Connective tissue

Connective tissue

- Maintain the form of organ
- Provide the matrix
- Connect tissue & cells
- Methabolic support

- Extracellular matrix

Protein fibers (collagen & elastic fiber)

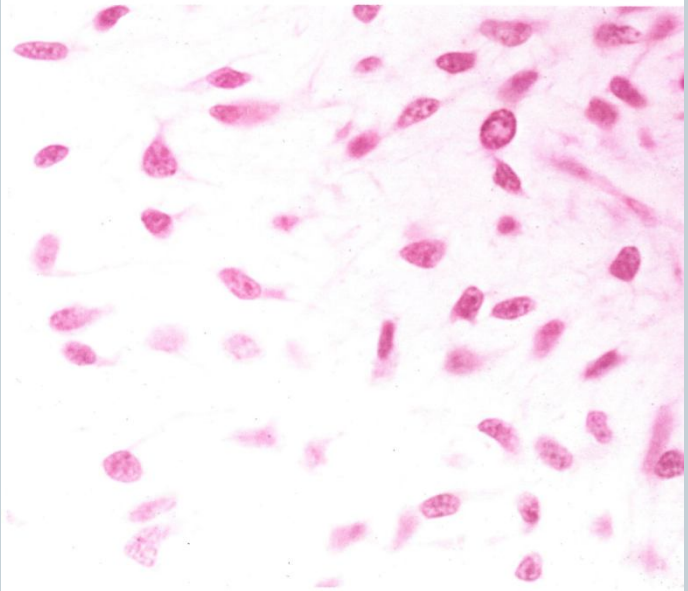
Ground substance (Pr.G,GAGs, GPr)

Connective tissue origine

Mesenchyme (mesoderm)
Mesenchymal cell
Undifferentiated cell
Large nucleus
Fine chromatin
Prominent nucleoli
Spindle shape
Scant cytoplasm
Migrate

bone, cartilage
Stem cells for blood, endothelium & muscle

FIGURE **5–1** **Embryonic mesenchyme.**



Mesenchyme consists of a population of undifferentiated cells, generally elongated but with many shapes, having large euchromatic nuclei and prominent nucleoli that indicate high levels of synthetic activity. These cells are called **mesenchymal cells**. Mesenchymal cells are surrounded by an ECM that they produced and that consists largely of a simple ground substance rich in hyaluronan (hyaluronic acid), but with very little collagen. X200. Mallory trichrome.

Cells of connective tissue

- Fibroblast
- Macrophage
- Plasma cell
- Mast cell
- adipocyte

Cellular and extracellular components of connective tissue.

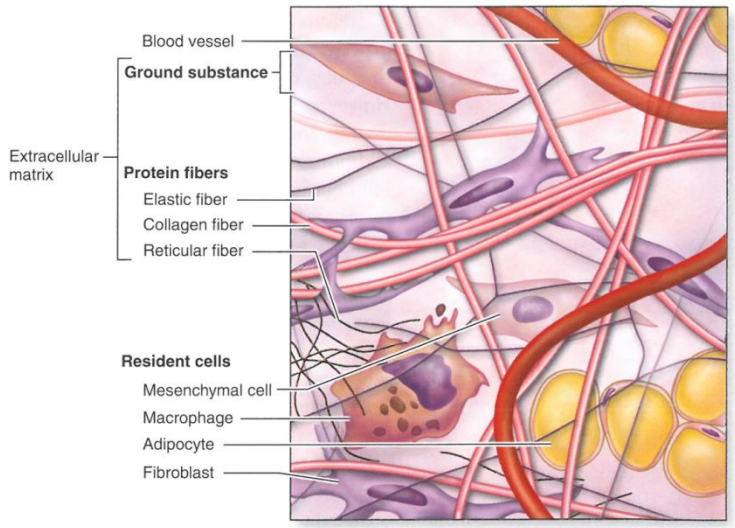


TABLE 5–1 Functions of cells in connective tissue proper.

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

Fibroblast

- Most cells
- Produce ECM

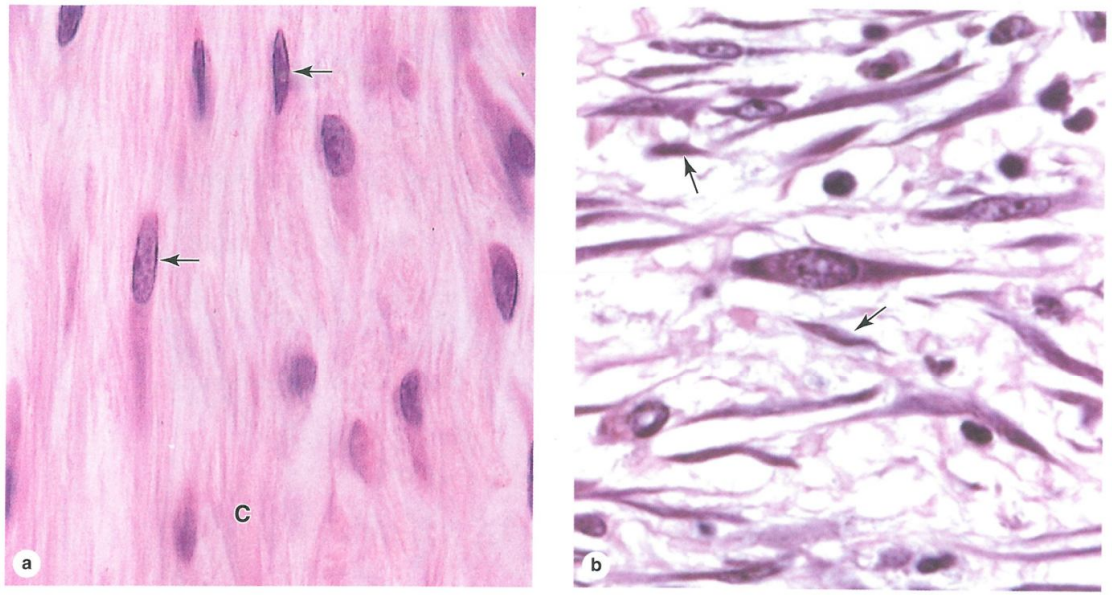
Much more cytoplasm
Large & oval nucleus
Prominent nucleoli
euchromatin
Expanded RER
Mature Golgi ap.

- Fibrocyte

Growth factors

Myofibroblast (wound healing)

FIGURE **5–3** **Fibroblasts.**



(a) Fibroblasts typically have large active nuclei and eosinophilic cytoplasm that tapers off in both directions along the axis of the nucleus, a morphology often referred to as "spindle-shaped." Nuclei (**arrows**) are clearly seen, but the eosinophilic cytoplasmic processes resemble the collagen bundles (**C**) that fill the ECM and are difficult to distinguish in H&E-stained sections.

(b) Both active and quiescent fibroblasts may sometimes be distinguished, as in this section of dermis. Active fibroblasts have large, euchromatic nuclei and basophilic cytoplasm, while inactive fibroblasts (or fibrocytes) are smaller with more heterochromatic nuclei (**arrows**). The round, very basophilic round cells are in leukocytes. Both X400. H&E.

Adipocyte

- Mesenchyme origin
- Fatt storage
- Heat production
- Cushen & insulate organ
- Metabolic significance

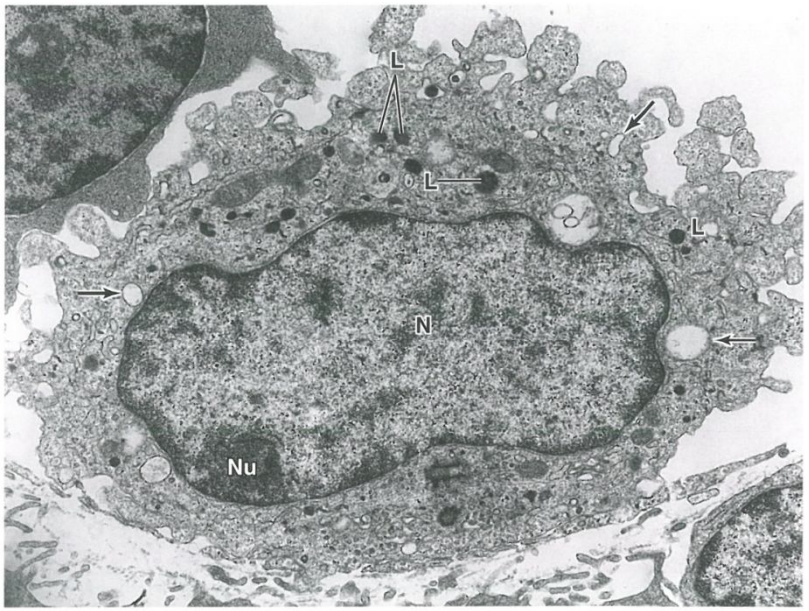
Macrophage & mononuclear phagocyte system

- Phagocytic function
- 10-30 µ
- Eccentric oval or kidney nucleus
- Named histiocyte
- Multinuclear giant cells
- Monocyte

- APCs

Kuppfer (Liver)
Microglial cell (CNS)
Osteoclast (Bone)
Langerhans ccell (Skin)

FIGURE **5–4** **Macrophage ultrastructure.**



Characteristic features of macrophages seen in this TEM of one such cell are the prominent nucleus (**N**) and the nucleolus (**Nu**) and the numerous secondary lysosomes (**L**). The arrows indicate phagocytic vacuoles near the protrusions and indentations of the cell surface. X10,000.

TABLE 5–2 Distribution and main functions of the cells of the mononuclear phagocyte system.

Cell Type	Major Locations	Main Function
Monocyte	Blood	Precursor of macrophages
Macrophage	Connective tissue, lymphoid organs, lungs, bone marrow, pleural and peritoneal cavities	Production of cytokines, chemotactic factors, and several other molecules that participate in inflammation (defense), antigen processing, and presentation
Kupffer cell	Liver (perisinusoidal)	Same as macrophages
Microglial cell	Central nervous system	Same as macrophages
Langerhans cell	Epidermis of skin	Antigen processing and presentation
Dendritic cell	Lymph nodes, spleen	Antigen processing and presentation
Osteoclast (from fusion of several macrophages)	Bone	Localized digestion of bone matrix
Multinuclear giant cell (several fused macrophages)	In connective tissue under various pathological conditions	Segregation and digestion of foreign bodies

Mast cells

- Oval or irregular cells
- 7-20 micrometer
- Basophilic granules
- Central nucleus
- Electron dense & heterogen granules
- Sulphated GAGs (metachromasia)
- Inflamatory, innate immunity & repaire

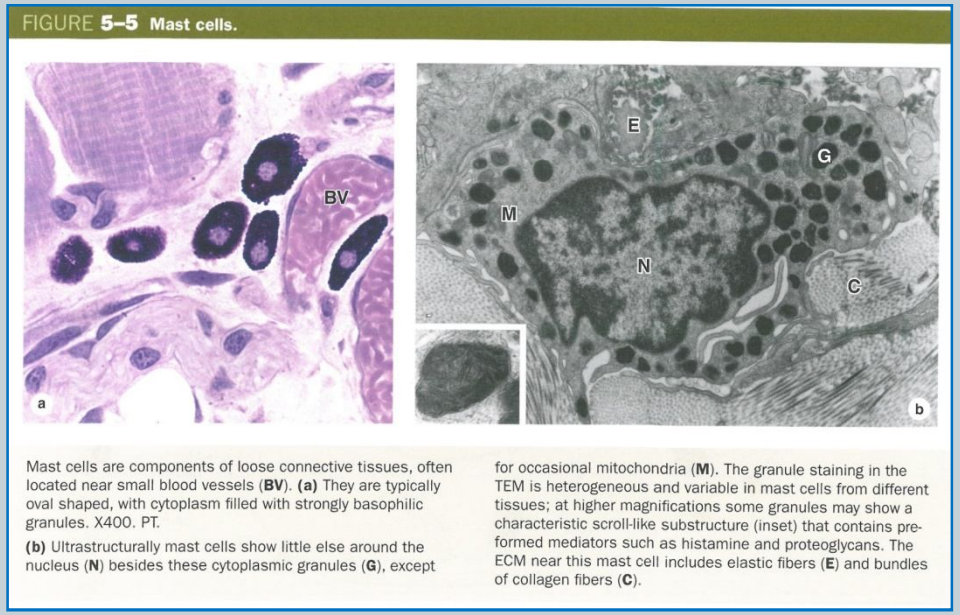


FIGURE **5–5** Mast cells.

Mast cells are components of loose connective tissues, often located near small blood vessels (**BV**). **(a)** They are typically oval shaped, with cytoplasm filled with strongly basophilic granules. X400. PT.

(b) Ultrastructurally mast cells show little else around the nucleus (**N**) besides these cytoplasmic granules (**G**), except for occasional mitochondria (**M**). The granule staining in the TEM is heterogeneous and variable in mast cells from different tissues; at higher magnifications some granules may show a characteristic scroll-like substructure (inset) that contains pre-formed mediators such as histamine and proteoglycans. The ECM near this mast cell includes elastic fibers (**E**) and bundles of collagen fibers (**C**).

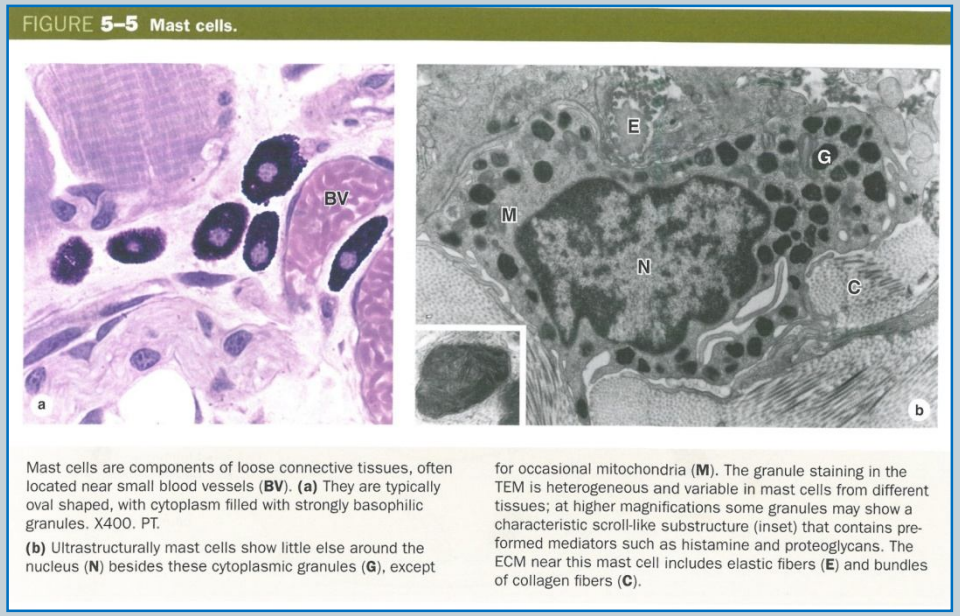
Mast cells products

- Heparin
- Histamin
- serin protease
- chemotactic factor
- Cytokines,
- Phospholipid

Prostaglandines

Leukoterienes

…



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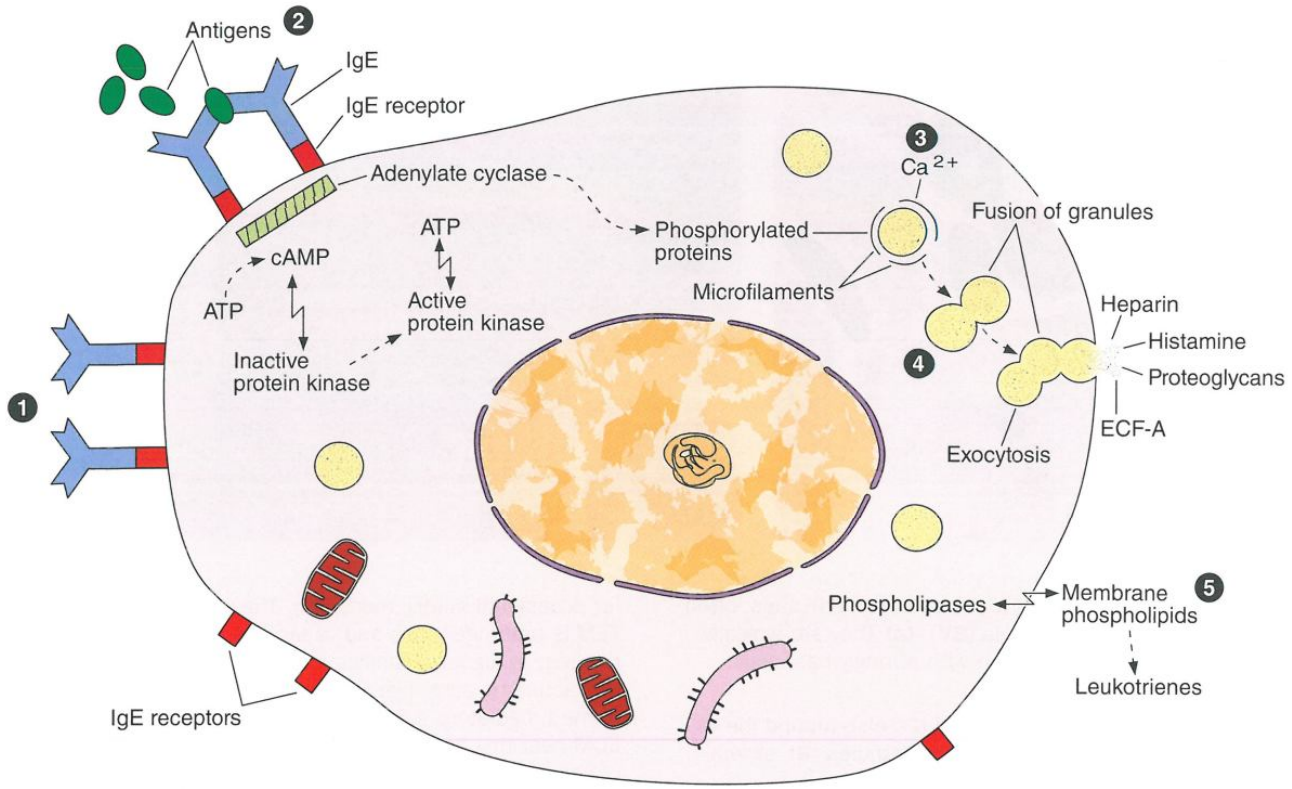
1. perivascular mast cell (skin & mesentere)
2. Mucosal mast cells (respiratory & digestive system)

Immediate hypersensitivity reaction (IgE)

FIGURE **5–6** **Mast cell secretion.**



Mast cell secretion is triggered by reexposure to certain antigens and allergens. Molecules of IgE antibody produced in an initial response to an allergen such as pollen or bee venom are bound to surface receptors for IgE (**1**), of which 300,000 are present per mast cell.

When a second exposure to the allergen occurs, IgE molecules bind this antigen and a few IgE receptors very rapidly become cross-linked (**2**). This activates adenylate cyclase, leading to phosphorylation of specific proteins (**3**), entry of Ca^{2+} and rapid exocytosis of some granules (**4**). In addition, phospholipases act on specific membrane phospholipids, leading to production and release of leukotrienes (**5**).

The components released from granules, as well as the leukotrienes, are immediately active in the local microenvironment and promote a variety of controlled local reactions that together normally comprise part of the inflammatory process called the **immediate hypersensitivity reaction**. "ECF-A" is the eosinophil chemotactic factor of anaphylaxis.

Plasma cells

- B Lymphocyte
- Antibody production
- Larg ovoid cells
- Basophilic cytoplasm (RER)
- Spherical eccentric nucleus
- Clock face (hetero & euchromatin)
- 10-20 days

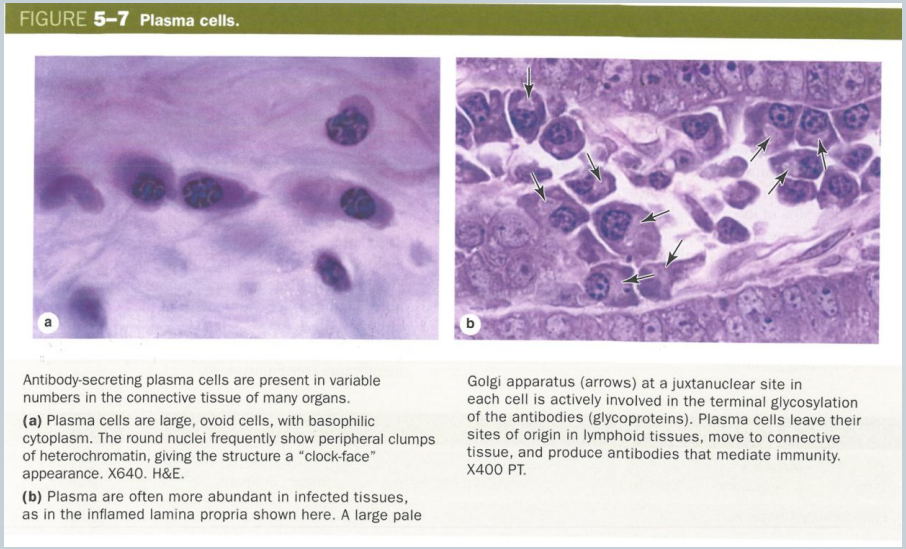


FIGURE **5–7** Plasma cells.

Antibody-secreting plasma cells are present in variable numbers in the connective tissue of many organs.

(a) Plasma cells are large, ovoid cells, with basophilic cytoplasm. The round nuclei frequently show peripheral clumps of heterochromatin, giving the structure a "clock-face" appearance. X640. H&E.

(b) Plasma are often more abundant in infected tissues, as in the inflamed lamina propria shown here. A large pale Golgi apparatus (arrows) at a juxtanuclear site in each cell is actively involved in the terminal glycosylation of the antibodies (glycoproteins). Plasma cells leave their sites of origin in lymphoid tissues, move to connective tissue, and produce antibodies that mediate immunity. X400 PT.

>> MEDICAL APPLICATION

Plasma cells are derived from B lymphocytes and are responsible for the synthesis of immunoglobulin antibodies. Each antibody is specific for the one antigen that stimulated the clone of B cells and reacts only with that antigen or molecules resembling it (see Chapter 14). The results of the antibody-antigen reaction are variable, but they usually neutralize harmful effects caused by antigens. An antigen that is a toxin (eg, tetanus, diphtheria) may lose its capacity to do harm when it binds to its specific antibody. Bound antigen-antibody complexes are quickly removed from tissues by phagocytosis.

Leukocytes

- Dipedesis
- Inflammatory reaction
- Hours – days

- Inflamation

Histamin (vasoactive sub.)
Mast cells
↑Vessele permeability
Edema
Redness
Heat
Pain (nerve ending)

- Chemotaxis

» MEDICAL APPLICATION

Increased vascular permeability is caused by the action of vasoactive substances such as histamine released from mast cells during **inflammation**. Increased blood flow and vascular permeability produce local swelling (edema), redness, and heat. **Pain** is due mainly to the action of the chemical mediators on nerve endings. All these activities help protect and repair the inflamed tissue. **Chemotaxis** (Gr. *chemeia*, alchemy + *taxis*, orderly arrangement), the phenomenon by which specific cell types are attracted by specific molecules, draws much larger numbers of leukocytes into inflamed tissues.

Fibers

- By fibroblast

1. Collagen
2. Reticular
3. Elastic (elastin)

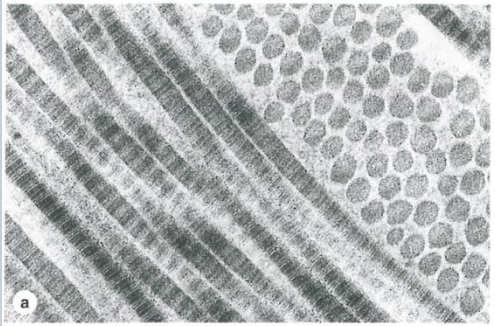
Collagens

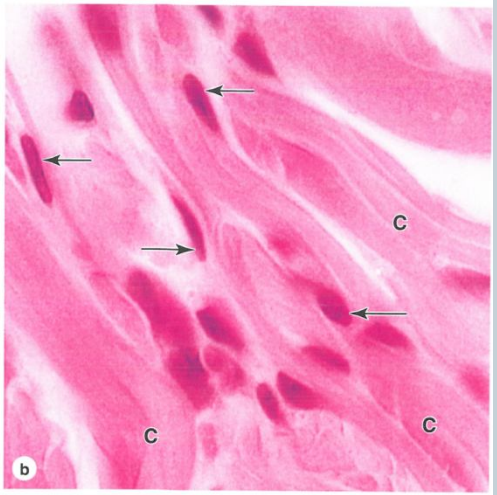
- Fiber
- Sheet
- Network

- Connective tissue
- Basement membrane
- External lamina of muscle
- External lamina of nerve cells

- Most common pr. (30%)
- 28 types

FIGURE **5–8** Type I collagen.





Subunits of type I collagen, the most abundant collagen, assemble to form extremely strong fibrils, which are then bundled together further by other collagens into much larger structures called **collagen fibers**.

(a) TEM shows fibrils cut longitudinally and transversely. In longitudinal sections fibrils display alternating dark and light bands; in cross section the cut ends of individual collagen molecules appear as dots. Ground substance completely surrounds the fibrils. X100,000.

(b) The large bundles of type I collagen fibrils (**C**) appear as acidophilic collagen fibers in connective tissues, where they may fill the extracellular space. Subunits for these fibers were secreted by the fibroblasts (**arrows**) associated with them. X400. H&E.

- Fibrillar collagens (I,II, III types, tendons, organ capsule, demis)
- Sheet forming collagens (IV, external lamina, basal lamina)
- Linking/anchoring collagens (VII, other collagen to ECM)

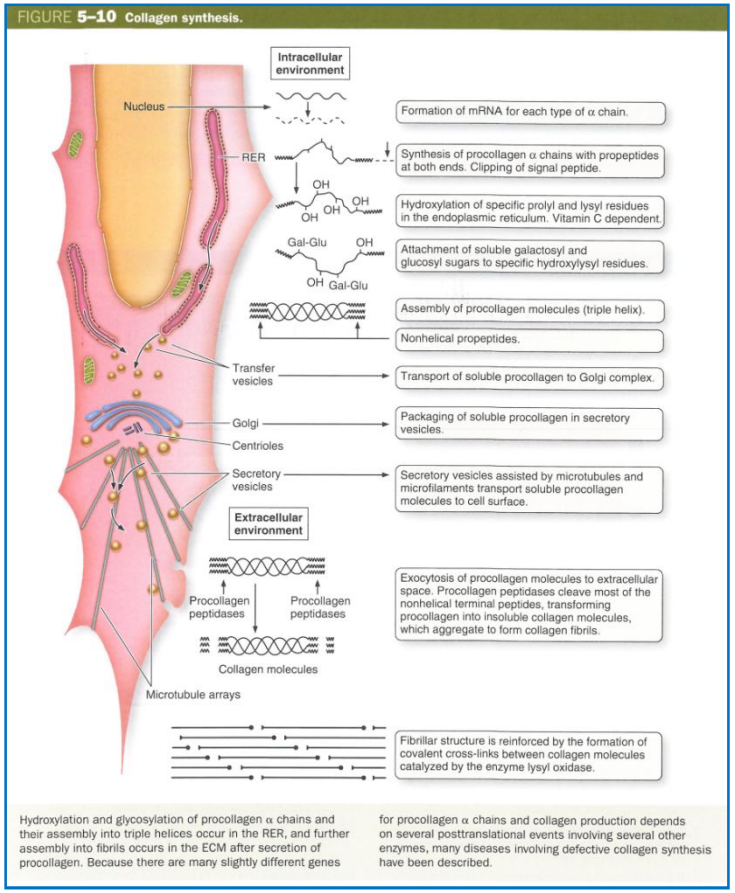
TABLE 5–3 Collagen types.

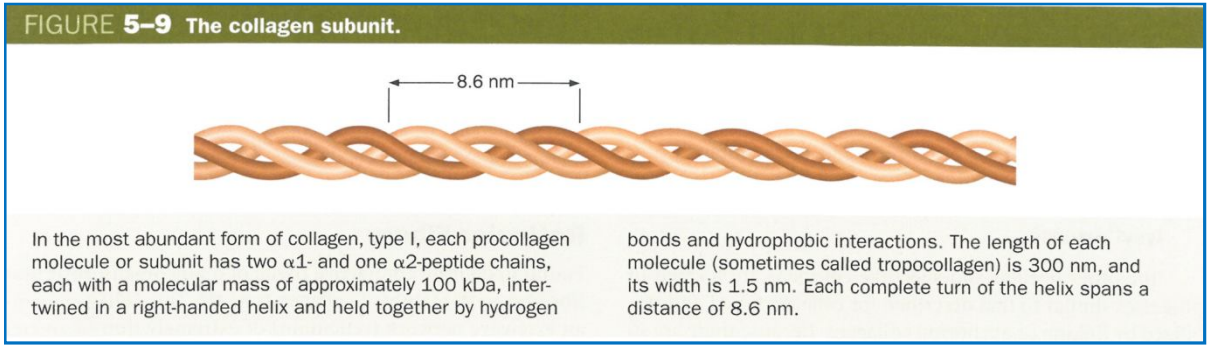
Type	Molecule Composition	Structure	Optical Microscopy	Major Locations	Main Function
Fibril-Forming Collagens					
I	$[\alpha 1\ (I)]_2[\alpha 2\ (I)]$	300-nm molecule, 67-nm banded fibrils	Thick, highly picrosirius birefringent, fibers	Skin, tendon, bone, dentin	Resistance to tension
II	$[\alpha 1\ (II)]_3$	300-nm molecule, 67-nm banded fibrils	Loose aggregates of fibrils, birefringent	Cartilage, vitreous body	Resistance to pressure
III	$[\alpha 1\ (III)]_3$	67-nm banded fibrils	Thin, weakly birefringent, argyrophilic (silver-binding) fibers	Skin, muscle, blood vessels, frequently together with type I	Structural maintenance in expansible organs
V	$[\alpha 1\ (V)]_3$	390-nm molecule, N-terminal globular domain	Frequently forms fiber together with type I	Fetal tissues, skin, bone, placenta, most interstitial tissues	Participates in type I collagen function
XI	$[\alpha 1\ (XI)]\ [\alpha 2\ (XI)]\ [\alpha 3\ (XI)]$	300-nm molecule	Small fibers	Cartilage	Participates in type II collagen function
Sheet-Forming Collagens					
IV	$[\alpha 1\ (VII)]_2\ [\alpha 1\ (IV)]$	2-dimensional cross-linked network	Detected by immunocytochemistry	All basal and external laminae	Support of epithelial cells; filtration
Linking/Anchoring Collagens					
VII	$[\alpha 1\ (VII)]_3$	450 nm, globular domain at each end	Detected by immunocytochemistry	Epithelial basement membranes	Anchors basal laminae to underlying reticular lamina
IX	$[\alpha 1\ (IX)]\ [\alpha 2\ (IX)]\ [\alpha 3\ (IX)]$	200-nm molecule	Detected by immunocytochemistry	Cartilage, vitreous body	Binds various proteoglycans; associated with type II collagen
XII	$[\alpha 1\ (XII)]_3$	Large N-terminal domain	Detected by immunocytochemistry	Placenta, skin, tendons	Interacts with type I collagen
XIV	$[\alpha 1\ (XIV)]_3$	Large N-terminal domain; cross-shaped molecule	Detected by immunocytochemistry	Placenta, bone	Binds type I collagen fibrils, with types V and XII, strengthening fiber formation

- α Procollagen (RER)
- 3 α Procollagen (Triple helix)

Disulphid bond (COOH end)

- Exocytose
- procollagen





Collagen synthesis

1. α-Procollagen(RER)
2. Prolin & lysin rich
3. Prolyl Hydroxilase (O2, Fe++, Vit C)
4. Glycosilation
5. Cystein (disulfid bond)
6. procollagen
7. exocytosis
8. Procollagen peptidase
9. Collagene molecule
10. Lysyl oxidase (binding)

Eosine (pink)
Trichorome mallory (blue)
Red cirius (red)

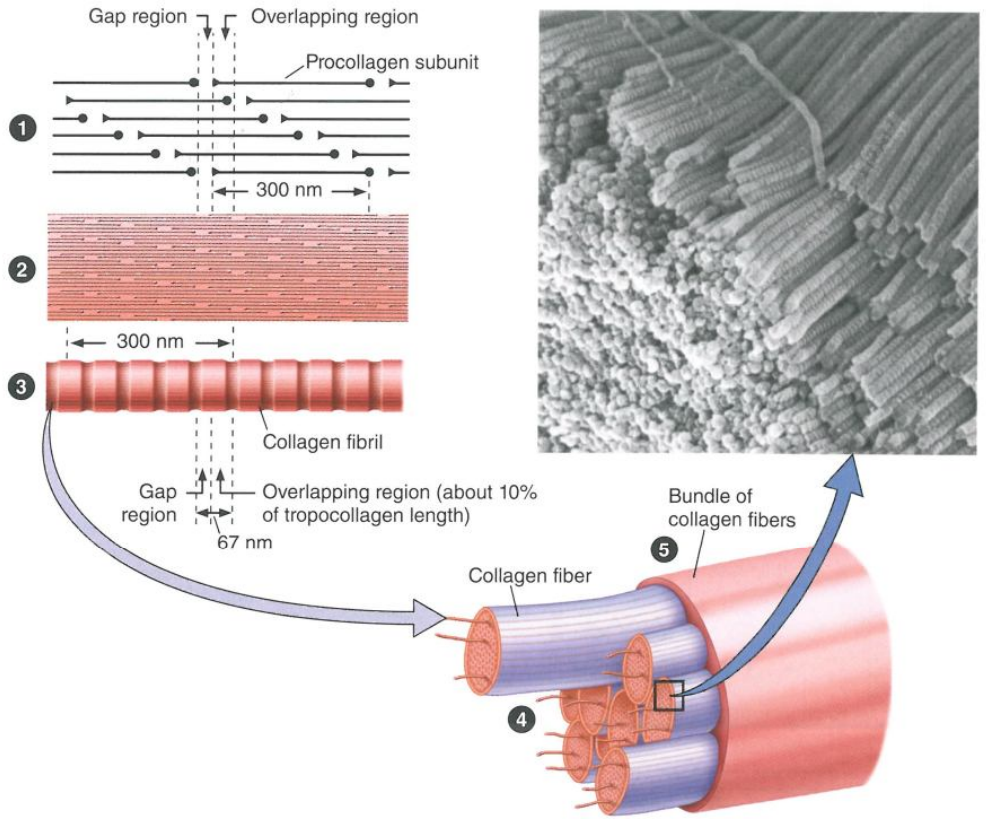
>> MEDICAL APPLICATION

A **keloid** is a local swelling caused by abnormally large amounts of collagen that form in scars of the skin. Keloids occur most often in individuals of African descent and can be a troublesome clinical problem to manage. Not only can they be disfiguring, but excision is almost always followed by recurrence.

TABLE **5–4** Examples of clinical disorders resulting from defects in collagen synthesis.

Disorder	Defect	Symptoms
Ehlers-Danlos type IV	Faulty transcription or translation of collagen type III	Aortic and/or intestinal rupture
Ehlers-Danlos type VI	Faulty lysine hydroxylation	Increased skin elasticity, rupture of eyeball
Ehlers-Danlos type VII	Decrease in procollagen peptidase activity	Increased articular mobility, frequent luxation
Scurvy	Lack of vitamin C, a required cofactor for prolyl hydroxylase	Ulceration of gums, hemorrhages
Osteogenesis imperfecta	Change of 1 nucleotide in genes for collagen type I	Spontaneous fractures, cardiac insufficiency

FIGURE 5–11 Assembly of type I collagen.



Shown here are the relationships among type I collagen molecules, fibrils, fibers, and bundles.

1. Rodlike triple-helix collagen molecules, each 300 nm long, self-assemble in a highly organized, lengthwise arrangement of overlapping regions.
2. The regular, overlapping arrangement of subunits continues as large collagen fibrils are assembled.
3. This structure causes fibrils to have characteristic cross striations with alternating dark and light bands when observed in the EM.
4. Fibrils assemble further and are linked together in larger collagen fibers visible by light microscopy.
5. Type I fibers often form into still larger aggregates bundled and linked together by other collagens.

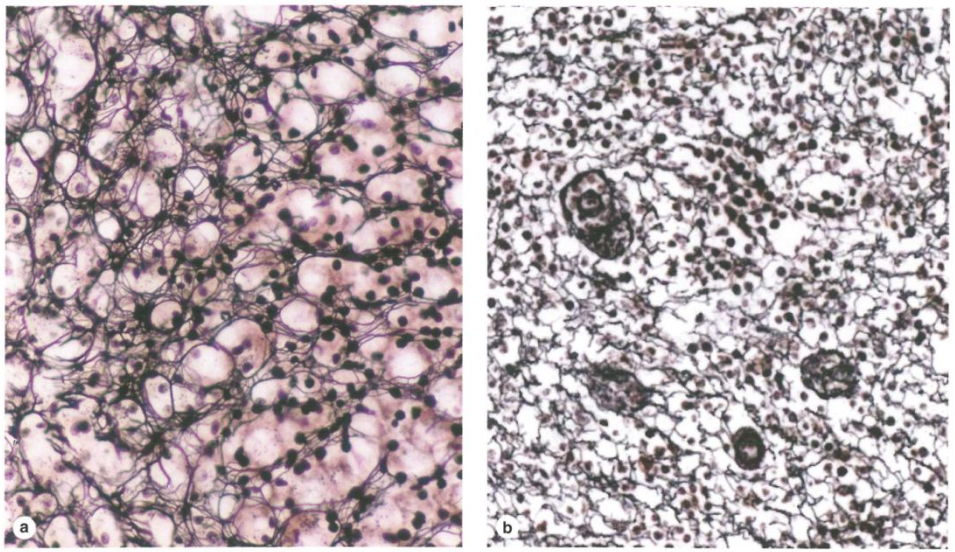
The photo shows an SEM view of type I collagen fibrils closely aggregated as part of a collagen fiber. Striations are visible on the surface of the fibrils.

Reticular fibers

- Collagen type III
- Network (reticulum)
- Highly glycosilaed (10%)
- Silver salts (argirophilic)
- PAS+

- Reticular lamina
- Adipocytes
- Smooth muscles
- Nerve fibers
- Small blood vessels

FIGURE **5–12** **Reticular fibers.**



In these silver-stained sections of adrenal cortex **(a)** and lymph node **(b)**, networks of delicate, black **reticular fibers** are prominent. These fibers serve as a supportive stroma in most lymphoid and hematopoietic organs and many endocrine glands. The fibers consist of type III collagen that is heavily glycosylated, producing the black argyrophilia. Cell nuclei are also dark, but cytoplasm is unstained. X100.

Function

- Supportive stroma for secretory parenchyma, liver vessel, endocrine gland
- Supportive stroma for hematopoietic tissue & bone marrow), lymphoid organ

Elastic fibers

- Thiner than collagen I
- Spares networks
- Bending & stretching condition
- Large blood wall
- Elastic lamellae

- Fibrillin microfibrils
- Elastin (Gly, Pro, Lys)
- Lysil oxidase
- Desmosine
- Elastase

- Not acidophilic
- Orsein
- Aldehyde fuschin

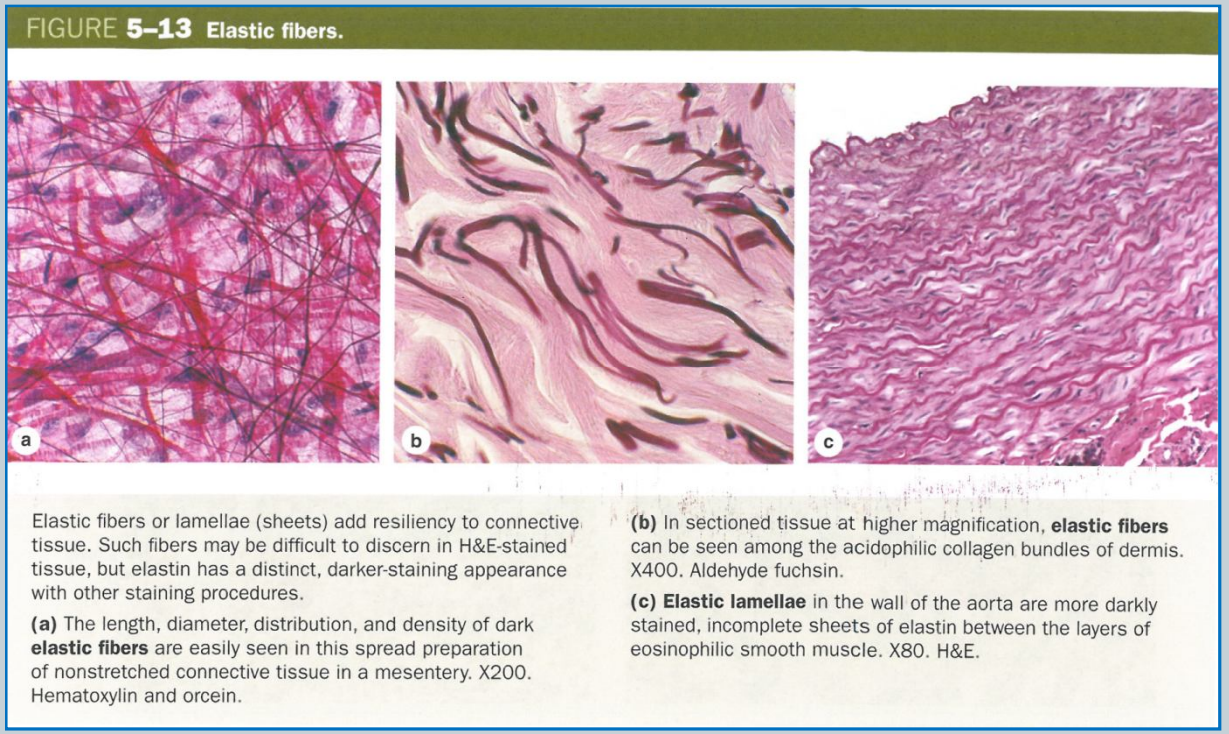
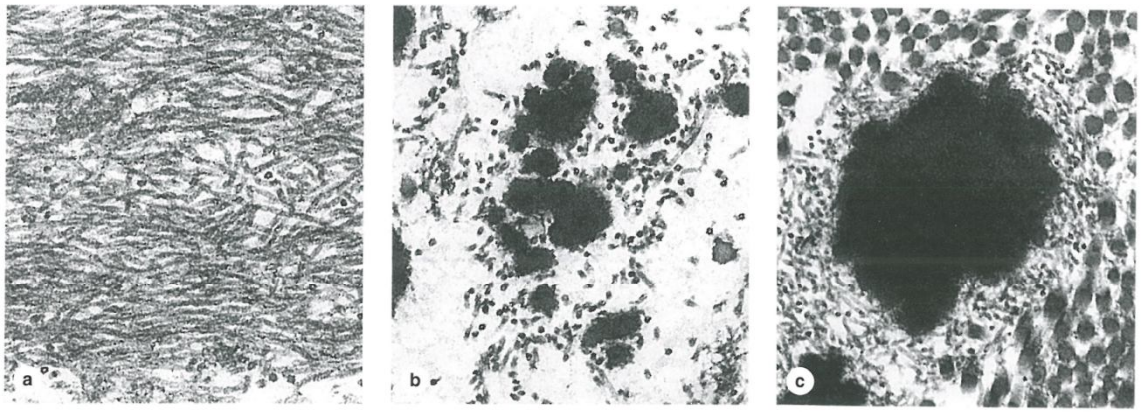


FIGURE **5–14** **Formation of elastic fibers.**



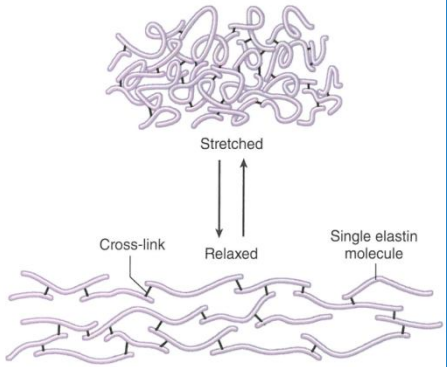
Stages in the formation of elastic fibers can be seen by TEM.

(a) Initially, a developing fiber consists of many 10-nm-diameter **fibrillin microfibrils** composed of molecular subunits secreted by fibroblasts and smooth muscle cells.

(b) Elastin is deposited on the scaffold of microfibrils, forming growing, amorphous composite structures. The elastin molecules are also secreted by the fibroblasts and quickly become cross-linked into larger assemblies.

(c) Elastin accumulates and ultimately occupies most of the electron-dense center of the single elastic fiber shown here. Fibrillin microfibrils typically remain at the fiber surface. Collagen fibrils, seen in cross section, are also present surrounding the elastic fiber. All X50,000.

FIGURE **5–15** **Molecular basis of elastic fiber elasticity.**



The diagram shows a small piece of an elastic fiber, in two conformations. Elastin polypeptides, the major components of elastic fibers, have multiple random-coil domains that straighten or stretch under force, and then relax. Most of the cross-links between elastin subunits consist of the covalent, cyclic structure **desmosine**, each of which involves four converted lysines in two elastin molecules. This unusual type of protein cross-link holds the aggregate together with little steric hindrance to elastin movements. These properties give the entire network its elastic quality.

- Fibrillin mutation
- Elastin deposition defect
- Marfan syndrome
- aneurysm

>> MEDICAL APPLICATION

Fibrillins comprise a family of proteins involved in making the scaffolding necessary for the deposition of elastin. Mutations in the fibrillin genes result in **Marfan syndrome**, a disease characterized by a lack of resistance in tissues rich in elastic fibers. Because the walls of large arteries are rich in elastic components and because the blood pressure is high in the aorta, patients with this disease often experience aortic swellings called **aneurysms**, which are life-threatening conditions.

Ground substance

- Hydrated

- GAGs

Disaccharid
Hyaloronic acid

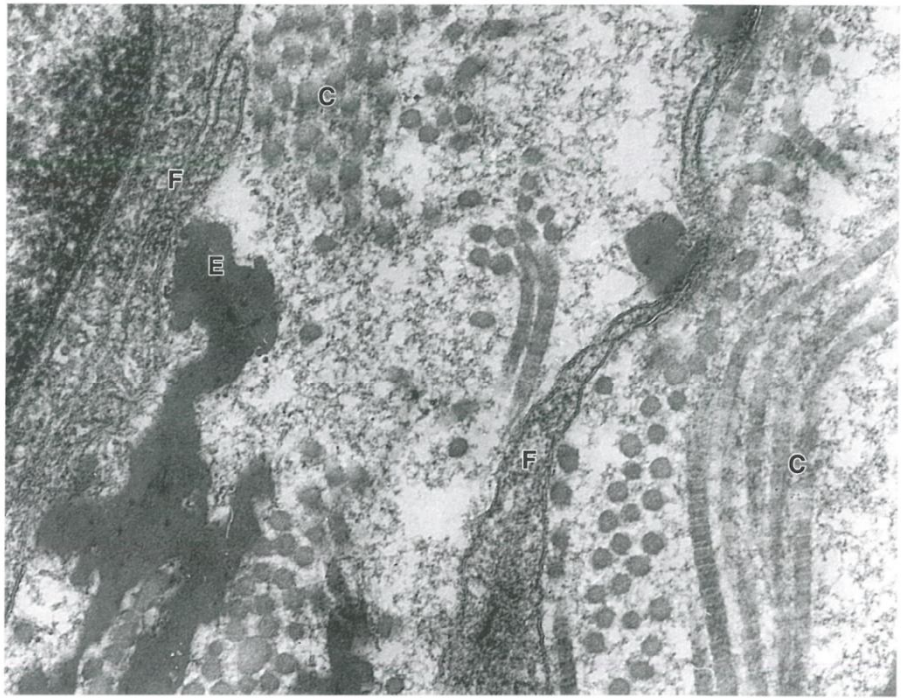
Dermatan sulphate
Heparan sulphate
Keratan sulphate
chondroitin sulphate in

- Proteoglycans

Decorin (col. I)
Syndecan (Integral pr.)
Aggrecan

- Glycoproteins

FIGURE **5–16** **Ultrastructure of the extracellular matrix (ECM).**

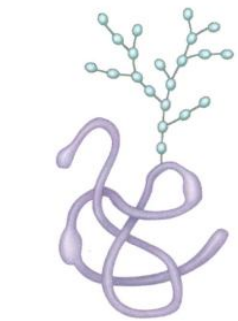


TEM of the connective tissue ECM reveals ground substance as either empty or containing fine granular material that fills spaces between the collagen (**C**) and elastic (**E**) fibers and surrounds fibroblast cells and processes (**F**). The granularity of ground substance is an artifact of the glutaraldehyde–tannic acid fixation procedure. X100,000.

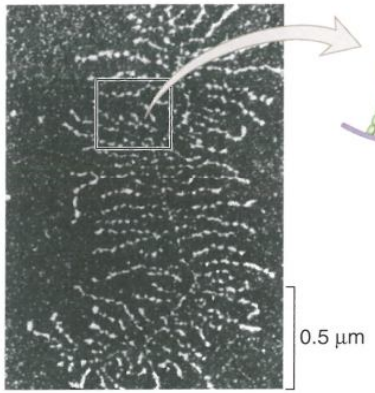
TABLE 5–5 Composition and distribution of glycosaminoglycans in connective tissue and their interactions with collagen fibers.

Glycosaminoglycan	Repeating Disaccharides		Distribution	Electrostatic Interaction with Collagen
	Hexuronic Acid	Hexosamine		
Hyaluronic acid	D-glucuronic acid	D-glucosamine	Umbilical cord, synovial fluid, vitreous humor, cartilage	
Chondroitin 4-sulfate	D-glucuronic acid	D-galactosamine	Cartilage, bone, cornea, skin, notochord, aorta	High levels of interaction, mainly with collagen type II
Chondroitin 6-sulfate	D-glucuronic acid	D-galactosamine	Cartilage, umbilical cord, skin, aorta (media)	High levels of interaction, mainly with collagen type II
Dermatan sulfate	L-iduronic acid or D-glucuronic acid	D-galactosamine	Skin, tendon, aorta (adventitia)	Low levels of interaction, mainly with collagen type I
Heparan sulfate	D-glucuronic acid or L-iduronic acid	D-galactosamine	Aorta, lung, liver, basal laminae	Intermediate levels of interaction, mainly with collagen types III and IV
Keratan sulfate	D-galactose	D-glucosamine	Cartilage, nucleus pulposus, annulus fibrosus	None

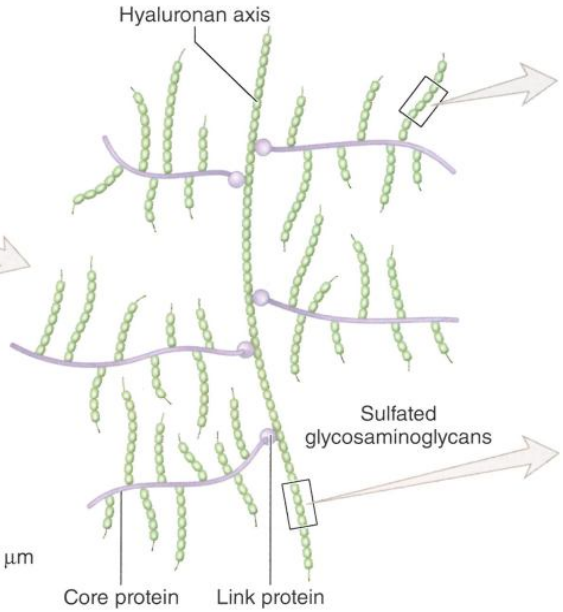
FIGURE 5–17 Glycoproteins and proteoglycans.

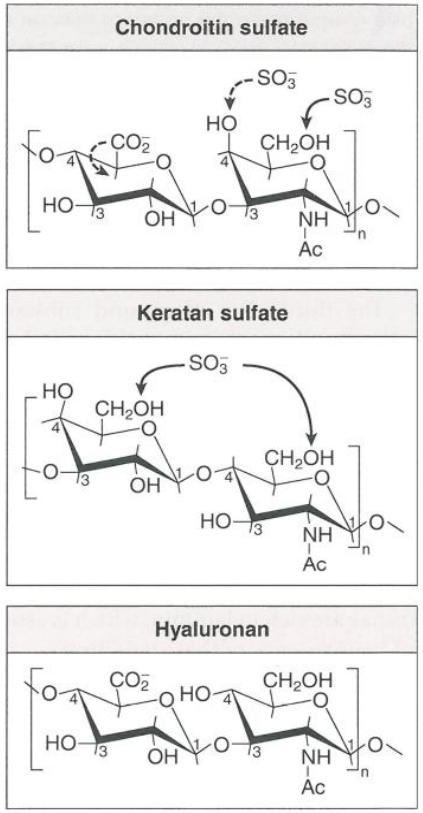


a A typical glycoprotein



b Proteoglycans linked to hyaluronan





Both macromolecules have a protein core that is glycosylated to variable degrees in the Golgi apparatus.

(a) Glycoproteins are usually globular proteins with branched oligosaccharide side-chains. Their polypeptide content is generally greater than their polysaccharide content.

(b) Proteoglycans contain a core of protein with one or many side chains of sulfated GAGs as well as branched oligosaccharides, generally having more carbohydrate than do glycoproteins. Shown here is a TEM darkfield image of many proteoglycans linked to an axis of hyaluronan. This large aggregate was purified from cartilage, where the major proteoglycan is **aggrecan**. The core protein of this extremely large proteoglycan has hydrated chondroitin sulfate and keratan sulfate side chains, and is attached to hyaluronan by link proteins. These features are included in the diagram representing a small portion of the photo. Chemical structures of the repeating disaccharide subunits of hyaluronan, chondroitin sulfate, and keratan sulfate are also indicated.

(*Figure 5-17b, Reproduced, with permission, from Rosenberg L, Hellman W, Kleinschmidt AK: Electron microscopic studies of proteoglycan aggregates from bovine articular cartilage.* J Biol Chem *1975;250:1877. © 1975 The American Society for Biochemistry and Molecular Biology.*)

Enzyme defect (proteoglycan & GAGs):
Hurler syn.
Sanfilipo syn.
Morquio syn.

Bacterial hyalorunidase

>> MEDICAL APPLICATION

The degradation of proteoglycans is carried out by several cell types and depends in part on the presence of several lysosomal enzymes. Several disorders have been described, including a deficiency in certain lysosomal enzymes causing degradation of certain GAGs, with the consequent accumulation of these macromolecules in tissues. The lack of specific hydrolases in the lysosomes has been found to be the cause of several disorders, including the **Hurler**, **Hunter**, **Sanfilippo**, and **Morquio syndromes**.

Because of their high viscosity, HA and proteoglycans tend to form a barrier against bacterial penetration of tissues. Bacteria that produce hyaluronidase, an enzyme that hydrolyzes hyaluronic acid and disassembles proteoglycans complexes, reduce the viscosity of the connective tissue ground substance and have greater invasive power.

Multiadhesive glycoproteins

- **Laminin**

(integrin, collagen IV, prg)
External & basal lamina

- **Fibronectin**

(collagen fiber, GAGs, integrin)

- **Integrin**

(laminin, fibronectin, collagen, ECM)
Talin & vinculin
Hemidesmosom

- Interstitial fluid

>> MEDICAL APPLICATION

Edema is the excessive accumulation of water in the extracellular spaces of connective tissue. This water comes from the blood, passing through the capillary walls that become more permeable during inflammation and normally producing slight swelling.

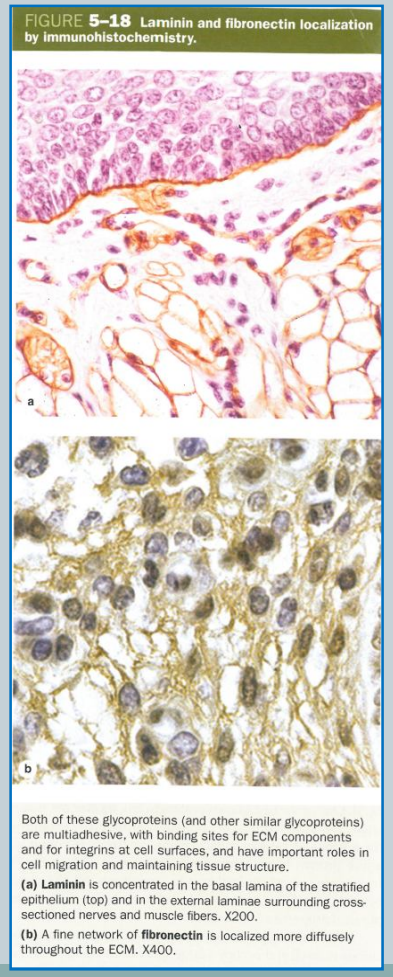


FIGURE **5–18** Laminin and fibronectin localization by immunohistochemistry.

Both of these glycoproteins (and other similar glycoproteins) are multiadhesive, with binding sites for ECM components and for integrins at cell surfaces, and have important roles in cell migration and maintaining tissue structure.

(a) Laminin is concentrated in the basal lamina of the stratified epithelium (top) and in the external laminae surrounding cross-sectioned nerves and muscle fibers. X200.

(b) A fine network of **fibronectin** is localized more diffusely throughout the ECM. X400.

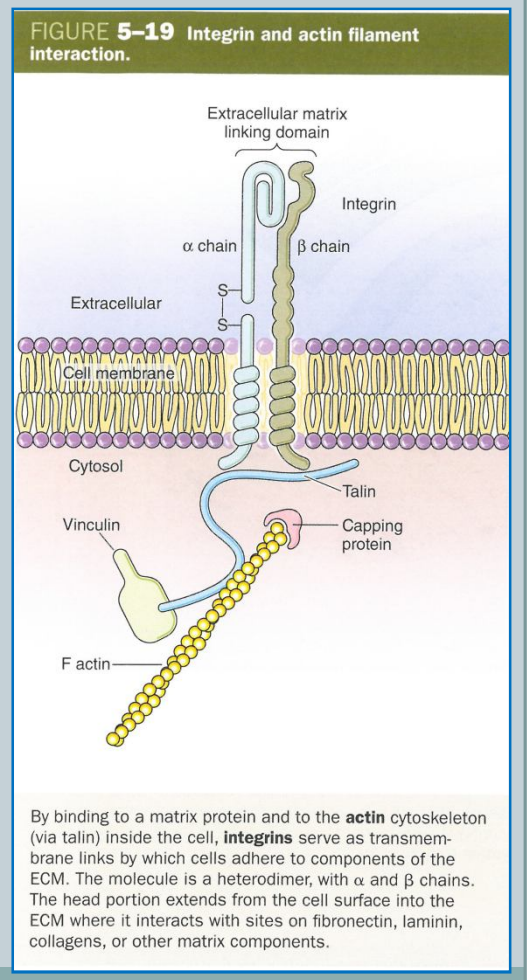
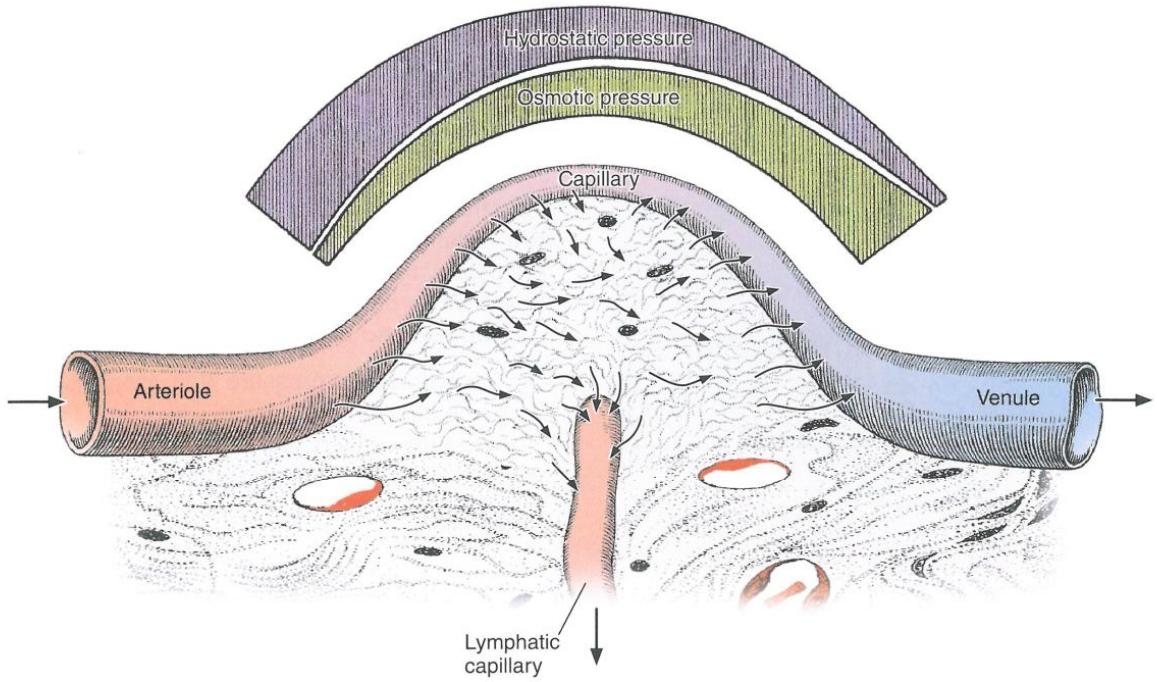


FIGURE **5–19** Integrin and actin filament interaction.

By binding to a matrix protein and to the **actin** cytoskeleton (via talin) inside the cell, **integrins** serve as transmembrane links by which cells adhere to components of the ECM. The molecule is a heterodimer, with α and β chains. The head portion extends from the cell surface into the ECM where it interacts with sites on fibronectin, laminin, collagens, or other matrix components.

FIGURE **5–20** **Movement of fluid in connective tissue.**



Water normally passes through capillary walls into the ECM of surrounding connective tissues primarily at the arterial end of a capillary, because the **hydrostatic pressure** is greater than the colloid **osmotic pressure**. However, hydrostatic pressure decreases toward the venous end of the capillary, as indicated at the top of the figure. The fall in hydrostatic pressure parallels a rise in osmotic pressure of the capillary blood because the plasma protein concentration increases as water is pushed out across the capillary wall.

As a result of the increased protein concentration and decreased hydrostatic pressure, osmotic pressure at the venous end is greater than hydrostatic pressure and water is drawn back into the capillary. In this way plasma and interstitial fluid constantly mix, nutrients in blood circulate to cells in connective tissue, and cellular wastes are removed.

Not all water that leaves capillaries by hydrostatic pressure is drawn back in by osmotic pressure. This excess tissue fluid is normally drained by the lymphatic capillaries, open-ended vessels that arise in connective tissue and enter the one-way lymphatic system that eventually delivers the fluid (now called **lymph**) back to veins.

Connective tissue types

- Connective tissue proper
1. Loose connective tissue (areolar tissue)
2. Dens connective tissue
- Irregular
- Regular

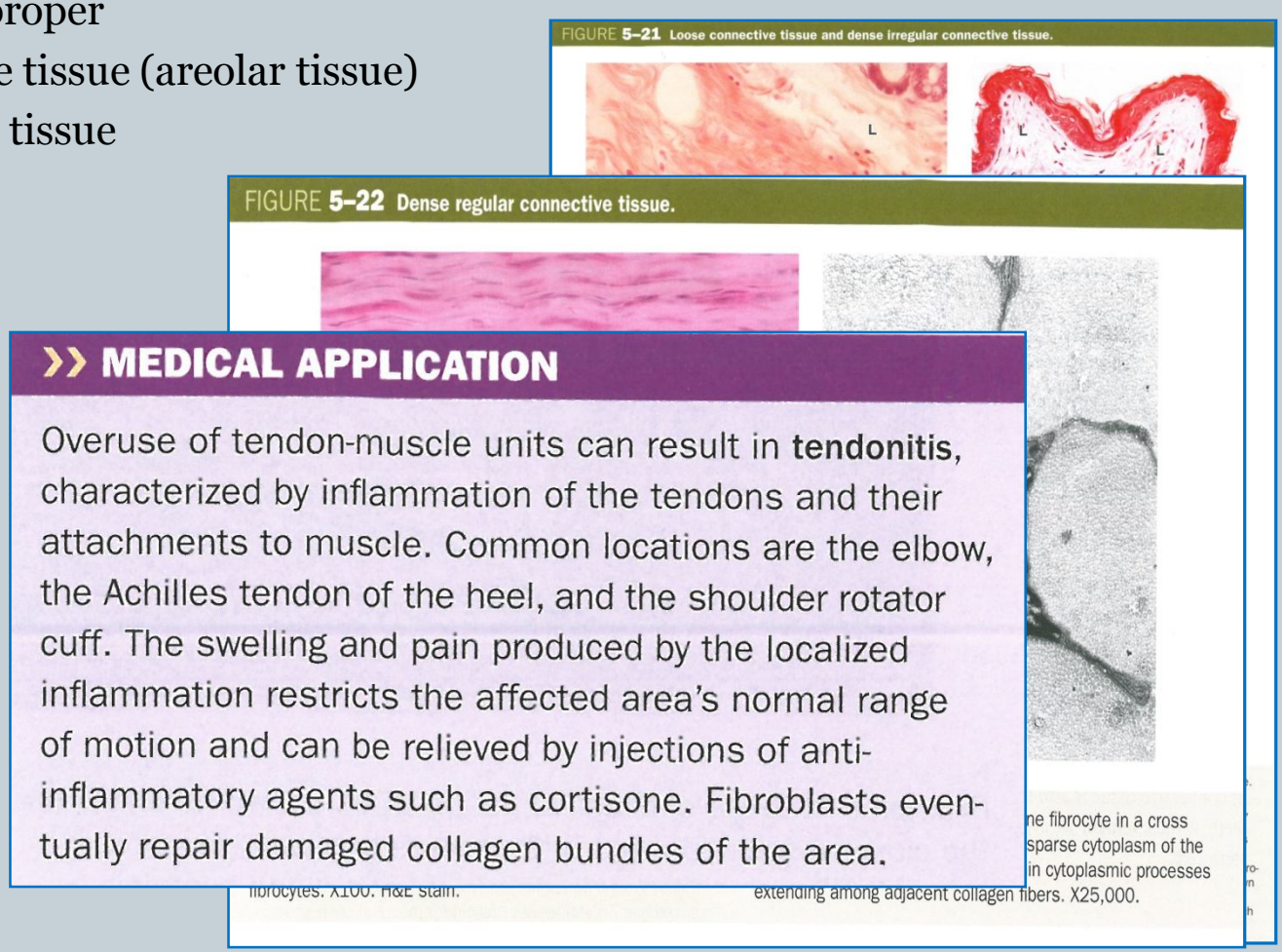


TABLE 5–6 Classification of connective or supporting tissues.

	General Organization	Major Functions	Examples
Connective Tissue Proper			
Loose (areolar) connective tissue	Much ground substance; many cells and little collagen, randomly distributed	Supports microvasculature, nerves, and immune defense cells	Lamina propria beneath epithelial lining of digestive tract
Dense irregular connective tissue	Little ground substance; few cells (mostly fibroblasts); much collagen in randomly arranged fibers	Protects and supports organs; resists tearing	Dermis of skin, organ capsules, submucosa layer of digestive tract
Dense regular connective tissue	Almost completely filled with parallel bundles of collagen; few fibroblasts, aligned with collagen	Provide strong connections within musculoskeletal system; strong resistance to force	Ligaments, tendons, aponeuroses, corneal stroma
Embryonic Connective Tissues			
Mesenchyme	Sparse, undifferentiated cells, uniformly distributed in matrix with sparse collagen fibers	Contains stem/progenitor cells for all adult connective tissue cells	Mesodermal layer of early embryo
Mucoid (mucous) connective tissue	Random fibroblasts and collagen fibers in viscous matrix	Supports and cushions large blood vessels	Matrix of the fetal umbilical cord
Specialized Connective Tissues			
Reticular connective tissue (see Chapter 14)	Delicate network of reticulin/collagen III with attached fibroblasts (reticular cells)	Supports blood-forming cells, many secretory cells, and lymphocytes in most lymphoid organs	Bone marrow, liver, pancreas, adrenal glands, all lymphoid organs except the thymus
Adipose Tissue (Chapter 6)			
Cartilage (Chapter 7)			
Bone (Chapter 8)			
Blood (Chapter 12)			

Connective tissue

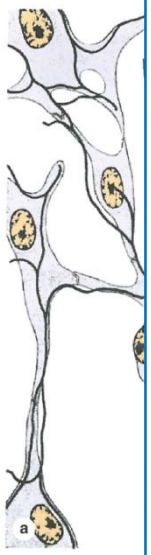
- Reticular tissue

Collagen III
Reticular cell (specialized fibroblast)
Hematopoietic tissue
Lymphoid organs
(bone marrow, luymph node, spleen)

- Mucoid or mucos tissue

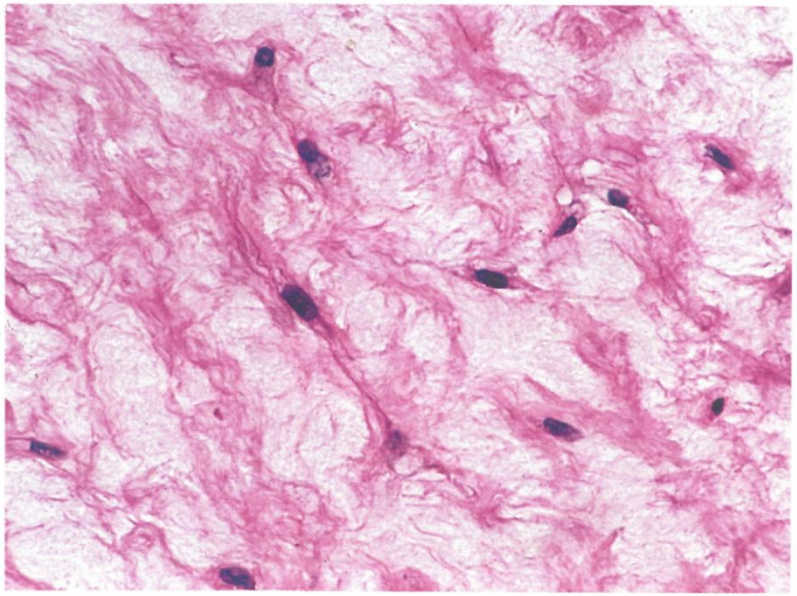
Umbilical cord (whartons jelly)
Fetal organ

FIGURE 5–23 R



(a) The diagram show
cells (free, transient c
of type III collagen are
cells, forming an elabo
fluid or lymph and war

FIGURE 5–24 Mucoid tissue.



A section of umbilical cord shows large fibroblasts surrounded by a large amount of very loose ECM containing mainly ground substances very rich in hyaluronan, with wisps of collagen. Histologically mucoid (or mucous) connective tissue resembles embryonic mesenchyme in many respects and is rarely found in adult organs. X200. H&E