General Characteristics

Connective (ko˘-nek′tiv) **tissues** comprise much of the body and are the most abundant type of tissue by weight. They bind structures, provide support and protection, serve as frameworks, fill spaces, store fat, produce blood cells, protect against infections, and help repair tissue damage.

The different types of connective tissue maintain the form of organs throughout the body. Connective tissues provide a matrix that supports and physically connects other tissues and cells together in organs. The interstitial fluid of connective tissue gives metabolic support to cells as the medium for diffusion of nutrients and waste products. Unlike the other tissue types (epithelium, muscle, and nerve), which consist mainly of cells, the major constituent of connective tissue is the **extracellular matrix** (**ECM**). Extracellular matrices consist of different combinations of **protein fibers** (such as **collagens** and **elastic fibers**) and **ground substance**. Ground substance is a complex of anionic, hydrophilic **proteoglycans**, **glycosaminoglycans** (**GAG**s), and multiadhesive **glycoproteins** (laminin, fibronectin, and others). GAGs (also called **mucopolysaccharides**) are long polysaccharides consisting of repeating disaccharide units, usually a uronic acid and a hexosamine. The largest, almost unique, and most ubiquitous GAG is **hyaluronic acid** (HA or hyaluronan). Others are **dermatan sulfate, chondroitin sulfates, keratan sulfate**, and **heparan sulfate**. Proteoglycans are composed of a core protein to which are covalently attached various numbers and combinations of the sulfated GAGs. Examples are **Aggrecan, Decorin**, **Syndecan** etc. Glycoproteins help stabilize the ECM by binding to other matrix components and to integrins in cell membranes. The hydrated nature of connective tissue ground substance provides the medium for the exchange of nutrients and metabolic wastes between cells and the blood supply.

Connective tissues originate from **embryonic mesenchyme**, a tissue developing mainly from the middle layer of the embryo, the mesoderm. Mesenchyme consists largely of viscous ground substance with few collagen fibers. Mesenchymal cells are undifferentiated and have large nuclei, with prominent nucleoli and fine chromatin.

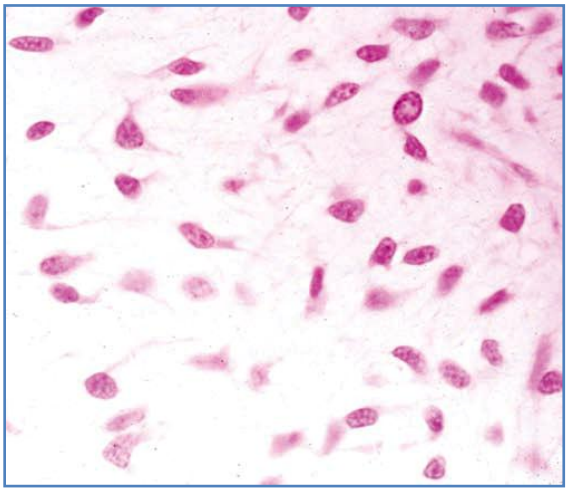

Figure. Embryonic mesenchyme.

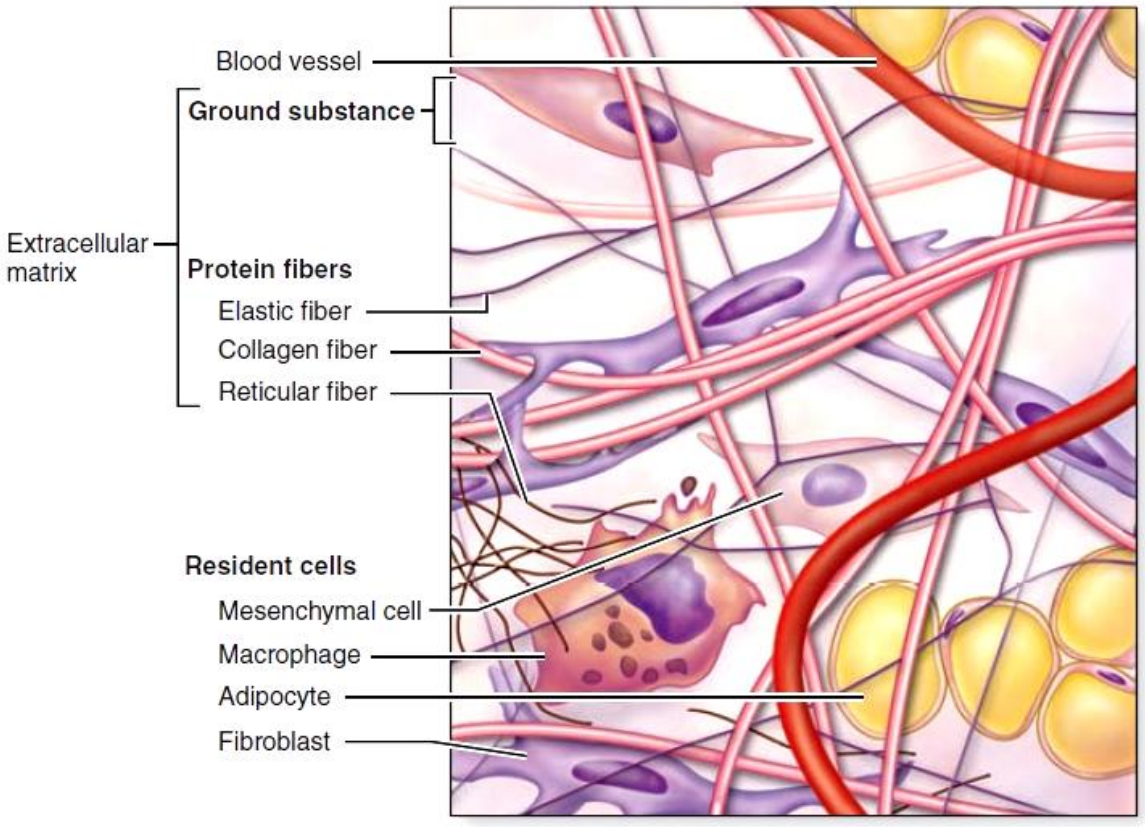

Figure. Cellular and extracellular components of connective tissue.

Connective tissue cells can usually divide. These tissues have varying degrees of vascularity, but in most cases, they have good blood supplies and are well nourished. Some connective tissues, such as bone and cartilage, are rigid. Loose connective tissue and dense connective tissue are more flexible.

Major Cell Types

Connective tissues include a variety of cell types. Some of them are called *fixed cells* because they reside in the specific connective tissue type for an extended period. These include fibroblasts, adipocytes, plasma cells and mast cells. Other cells, such as macrophages, are *wandering cells*. They move through and appear in tissues temporarily, usually in response to an injury or infection.

Fibroblasts and adipocytes originate locally from mesenchymal cells and are permanent residents of connective tissue; other cells found here, such as macrophages , plasma cells , and mast cells , originate from hematopoietic stem cells in bone marrow, circulate in the blood, and then move into connective tissue where they function.

FIGURE A scanning electron micrograph of a fibroblast (4,000×).

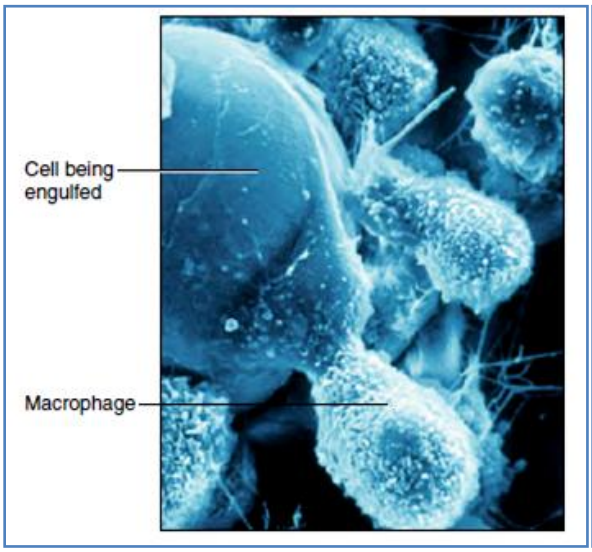

FIGURE. Macrophages are scavenger cells common in connective tissues. This scanning electron micrograph shows a number of macrophages engulfi ng parts of a larger cell (3,330×).

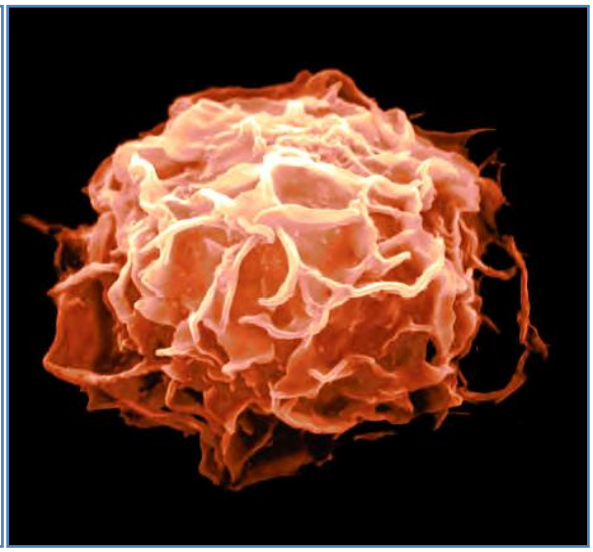

FIGURE. Scanning electron micrograph of a mast cell (6,600×).

TABLE 5–1 Functions of cells in connective tissue proper.

Cell Type	Major Product or Activity
Fibroblasts (fibrocytes)	Extracellular fibers and ground substance
Plasma cells	Antibodies
Lymphocytes (several types)	Various immune/defense functions
Eosinophilic leukocytes	Modulate allergic/vasoactive reactions and defense against parasites
Neutrophilic leukocytes	Phagocytosis of bacteria
Macrophages	Phagocytosis of ECM components and debris; antigen processing and presentation to immune cells; secretion of growth factors, cytokines, and other agents
Mast cells and basophilic leukocytes	Pharmacologically active molecules (eg, histamine)
Adipocytes	Storage of neutral fats

Connective Tissue Fibers

The fibrous components of connective tissue are elongated structures formed from proteins that polymerize after secretion from fibroblasts. The three main types of fibers include collagen, reticular, and elastic fibers. Collagen and reticular fibers are both formed by proteins of the collagen family, and elastic fibers are composed mainly of the protein elastin. These fibers are distributed unequally among the different types of connective tissue, with the predominant fiber type usually responsible for conferring specific tissue properties.

Collagenous fibers are thick threads of the protein collagen, the major and most abundant structural protein of the body. Collagenous fibers are grouped in long, parallel bundles, and they are flexible but only slightly elastic. More importantly, they have great tensile strength—that is, they can resist considerable pulling force. Thus, collagenous fibers are important components of body parts that hold structures together, such as ligaments (which connect bones to bones) and tendons (which connect muscles to bones).

Tissue containing abundant collagenous fibers is called *dense connective tissue.* Such tissue appears white, and for this reason collagenous fibers of dense connective tissue are sometimes called white fibers. *Loose connective tissue,* on the other hand, has sparse collagenous fibers.

Elastic fibers are composed of a springlike protein called **elastin.** These fibers branch, forming complex networks in various tissues. They are weaker than collagenous fibers but elastic. That is, they are easily stretched or deformed and will resume their original lengths and shapes when the force acting upon them is removed. Elastic fibers are common in body parts normally subjected to stretching, such as the vocal cords and air passages of the respiratory system. Elastic fibers are sometimes called yellow fibers, because tissues amply supplied with them appear yellowish.

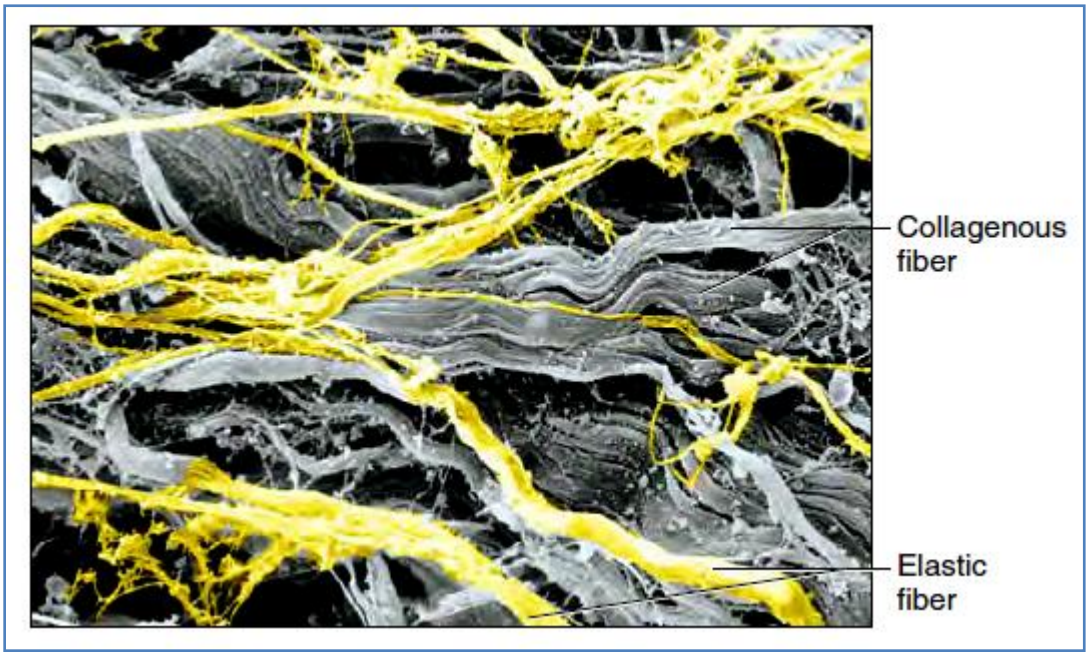

FIGURE. Scanning electron micrograph of collagenous fi bers (shades of white to gray) and elastic fi bers (yellow) (4,100×).

Reticular fibers are thin collagenous fibers. They are highly branched and form delicate supporting networks in a variety of tissues, including those of the spleen.

TABLE 5.6 | Components of Connective Tissue

Component	Characteristic	Function
Fibroblasts	Widely distributed, large, star-shaped cells	Secrete proteins that become fibers
Macrophages	Motile cells sometimes attached to fibers	Clear foreign particles from tissues by phagocytosis
Mast cells	Large cells, usually located near blood vessels	Release substances that may help prevent blood clotting and promote inflammation
Collagenous fibers (white fibers)	Thick, threadlike fibers of collagen with great tensile strength	Hold structures together
Elastic fibers (yellow fibers)	Bundles of microfibrils embedded in elastin	Provide elastic quality to parts that stretch
Reticular fibers	Thin fibers of collagen	Form supportive networks within tissues

Categories of Connective Tissues

Connective tissue is divided into two major categories. *Connective tissue proper* includes loose connective tissue (areolar, adipose, reticular) and dense connective tissue (dense regular, dense irregular, elastic). The *specialized connective tissues* include cartilage, bone, and blood.

A) Loose Connective Tissue

1. Areolar Tissue

Areolar tissue, forms delicate, thin membranes throughout the body. The cells of this tissue, mainly fibroblasts, are located some distance apart and are separated by a gel-like ground substance that contains many collagenous and elastic fibers that fibroblasts secrete. Areolar tissue binds the skin to the underlying organs and fills spaces between muscles. It underlies most layers of epithelium, where its many blood vessels nourish nearby epithelial cells.

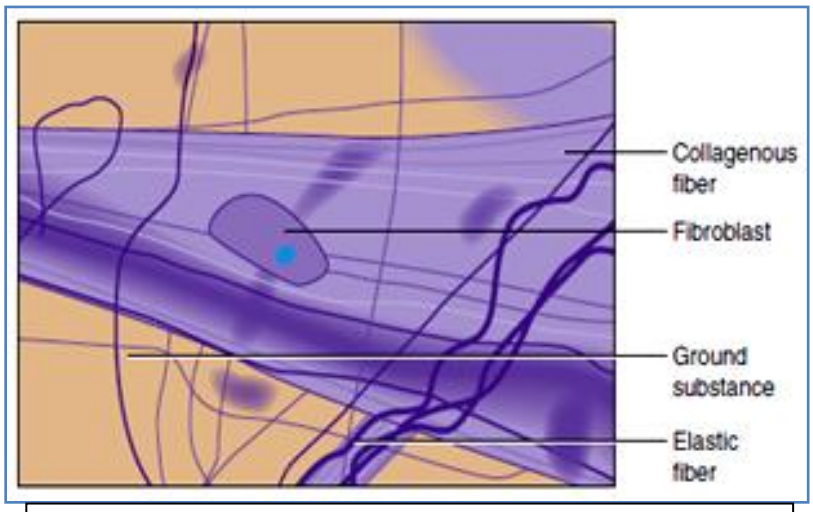

FIGURE. Areolar tissue contains numerous fibroblasts that produce collagenous and elastic fibers (800×).

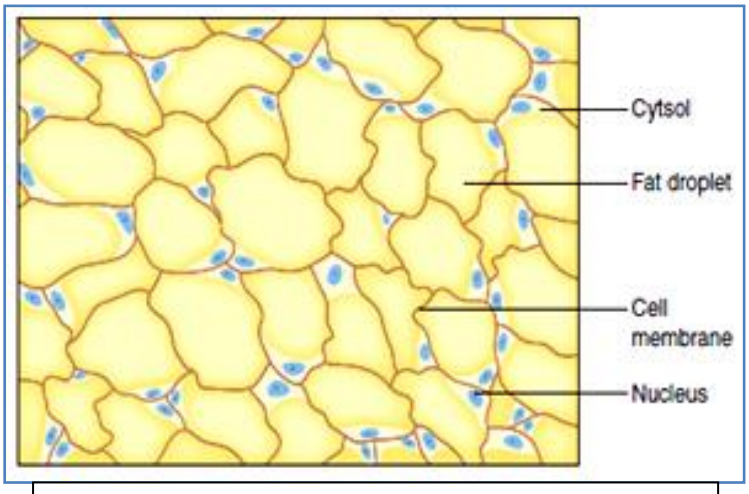

FIGURE. Adipose tissue cells contain large fat droplets that push the nuclei close to the cell membranes (400×).

2. Adipose Tissue

Adipose tissue, or fat, develops when certain cells (adipocytes) store fat in droplets in their cytoplasm. These cells resemble fibroblasts, but as they accumulate fat, they enlarge, and their nuclei are pushed to one side. When adipocytes become so abundant that they crowd out other cell types, they form adipose tissue. This tissue lies beneath the skin, in spaces between muscles, around the kidneys, behind the eyeballs, in certain abdominal membranes, on the surface of the heart, and around certain joints. Adipose tissue cushions joints and some organs, such as the kidneys. It also insulates beneath the skin, and it stores energy in fat molecules.

3. Reticular Connective Tissue

Reticular connective tissue is composed of thin, collagenous fibers in a three-dimensional network. It helps provide the framework of certain internal organs, such as the liver, spleen, and lymphatic organs.

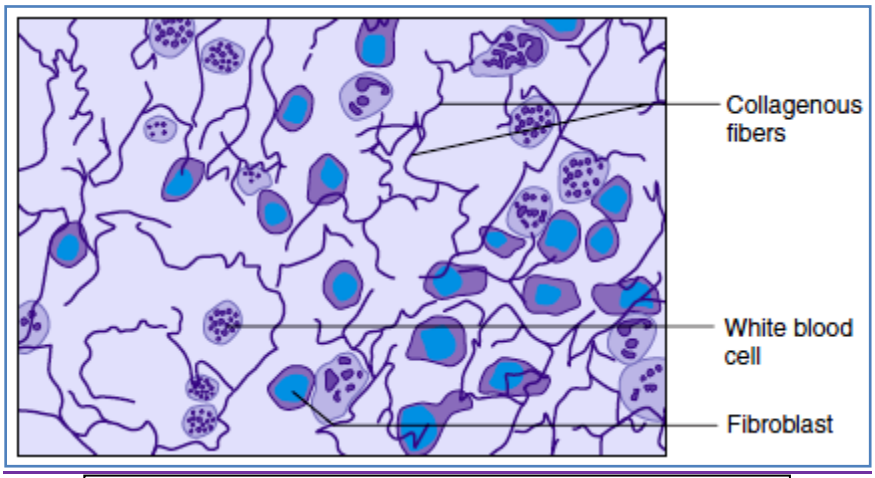

FIGURE 5.20 Reticular connective tissue is a network of thin collagenous fibers, which contains numerous fibroblasts and white blood cells (1,000×).

B) Dense Connective Tissue

1. Dense Regular Connective Tissue

Dense regular connective tissue consists of many closely packed, thick, collagenous fibers; a fine network of elastic fibers; and a few cells, mostly fibroblasts. Collagenous fibers of dense regular connective tissue are very strong, enabling the tissue to withstand pulling forces. It often binds body parts as parts of *tendons* and *ligaments*. The blood supply to dense regular connective tissue is poor, slowing tissue repair. This is why a sprain, which damages tissues surrounding a joint, may take considerable time to heal.

1. Dense Irregular Connective Tissue

Fibers of **dense irregular connective tissue** are thicker, interwoven, and more randomly organized. This allows the tissue to sustain tension exerted from many different directions. Dense irregular connective tissue is in the dermis, the inner skin layer.

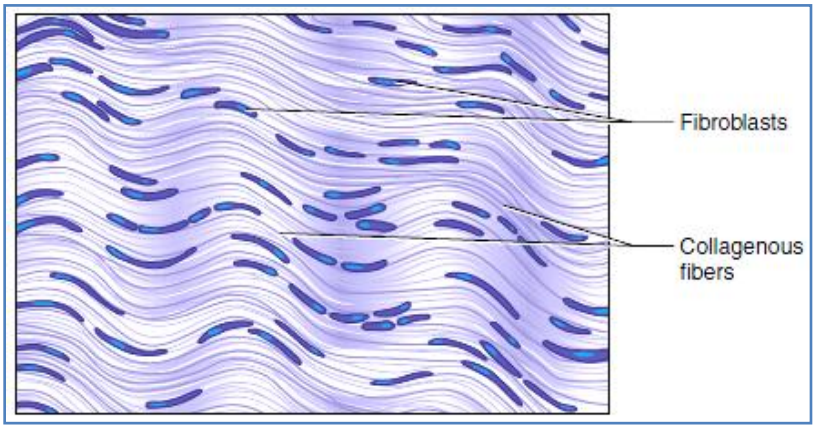

FIGURE. Dense regular connective tissue consists largely of tightly packed collagenous fibers (500×).

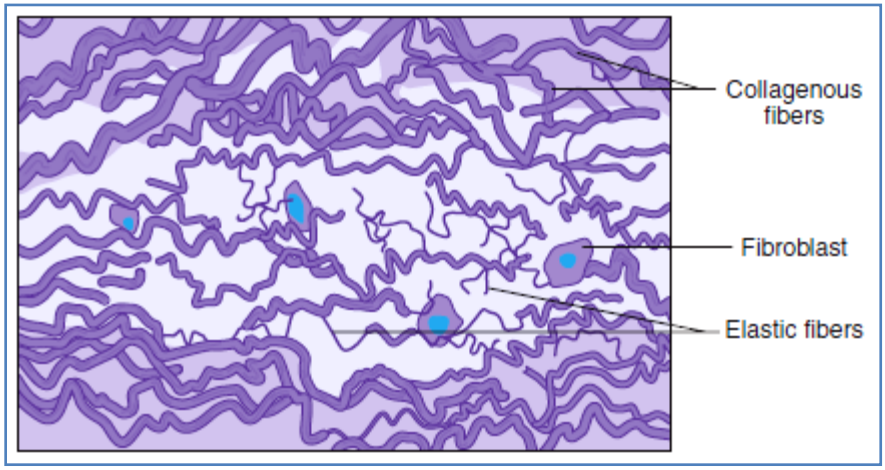

FIGURE. Elastic connective tissue contains many elastic fibers with collagenous fibers between them (160×).

2. Elastic Connective Tissue

Elastic connective tissue mainly consists of yellow, elastic fibers in parallel strands or in branching networks. Between these fibers are collagenous fibers and fibroblasts. This tissue is found in the attachments between bones of the spinal column (ligamenta flava). It is also in the layers within the walls of certain hollow internal organs, including the larger arteries; some portions of the heart; and the larger airways, where it imparts an elastic quality.

C) Specialized Connective Tissue

1. Cartilage

Cartilage is a rigid connective tissue. It provides support, frameworks, and attachments; protects underlying tissues; and forms structural models for many developing bones. In cartilage extracellular matrix is abundant and is largely composed of collagenous fibers embedded in a gel-like ground substance. This ground substance is rich in a proteinpolysaccharide complex (chondromucoprotein) and contains a large volume of water. Cartilage cells, or **chondrocytes**, occupy small chambers called *lacunae*

and lie completely within the extracellular matrix. A cartilaginous structure is enclosed in a covering of connective tissue called *perichondrium.* Although cartilage tissue lacks a direct blood supply, blood vessels are in the surrounding perichondrium. Cartilage cells near the perichondrium obtain nutrients from these vessels by diffusion, aided by the water in the extracellular matrix. This lack of a direct blood supply is why torn cartilage heals slowly and why chondrocytes do not divide frequently. The three types of cartilage are distinguished by their different types of extracellular matrix.

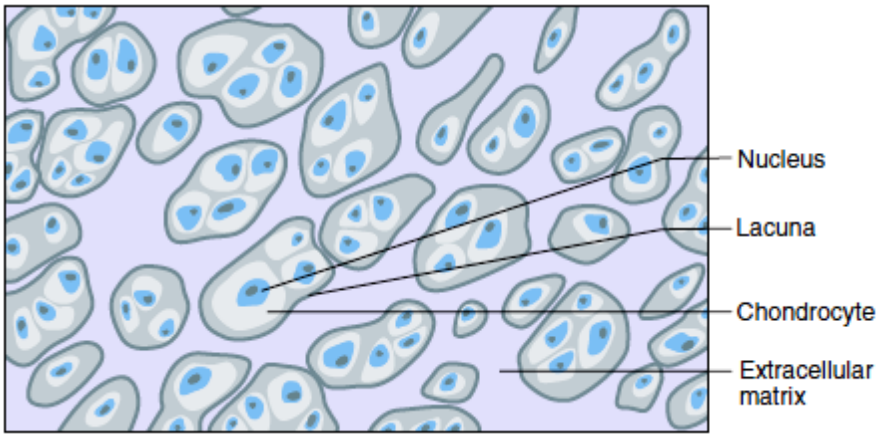

FIGURE. Cartilage cells (chondrocytes) are located in lacunae, in turn surrounded by extracellular matrix containing very fine collagenous fibers (400×). This is hyaline cartilage, the most common type.

Hyaline cartilage, the most common type, has very fine collagenous fibers in its extracellular matrix and looks somewhat like white glass. It is found on the ends of bones in many joints, in the soft part of the nose, and in the supporting rings of the respiratory passages. Parts of an embryo's skeleton begin as hyaline cartilage "models" that bone gradually replaces. Hyaline cartilage is also important in the development and growth of most bones.

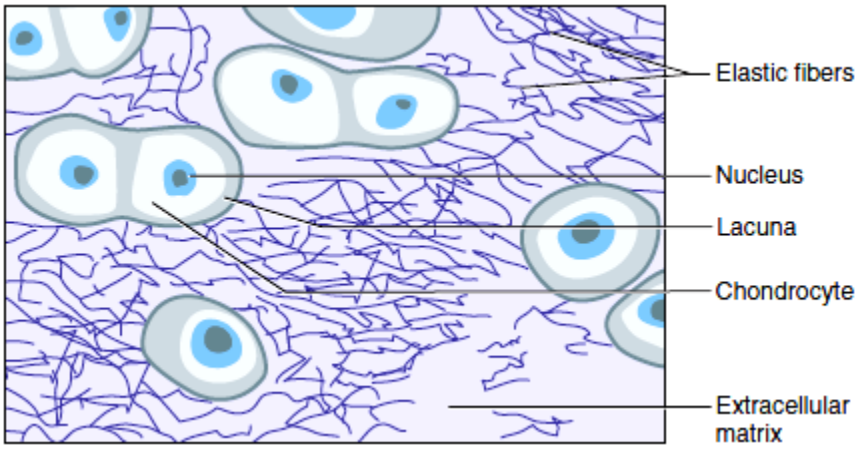

FIGURE. Elastic cartilage contains many elastic fibers in its extracellular matrix (1,200×).

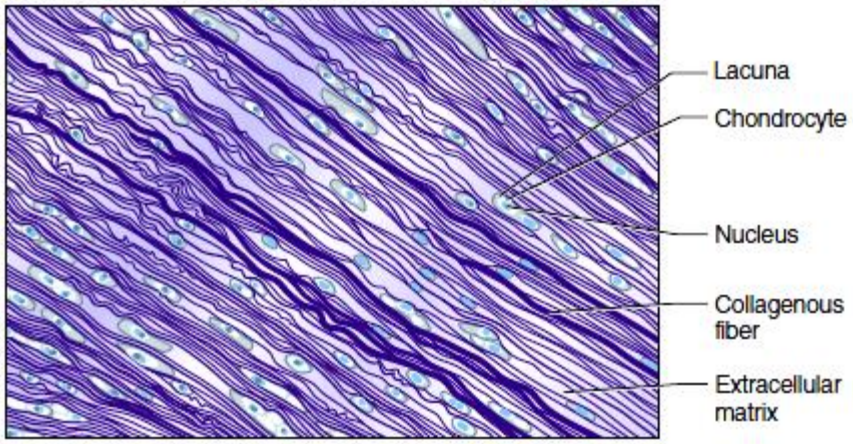

FIGURE. Fibrocartilage contains many large collagenous fibers in its extracellular matrix (400×).

Elastic cartilage is more flexible than hyaline cartilage because its extracellular matrix has a dense network of elastic fibers. It provides the framework for the external ears and parts of the larynx.

Fibrocartilage, a very tough tissue, has many collagenous fibers. It is a shock absorber for structures subjected to pressure. For example, fibrocartilage forms pads (intervertebral discs) between the individual bones (vertebrae) of the spinal column. It also cushions bones in the knees and in the pelvic girdle.

2. Bone

Bone (osseous tissue) is the most rigid connective tissue. Its hardness is largely due to mineral salts, such as calcium phosphate and calcium carbonate, between cells. This extracellular matrix also contains abundant collagenous fibers, which are flexible and reinforce the mineral components of bone.

As the main constituent of the adult skeleton, bone tissue provides solid support for the body, protects vital organs such as those in the cranial and thoracic cavities, and harbors cavities containing bone marrow where blood cells are formed. Bone (or osseous) tissue also serves as a reservoir of calcium, phosphate, and other ions that can be released or stored in a controlled fashion to maintain constant concentrations in body fluids. In addition, bones form a system of levers that multiply the forces generated during skeletal muscle contraction and transform them into bodily movements. This mineralized tissue therefore confers mechanical and metabolic functions to the skeleton. Bone is a specialized connective tissue composed of calcified extracellular material, the bone matrix , and three major cell types :

■ Osteocytes (Gr. *osteon* , bone + *kytos* , cell), which are found in cavities (lacunae) between bone matrix layers (lamellae), with cytoplasmic processes extending into small canaliculi (L. *canalis* , canal) between lamellae.
■ Osteoblasts (*osteon* + Gr. *blastos* , germ), which synthesize the organic components of the matrix
■ Osteoclasts (*osteon* + Gr. *klastos* , broken), which are multinucleated, giant cells involved in the resorption and remodeling of bone tissue.

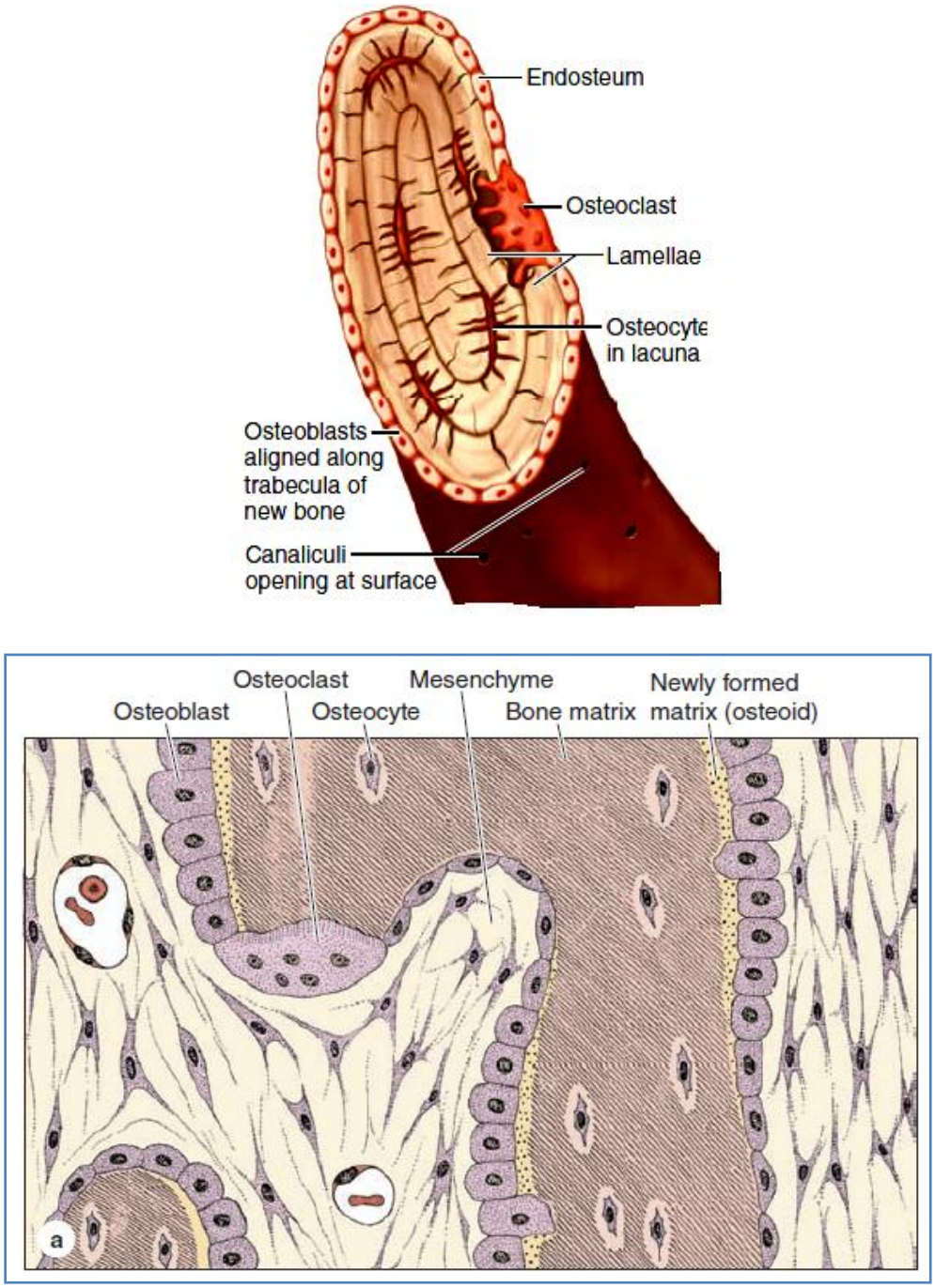

Figure. Diagram showing the relationship of osteoblasts to osteoid, bone matrix, and osteocytes. Osteoblasts and most of the larger osteoclasts are part of the endosteum covering the bony trabeculae.

Because metabolites are unable to diffuse through the calcified matrix of bone, the exchanges between osteocytes and blood capillaries depend on communication through the very thin, cylindrical spaces of the canaliculi. All bones are lined on both internal and external surfaces by layers of connective tissue containing osteogenic cells − endosteum on the internal surface surrounding the marrow cavity and periosteum on the external surface.

3. Blood

Blood, another type of connective tissue, is composed of cells suspended in a fluid extracellular matrix called *plasma*. These cells include *red blood cells*, *white blood cells*, and cellular fragments called *platelets*. Red blood cells transport gases; white blood cells fight infection; and platelets are involved in blood clotting. Most blood cells form in special tissues (hematopoietic tissues) in red marrow within the hollow parts of certain bones.Red blood cells are the only type of blood cells that function entirely in the blood vessels. In contrast, white blood cells typically migrate from the blood through capillary walls to connective tissues, where they carry on their major activities. The white blood cells usually reside in the connective tissues until they die.

FIGURE **12–1** **Composition of whole blood.**