

The background features a light gray gradient with several realistic water droplets of various sizes scattered across the surface. The droplets have highlights and shadows, giving them a three-dimensional appearance. The text 'Connective Tissue' is centered in the middle of the page.

Connective Tissue

General Features

- Connective tissue provides a matrix that supports and physically connects other tissues and cells together to form the organs of the body.
- The interstitial fluid of connective tissue gives metabolic support to cells as the medium for diffusion of nutrients and waste products.
- Composed of cells (fixed and wandering), fibers and ground substance.
- Variable vascularity.
- Variable regenerative power.

Functions

1. Structural framework for body.
2. Transportation of fluids and dissolved substances.
3. Protection of delicate organs.
4. Supports, surrounds, and connects other tissues.
5. Storage of energy in the form of lipids.
6. Defend the body against microorganisms.

Origin

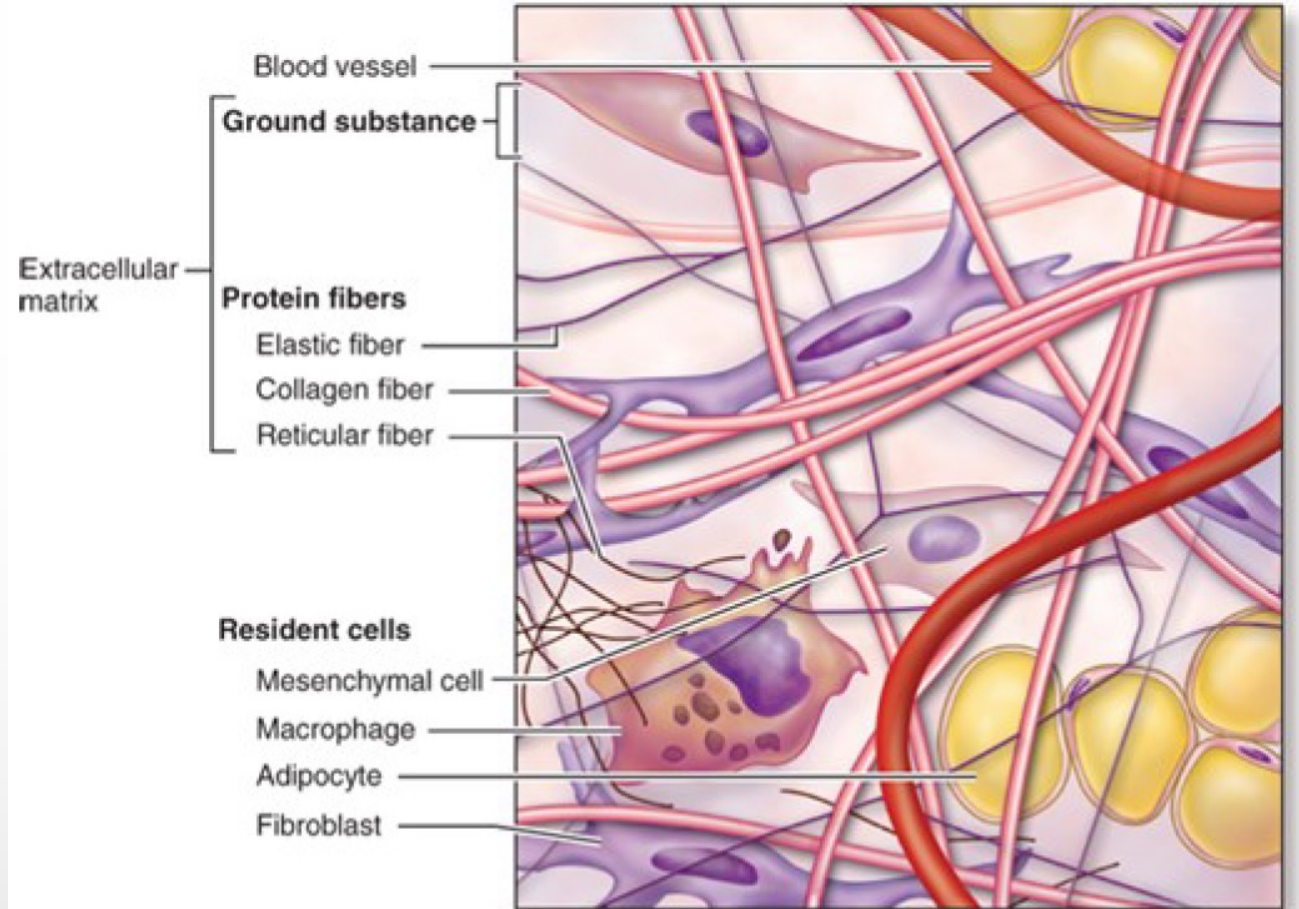
- All connective tissues originate from embryonic mesenchyme, a tissue developing mainly from the middle layer of the embryo, the mesoderm.
- Mesenchyme consists largely of viscous ground substance with few collagen fibers.
- Mesenchymal cells are undifferentiated and have large nuclei, with prominent nucleoli and fine chromatin.
- Mesenchymal cells are spindle-shaped---- with their scant cytoplasm extended as two or more thin cytoplasmic processes

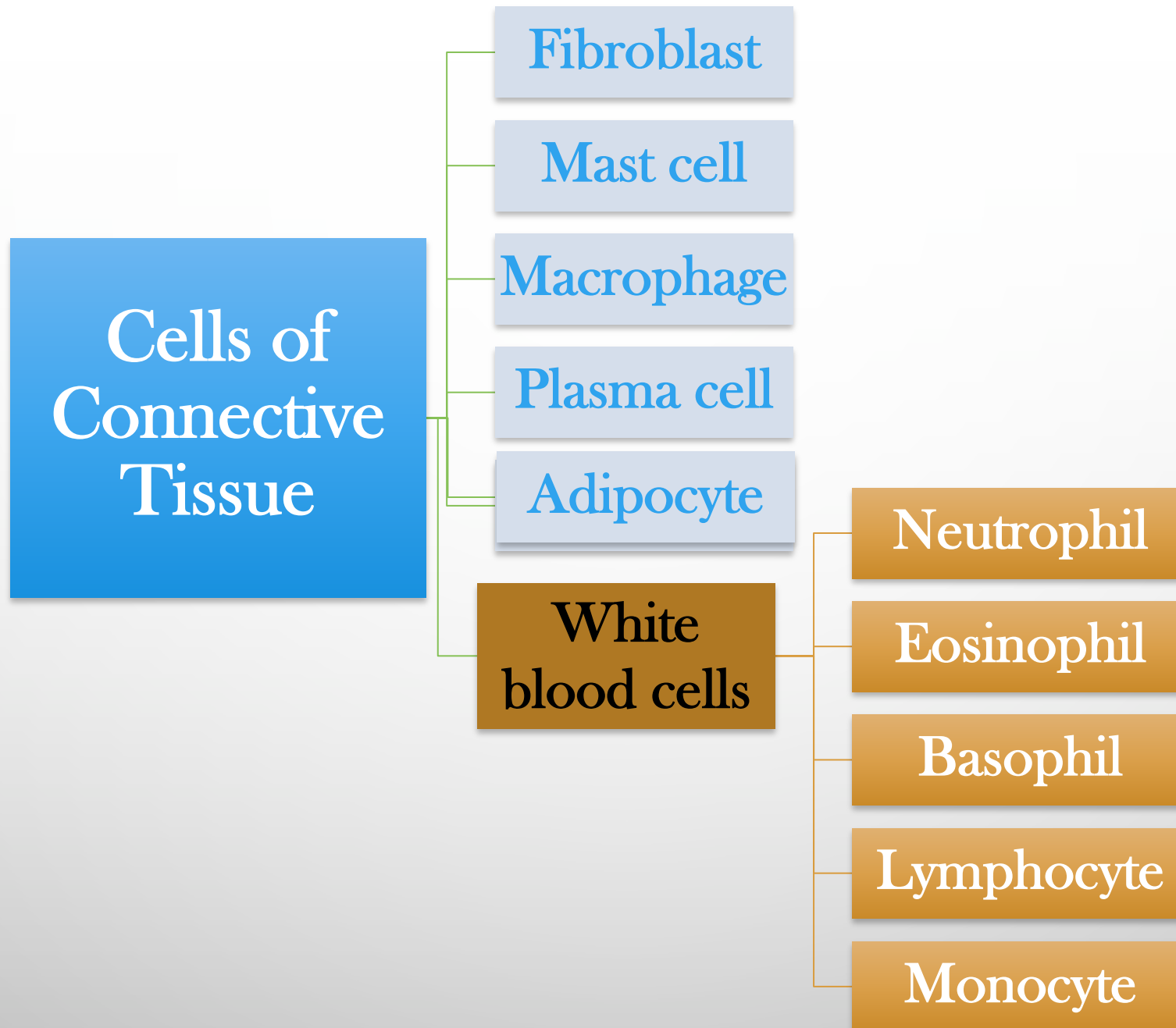
Components

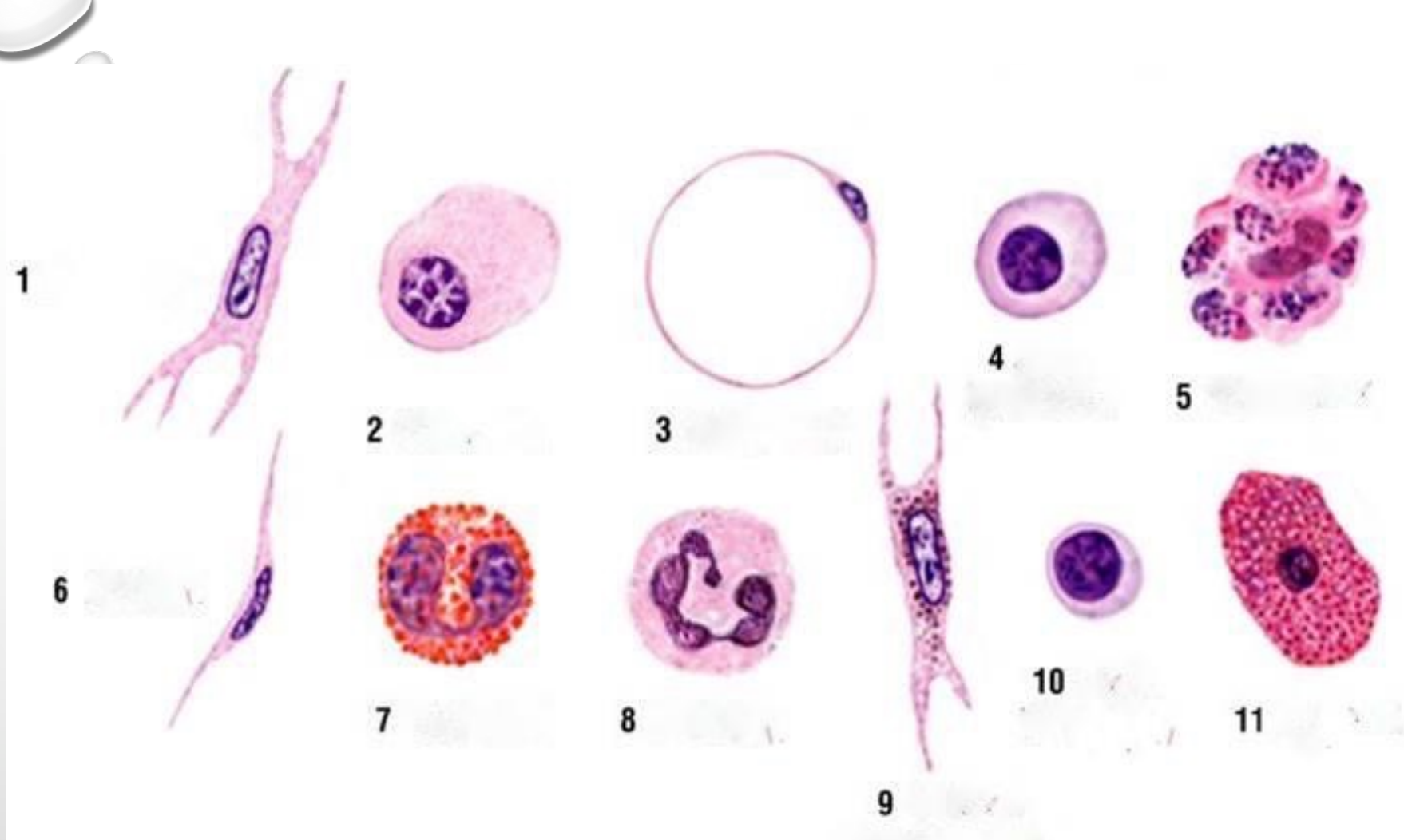
- Cells
- Fibers
- Ground substance

Ground substance

- Ground substance is a complex of anionic, hydrophilic proteoglycans, glycosaminoglycans (GAGs), and multiadhesive glycoproteins (laminin, fibronectin, etc.)







- | | | | |
|-------------------------------|----------------|----------------------|---------------------|
| 1. Fibroblast | 2. Plasma cell | 3. Adipocyte | 4. large lymphocyte |
| 5. Macrophage | 6. Fibrocyte | 7. Eosinophil | 8. Neutrophil |
| 9. Cell with pigment granules | | 10. Small lymphocyte | |
| 11. Mast cell | | | |

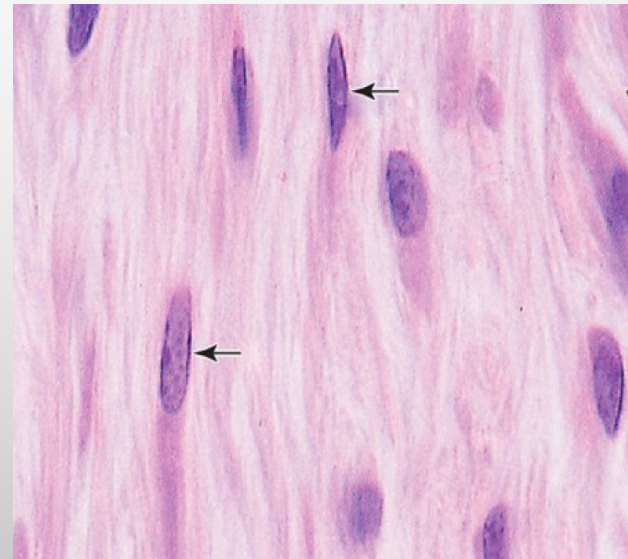
Connective tissue cells

| 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 |

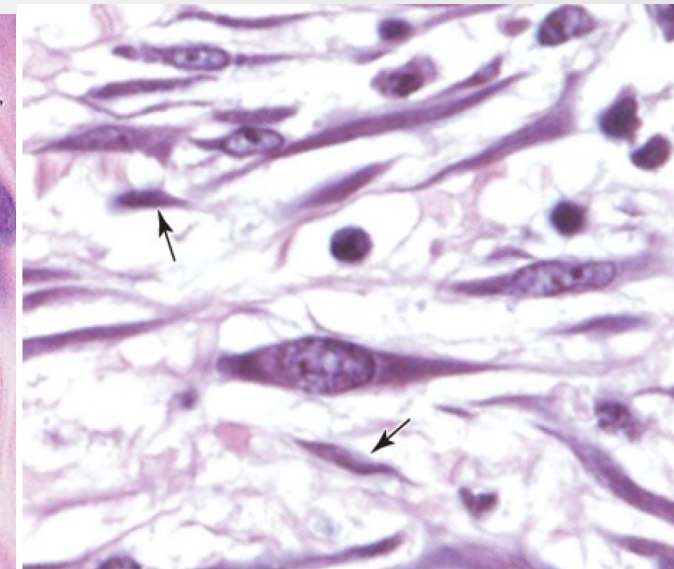
Fibroblast

- The most common cells in connective tissue proper
- Produce and maintain most of the tissue's extracellular components.
- Most of the secreted ECM components undergo further modification outside the cell before assembling as a matrix.

Fibroblast



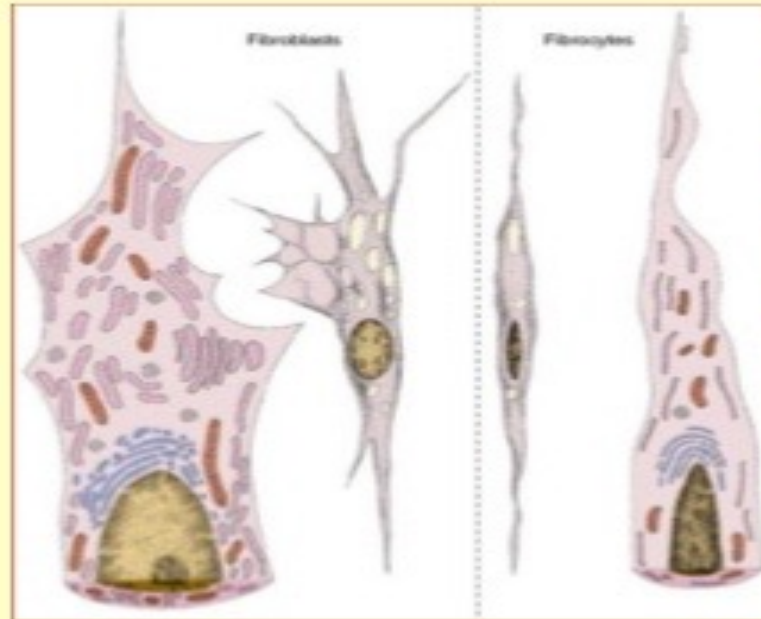
Fibrocyte



Fibroblasts _ Fibrocytes

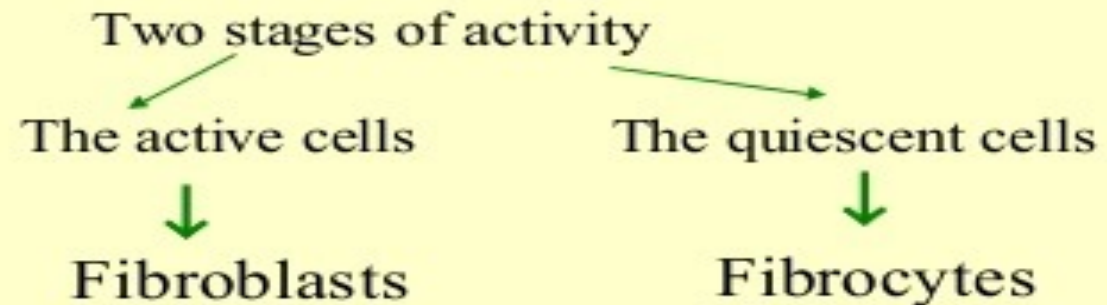
✓ Fibroblasts

- the most common cells in connective tissue
- cells responsible for the synthesis of extracellular matrix components
- an abundant and irregularly branched cytoplasm
- ovoid, large and pale staining nucleus with nucleolus
- rich in RER and well developed Golgi complex
- produce the growth factors → influence growth and cells differentiation
- proliferate when the additional fibroblasts are required



✓ Fibrocytes

- smaller than fibroblasts
- fewer processes
- smaller, darker, elongated nucleus
- small amount of RER

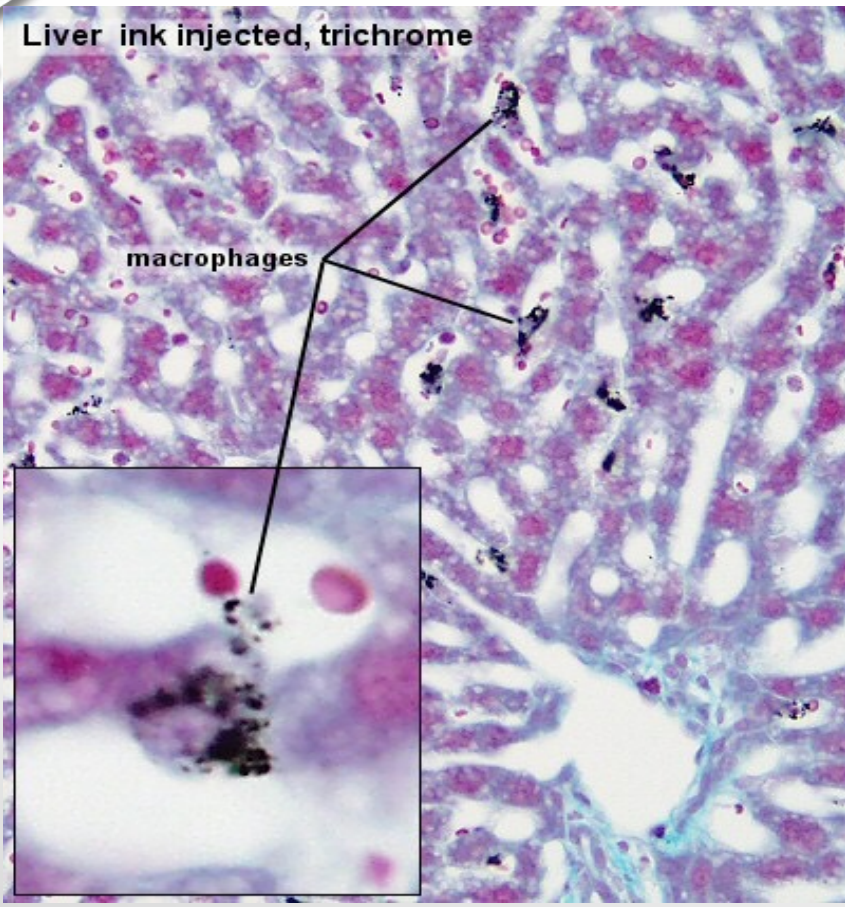


Macrophage

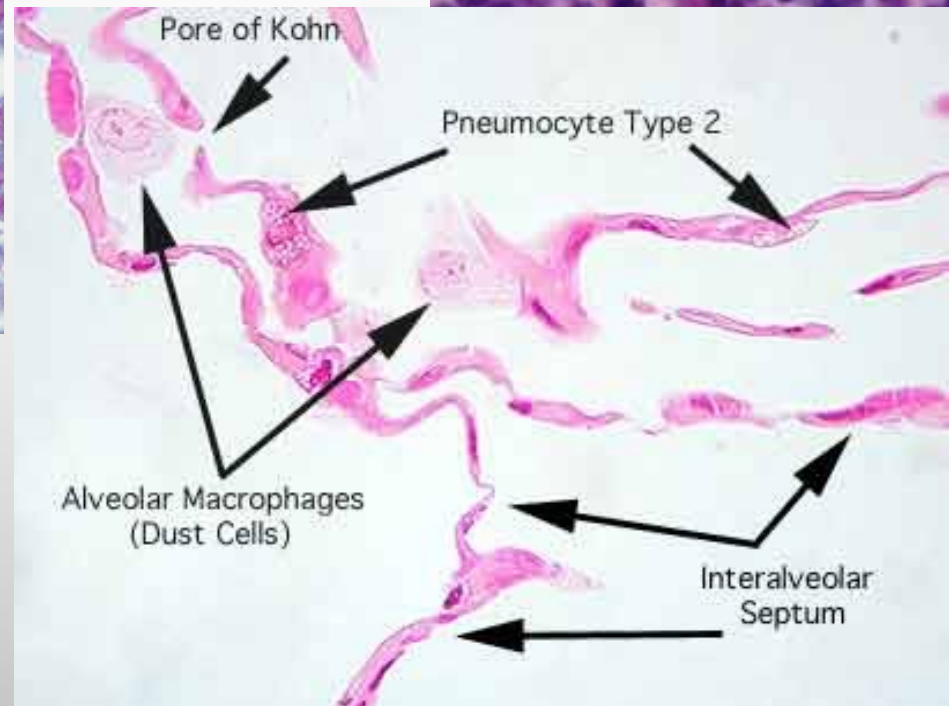
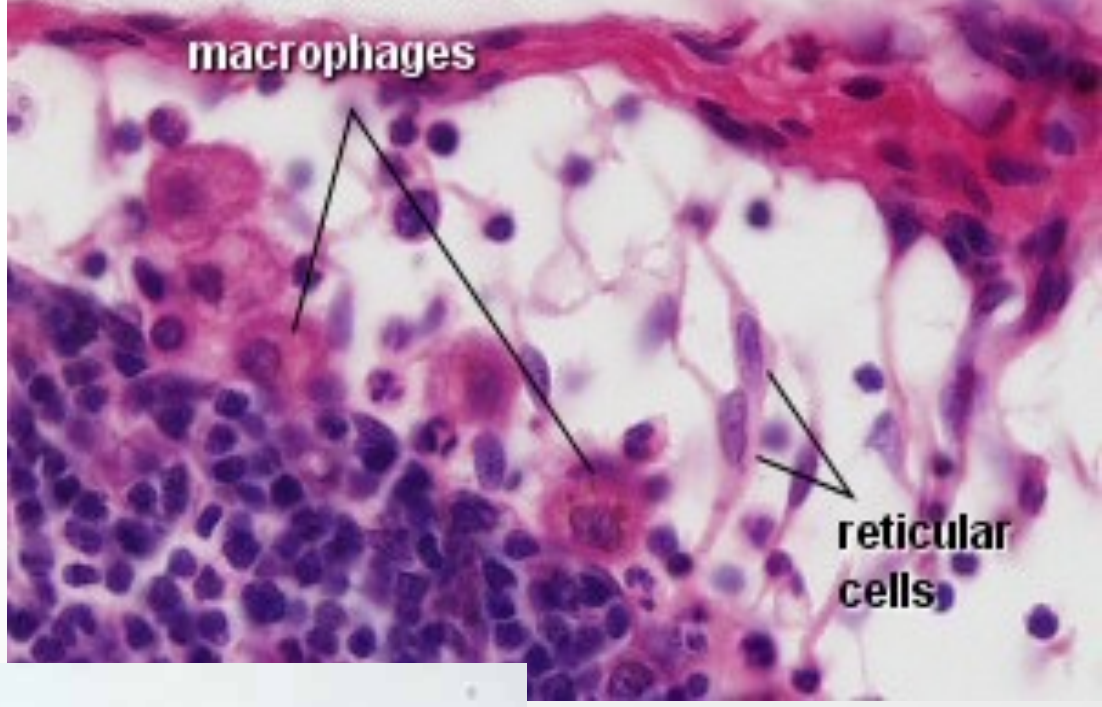
- Macrophages have highly developed phagocytic ability and specialize in turnover of protein fibers and removal of apoptotic cells, tissue debris, or other particulate material
- Being especially abundant at sites of inflammation.
- Size and shape vary considerably, corresponding to their state of functional activity.
- A typical macrophage measures between 10 and 30 μm in diameter and has an eccentrically located, oval or kidney-shaped nucleus.
- They generally have well-developed Golgi complexes and many lysosomes.

Mononuclear Phagocyte System

| Cell Type | Major Location | 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 |



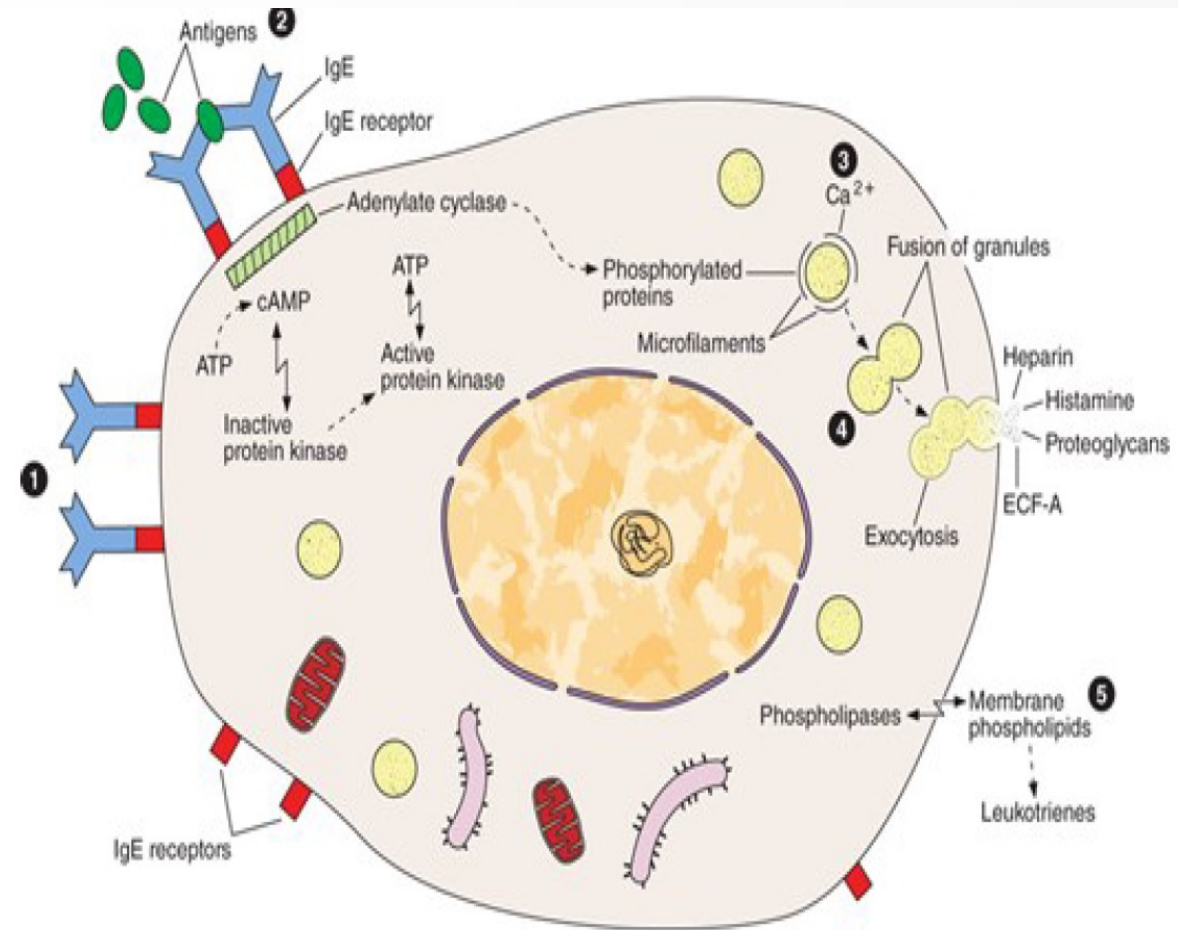
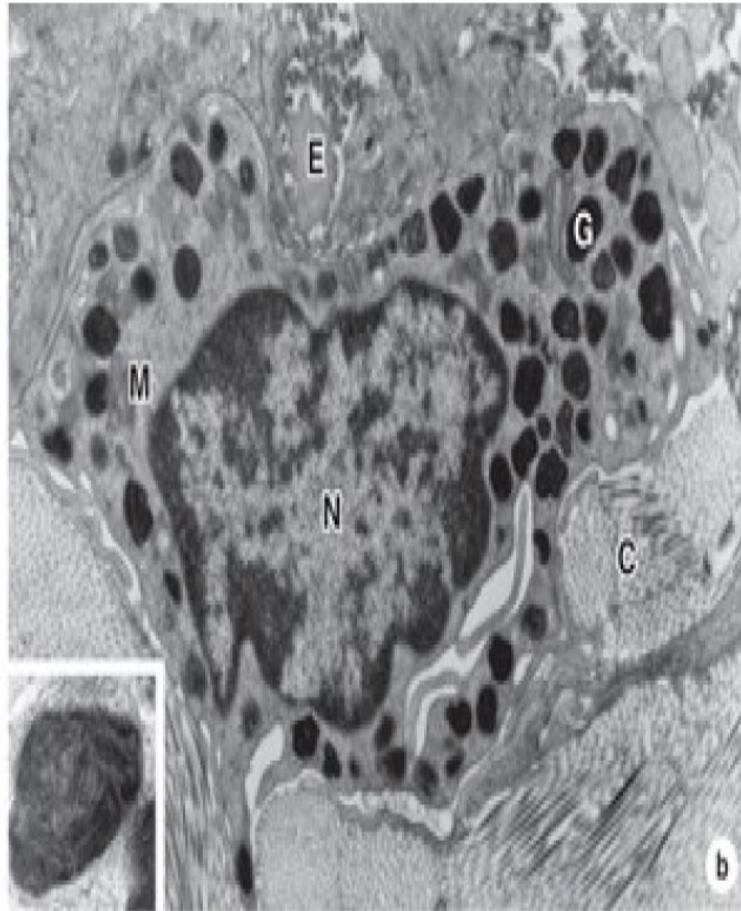
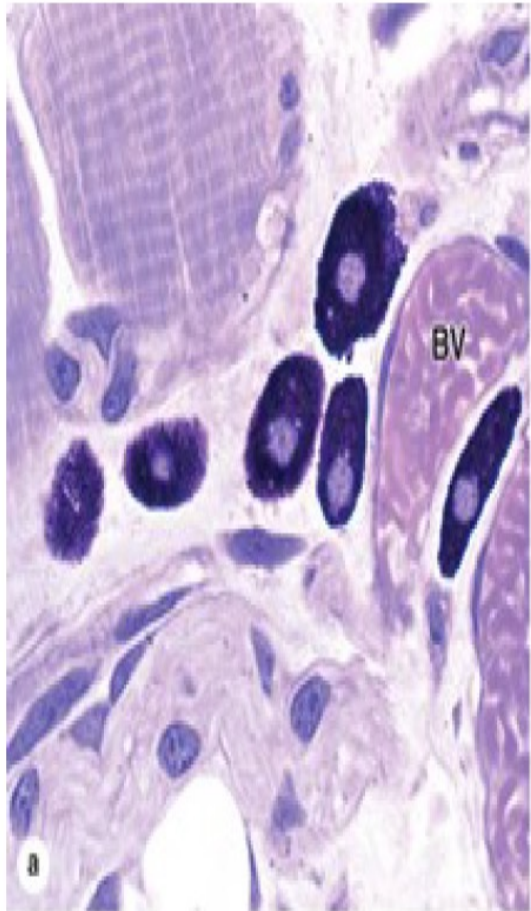
H&E - subcapsular sinus



Mast Cell

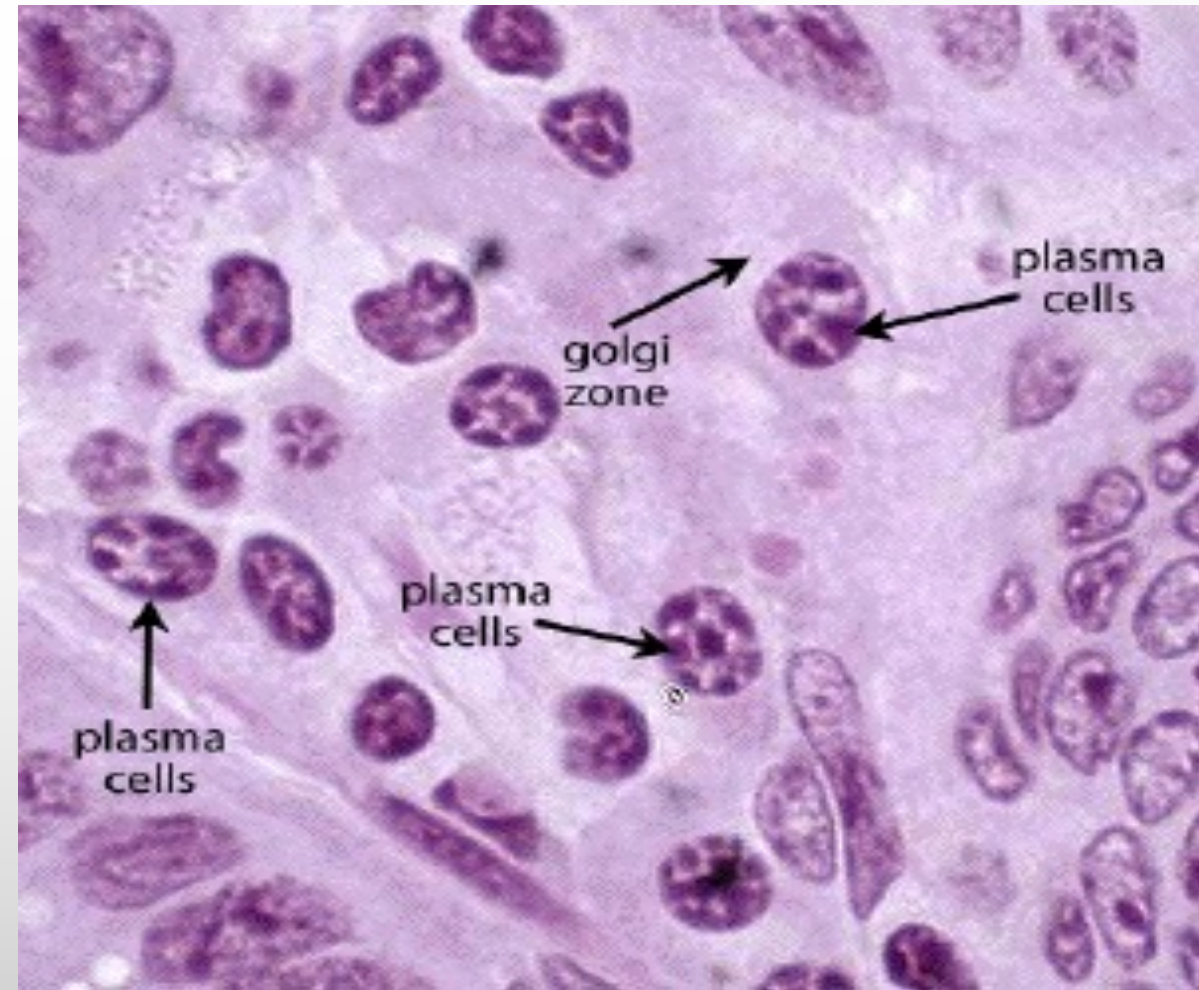
- Mast cells are oval or irregularly shaped cells of connective tissue,
- Filled with basophilic secretory granules that often obscure the central nucleus
- Mast cells function in the localized release of many bioactive substances, includes the following:
 1. Heparin, a sulfated GAG that acts locally as an anticoagulant
 2. Histamine: promotes increased vascular permeability and smooth muscle contraction
 3. Serine proteases: activate various mediators of inflammation
 4. Eosinophil and neutrophil chemotactic factors: attract those leukocytes
 5. Phospholipid precursors: converted to other important lipid mediators of the inflammatory reaction.

MAST CELL



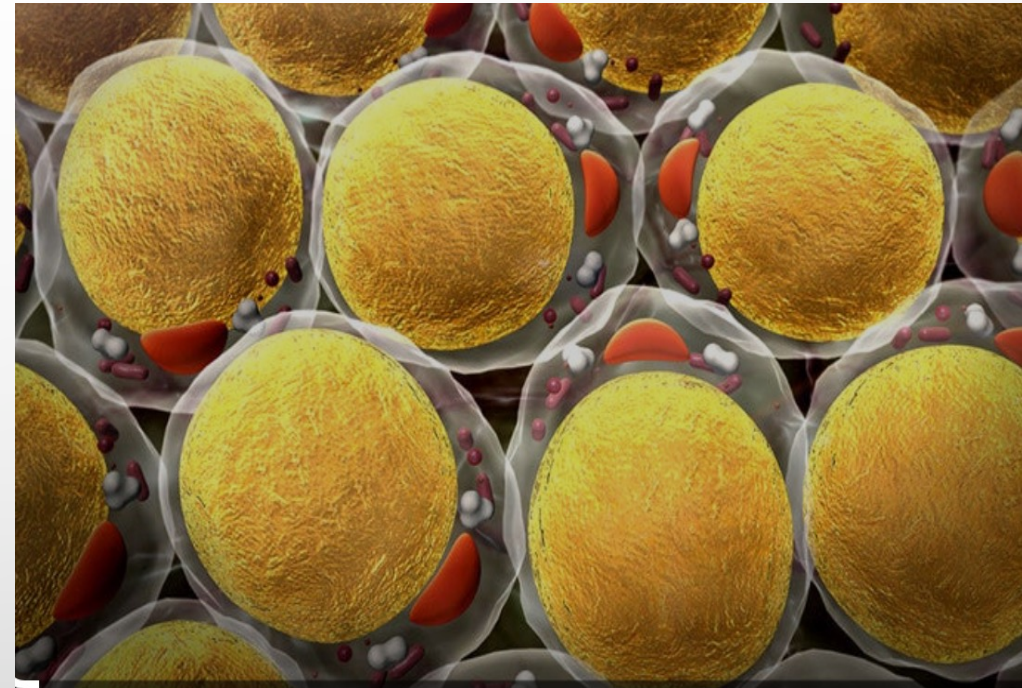
Plasma Cell

- Plasma cells are B lymphocyte-derived, antibody-producing cells.
- Relatively large, ovoid cells have basophilic cytoplasm rich in RER.
- Large Golgi apparatus near the nucleus that may appear pale in routine histologic preparations



Adipose Cells

- Fat cells
- Found in the connective tissue of many organs.
- Large, mesenchymal-derived cells are specialized for cytoplasmic storage of lipid as neutral fats, or less commonly for the production of heat.
- Tissue with a large population of adipocytes, called adipose connective tissue, serves to cushion and insulate the skin and other organs.

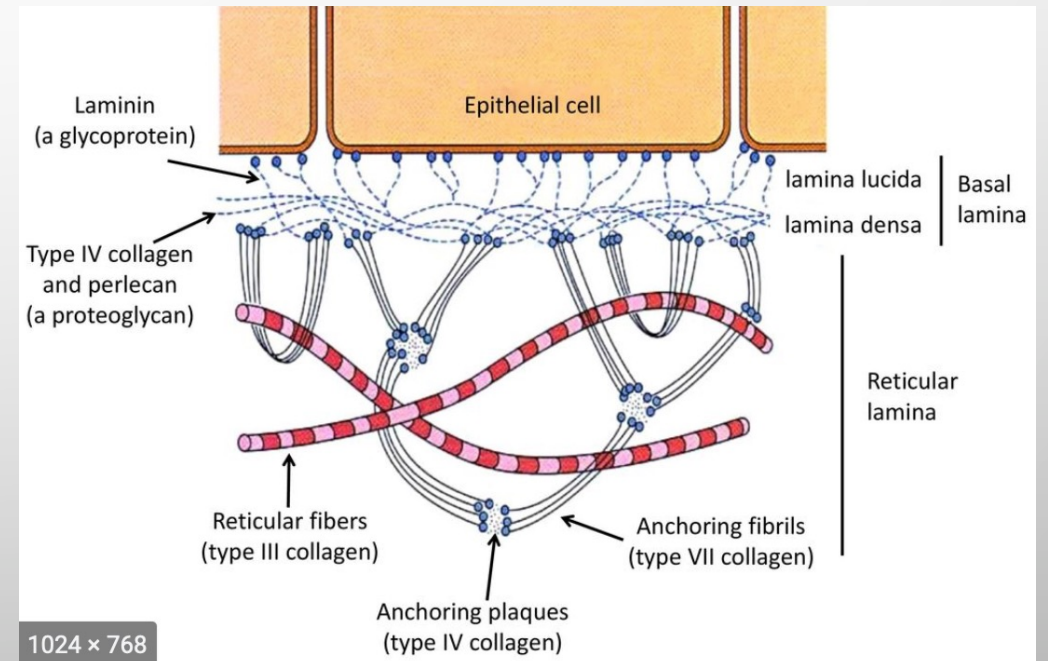
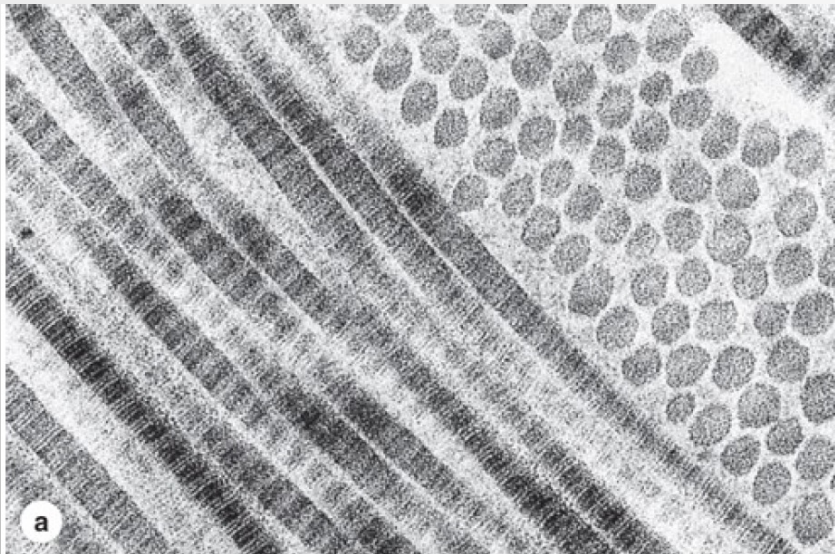


Connective Tissue Fibers/Collagen

- Form various extracellular fibers, sheets, and networks.
- Extremely strong and resistant to normal shearing and tearing forces.
- Collagen is a key element of all connective tissues, as well as epithelial basement membranes and the external laminae of muscle and nerve cells.
- Most abundant protein in the human body, representing 30% of its dry weight.
- A family of 28 collagens exists in vertebrates.

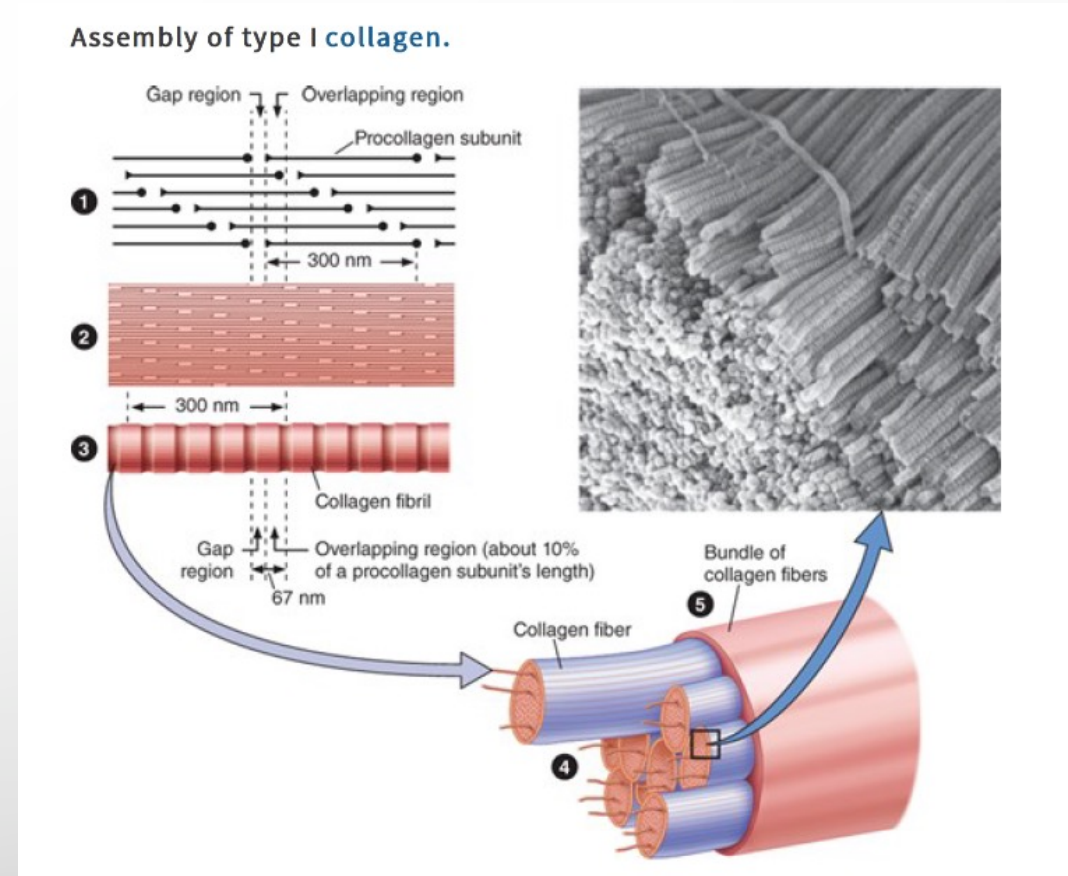
Collagen types

- **Fibrillar collagens**, notably collagen types I, II, and III. Form structures such as tendons, organ capsules, and dermis.
- **Network or sheet-forming collagens** such as type IV collagen have subunits produced by epithelial cells and are major structural of external laminae and all epithelial basal laminae.
- **Linking/anchoring collagens** are short.



Collagen Assembly

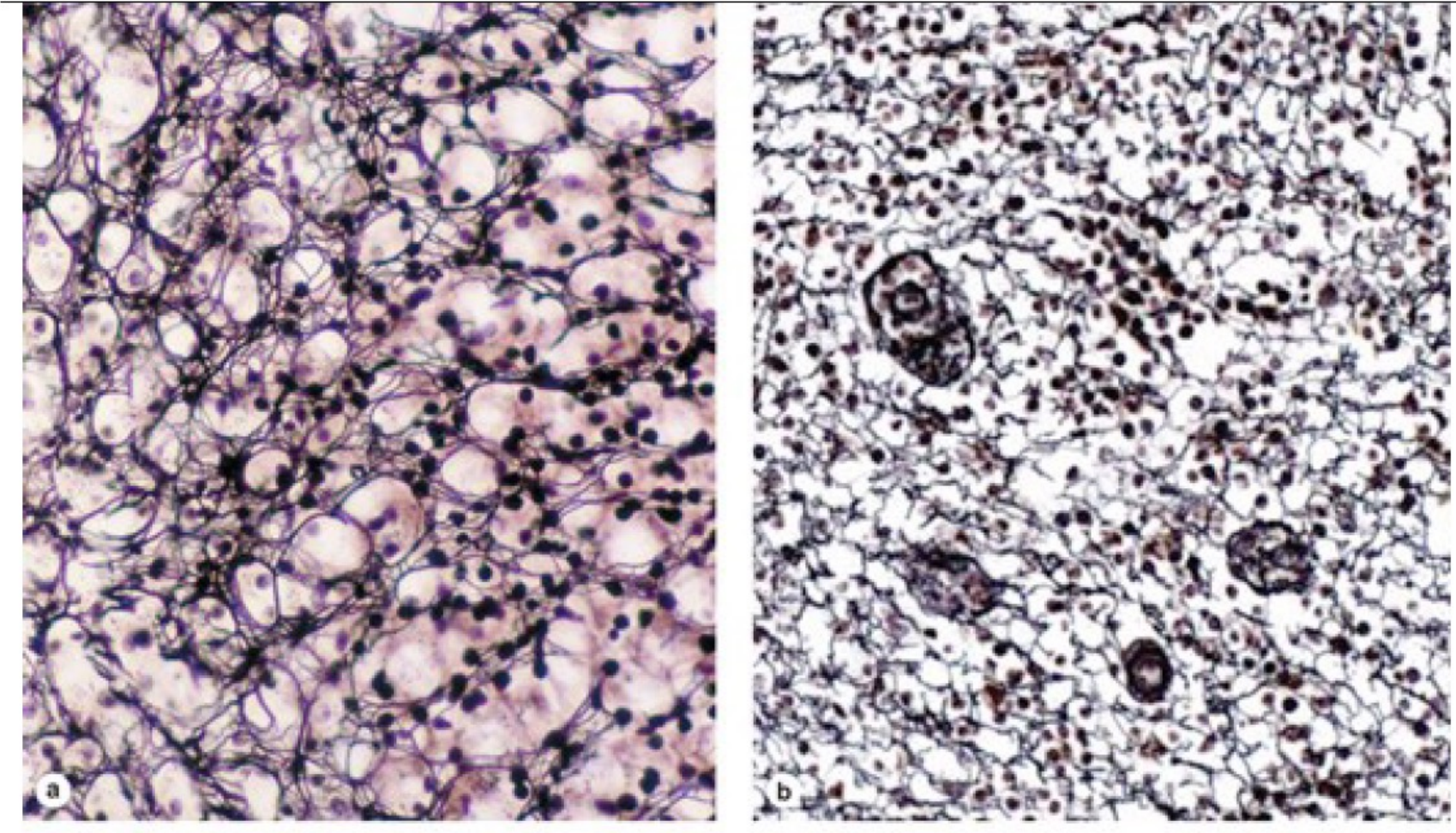
1. Rodlike triple-helix collagen molecules, each 300-nm long, self-assemble in a highly organized, lengthwise arrangement of overlapping regions.
2. The regular, overlapping arrangement of subunits continues as large collagen fibrils are assembled.
3. This structure causes fibrils to have characteristic 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.



Connective Tissue Fibers/Reticular

- Found in delicate connective tissue of many organs, notably in the immune system.
- Consist mainly of collagen type III, which forms an extensive network.
- Seldom visible in hematoxylin and eosin (H&E) but are stained black after impregnation with **silver** salts.
- Periodic Acid–Schiff (PAS) positive-----due to the high content of sugar chains.
- Reticular fibers contain up to 10% carbohydrate as opposed to 1% in most other collagen fibers.
- Produced by fibroblasts.
- Surround adipocytes, smooth muscle and nerve fibers, and small blood vessels.
- Serve as the supportive stroma for the parenchymal secretory cells, liver and endocrine glands.
- Stroma of hemopoietic tissue (bone marrow), the spleen, and lymph nodes

RETICULAR FIBERS

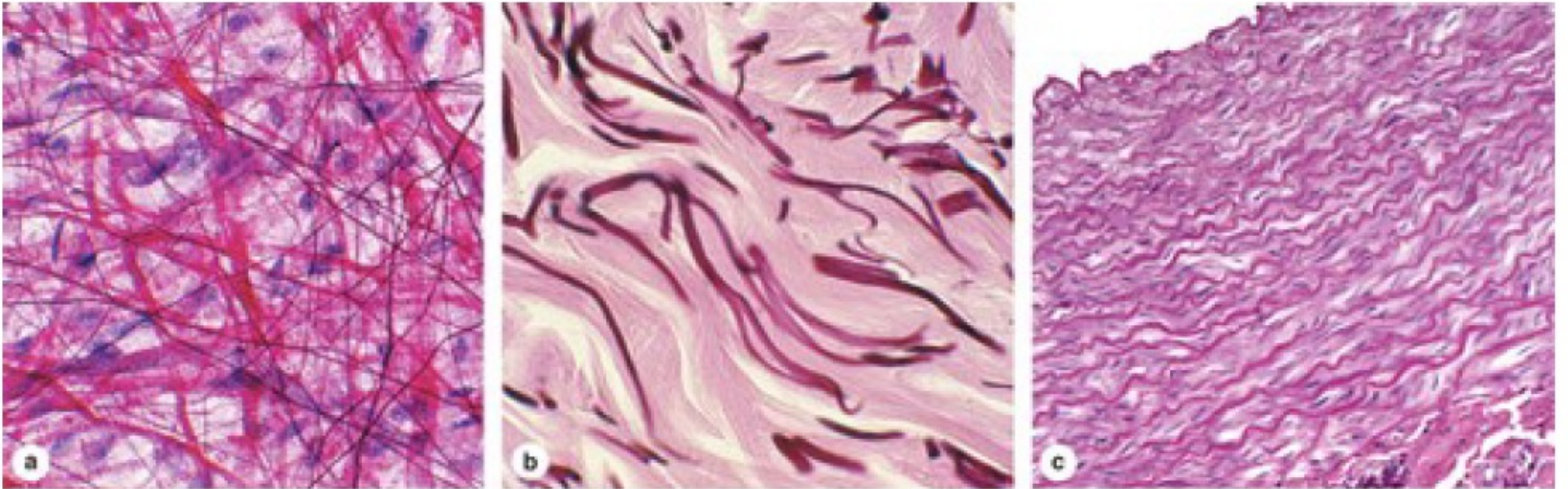


Lymph nodes-
silver stain

Connective Tissue Fibers/Elastic

- Thinner than the type I collagen fibers and form sparse networks interspersed with collagen bundles in many organs (subject to regular stretching or bending).
- Have rubberlike properties that allow tissue containing to be stretched or distended (lungs).
- In the wall of large blood vessels, especially arteries, elastin also occurs as fenestrated sheets called **elastic lamellae**.
- Elastic fibers and lamellae are not strongly acidophilic and stain poorly with H&E.
- Stained more darkly than collagen with other stains such as orcein and aldehyde fuchsin.

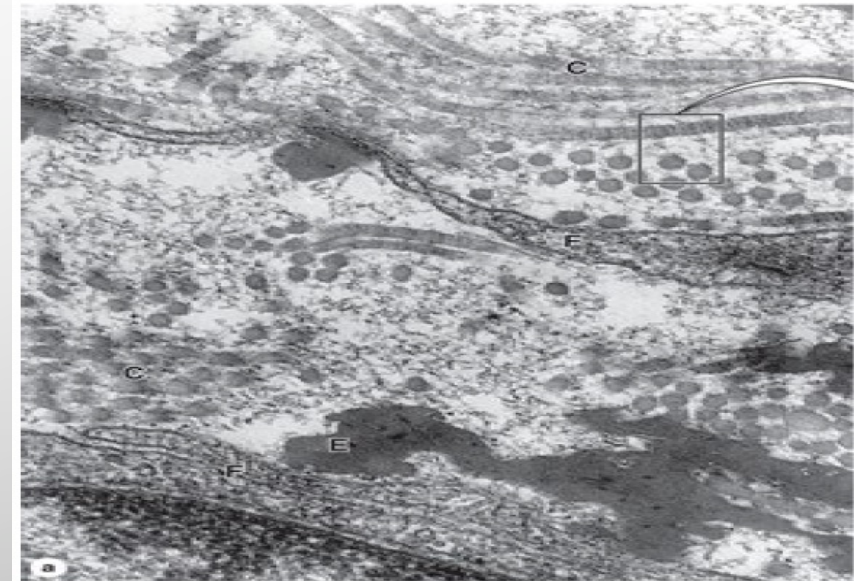
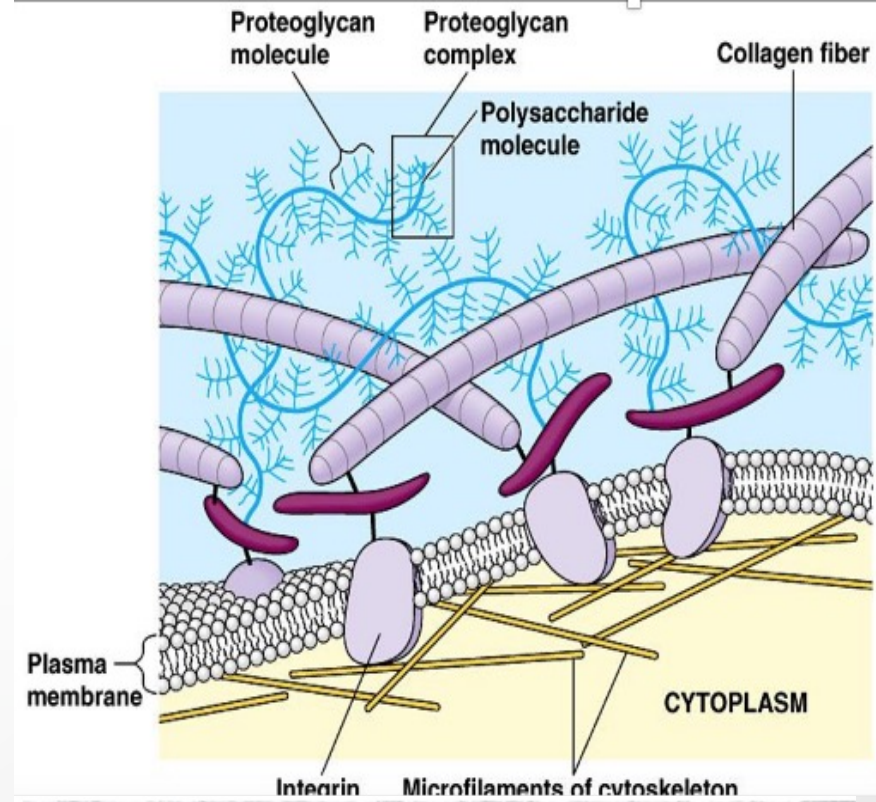
Connective Tissue Fibers/Elastic



- A- Hematoxylin and orcein)
- B-Aldehyde fuchsin)
- C- H&E

Ground Substance

- A semi- fluid gel (highly hydrated) and transparent material
- The ground substance of the ECM is a highly hydrated (with much bound water), transparent, complex mixture of three major kinds of macromolecules: glycosaminoglycans (GAGs), proteoglycans, and multiadhesive glycoproteins.
- Filling the space between cells and fibers in connective tissue.
- Allows diffusion of small molecules.
- Because it is viscous---lubricant and a barrier to the penetration of invaders.



GAGs

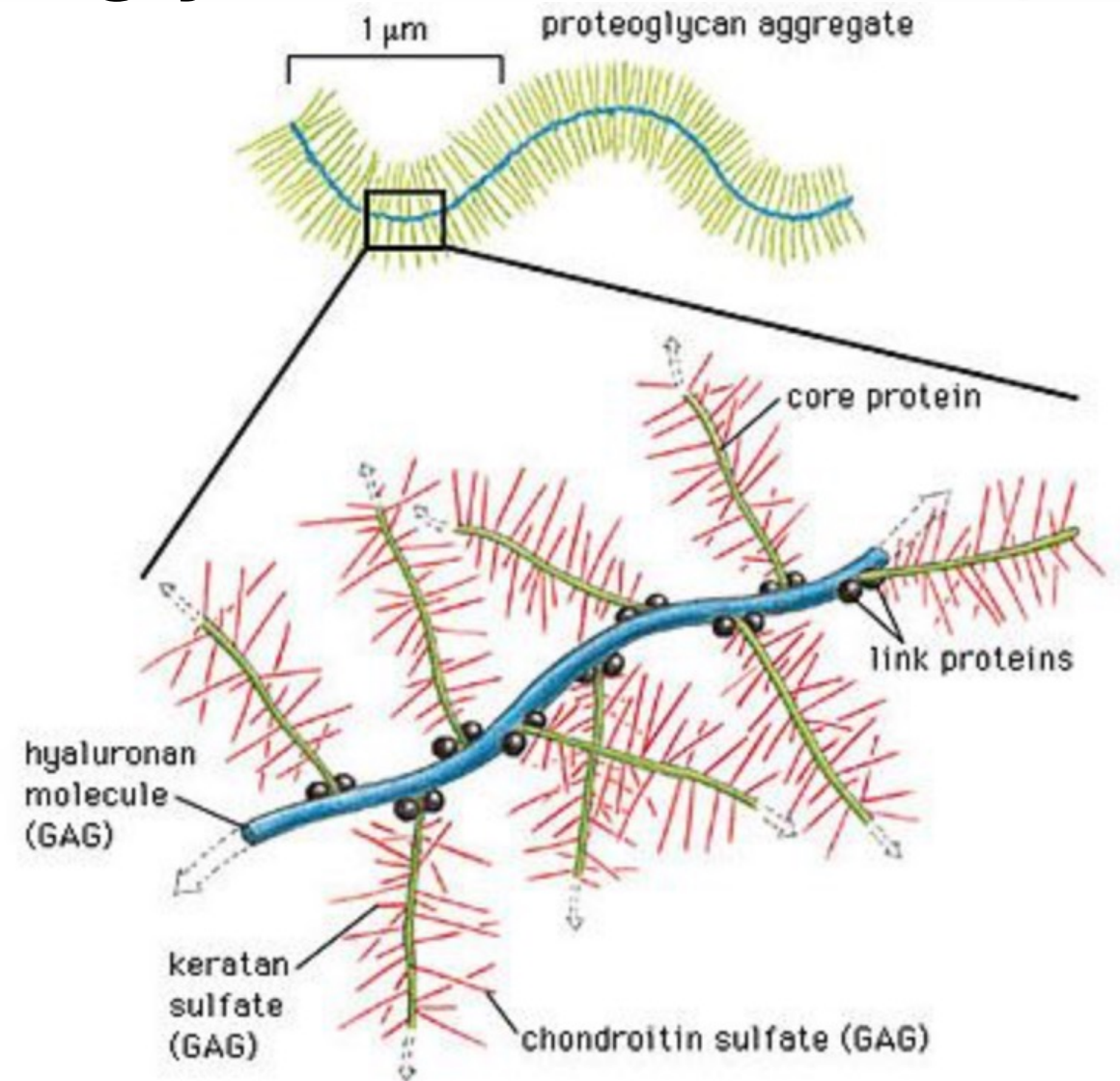
- GAGs (mucopolysaccharides) are long polymers of repeating disaccharide units, usually a hexosamine and uronic acid.
- The largest and most ubiquitous is hyaluronan (hyaluronate or hyaluronic acid).
- Hyaluronan forms a viscous, pericellular network that binds a considerable amount of water (diffusion through connective tissue and in lubricating various organs and joints).

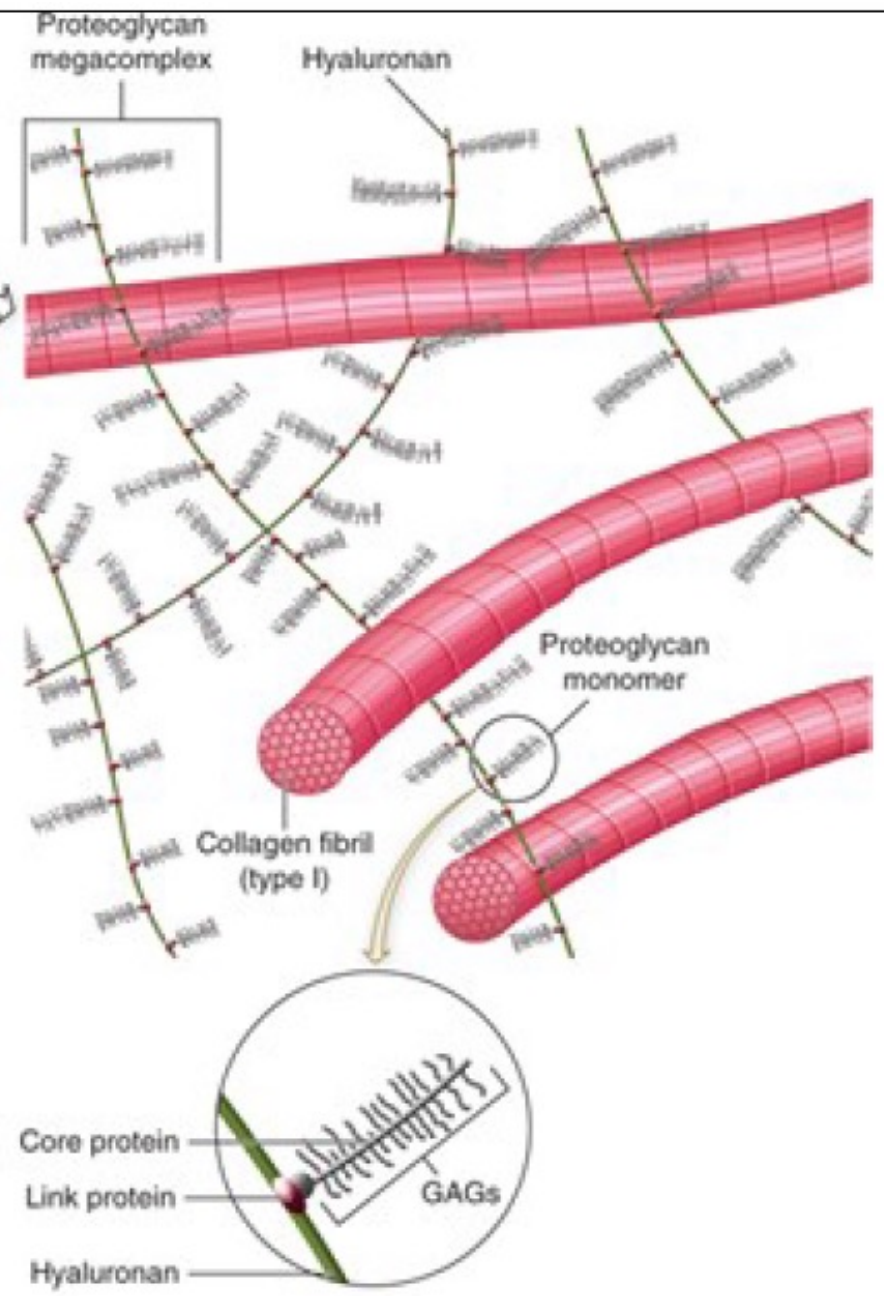
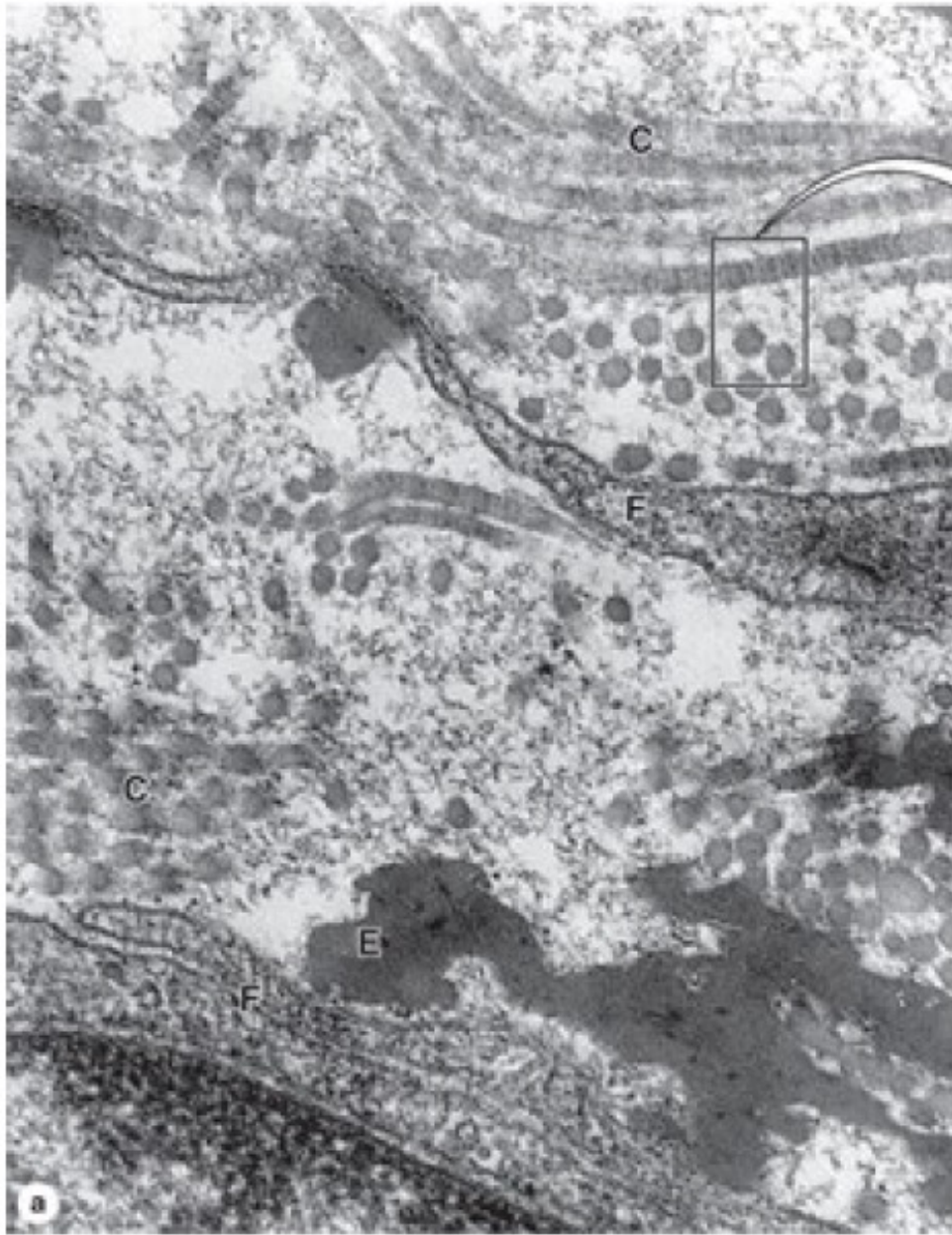
GAGs

- All other GAGs are much smaller, sulfated, bound to proteins (as parts of proteoglycans).
- Major GAGs found in proteoglycans are dermatan sulfate, chondroitin sulfates, keratan sulfate, and heparan sulfate (different disaccharide units)
- Their high negative charge forces GAGs to an extended conformation and causes them to sequester cations as well as water.
- These features provide GAGs with space-filling, cushioning, and lubricant functions.

GAGs that form proteoglycans

- Hyaluronic acid
- Chondroitin 4-sulfate
- Chondroitin 6-sulfate
- Dermatan sulfate
- Heparan sulfate
- Heparin
- Keratan sulfate



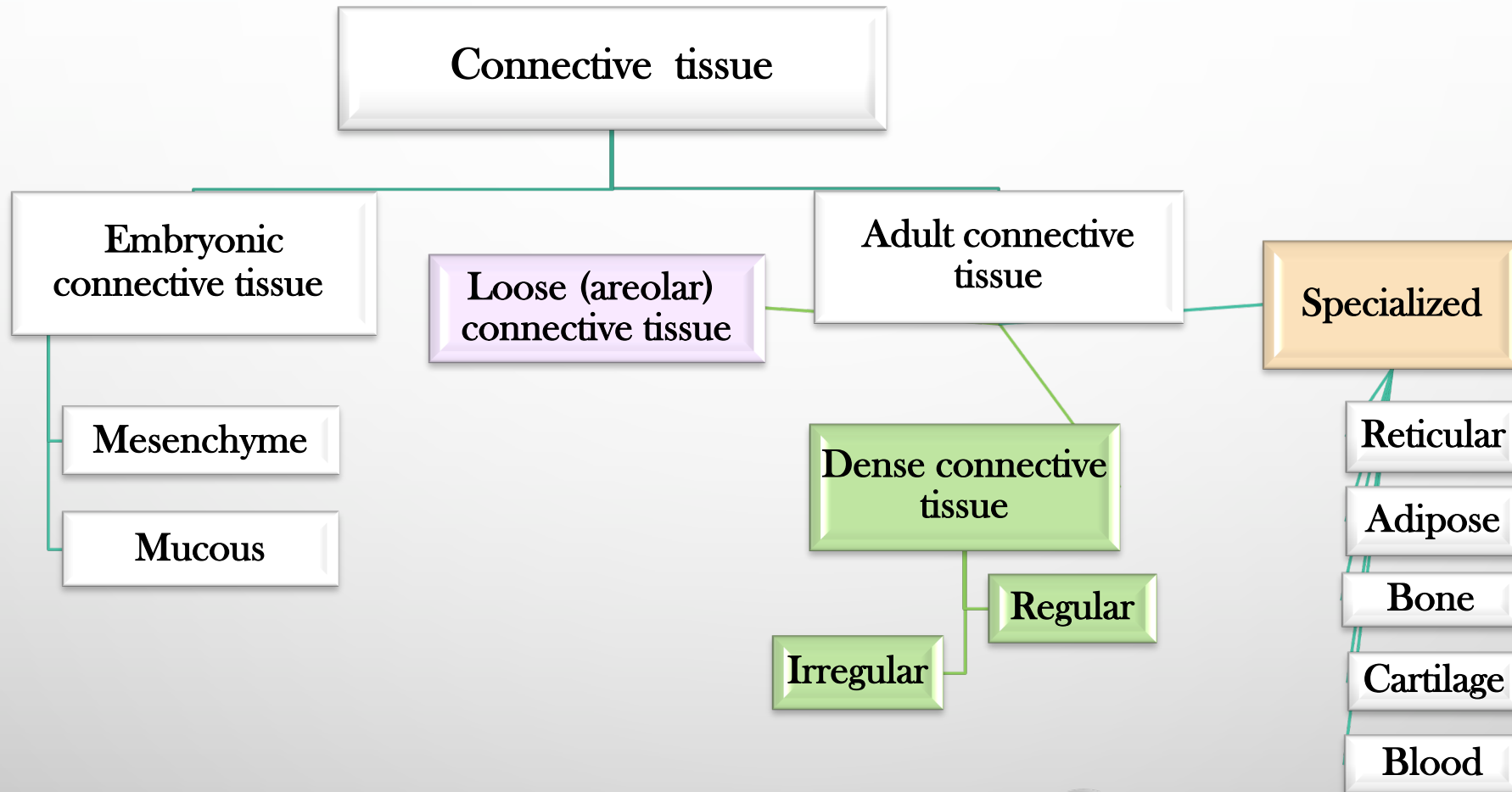


b

GAGs

| 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 |

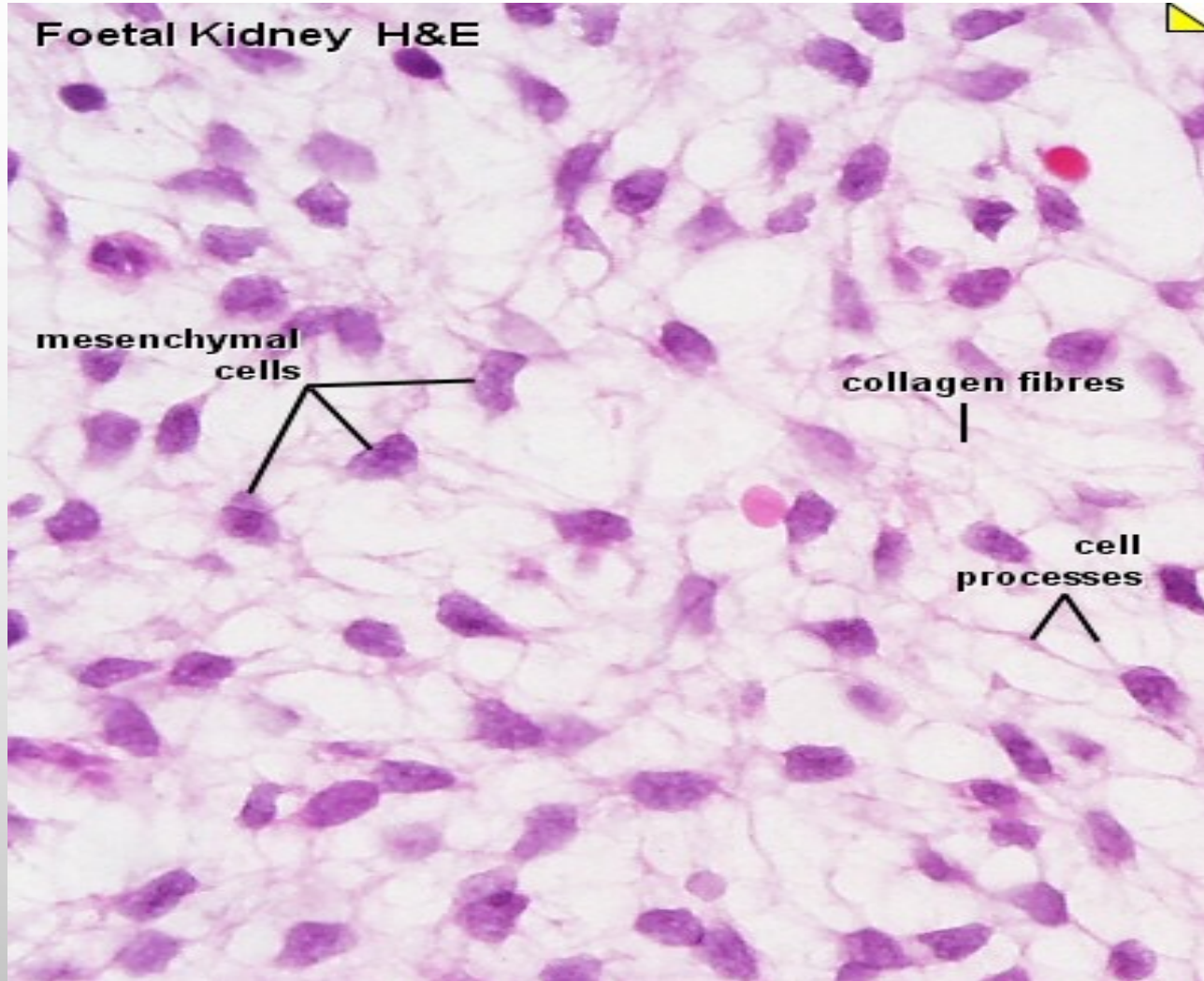
Classification Of Connective Tissue



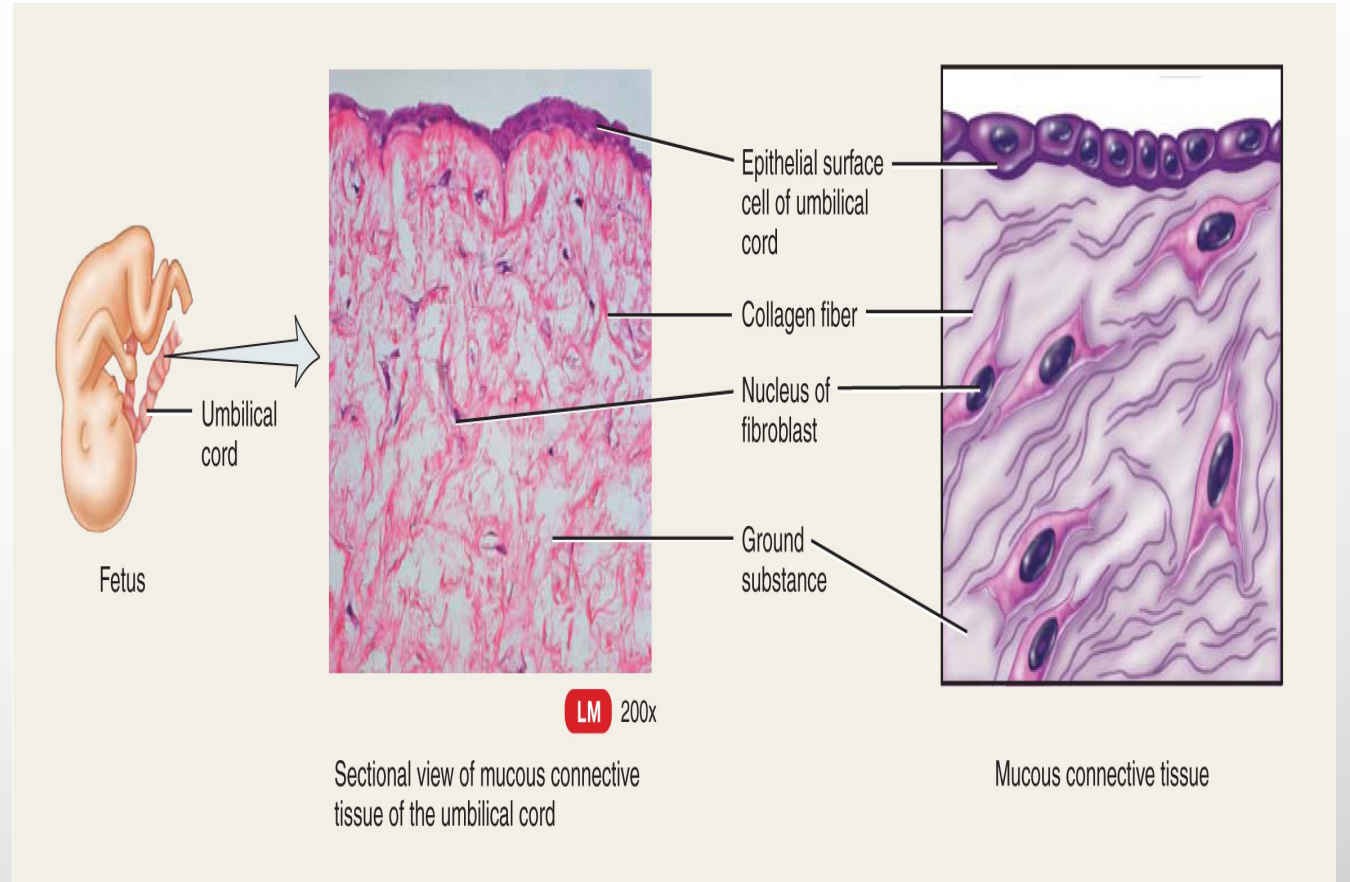
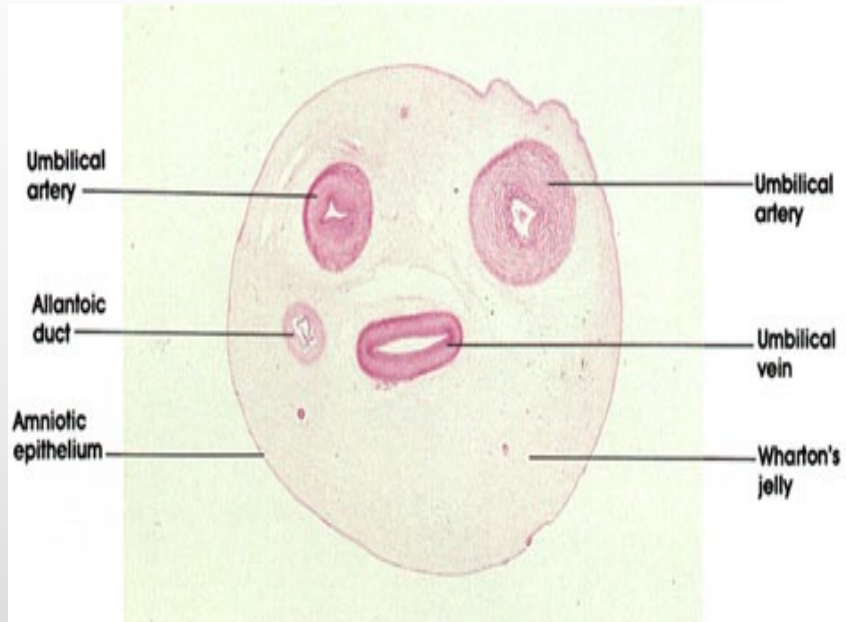
Classification-Embryonic CT

| Embryonic Connective Tissues | | | |
|-----------------------------------|---|--|------------------------------------|
| | General Organization | Major Functions | Examples |
| 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 |

Mesenchyme



Mucous Connective Tissue



Classification-Adult CT

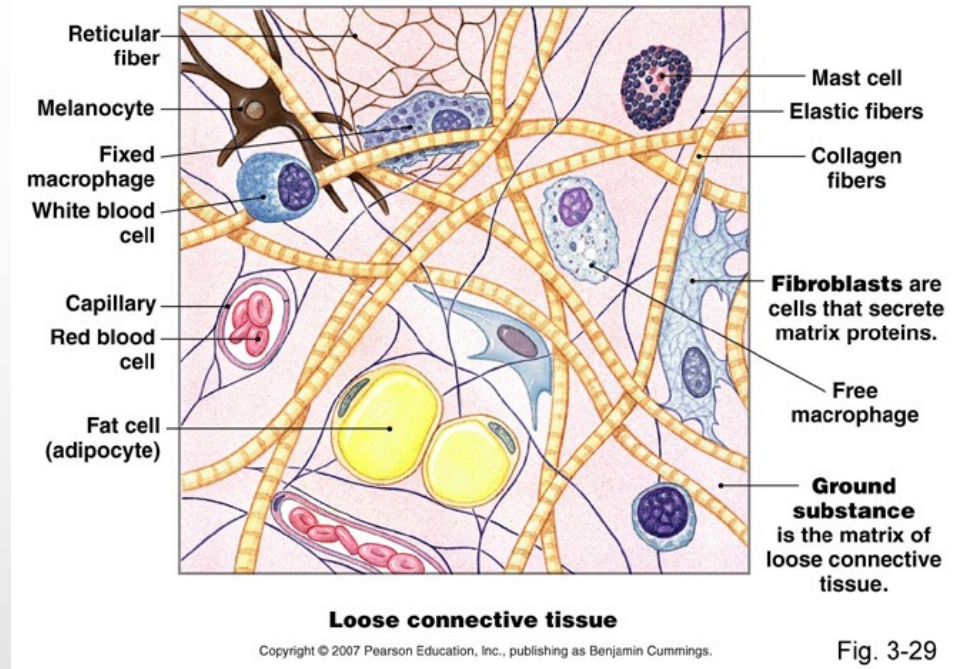
| | General Organization | Major Functions | Examples |
|-----------------------------------|--|--|--|
| Connective Tissue Proper | | | |
| Loose (areolar) connective tissue | Much ground substance; many cells and little collagen, randomly distributed | Supports microvasculature, nerves, and immune defense 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 |

Classification-Specialized CT

| | General Organization | Major Functions | Examples |
|--|--|---|---|
| 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 |

Loose (Areolar) Connective Tissue

- Consists of all 3 types of fibers, several types of cells, and semi-fluid ground substance.
- Found in subcutaneous layer and mucous membranes, and around blood vessels, nerves and organs
- Function = strength, support and elasticity



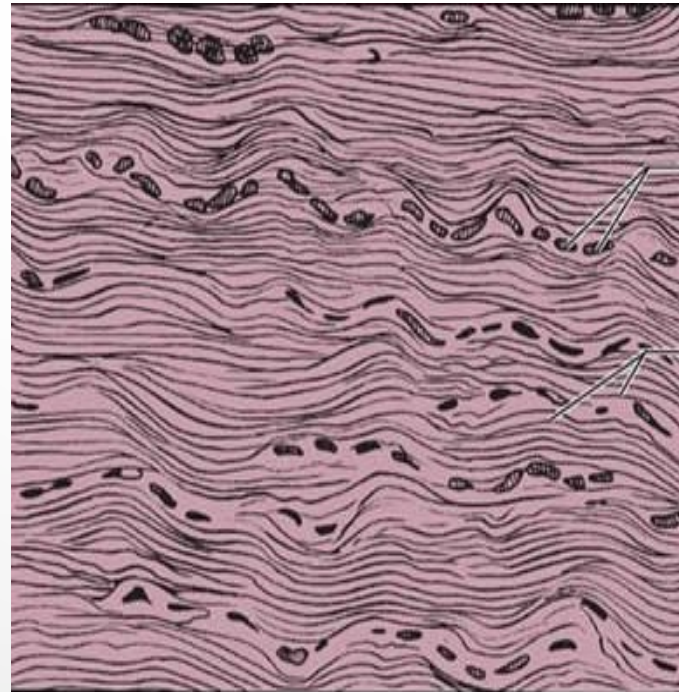
Dense Connective Tissue

Contains more numerous and thicker fibers and far fewer cells than loose CT.

- a. Dense regular connective tissue
Tendons and ligaments
- b. Dense irregular connective tissue
Dermis of skin

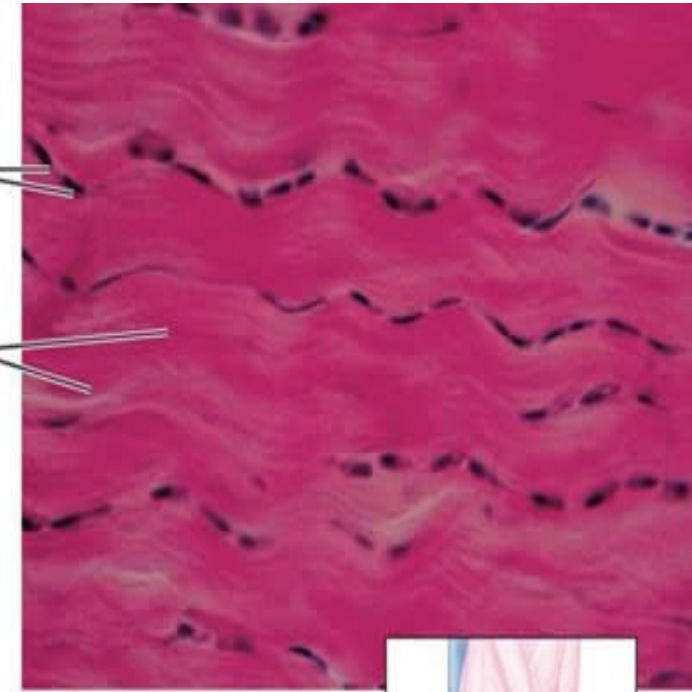
Dense Regular Connective Tissue

- Consists of bundles of collagen fibers and fibroblasts.
- Forms tendons, ligaments.
- Function = provide strong attachment between various structures.

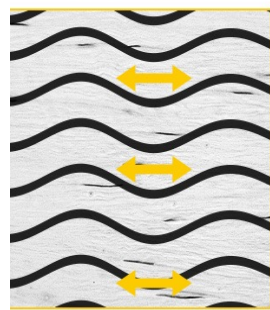


fibroblasts

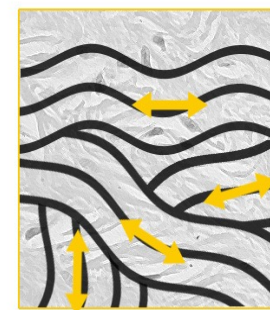
collagenous fibers



Direction of Dense Connective Tissue Fibers



Dense Regular



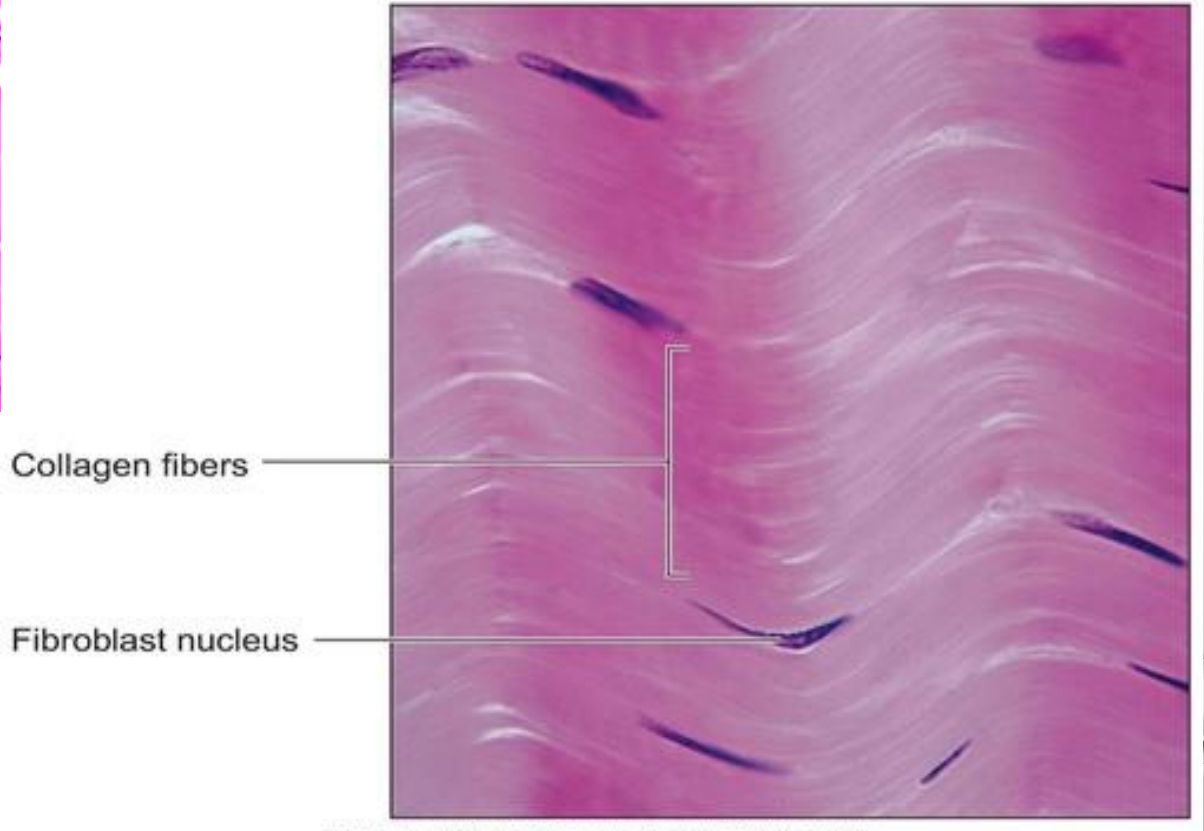
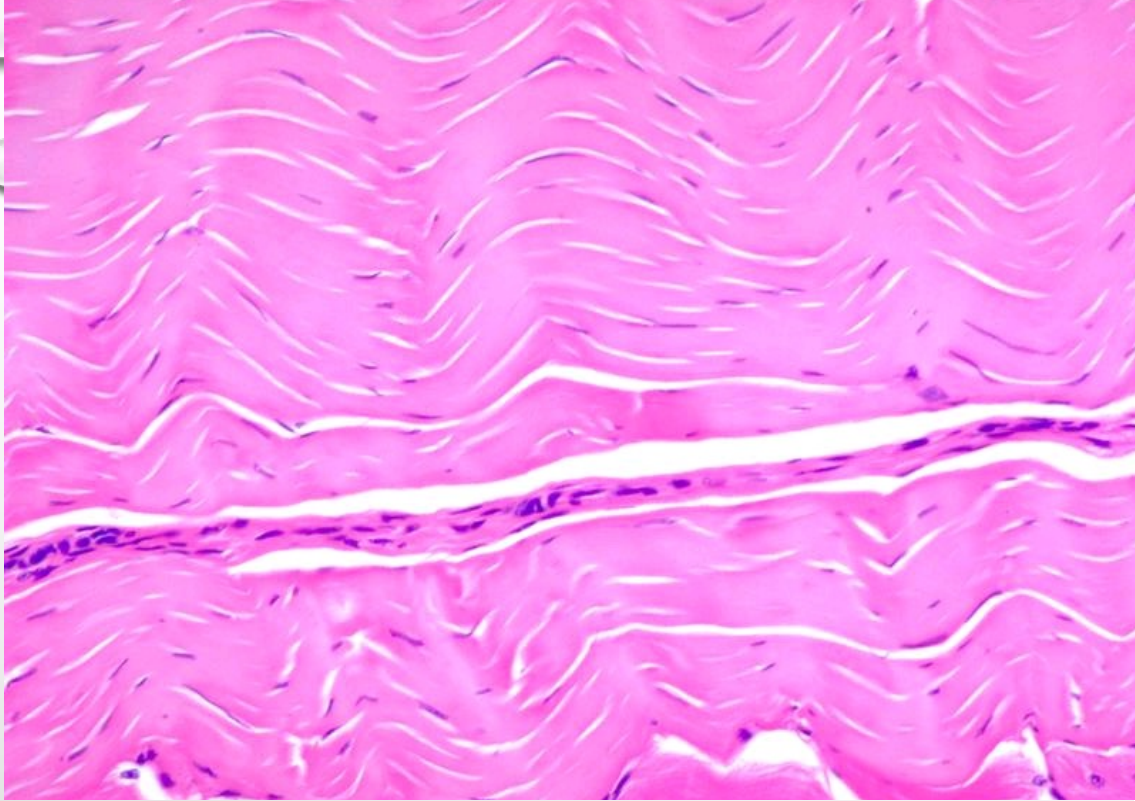
Dense Irregular

Connective Tissue

: Tendons; ligaments

: Binds organs together





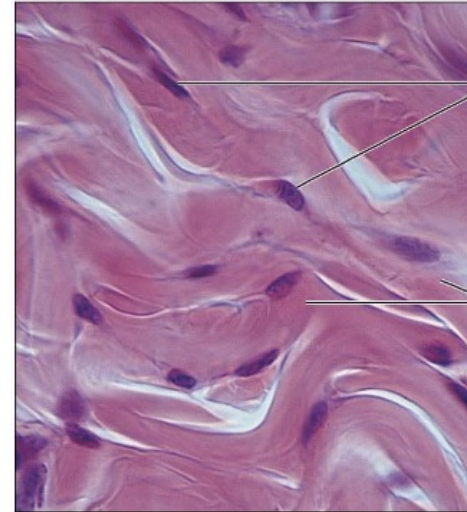
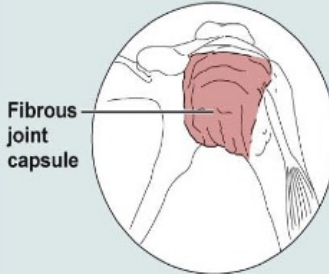
Dense Irregular CT

- Consists Of Randomly-arranged Collagen Fibers And A Few Fibroblasts.
- Found In Dermis Of Skin, capsules of joints and organs
- Function = Provide Strength and protection

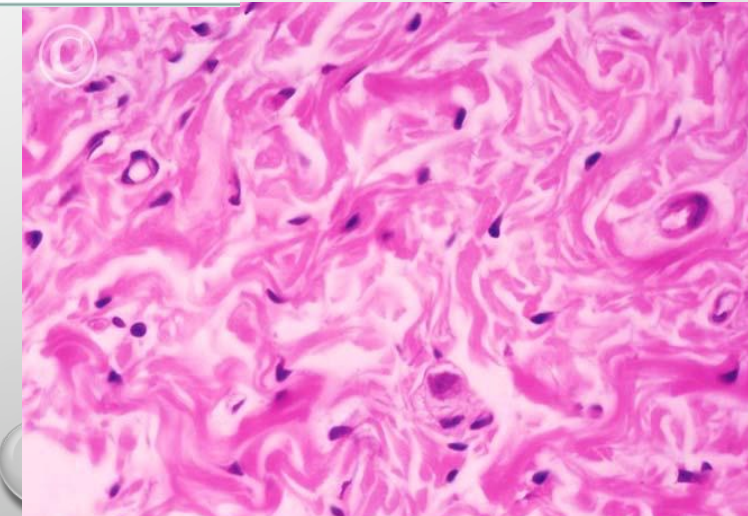
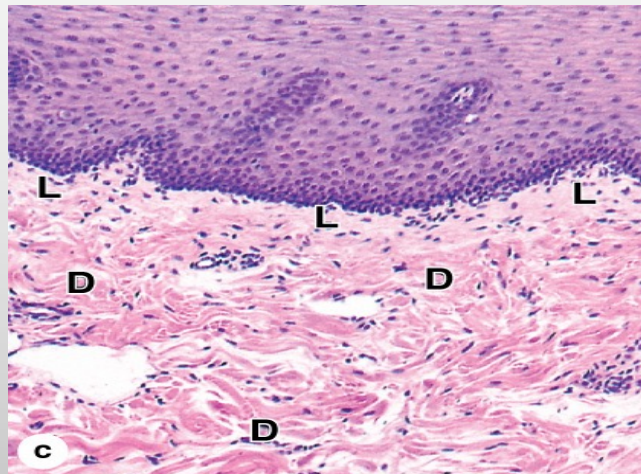
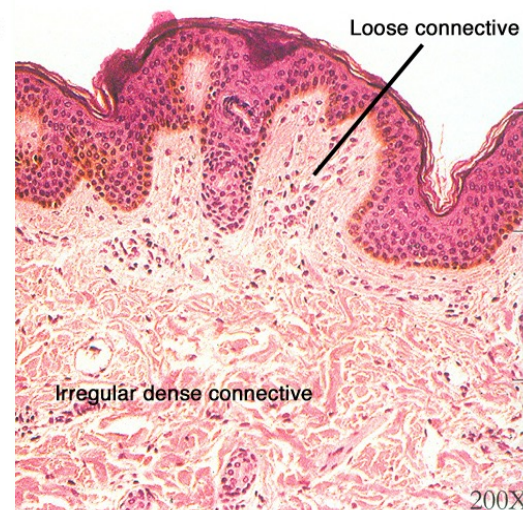
Description: Primarily irregularly arranged collagen fibers; some elastic fibers; major cell type is the fibroblast.

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

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



Photomicrograph: Dense irregular connective tissue from the dermis of the skin (600x).



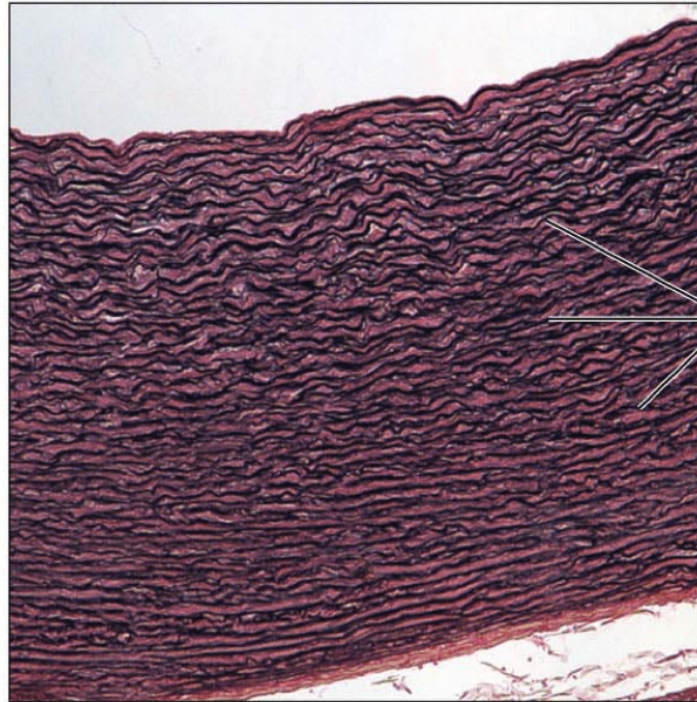
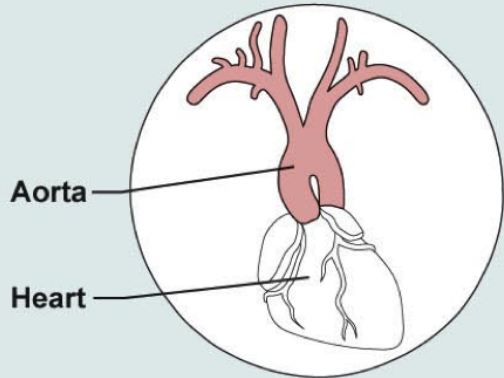
Elastic Connective Tissue

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

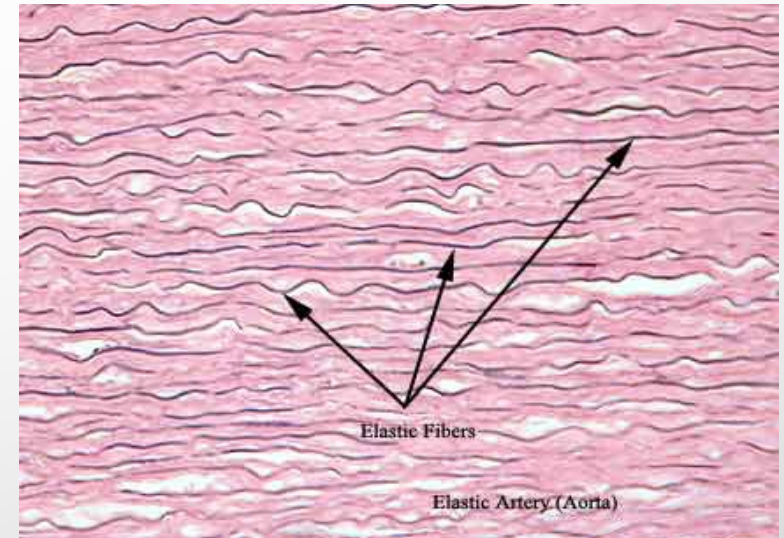
Description: Dense regular connective tissue containing a high proportion of elastic fibers.

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

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

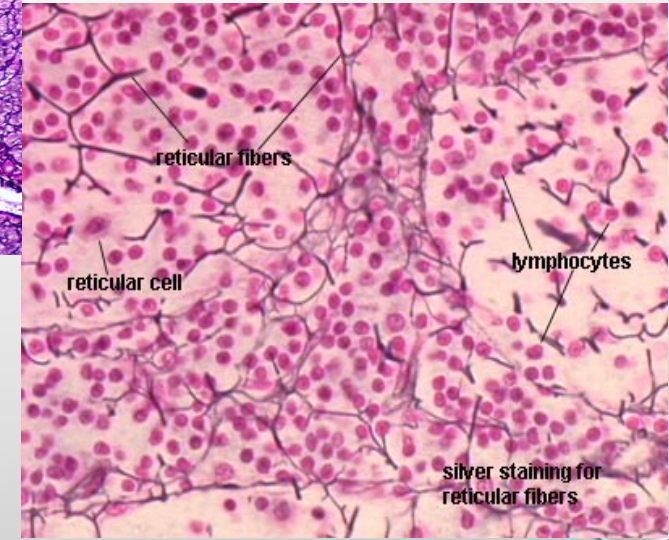
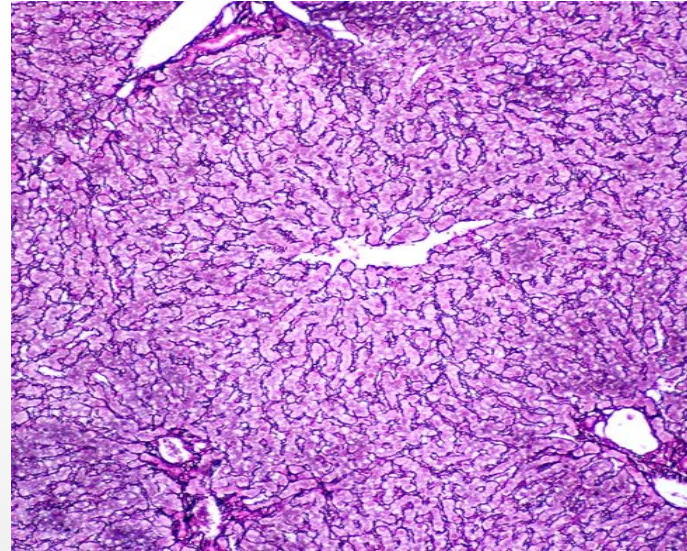


Photomicrograph: Elastic connective tissue in the wall of the aorta (85 \times).



RETICULAR CT

- Consists of fine interlacing reticular fibers and reticular cells.
- Found in liver, spleen and lymph nodes.
- Function = forms the framework (stroma) of organs and binds together smooth muscle tissue cells.



Medical Application Collagen

| | | |
|-------------------------|---|--|
| 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 |