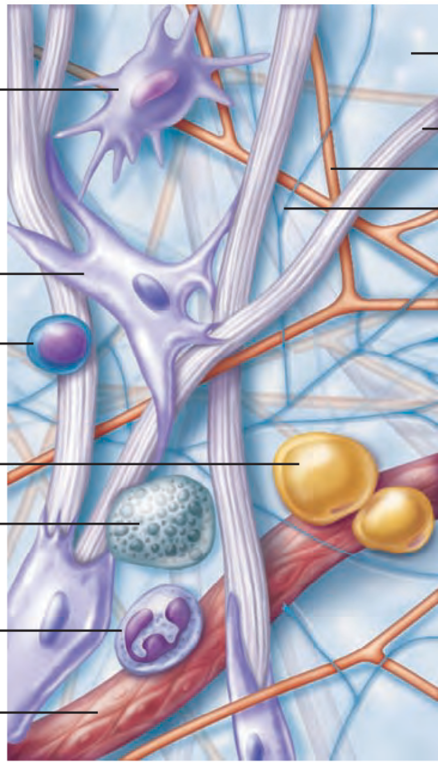


Figure 4.7 Areolar connective tissue: A prototype (model) connective tissue. This tissue underlies epithelia and surrounds capillaries. Notice the various cell types and three classes of fibers (collagen, reticular, elastic) embedded in the ground substance. (See Figure 4.8a for a less idealized version.)

Connective Tissue Cells

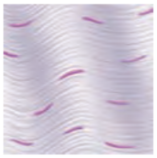
Each major class of connective tissue has a resident cell type that exists in immature and mature forms (see Table 4.1). The immature (undifferentiated) cells, indicated by the suffix *blast* (literally, "bud" or "sprout," but the suffix means "forming"), are actively mitotic cells that secrete the ground substance and the fibers characteristic of their particular matrix. As listed in the third column of Table 4.1, the primary blast cell types by connective tissue class are (1) connective tissue proper: **fibroblast**; (2) cartilage: **chondroblast** (kon′dro-blast″); and (3) bone: **osteoblast** (os′te-o-blast″). The **hematopoietic stem cell** (hem″ah-to-poy-et′ik), which is the undifferentiated blast cell that produces blood cells, is not included in Table 4.1 because it is not located in "its" tissue (blood) and does not make the fluid matrix (plasma) of that tissue. Blood formation is considered in Chapter 17.

Once they synthesize the matrix, the blast cells assume their mature, less active mode, indicated by the suffix *cyte* (Table 4.1, third column). The mature cells maintain the health of the matrix. However, if the matrix is injured, they can easily revert to their more active state to repair and regenerate the matrix. (The blood-forming stem cells are always actively mitotic.)

Additionally, connective tissue is home to an assortment of other cell types, such as

- **Fat cells**, which store nutrients.
- **White blood cells** (neutrophils, eosinophils, lymphocytes), and other cell types that are concerned with tissue response to injury.
- **Mast cells**, which typically cluster along blood vessels. These oval cells detect foreign microorganisms (e.g., bacteria, fungi) and initiate local inflammatory responses against them. In mast cell cytoplasm are secretory granules (*mast* = stuffed full of granules) containing chemicals that mediate inflammation, especially in severe allergies. These chemicals include
  - *Heparin* (hep′ah-rin), an anticoagulant chemical that prevents blood clotting when free in the bloodstream (but in human mast cells it appears to regulate the action of other mast cell chemicals)
  - *Histamine* (his′tah-mēn), a substance that makes capillaries leaky
  - *Proteases* (protein-degrading enzymes)
  - Various other enzymes
- **Macrophages** (mak′ro-fāj″-es; *macro* = large; *phago* = eat), large, irregularly shaped cells that avidly phagocytize a broad variety of foreign materials, ranging from foreign molecules to entire bacteria to dust particles. These "big eaters" also dispose of dead tissue cells, and they are central actors in the immune system. Macrophages, which are peppered throughout loose connective tissue, bone marrow, and lymphatic tissue, may be attached to connective tissue fibers (fixed) or may migrate freely through the matrix. Some macrophages have

Table 4.1 Comparison of Classes of Connective Tissues

		COMPONENTS		
TISSUE CLASS AND EXAMPLE	**SUBCLASSES**	**CELLS**	**MATRIX**	**GENERAL FEATURES**
Connective Tissue Proper  *Dense regular connective tissue*	1. Loose connective tissue ▪ Areolar ▪ Adipose ▪ Reticular 2. Dense connective tissue ▪ Regular ▪ Irregular ▪ Elastic	Fibroblasts Fibrocytes Defense cells Adipocytes	Gel-like ground substance All three fiber types: collagen, reticular, elastic	Six different types; vary in density and types of fibers Functions as a binding tissue Resists mechanical stress, particulary tension Provides reservoir for water and salts Nutrient (fat) storage
Cartilage  *Hyaline cartilage*	1. Hyaline cartilage 2. Elastic cartilage 3. Fibrocartilage	Chondroblasts found in growing cartilage Chondrocytes	Gel-like ground substance Fibers: collagen, elastic fibers in some	Resists compression because of the large amounts of water held in the matrix Functions to cushion and support body structures
Bone Tissue  *Compact bone*	1. Compact bone 2. Spongy bone	Osteoblasts Osteocytes	Gel-like ground substance calcified with inorganic salts Fibers: collagen	Hard tissue that resists both compression and tension Functions in support
Blood 	See Chapter 17 for details on blood cell formation and differentiation.	Erythrocytes (RBC) Leukocytes (WBC) Platelets	Plasma No fibers	A fluid tissue Functions to carry O_2, CO_2, nutrients, wastes, and other substances (hormones, for example)

selective appetites. For example, those of the spleen primarily dispose of aging red blood cells, but they will not turn down other "delicacies" that come their way.

☑ Check Your Understanding

11. What are four functions of connective tissue?

12. What are the three types of fibers found in connective tissues?

For answers, see Appendix H.

Types of Connective Tissue

✓ Describe the types of connective tissue found in the body, and indicate their characteristic functions.

As noted, all classes of connective tissue consist of living cells surrounded by a matrix. Their major differences reflect cell type, and types and relative amounts of fibers, as summarized in Table 4.1.

As mentioned earlier, mature connective tissues arise from a common embryonic tissue, called **mesenchyme** (meh′zin-kīm). Mesenchyme has a fluid ground substance containing fine sparse fibers and star-shaped *mesenchymal cells*. It arises during the early weeks of embryonic development and eventually differentiates (specializes) into all other connective tissue cells. However, some mesenchymal cells remain and provide a source of new cells in mature connective tissues.

Figure 4.8 illustrates the connective tissues that we describe in the next sections. Study this figure as you read along.

4

Connective Tissue Proper—Loose Connective Tissues

Connective tissue proper has two subclasses: **loose connective tissues** (areolar, adipose, and reticular) and **dense connective tissues** (dense regular, dense irregular, and elastic). Except for bone, cartilage, and blood, all mature connective tissues are connective tissue proper.

Areolar Connective Tissue The functions of **areolar connective tissue** (Figure 4.8a) include:

- Supporting and binding other tissues (the job of the fibers)
- Holding body fluids (the ground substance's role)
- Defending against infection (via the activity of white blood cells and macrophages)
- Storing nutrients as fat (in fat cells)

Fibroblasts, flat branching cells that appear spindle shaped in profile, predominate, but numerous macrophages are also seen and present a formidable barrier to invading microorganisms. Fat cells appear singly or in clusters, and occasional mast cells are identified easily by the large, darkly stained cytoplasmic granules that often obscure their nuclei. Other cell types are scattered throughout.

The most obvious structural feature of this tissue is the loose arrangement of its fibers. The rest of the matrix, occupied by ground substance, appears to be empty space when viewed through the microscope, and in fact, the Latin term *areola* means "a small open space." Because of its loose nature, areolar connective tissue provides a reservoir of water and salts for surrounding body tissues, always holding approximately as much fluid as there is in the entire bloodstream. Essentially all body cells obtain their nutrients from and release their wastes into this "tissue fluid."

The high content of hyaluronic acid makes its ground substance viscous, like molasses, which may hinder the movement of cells through it. Some white blood cells, which protect the body from disease-causing microorganisms, secrete the enzyme hyaluronidase to liquefy the ground substance and ease their passage. (Unhappily, some harmful bacteria have the same ability.) When a body region is inflamed, the areolar tissue in the area soaks up excess fluids like a sponge, and the affected area swells and becomes puffy, a condition called **edema** (ĕ-de′mah).

Areolar connective tissue is the most widely distributed connective tissue in the body, and it serves as a universal packing material between other tissues. It binds body parts together while allowing them to move freely over one another; wraps small blood vessels and nerves; surrounds glands; and forms the subcutaneous tissue, which cushions and attaches the skin to underlying structures. It is the connective tissue that most epithelia rest on and is present in all mucous membranes as the *lamina propria*. (Mucous membranes line body cavities open to the exterior.)

Adipose (Fat) Tissue **Adipose tissue** (ad′ĭ-pōs) is similar to areolar tissue in structure and function, but its nutrient-storing ability is much greater. Consequently, **adipocytes** (ad′ĭ-po-sītz), commonly called *adipose* or *fat cells*, account for 90% of this tissue's mass. The matrix is scanty and the cells are packed closely together, giving a chicken-wire appearance to the tissue. A glistening oil droplet (almost pure triglyceride) occupies most of a fat cell's volume and displaces the nucleus to one side (Figure 4.8b). Mature adipocytes are among the largest cells in the body. As they take up or release fat, they become plumper or more wrinkled, respectively.

Adipose tissue is richly vascularized, indicating its high metabolic activity. Without the fat stores in our adipose tissue, we could not live for more than a few days without eating. Adipose tissue is certainly abundant: It constitutes 18% of an average person's body weight, and a chubby person's body can be 50% fat without being considered morbidly obese.

Adipose tissue may develop almost anywhere areolar tissue is plentiful, but it usually accumulates in subcutaneous tissue, where it acts as a shock absorber, as insulation, and as an energy storage site. Because fat is a poor conductor of heat, it helps prevent heat loss from the body. Other sites where fat accumulates include surrounding the kidneys, behind the eyeballs, and at genetically determined fat depots such as the abdomen and hips.

The abundant fat beneath the skin serves the general nutrient needs of the entire body, and 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 rapid rate. Many of these local depots are highly enriched in special lipids.

The adipose tissue just described is sometimes called *white fat*, or *white adipose tissue*, to distinguish it from **brown fat**, or **brown adipose tissue**. White fat stores nutrients (mainly for other cells), but brown fat contains abundant mitochondria, which use the lipid fuels to heat the bloodstream to warm the body (rather than to produce ATP molecules). The richly vascular brown fat occurs mainly on the back of babies who (as yet) lack the ability to produce body heat by shivering. Scant deposits occur in adults, mostly above the collar bones, on the neck and abdomen, and around the spine.

Reticular Connective Tissue **Reticular connective tissue** resembles areolar connective tissue, but the only fibers in its matrix are reticular fibers, which form a delicate network along which fibroblasts called **reticular cells** (Figure 4.8c) are scattered. Although reticular *fibers* are widely distributed in the body, reticular tissue is limited to certain sites. It forms a labyrinth-like **stroma** (literally, "bed" or "mattress"), or internal framework, that can support many free blood cells (mostly lymphocytes) in lymph nodes, the spleen, and bone marrow.

Connective Tissue Proper—Dense Connective Tissues

The three varieties of dense connective tissue are dense regular, dense irregular, and elastic. Since all three have fibers as their prominent element, dense connective tissues are often called **fibrous connective tissues**.

Dense Regular Connective Tissue **Dense regular connective tissue** contains closely packed bundles of collagen fibers running in the same direction, parallel to the direction of pull (Figure 4.8d). This arrangement results in white, flexible structures

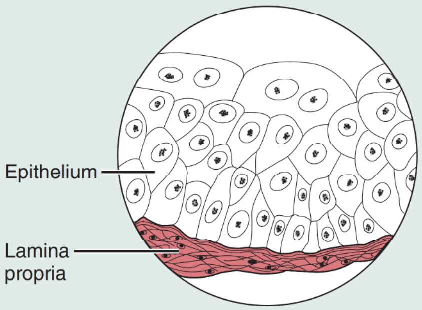
4

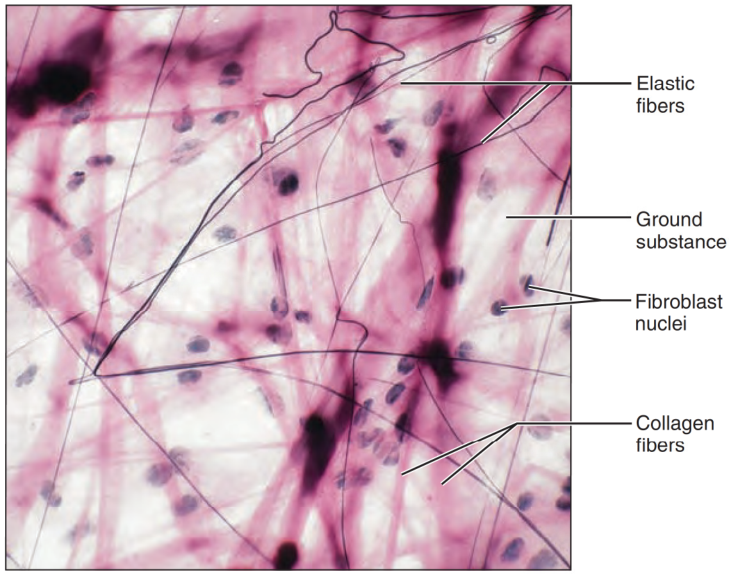
(a) Connective tissue proper: loose connective tissue, areolar

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.





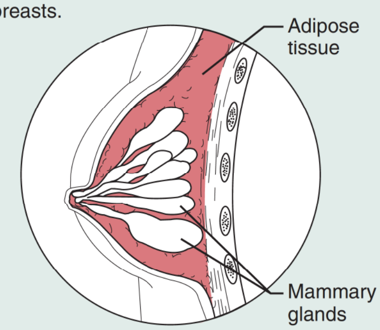
Photomicrograph: Areolar connective tissue, a soft packaging tissue of the body (340×).

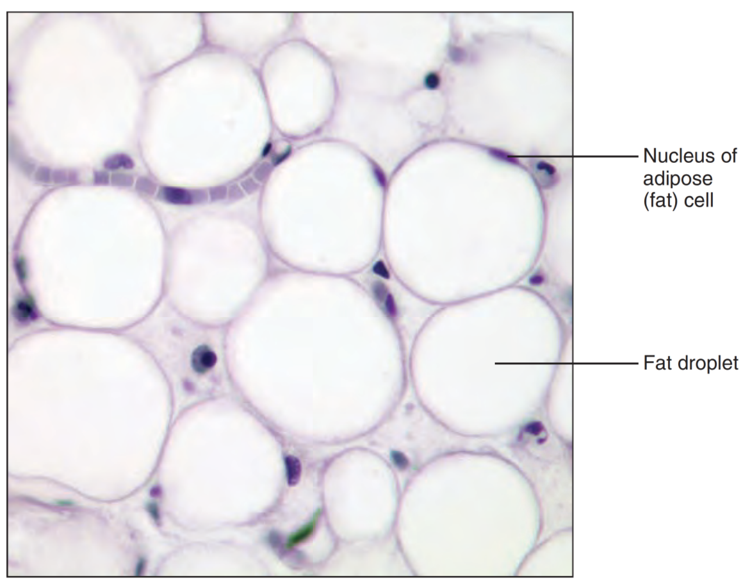
(b) Connective tissue proper: loose connective tissue, adipose

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 subcutaneous tissue; around kidneys and eyeballs; within abdomen; in breasts.





Photomicrograph: Adipose tissue from the subcutaneous layer under the skin (350×).

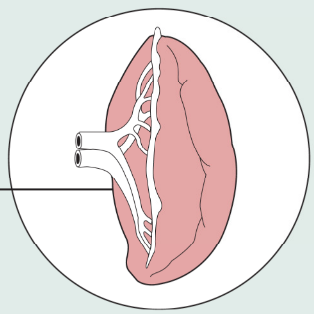
Figure 4.8 Connective tissues. (a) and **(b)** Connective tissue proper. (For related images, see *A Brief Atlas of the Human Body*, Plates 11 and 12.)

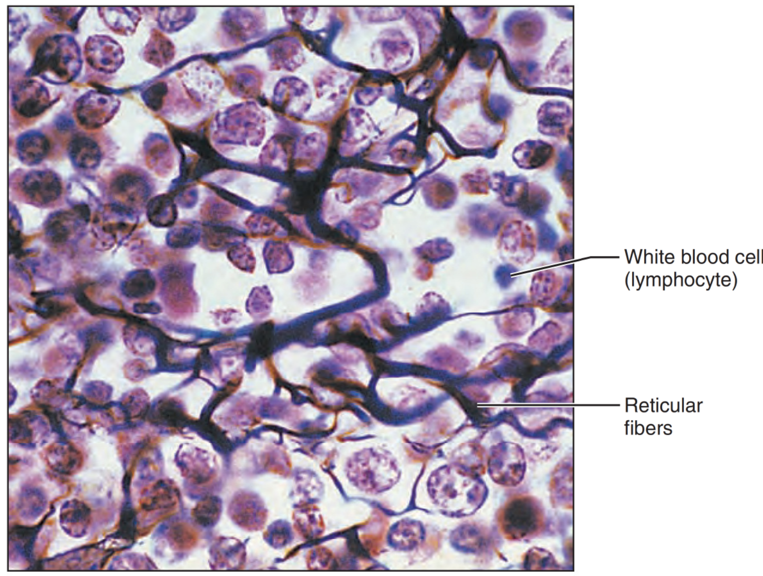
(c) Connective tissue proper: loose connective tissue, reticular

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).





Photomicrograph: Dark-staining network of reticular connective tissue fibers forming the internal skeleton of the spleen (350×).

Figure 4.8 *(continued)* **Connective tissues. (c)** Connective tissue proper. (For a related image, see *A Brief Atlas of the Human Body*, Plate 13.)

with great resistance to tension (pulling forces) where the tension is exerted in a single direction. Crowded between the collagen fibers are rows of fibroblasts that continuously manufacture the fibers and scant ground substance.

Collagen fibers are slightly wavy (see Figure 4.8d). This allows the tissue to stretch a little, but once the fibers straighten out, there is no further "give" to this tissue. Unlike our model (areolar) connective tissue, this tissue has few cells other than fibroblasts and is poorly vascularized.

With its enormous tensile strength, dense regular connective tissue forms *tendons*, which are cords that attach muscles to bones; flat, sheetlike tendons called *aponeuroses* (ap″o-nu-ro′sēz) that attach muscles to other muscles or to bones; and the *ligaments* that bind bones together at joints. Ligaments contain more elastic fibers than tendons and are slightly more stretchy. Dense regular connective tissue also forms fascia (fash′e-ah; "a bond"), a fibrous membrane that wraps around muscles, groups of muscles, blood vessels, and nerves, binding them together like plastic sandwich wrap.

Dense Irregular Connective Tissue **Dense irregular connective tissue** has the same structural elements as the regular variety. However, the bundles of collagen fibers are much thicker and they are arranged irregularly; that is, they run in more than one plane (Figure 4.8e). This type of tissue forms sheets in body areas where tension is exerted from many different directions. It is found in the skin as the leathery *dermis*, and it forms fibrous joint capsules and the fibrous coverings that surround some organs (kidneys, bones, cartilages, muscles, and nerves).

Elastic Connective Tissue A few ligaments, such as those connecting adjacent vertebrae, are very elastic. The dense regular connective tissue in those structures is called **elastic connective tissue** (Figure 4.8f). Additionally, many of the larger arteries have stretchy sheets of elastic connective tissue in their walls.

Cartilage

Cartilage (kar′tĭ-lij), which stands up to both tension *and* compression, has qualities intermediate between dense connective tissue and bone. It is tough but flexible, providing a resilient rigidity to the structures it supports.

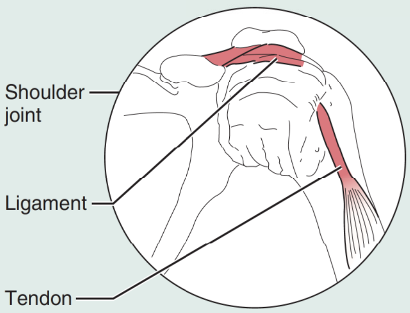
Cartilage lacks nerve fibers and is avascular. It receives its nutrients by diffusion from blood vessels located in the connective tissue membrane (perichondrium) surrounding it. Its ground substance contains large amounts of the GAGs chondroitin sulfate and hyaluronic acid, firmly bound collagen fibers (and in some cases elastic fibers), and is quite firm. Cartilage matrix also contains an exceptional amount of tissue fluid. In fact, cartilage is up to 80% water! The movement of tissue fluid in its matrix enables cartilage to rebound after being compressed and also helps to nourish the cartilage cells.

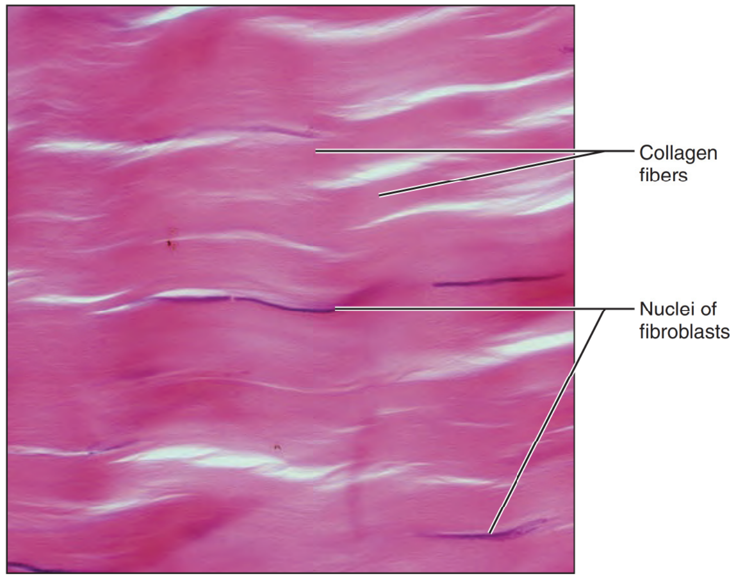
(d) Connective tissue proper: dense connective tissue, dense regular

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.





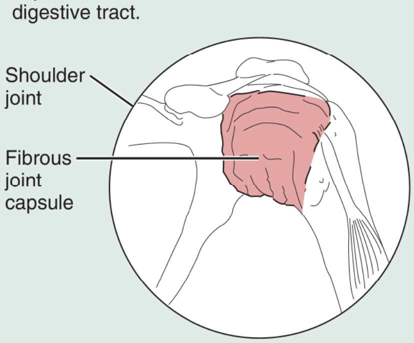
Photomicrograph: Dense regular connective tissue from a tendon (430×).

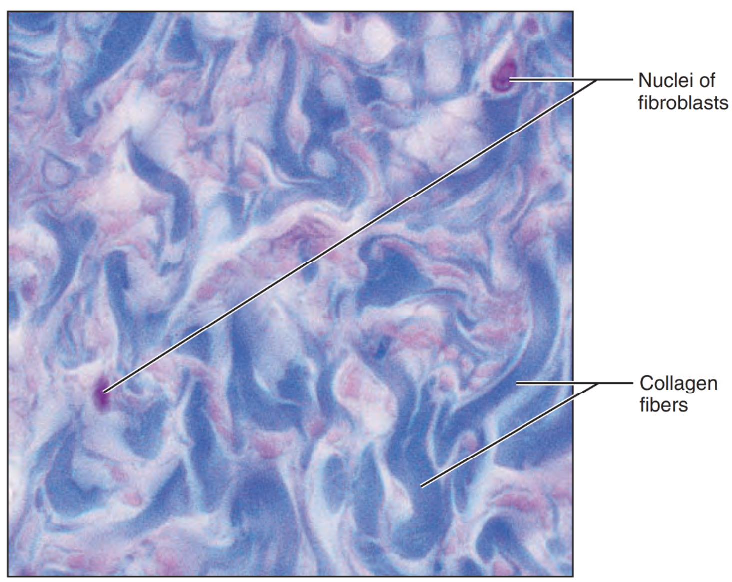
(e) Connective tissue proper: dense connective tissue, dense irregular

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

Function: Withstands 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 fibrous capsule of a joint (430×).

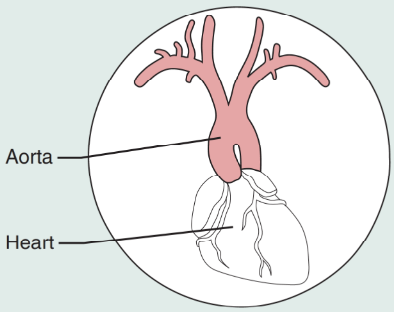
Figure 4.8 *(continued)* **(d)** and **(e)** Connective tissue proper. (For related images, see *A Brief Atlas of the Human Body*, Plates 14 and 15.)

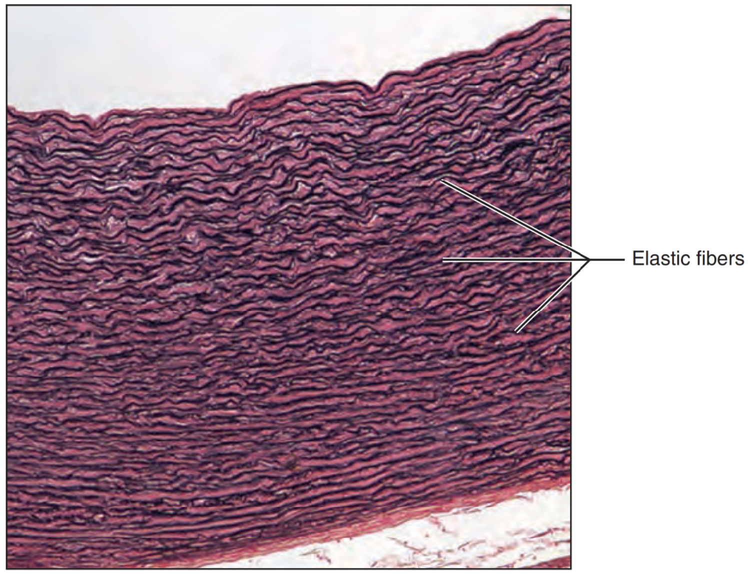
(f) Connective tissue proper: dense connective tissue, elastic

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

Function: Allows tissue to recoil after 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 (250×).

Figure 4.8 *(continued)* **Connective tissues. (f)** Connective tissue proper. (For a related image, see *A Brief Atlas of the Human Body*, Plate 16.)

Chondroblasts, the predominant cell type in growing cartilage, produce new matrix until the skeleton stops growing at the end of adolescence. The firmness of the cartilage matrix prevents the cells from becoming widely separated, so **chondrocytes**, or mature cartilage cells, are typically found in small groups within cavities called *lacunae* (lah-ku′ne; "pits").

Homeostatic Imbalance 4.2

Because cartilage is avascular and aging cartilage cells lose their ability to divide, injured cartilages heal slowly. This phenomenon is excruciatingly familiar to those who have experienced sports injuries. During later life, cartilages tend to calcify or even ossify (become bony). In such cases, the chondrocytes are poorly nourished and die. ✚

There are three varieties of cartilage: *hyaline cartilage*, *elastic cartilage*, and *fibrocartilage*, each dominated by a particular fiber type.

Hyaline Cartilage **Hyaline cartilage** (hi′ah-līn), or *gristle*, is the most abundant cartilage in the body. Although it contains large numbers of collagen fibers, they are not apparent and the matrix appears glassy (*hyal* = glass, transparent) blue-white when viewed by the unaided eye. Chondrocytes account for only 1–10% of the cartilage volume (Figure 4.8g).

Hyaline cartilage provides firm support with some pliability. It covers the ends of long bones as *articular cartilage*, providing springy pads that absorb compression at joints. Hyaline cartilage also supports the tip of the nose, connects the ribs to the sternum, and supports most of the respiratory system passages. Most of the embryonic skeleton consists of hyaline cartilage before bone forms. Skeletal hyaline cartilage persists during childhood as the *epiphyseal plates* (e″pĭ-fis′e-ul), actively growing regions near the ends of long bones.

Elastic Cartilage Histologically, **elastic cartilage** (Figure 4.8h) is nearly identical to hyaline cartilage. However, elastic cartilage has many more elastic fibers. Found where strength and exceptional stretchability are needed, elastic cartilage forms the "skeletons" of the external ear (the pinna) and the epiglottis (the flap that covers the opening to the respiratory passageway when we swallow).

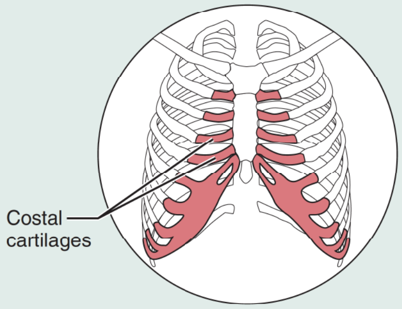
Fibrocartilage Structurally, **fibrocartilage** is intermediate between hyaline cartilage and dense regular connective tissues. Its rows of chondrocytes (a cartilage feature) alternate with rows of thick collagen fibers (characteristic of dense regular connective tissue) (Figure 4.8i). Because it is compressible and resists tension well, fibrocartilage is found where strong support and the ability to withstand heavy pressure are required: for example, the intervertebral discs (resilient cushions between the bony vertebrae) and the spongy cartilages of the knee (menisci) (see Figure 6.1, p. 175).

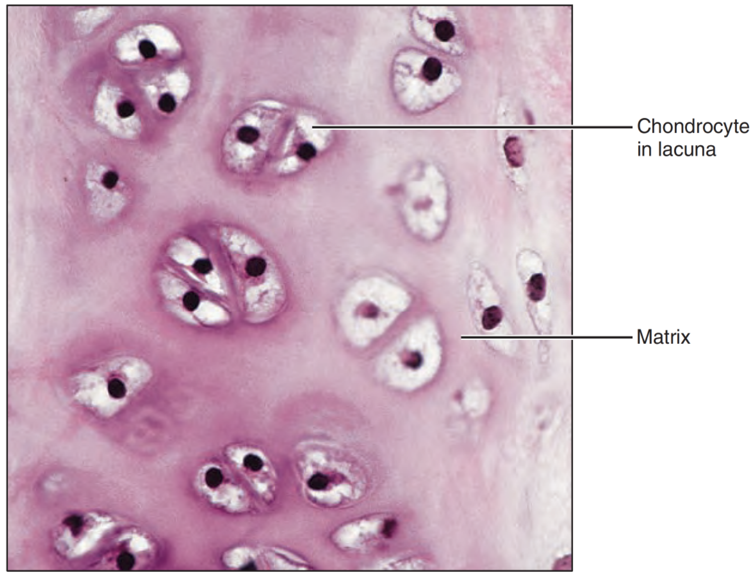
(g) Cartilage: hyaline

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; serves as resilient cushion; 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.





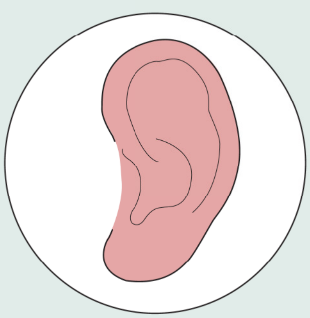
Photomicrograph: Hyaline cartilage from a costal cartilage of a rib (470×).

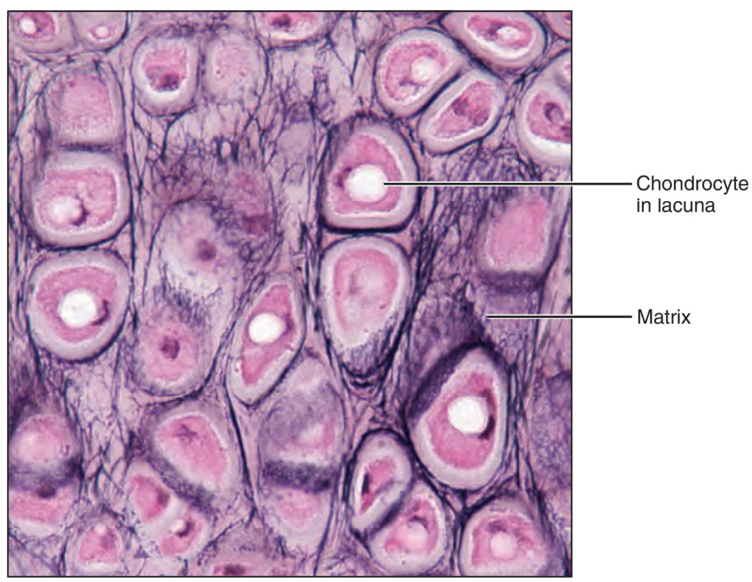
(h) Cartilage: elastic

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.





Photomicrograph: Elastic cartilage from the human ear pinna; forms the flexible skeleton of the ear (800×).

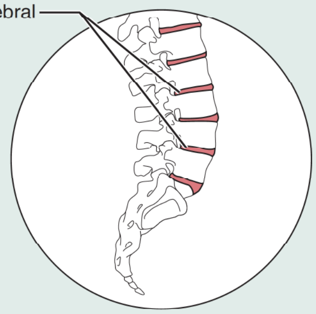
Figure 4.8 *(continued)* **(g)** and **(h)** Cartilage. (For related images, see *A Brief Atlas of the Human Body*, Plates 17 and 18.)

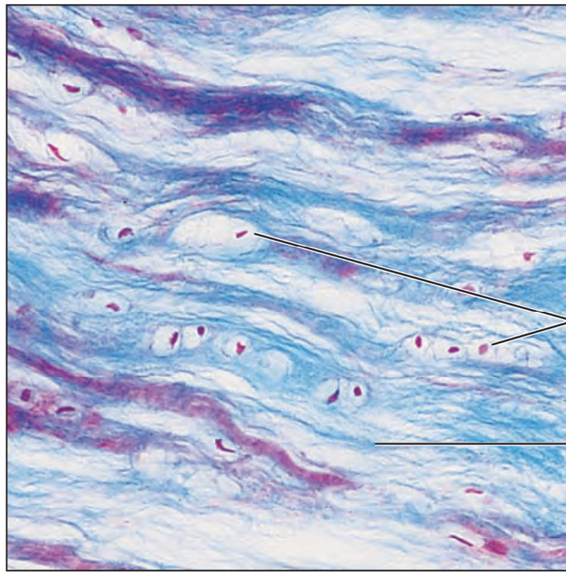
(i) Cartilage: fibrocartilage

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

Function: Tensile strength allows it to absorb compressive shock.

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





Photomicrograph: Fibrocartilage of an intervertebral disc (125×). Special staining produced the blue color seen.

Figure 4.8 *(continued)* **Connective tissues. (i)** Cartilage. (For a related image, see *A Brief Atlas of the Human Body*, Plate 19.)

Bone (Osseous Tissue)

Because of its rocklike hardness, **bone**, or **osseous tissue** (os′e-us), has an exceptional ability to support and protect body structures. Bones of the skeleton also provide cavities for storing fat and synthesizing blood cells. Bone matrix is similar to that of cartilage but is harder and more rigid because, in addition to its more abundant collagen fibers, bone has an added matrix element—inorganic calcium salts (bone salts).

Osteoblasts produce the organic portion of the matrix, and then bone salts are deposited on and between the fibers. Mature bone cells, or **osteocytes**, reside in the lacunae within the matrix they have made (Figure 4.8j). A cross section of bone tissue reveals closely packed structural units called *osteons* formed of concentric rings of bony matrix (lamellae) surrounding central canals containing the blood vessels and nerves serving the bone. Unlike cartilage, the next firmest connective tissue, bone is well supplied by invading blood vessels.

Blood

Blood, the fluid within blood vessels, is the most atypical connective tissue. It does *not* connect things 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 fluid matrix called *blood plasma* (Figure 4.8k).

The vast majority of blood cells are red blood cells, or erythrocytes, but scattered white blood cells and platelets (needed for blood clotting) are also seen. The "fibers" of blood are soluble protein molecules that precipitate, forming visible fiberlike structures during blood clotting. Blood functions as the transport vehicle for the cardiovascular system, carrying nutrients, wastes, respiratory gases, and many other substances throughout the body.

☑ Check Your Understanding

13. Which connective tissue has a soft weblike matrix capable of serving as a fluid reservoir?
14. What type of connective tissue is damaged when you cut your index finger tendon?
15. John wants to become a professional basketball player. Unfortunately he is short for his age and his epiphyseal plates have already fused. What type of connective tissue forms the epiphyseal plates?

For answers, see Appendix H.

Muscle Tissue

✓ Compare and contrast the structures and body locations of the three types of muscle tissue.

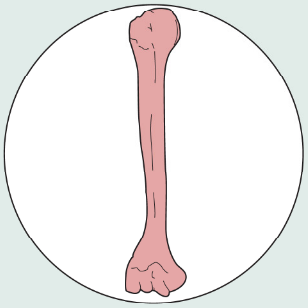
Muscle tissues are highly cellular, well-vascularized tissues that are responsible for most types of body movement. Muscle cells possess **myofilaments**, elaborate versions of the *actin* and *myosin* filaments that bring about movement or contraction in all

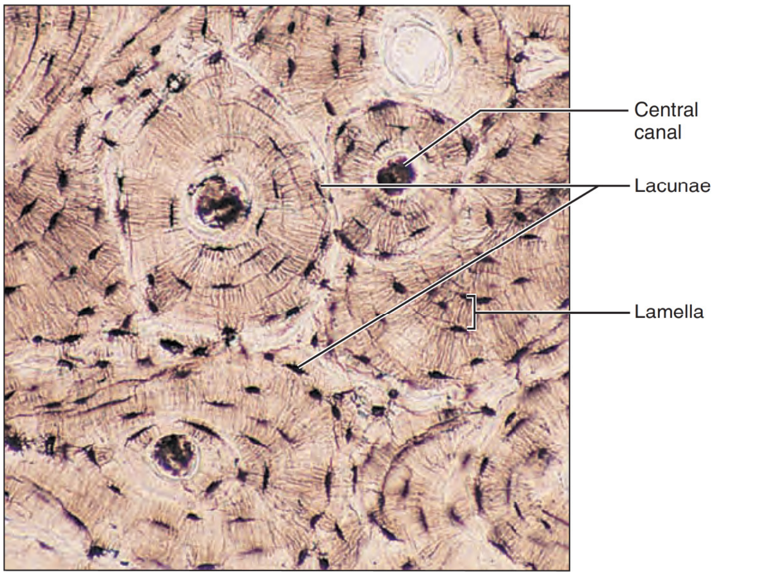
(j) Others: bone (osseous tissue)

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

Function: 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





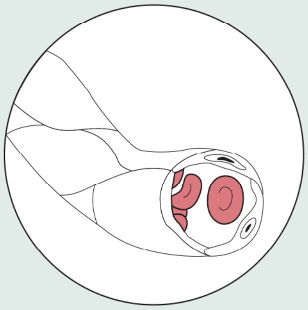
Photomicrograph: Cross-sectional view of bone (125×).

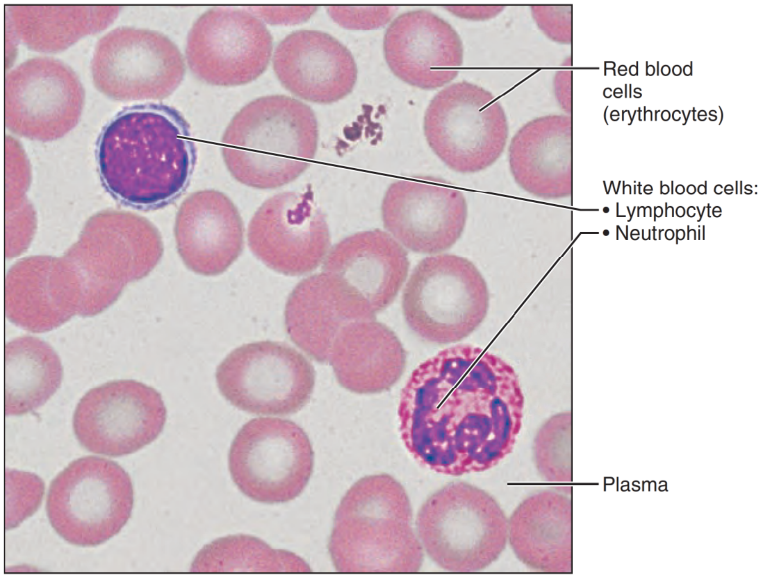
(k) Connective tissue: blood

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

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

Location: Contained within blood vessels.



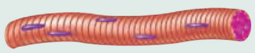


Photomicrograph: Smear of human blood (1670×); shows two white blood cells surrounded by red blood cells.

Figure 4.8 *(continued)* **(j)** Bone. (For a related image, see *A Brief Atlas of the Human Body*, Plate 20.) **(k)** Blood. (For related images, see *A Brief Atlas of the Human Body*, Plates 22–27.)

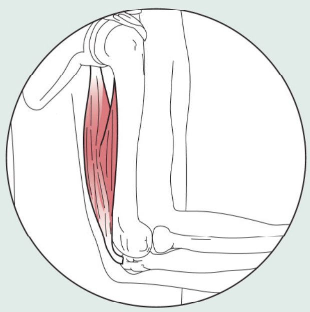
(a) Skeletal muscle

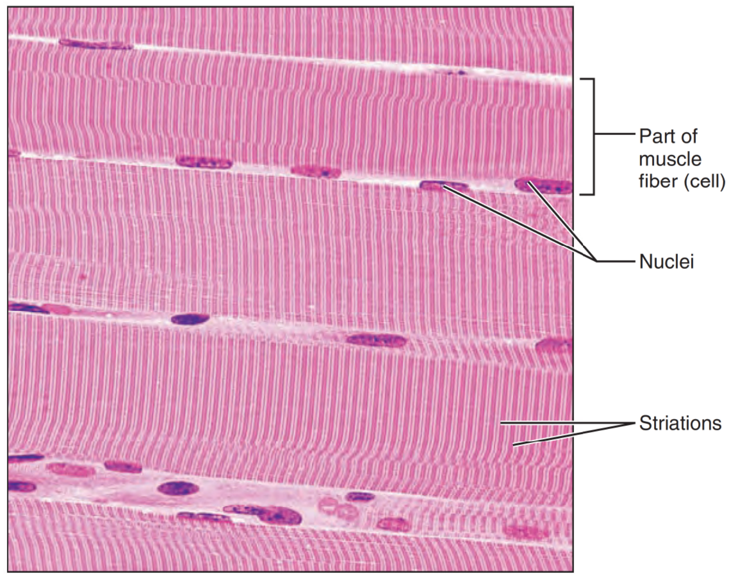
Description: Long, cylindrical, multinucleate cells; obvious striations.



Function: Voluntary movement; locomotion; manipulation of the environment; facial expression; voluntary control.

Location: In skeletal muscles attached to bones or occasionally to skin.





Photomicrograph: Skeletal muscle (approx. 440×). Notice the obvious banding pattern and the fact that these large cells are multinucleate.

Figure 4.9 Muscle tissues. (a) Skeletal muscle tissue. (For a related image, see *A Brief Atlas of the Human Body*, Plate 28.)

cell types. There are three kinds of muscle tissue: skeletal, cardiac, and smooth.

Skeletal Muscle

Skeletal muscle tissue is packaged by connective tissue sheets into organs called *skeletal muscles* that are attached to the bones of the skeleton. These muscles form the flesh of the body, and as they contract they pull on bones or skin, causing body movements.

Skeletal muscle cells, also called **muscle fibers**, are long, cylindrical cells that contain many peripherally located nuclei. Their obvious banded, or striated, appearance reflects the precise alignment of their myofilaments **(Figure 4.9a)**.

Cardiac Muscle

Cardiac muscle is found only in the walls of the heart. Its contractions help propel blood through the blood vessels to all parts of the body. Like skeletal muscle cells, cardiac muscle cells are striated. However, cardiac cells differ structurally in that they are

- Generally uninucleate (one nucleus) with the nucleus situated centrally
- Branching cells that fit together tightly at unique junctions called **intercalated discs** (in-ter′kah-la″ted) (Figure 4.9b)

Smooth Muscle

Smooth muscle is so named because its cells have no visible striations. Individual smooth muscle cells are spindle shaped and contain one centrally located nucleus (Figure 4.9c). Smooth muscle is found mainly in the walls of hollow organs other than the heart (digestive and urinary tract organs, uterus, and blood vessels). It squeezes substances through these organs by alternately contracting and relaxing.

Because skeletal muscle contraction is under our conscious control, skeletal muscle is often referred to as **voluntary muscle**, and the other two types are called **involuntary muscle** because we do not consciously control them. We describe skeletal muscle and smooth muscle in detail in Chapter 9, and cardiac muscle in Chapter 18.

☑ Check Your Understanding

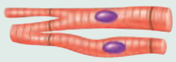
16. You are looking at muscle tissue through the microscope and you see striped branching cells that connect with one another. What type of muscle are you viewing?

17. Which muscle type(s) is voluntary? Which is injured when you pull a muscle while exercising?

For answers, see Appendix H.

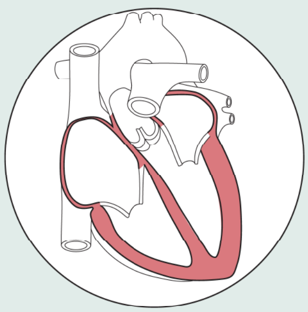
(b) Cardiac muscle

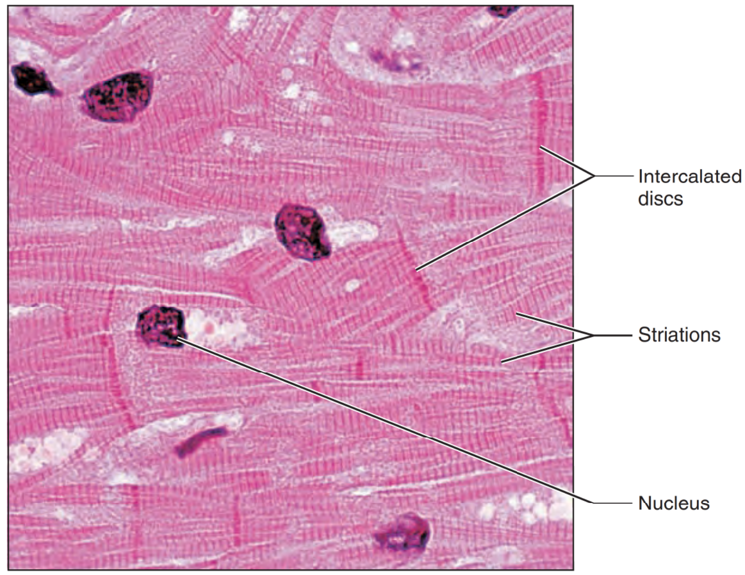
Description: Branching, striated, generally uninucleate cells that interdigitate at specialized junctions (intercalated discs).



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

Location: The walls of the heart.

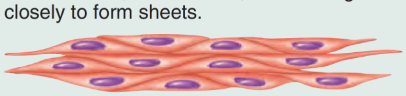




Photomicrograph: Cardiac muscle (900×); notice the striations, branching of cells, and the intercalated discs.

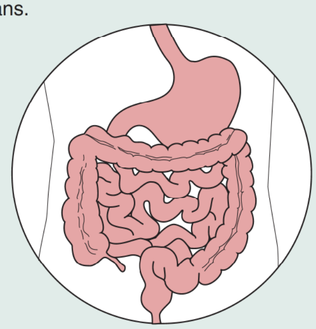
(c) Smooth muscle

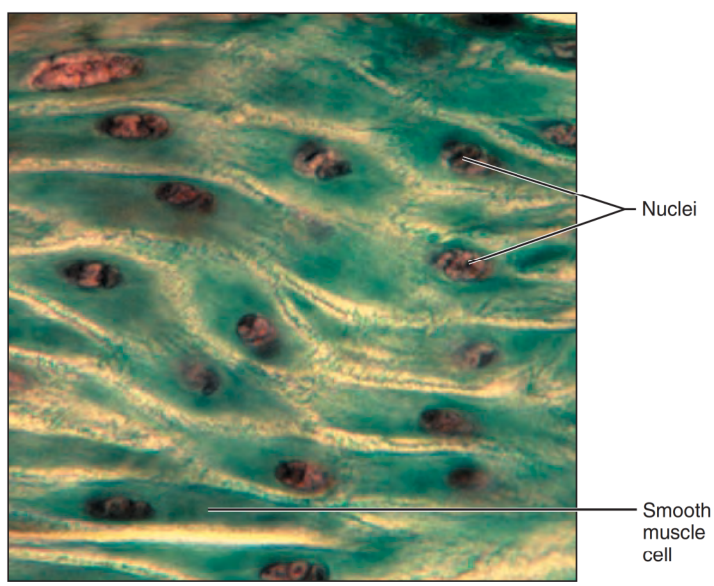
Description: Spindle-shaped cells with central nuclei; no striations; cells arranged closely to form sheets.



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

Location: Mostly in the walls of hollow organs.



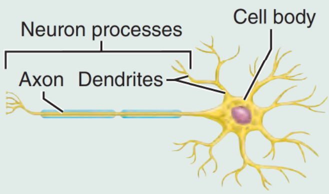


Photomicrograph: Sheet of smooth muscle (720×).

Figure 4.9 *(continued)* **(b)** Cardiac muscle tissue. (For a related image, see *A Brief Atlas of the Human Body*, Plate 31.) **(c)** Smooth muscle tissue. (For a related image, see *A Brief Atlas of the Human Body*, Plate 32.

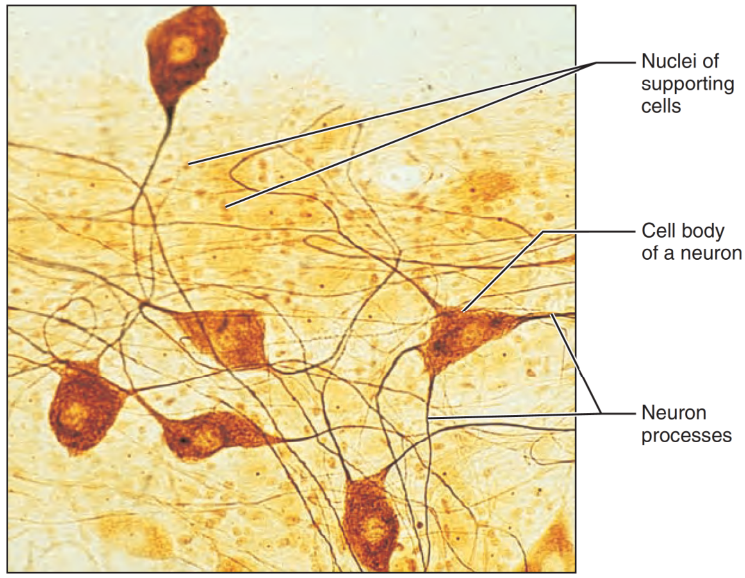
Nervous tissue

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 nonexcitable supporting cells.



Function: Neurons transmit electrical signals from sensory receptors and to effectors (muscles and glands) which control their activity; supporting cells support and protect neurons.

Location: Brain, spinal cord, and nerves.



Photomicrograph: Neurons (350×)

Figure 4.10 Nervous tissue. (For a related image, see *A Brief Atlas of the Human Body*, Plate 33.)

Nervous Tissue

✓ Indicate the general characteristics of nervous tissue.

Nervous tissue is the main component of the nervous system—the brain, spinal cord, and nerves—which regulates and controls body functions. It contains two major cell types: neurons and supporting cells.

Neurons are highly specialized nerve cells that generate and conduct nerve impulses **(Figure 4.10)**. Typically, they are branching cells with cytoplasmic extensions or processes that enable them to

- Respond to stimuli (via processes called *dendrites*)
- Transmit electrical impulses over substantial distances within the body (via processes called *axons*)

Supporting cells are nonconducting cells that support, insulate, and protect the delicate neurons. Chapter 11 presents a more complete discussion of nervous tissue.

Check Your Understanding

18. How does the extended length of a neuron's processes aid its function in the body?

For answers, see Appendix H.

Covering and Lining Membranes

✓ Describe the structure and function of cutaneous, mucous, and serous membranes.

Now that we have described all four primary tissues, we can consider the body's membranes that incorporate more than one type of tissue. The covering and lining membranes are of three types: *cutaneous*, *mucous*, or *serous*. Essentially they all are continuous multicellular sheets composed of at least two primary tissue types: an epithelium bound to an underlying layer of connective tissue proper. Hence, these membranes are simple organs. We describe the *synovial membranes*, which line joint cavities and consist of connective tissue only, in Chapter 8.

Cutaneous Membrane

The **cutaneous membrane** (ku-ta′ne-us; *cutis* = skin) is your skin **(Figure 4.11a)**. It is an organ system consisting of a keratinized stratified squamous epithelium (epidermis) firmly attached to a thick layer of connective tissue (dermis). Unlike other epithelial membranes, the cutaneous membrane is exposed to the air and is a dry membrane. Chapter 5 is devoted to this unique organ system.

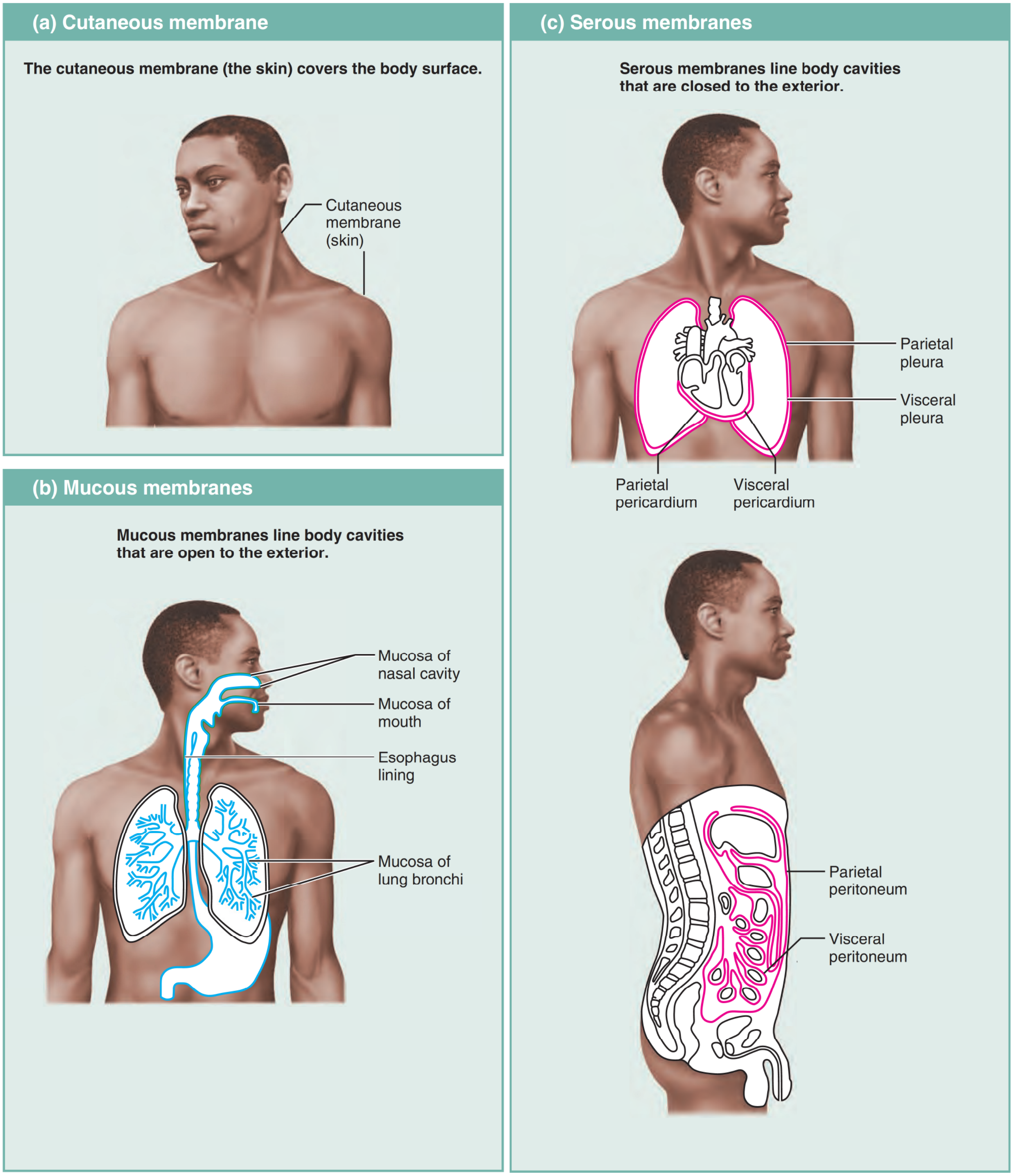


Figure 4.11 Classes of membranes.

Mucous Membranes

Mucous membranes, or **mucosae** (mu-ko′se), line all body cavities that open to the outside of the body, such as the hollow organs of the digestive, respiratory, and urogenital tracts (Figure 4.11b). In all cases, they are "wet," or moist, membranes bathed by secretions or, in the case of the urinary mucosa, urine. Notice that the term *mucosa* refers to the location of the membrane, *not* its cell composition, which varies. However, most mucosae contain either stratified squamous or simple columnar epithelia. The epithelial sheet lies directly over a layer of loose connective tissue called the **lamina propria** (lam′ĭ-nah pro′pre-ah; "one's own layer"). In some mucosae, the lamina propria rests on a third (deeper) layer of smooth muscle cells.

Mucous membranes are often adapted for absorption and secretion. Although many mucosae secrete mucus, this is not a requirement. The mucosae of both the digestive and respiratory tracts secrete copious amounts of lubricating mucus, but that of the urinary tract does not.

Serous Membranes

Serous membranes, or **serosae** (se-ro′se), introduced in Chapter 1, are the moist membranes found in closed ventral body cavities (Figure 4.11c). A serous membrane consists of simple squamous epithelium (a mesothelium) resting on a thin layer of loose connective (areolar) tissue. The mesothelial cells add hyaluronic acid to the fluid that filters from the capillaries in the associated connective tissue. The result is the thin, clear *serous fluid* that lubricates the facing surfaces of the parietal and visceral layers, so that they slide across each other easily.

The serosae are named according to their site and specific organ associations. For example, the **pleurae** line the thoracic wall and cover the lungs; the **pericardium** encloses the heart; and the **peritoneum** encloses the abdominopelvic viscera.

☑ Check Your Understanding

19. What type of membrane consists of epithelium and connective tissue, and lines body cavities open to the exterior?

20. What type of membrane lines the thoracic walls and covers the lungs, and what is it called?

For answers, see Appendix H.

Tissue Repair

✓ Outline the process of tissue repair involved in normal healing of a superficial wound.

The body has many techniques for protecting itself from uninvited "guests" or injury. Intact mechanical barriers such as the skin and mucosae, the cilia of epithelial cells lining the respiratory tract, and the strong acid (chemical barrier) produced by stomach glands represent three defenses at the body's external boundaries.

When tissue is injured, these barriers are penetrated. This stimulates the body's inflammatory and immune responses, which wage their battles largely in the connective tissues of the body. The *inflammatory response* is a relatively nonspecific reaction that develops quickly wherever tissues are injured, while the *immune response* is extremely specific, but takes longer to swing into action. We consider the inflammatory and immune responses in detail in Chapter 21.

Steps of Tissue Repair

Tissue repair requires that cells divide and migrate, activities that are initiated by growth factors (wound hormones) released by injured cells. Repair occurs in two major ways:

- **Regeneration** replaces destroyed tissue with the same kind of tissue.
- In **fibrosis**, fibrous connective tissue proliferates to form **scar tissue**.

Which of these occurs depends on (1) the type of tissue damaged and (2) the severity of the injury. In skin, the tissue we will use as our example, repair involves both activities **(Figure 4.12)**.

① **Inflammation sets the stage.** Tissue trauma causes injured tissue cells, macrophages, mast cells, and others to release inflammatory chemicals, which cause the capillaries to dilate and become very permeable. White blood cells (neutrophils, monocytes) and plasma fluid rich in clotting proteins, antibodies, and other substances seep into the injured area. The leaked clotting proteins construct a clot, which stops the loss of blood, holds the edges of the wound together, and effectively walls in, or isolates, the injured area, preventing bacteria, toxins, or other harmful substances from spreading to surrounding tissues. The part of the clot exposed to air quickly dries and hardens, forming a *scab*. The inflammatory events leave behind excess fluid, bits of destroyed cells, and other debris, which are eventually removed via lymphatic vessels or phagocytized by macrophages.

② **Organization restores the blood supply.** Even while the inflammatory process is going on, the first phase of tissue repair, called **organization**, begins. During organization the blood clot is replaced by **granulation tissue**, a delicate pink tissue composed of several elements. It contains capillaries that grow in from nearby areas and lay down a new capillary bed. Granulation tissue is actually named for these capillaries, which protrude nublike from its surface, giving it a granular appearance. These capillaries are fragile and bleed freely, as we see when someone picks at a scab. Proliferating fibroblasts in granulation tissue produce growth factors as well as new collagen fibers to bridge the gap. Some of these fibroblasts have contractile properties that allow them to pull the margins of the wound together or to pull existing blood vessels into the healing wound. As organization proceeds, macrophages digest the original blood clot and collagen fiber deposit continues. The granulation tissue, destined to become scar tissue (a permanent fibrous patch), is highly resistant to infection because it produces bacteria-inhibiting substances. As a rule, wound healing is a self-limited response. Once enough matrix has accumulated in the injured area, the fibroblasts either revert to the resting stage or undergo apoptosis.

③ **Regeneration and fibrosis effect permanent repair.** During organization, the surface epithelium begins to *regenerate*, growing under the scab, which soon detaches. As the fibrous tissue beneath matures and contracts, the regenerating

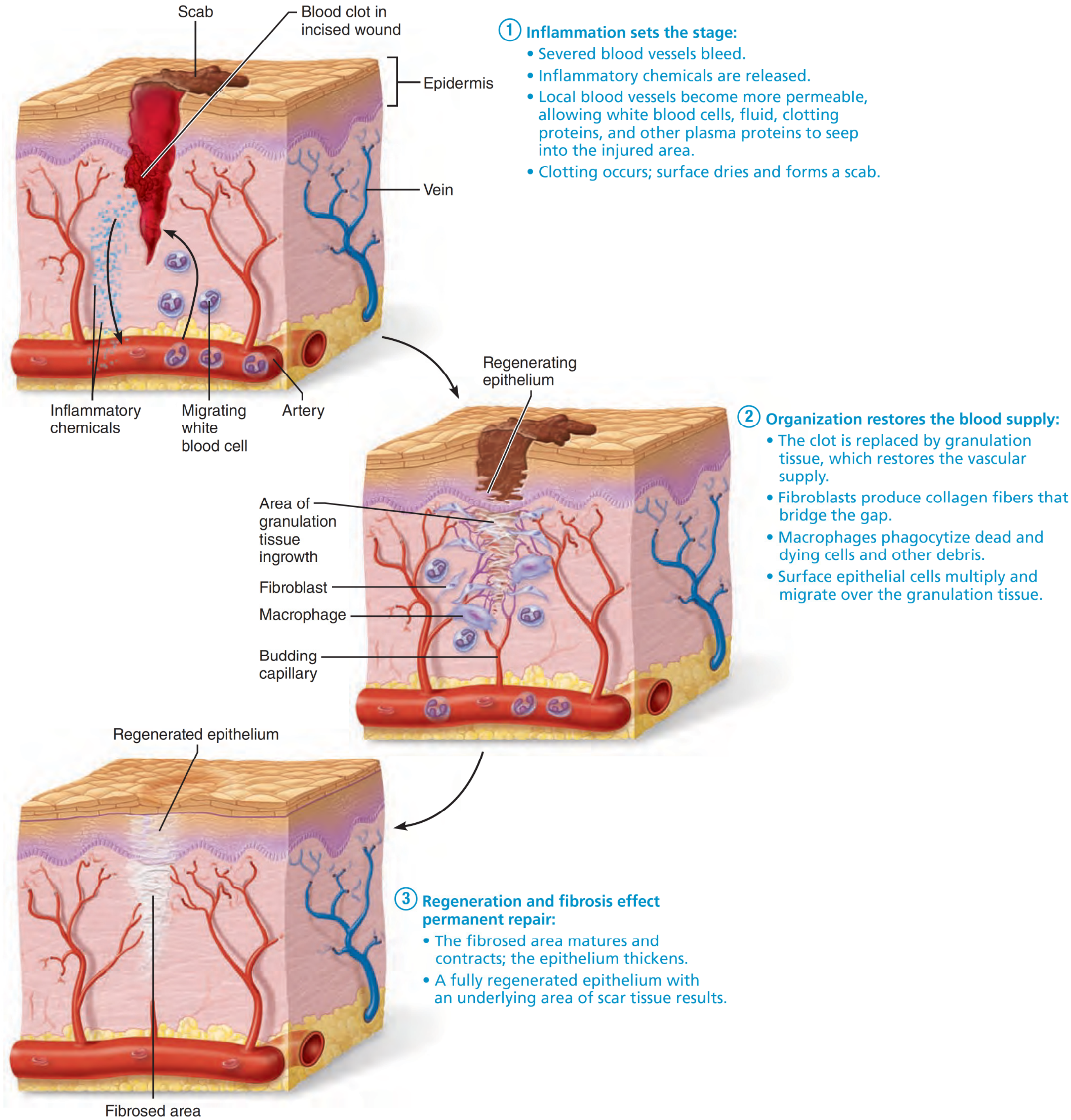


Figure 4.12 Tissue repair of a nonextensive skin wound: regeneration and fibrosis.

epithelium thickens until it finally resembles the adjacent skin. The end result is a fully regenerated epithelium, and an underlying area of scar tissue. The scar may be invisible, or visible as a thin white line, depending on the severity of the wound.

The repair process that we have just described follows healing of a wound (cut, scrape, puncture) that breaches an epithelial barrier. In simple *infections* (a pimple or sore throat), healing is solely by regeneration. Only severe (destructive) infections lead to clot formation or scarring.

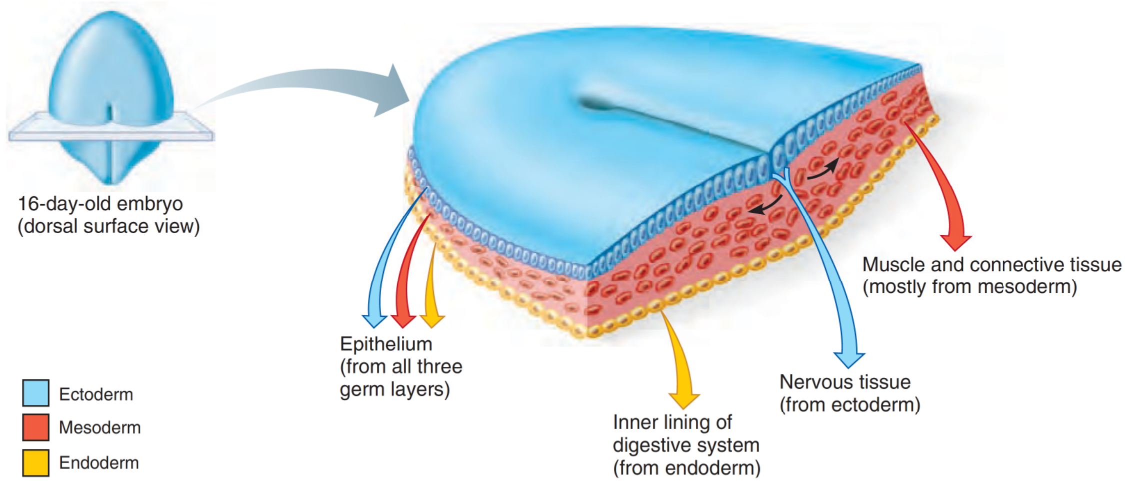


Figure 4.13 Embryonic germ layers and the primary tissue types they produce. The three embryonic layers collectively form the very early embryonic body.

Regenerative Capacity of Different Tissues

Tissues vary widely in their capacity for regeneration. Epithelial tissues, bone, areolar connective tissue, dense irregular connective tissue, and blood-forming tissue regenerate extremely well. Smooth muscle and dense regular connective tissue have a moderate capacity for regeneration, but skeletal muscle and cartilage have a weak regenerative capacity. Cardiac muscle and the nervous tissue in the brain and spinal cord have virtually no *functional* regenerative capacity, and they are routinely replaced by scar tissue. However, recent studies show that some unexpected (and highly selective) 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. Over a period of months, the fibrous mass shrinks and becomes more and more compact. The resulting scar appears as a pale, often shiny area composed mostly of collagen fibers. Scar tissue is strong, but it lacks the flexibility and elasticity of most normal tissues. Also, it cannot perform the normal functions of the tissue it has replaced.

Homeostatic Imbalance 4.3

Scar tissue that forms in the wall of the urinary bladder, heart, or other muscular organ may severely hamper the organ's function. The normal shrinking of the scar reduces the internal volume and may hinder or even block substances from moving through a hollow organ. Scar tissue hampers muscle's ability to contract and may interfere with its normal excitation by the nervous system. In the heart, these problems may lead to progressive heart failure. In irritated visceral organs, particularly following abdominal surgery, *adhesions* may form as the newly forming scar tissue connects adjacent organs together. Such adhesions can prevent the normal shifting about (churning) of loops of the intestine, dangerously obstructing the flow of foodstuffs. Adhesions can also restrict heart movements and immobilize joints. ✚

☑ Check Your Understanding

21. What are the three main steps of tissue repair?
22. Why does a deep injury to the skin result in abundant scar tissue?

For answers, see Appendix H.

Developmental Aspects of Tissues

✓ Indicate the embryonic origin of each tissue class.

✓ Briefly describe tissue changes that occur with age.

One of the first events of embryonic development is the formation of the three **primary germ layers**, which lie one atop the next like a three-layered cellular pancake. From superficial to deep, these layers are the **ectoderm**, **mesoderm** (mez′o-derm), and **endoderm** **(Figure 4.13)**. These primary germ layers then specialize to form the four primary tissues—epithelium, nervous tissue, muscle, and connective tissues—that make up all body organs.

By the end of the second month of development, the primary tissues have appeared, and all major organs are in place. In general, tissue cells remain mitotic and produce the rapid 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 achieved. Cellular division then slows greatly, although many tissues retain some ability to regenerate.

In adults, only epithelia and blood-forming tissues are highly mitotic. Some tissues that regenerate through life, such as the glandular cells of the liver, do so through division of their mature (specialized) cells. Others, like the epidermis of the skin and cells lining the intestine, have abundant *stem cells*, relatively undifferentiated cells that divide as necessary to produce new cells.

A CLOSER LOOK

Cancer—The Intimate Enemy

The word **cancer** elicits **dread** in everyone. Why does cancer strike some and not others?

Although once perceived as disorganized cell growth, this disease is now known to be a logical, coordinated process in which a precise sequence of **tiny alterations** changes a normal cell into a **killer**.

When cells fail to follow 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 is strictly a local affair. Its cells remain compacted, are often encapsulated, tend to grow slowly, and seldom kill their hosts if 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." Whereas normal cells become fatally "homesick" and die when they lose contact with the surrounding matrix, malignant cells tend to 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 for traveling to other parts of the body, called **metastasis** (mĕ-tas′tah-sis), probably has a lot to do with signaling molecules and the cell-surface glycoproteins the cancer cells bear. 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.

Carcinogenesis

Autopsies on individuals aged 50–70 who died of another cause have revealed that most of us have microscopic (but dormant) in situ (confined to origin site) neoplasms. So what changes a normal cell into a cancerous one? Some physical factors (radiation, mechanical trauma), certain viral infections, chronic inflammations, and many chemicals (tobacco tars, saccharine, some natural food chemicals).

All these factors cause *mutations*—changes in DNA that alter the expression of certain genes. However, not all carcinogens do damage because most are eliminated by peroxisomal or lysosomal enzymes or by the immune system. Furthermore, one mutation usually isn't enough. It takes several genetic changes to transform (convert) a normal cell into a cancerous cell.

The discovery of **oncogenes** (Greek *onco* = tumor), or cancer-causing genes, in rapidly spreading cancers provided a clue to the role of genes in cancer. **Proto-oncogenes**, benign forms of oncogenes in normal cells, were discovered later. Proto-oncogenes code for proteins that are essential for cell division, growth, and cellular adhesion, among other things. Many proto-oncogenes have fragile sites that break when exposed to carcinogens, converting them to oncogenes. Failure to code for certain proteins may lead to loss of an enzyme that controls an important metabolic process. Oncogenes may also "switch on" dormant genes that allow cells to become invasive and metastasize. Known oncogenes now number over 100.

Oncogenes have been detected in only 15–20% of human cancers, so investigators were not too surprised by the discovery of **tumor suppressor genes**, or **anti-oncogenes**, which suppress cancer by inactivating carcinogens, aiding DNA repair, or enhancing the immune system's counterattack. In fact, over half of all cancers involve malfunction or loss of just 2 of the 15 identified tumor suppressor genes—*p53* and *p16*. This is not surprising when you learn that *p53* prompts most cells to make proteins that stop cell division in stressed cells by promoting apoptosis or cell cycle arrest.

Furthermore, although each type of cancer is genetically distinct, human cancers appear to share a master set of genes—an activated group of 67 genes—and almost all cancer cells have gained or lost entire chromosomes. Whatever genetic factors are at work, the "seeds" of cancer appear to be in our own genes. Cancer is an intimate enemy indeed.

Let's look at the carcinogenesis of colorectal cancer, one of the best-understood human cancers. As with most cancers, a metastasis develops gradually. One of the first signs is a polyp (see photo on p. 146), a small benign growth consisting of apparently normal mucosa cells. As cell division continues, the polyp enlarges, becoming an adenoma (a term for any neoplasm of glandular epithelium). As various tumor suppressor genes are inactivated and the *K-ras* oncogene is mobilized, the mutations pile up and the adenoma becomes increasingly abnormal. The final consequence is colon carcinoma, a form of cancer that metastasizes quickly.

Cancer Prevalence

Almost half of all Americans develop cancer in their lifetime and a fifth of us will die of it. Cancer can arise from almost any cell type, but the most common cancers originate in the skin, lung, colon, breast, and prostate. Although stomach and colon cancer incidence is down, skin and lymphoid cancer rates are up.

Many cancers are preceded by observable lumps or other structural changes in tissue—for instance, *leukoplakia*, white patches in the mouth caused by the chronic irritation of ill-fitting dentures or heavy smoking. Although these lesions sometimes progress to cancer, in many cases they remain stable or even revert to normal if the environmental irritant is removed.

Diagnosis and Staging

Screening procedures are vital for early detection. Examples include *mammography* (X-ray examination of the breasts), examining breasts or testicles for lumps, examining the blood for cancer markers, and checking fecal samples for blood.

Unfortunately, most cancers are diagnosed only after symptoms have already appeared. In this case diagnosis is usually by **biopsy**: removing a tissue sample surgically and examining it microscopically for malignant cells. Increasingly, diagnosis includes chemical or genetic analysis of the sample—typing cancer cells by which genes are switched on or off, a technique described below.

Physical and histological examinations, lab tests, and imaging techniques (MRI, CT) can determine the extent of the disease (size of the neoplasm, degree of metastasis, etc.). Then, the cancer is assigned a **stage** from 1 to 4 according to the probability of cure. Stage 1 has the best probability of cure, stage 4 the worst.

Cancer Treatments

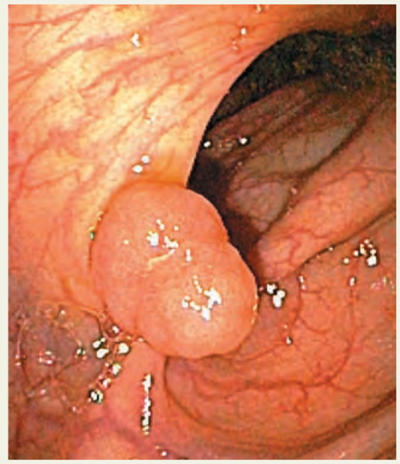
Most cancers are removed surgically if possible. To destroy metastasized cells, surgery is commonly followed by X irradiation and/or treatment with radioisotopes and chemotherapy (treatment with cytotoxic drugs). Recently, some oncologists have been using heat therapy (a slight upward temperature change) to make cancer cells more vulnerable to chemotherapy or radiation.

Chemotherapy is beset with the problem of resistance. Some cancer cells can eject the drugs in tiny bubbles or flattened vesicles dubbed exosomes, and these cells proliferate, forming new tumors that are resistant to chemotherapy. Furthermore, anticancer drugs have unpleasant side effects—nausea, vomiting, hair loss—because they kill *all* rapidly dividing cells, including normal tissue cells. The anticancer drugs also can damage the brain, producing a phenomenon called chemobrain—mental fuzziness and memory loss reported by many cancer patients. X rays also have side effects because, in passing through the body, they destroy healthy tissue as well as cancer cells.

Promising New Therapies

Traditional cancer treatments—"cut, burn, and poison"—are widely recognized as crude and painful. Promising new therapies focus on

- *Interrupting the signaling pathways that fuel cancer growth.* Imatinib (brand name Gleevec) incapacitates a mutated enzyme that triggers uncontrolled division of cells in two rare blood and digestive system cancers. Trastuzumab (Herceptin) is used to treat breast cancer. These drugs can provide a few extra weeks of life, before their protective effects wear off and the disease progresses again.
- *Delivering treatments more precisely to the cancer while sparing normal tissue.* One approach is to inject the patient with tiny drug-coated metal beads; then a powerful magnet positioned over the cancer guides the beads to the tumor. Or, a patient might take light-sensitive drugs that are drawn naturally into rapidly dividing cancer cells. Then, exposure to certain frequencies of laser light sets off reactions that kill the malignant cells. Proton therapy delivers highly targeted killing doses of protons (radiation) with incredible precision and effectiveness. Unlike X rays, which pass through the cancer and onward through the patient's body, protons can be slowed down and even directed to stop in the neoplasm.
- *Using genetically modified immune cells to target cancer cells.* One promising technique harvests a patient's most aggressive cancer-killing immune cells (T lymphocytes), inserts modified genes into them that make them even more efficient, multiplies the cells in the lab, and infuses them back into the patient.
- *Testing genotypes.* A few major cancer centers are beginning to genotype (test for genetic markers) every patient's tumor. The hope is to match personalized markers with drugs tailored to go after the tumor's genetic weak spot. For example, taxol, quite successful in treating breast and ovarian cancer, works only against tumors with a specific genetic makeup.



A polyp in the colon

Other experimental treatments seek to starve cancer cells by cutting off their blood supply, fix defective tumor suppressor genes and oncogenes, destroy cancer cells with viruses, or signal cancer cells to commit suicide by apoptosis. A cancer vaccine (TRICOM) contains genetically engineered viruses carrying genes for a cancer protein called carcinoembryonic antigen (CEA). When CEA proteins are delivered into the patient's body, they stimulate an immune response that orchestrates an attack on all CEA-bearing cancer cells.

At present, about half of all cancer cases are cured. Although average survival rates have not increased, cancer patients' quality of life has improved in the last decade. We can offer better treatments for cancer-associated pain, and antinausea drugs and other helpful medicines can soothe the side effects of chemotherapy.

Given good nutrition, good circulation, and relatively infrequent wounds and infections, our tissues normally function efficiently through youth and middle age. But with increasing age, epithelia thin and are more easily breached. Tissue repair is less efficient, and bone, muscle, and nervous tissues begin to atrophy, particularly when a person is not physically active. These events are due partly to decreased circulatory efficiency, which reduces delivery of nutrients to the tissues, but in some cases, diet is a contributing factor. As income declines or as chewing becomes more difficult, older people tend to eat soft foods, which may be low in protein and vitamins. As a result, tissue health suffers.

Another problem of aging tissues is the likelihood of DNA mutations in the most actively mitotic cells, which increases the risk of cancer (see *A Closer Look* on p. 145).

☑ Check Your Understanding

23. What are the names of the three embryonic germ layers?
24. Which germ layer gives rise to the nervous system?
25. Which two tissue types remain highly mitotic throughout life?

For answers, see Appendix H.

As we have seen, body cells combine to form four discrete tissue types: epithelial, connective, nervous, and muscle tissues. The cells making up each of these tissues share certain features but are by no means identical. They "belong" together because they have basic functional similarities. The important concept to carry away with you is that tissues, despite their unique abilities, cooperate to keep the body safe, healthy, and whole.

Chapter Summary

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Tissues are collections of structurally similar cells with related functions. The four primary tissues are epithelial, connective, nervous, and muscle tissues.

Preparing Human Tissue for Microscopy (pp. 117–118)

1. Preparation of tissues for microscopic examination involves cutting thin sections of the tissue and using dyes to stain the tissue. Minor distortions called artifacts can be introduced by the tissue preparation process.

Epithelial Tissue (pp. 118–126)

1. Epithelial tissue is the covering, lining, and glandular tissue of the body. Its functions include protection, absorption, excretion, filtration, secretion, and sensory reception.

Special Characteristics of Epithelium (pp. 118–119)

2. Epithelial tissues exhibit specialized contacts, polarity, avascularity, support from connective tissue, and high regenerative capacity.

Classification of Epithelia (pp. 119–124)

3. Epithelium is classified by arrangement as simple (one layer) or stratified (more than one layer) and by cell shape as squamous, cuboidal, or columnar. The terms denoting cell shape and arrangement are combined to describe the epithelium fully.
4. Simple squamous epithelium is a single layer of squamous cells. Highly adapted for filtration and exchange of substances, it forms walls of air sacs of the lungs and lines blood vessels. It contributes to serosae as mesothelium and lines all hollow circulatory system organs as endothelium.
5. Simple cuboidal epithelium, commonly active in secretion and absorption, is found in glands and in kidney tubules.
6. Simple columnar epithelium, specialized for secretion and absorption, consists of a single layer of tall columnar cells that exhibit microvilli and often mucus-producing cells. It lines most of the digestive tract.
7. Pseudostratified columnar epithelium is a simple columnar epithelium that appears stratified. Its ciliated variety, rich in mucus-secreting cells, lines most of the upper respiratory passages.
8. Stratified squamous epithelium is multilayered; cells at the free surface are squamous. It is adapted to resist abrasion. It lines the esophagus and vagina; its keratinized variety forms the skin epidermis.
9. Stratified cuboidal epithelia are rare in the body, and are found chiefly in ducts of large glands. Stratified columnar epithelium has a very limited distribution, found mainly in the male urethra and at transition areas between other epithelia types.
10. Transitional epithelium is a modified stratified squamous epithelium, adapted for responding to stretch. It lines hollow urinary system organs.

Glandular Epithelia (pp. 124–126)

11. A gland is one or more cells specialized to secrete a product.
12. On the basis of site of product release, glands are classified as exocrine or endocrine. Glands are classified structurally as multicellular or unicellular.
13. Unicellular glands, typified by goblet cells and mucous cells, are mucus-secreting single-celled glands.
14. Multicellular exocrine glands are classified according to duct structure as simple or compound, and according to the structure of their secretory parts as tubular, alveolar, or tubuloalveolar.
15. Multicellular exocrine glands of humans are classified functionally as merocrine or holocrine.

Connective Tissue (pp. 127–136)

1. Connective tissue is the most abundant and widely distributed tissue of the body. Its functions include binding and support, protection, insulation, fat storage, and transportation (blood).

Common Characteristics of Connective Tissue (p. 127)

2. Connective tissues originate from embryonic mesenchyme and have a matrix. Depending on type, a connective tissue may be well vascularized (most), poorly vascularized (dense connective tissue), or avascular (cartilage).

Structural Elements of Connective Tissue (pp. 127–129)

3. The structural elements of all connective tissues are extracellular matrix and cells.
4. The extracellular matrix consists of ground substance and fibers (collagen, elastic, and reticular). It may be fluid, gel-like, or firm.
5. Each connective tissue type has a primary cell type that can exist as a mitotic, matrix-secreting cell (blast) or as a mature cell (cyte) responsible for maintaining the matrix. The undifferentiated cell type of connective tissue proper is the fibroblast; that of cartilage is the chondroblast; that of bone is the osteoblast; and that of blood-forming tissue is the hematopoietic stem cell (see Chapter 17).

Types of Connective Tissue (pp. 129–136)

6. Embryonic connective tissue is called mesenchyme.
7. Connective tissue proper consists of loose and dense varieties. The loose connective tissues are
   - Areolar: gel-like ground substance; all three fiber types loosely interwoven; a variety of cells; forms the lamina propria and soft packing around body organs; the prototype.
   - Adipose: consists largely of adipocytes; scant matrix; insulates and protects body organs; provides reserve energy fuel. Brown fat is more important for generating body heat.
   - Reticular: finely woven reticular fibers in soft ground substance; the stroma of lymphoid organs and bone marrow.
8. Dense connective tissue proper includes
   - Dense regular: dense parallel bundles of collagen fibers; few cells, little ground substance; high tensile strength; forms tendons, ligaments, aponeuroses; in cases where this tissue also contains numerous elastic fibers it is called elastic connective tissue.
   - Dense irregular: like regular variety, but fibers are arranged in different planes; resists tension exerted from many

different directions; forms the dermis of the skin and organ capsules.

9. Cartilage exists as
   - Hyaline: firm ground substance containing collagen fibers; resists compression well; found in fetal skeleton, at articulating surfaces of bones, and trachea; most abundant type.
   - Elastic cartilage: elastic fibers predominate; provides flexible support of the external ear and epiglottis.
   - Fibrocartilage: parallel collagen fibers; provides support with compressibility; forms intervertebral discs and knee cartilages.
10. Bone (osseous tissue) consists of a hard, collagen-containing matrix embedded with calcium salts; forms the bony skeleton.
11. Blood consists of blood cells in a fluid matrix (plasma).

Muscle Tissue (pp. 136–139)

1. Muscle tissue consists of elongated cells specialized to contract and cause movement.
2. Based on structure and function, the muscle tissues are
   - Skeletal muscle: attached to and moves the bony skeleton; cells are cylindrical and striated.
   - Cardiac muscle: forms the walls of the heart; pumps blood; cells are branched and striated.
   - Smooth muscle: in the walls of hollow organs; propels substances through the organs; cells are spindle shaped and lack striations.

Nervous Tissue (p. 140)

1. Nervous tissue forms organs of the nervous system. It is composed of neurons and supporting cells.
2. Neurons are branching cells that receive and transmit electrical impulses. They are involved in body regulation. Supporting cells support and protect neurons.

iP Nervous System I; Topic: Anatomy Review, pp. 1, 3.

Covering and Lining Membranes (pp. 140–142)

1. Membranes are simple organs, consisting of an epithelium bound to an underlying connective tissue layer. They include mucosae, serosae, and the cutaneous membrane.

Tissue Repair (pp. 142–144)

1. Inflammation is the body's response to injury. Tissue repair begins during the inflammatory process. It may lead to regeneration, fibrosis, or both.
2. Tissue repair begins with organization, during which the blood clot is replaced by granulation tissue. If the wound is small and the damaged tissue is actively mitotic, the tissue will regenerate and cover the fibrous tissue. When a wound is extensive or the damaged tissue amitotic, it is repaired only by fibrous connective (scar) tissue.

Developmental Aspects of Tissues (pp. 144–146)

1. Epithelium arises from all three primary germ layers (ectoderm, mesoderm, endoderm); muscle and connective tissue from mesoderm; and nervous tissue from ectoderm.
2. The decrease in mass and viability seen in most tissues during old age often reflects circulatory deficits or poor nutrition.

Review Questions

Multiple Choice/Matching

(Some questions have more than one correct answer. Select the best answer or answers from the choices given.)

1. Use the key to classify each of the following described tissue types into one of the four major tissue categories.

   Key: **(a)** connective tissue **(b)** epithelium **(c)** muscle **(d)** nervous tissue

   ____ **(1)** Tissue type composed largely of nonliving extracellular matrix; important in protection and support
   ____ **(2)** The tissue immediately responsible for body movement
   ____ **(3)** The tissue that enables us to be aware of the external environment and to react to it
   ____ **(4)** The tissue that lines body cavities and covers surfaces
2. An epithelium that has several layers, with an apical layer of flattened cells, is called (choose all that apply): **(a)** ciliated, **(b)** columnar, **(c)** stratified, **(d)** simple, **(e)** squamous.
3. Match the epithelial types named in column B with the appropriate description(s) in column A.

Column A	Column B
____ **(1)** Lines most of the digestive tract	**(a)** pseudostratified ciliated columnar
____ **(2)** Lines the esophagus	**(b)** simple columnar
____ **(3)** Lines much of the respiratory tract	**(c)** simple cuboidal
____ **(4)** Forms the walls of the air sacs of the lungs	**(d)** simple squamous
____ **(5)** Found in urinary tract organs	**(e)** stratified columnar
____ **(6)** Endothelium and mesothelium	**(f)** stratified squamous
	(g) transitional

4. The gland type that secretes products such as milk, saliva, bile, or sweat through a duct is **(a)** an endocrine gland, **(b)** an exocrine gland.
5. The membrane which lines body cavities that open to the exterior is a(n) **(a)** endothelium, **(b)** cutaneous membrane, **(c)** mucous membrane, **(d)** serous membrane.
6. Scar tissue is a variety of **(a)** epithelium, **(b)** connective tissue, **(c)** muscle tissue, **(d)** nervous tissue, **(e)** all of these.

Short Answer Essay Questions

7. Define tissue.
8. Name four important functions of epithelial tissue and provide at least one example of a tissue that exemplifies each function.
9. Describe the criteria used to classify covering and lining epithelia.
10. Explain the functional classification of multicellular exocrine glands and supply an example for each class.
11. Provide examples from the body that illustrate four of the major functions of connective tissue.
12. Name the primary cell type in connective tissue proper; in cartilage; in bone.
13. Name the two major components of matrix and, if applicable, subclasses of each component.
14. Matrix is extracellular. How does the matrix get to its characteristic position?

15. Name the specific connective tissue type found in the following body locations: (a) forming the soft packing around organs, (b) supporting the ear pinna, (c) forming "stretchy" ligaments, (d) first connective tissue in the embryo, (e) forming the intervertebral discs, (f) covering the ends of bones at joint surfaces, (g) main component of subcutaneous tissue.
16. What is the function of macrophages?
17. Differentiate between the roles of neurons and the supporting cells of nervous tissue.
18. Compare and contrast skeletal, cardiac, and smooth muscle tissue relative to structure, body location, and specific function.
19. Describe the process of tissue repair, making sure you indicate factors that influence this process.
20. Indicate which primary tissue classes derive from each embryonic germ layer.
21. In what ways are adipose tissue and bone similar? How are they different?

Critical Thinking and Clinical Application Questions

1. John sustained a severe injury during football practice and is told that he has a torn knee cartilage. Can he expect a quick, uneventful recovery? Explain your response.
2. The epidermis (epithelium of the cutaneous membrane or skin) is a keratinized stratified squamous epithelium. Explain why that epithelium is much better suited for protecting the body's external surface than a mucosa consisting of a simple columnar epithelium would be.
3. Your friend is trying to convince you that if the ligaments binding the bones together at your freely movable joints (such as your knee, shoulder, and hip joints) contained more elastic fibers, you would be much more flexible. Although there is some truth to this statement, such a condition would present serious problems. Why?
4. In adults, over 90% of all cancers are either adenomas (adenocarcinomas) or carcinomas. (See Related Clinical Terms for this chapter.) 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 do you think this is so?
5. Cindy, an overweight high school student, is overheard telling her friend that she's going to research how she can transform some of her white fat to brown fat. What is her rationale here (assuming it is possible)?
6. Mrs. Delancy went to the local meat market and bought a beef tenderloin (cut from the loin, the region along the steer's vertebral column) and some tripe (cow's stomach). What type of muscle was she preparing to eat in each case?

AT THE CLINIC

Related Clinical Terms

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

Autopsy (aw′top-se) Examination of the body, its organs, and its tissues after death to determine the actual cause of death; also called postmortem examination and necropsy.

Carcinoma (kar″sĭ-no′mah; *karkinos* = crab, cancer) Cancer arising in an epithelium; accounts for 90% of human cancers.

Healing by first intention The simplest type of healing; occurs when the edges of the wound are brought together by sutures, staples, or other means used to close surgical incisions. Only small amounts of granulation tissue need be formed.

Healing by second intention The wound edges remain separated, and relatively large amounts of granulation tissue bridge the gap; the manner in which unattended wounds heal. Healing is slower than in wounds in which the edges are brought together, and larger scars result.

Keloid (ke′loid) Abnormal proliferation of connective tissue during healing of skin wounds; results in large, unsightly mass of scar tissue at the skin surface.

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).

Marfan's syndrome Genetic disease resulting in abnormalities of connective tissues due to a defect in fibrillin, a protein that is associated with elastin in elastic fibers. Clinical signs include loose-jointedness, long limbs and spiderlike fingers and toes, visual problems, and weakened blood vessels (especially the aorta) due to poor connective tissue reinforcement.

Osteogenesis imperfecta (brittle bone disease) An inherited condition that causes defective collagen production. Because collagen reinforces many body structures including bones, the result is weak bones that break easily. It is not unusual for its victims to have 30 or more fractures during their lifetime. Occurs in 1 out of 20,000 births. Misdiagnosis results in many infants coming to the ER with multiple fractures being treated as battered babies.

Pathology (pah-thol′o-je) Scientific study of changes in organs and tissues produced by disease.

Pus A collection of tissue fluid, bacteria, dead and dying tissue cells, white blood cells, and macrophages in an inflamed area.

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

Scurvy A nutritional deficiency caused by lack of adequate vitamin C needed to synthesize collagen; signs and symptoms include blood vessel disruption, delay in wound healing, weakness of scar tissue, and loosening of teeth.

VAC (vacuum-assisted closure) Innovative healing process for open-skin wounds and skin ulcers. Often induces healing when all other methods fail. Involves covering the wound with a special sponge, and then applying suction through the sponge. In response to the subsequent skin stretching, fibroblasts in the wound form more collagen tissue and new blood vessels proliferate, bringing more blood into the injured area, which also promotes healing.