

The background of the slide is a light gray gradient with several realistic water droplets of various sizes scattered across it. The droplets have highlights and shadows, giving them a three-dimensional appearance. Some are near the top, some near the bottom, and some are partially cut off by the edges of the frame.

# Connective TISSUE

Connective tissue provides a matrix that supports and physically connects other tissues and cells together to form the organs of the body.

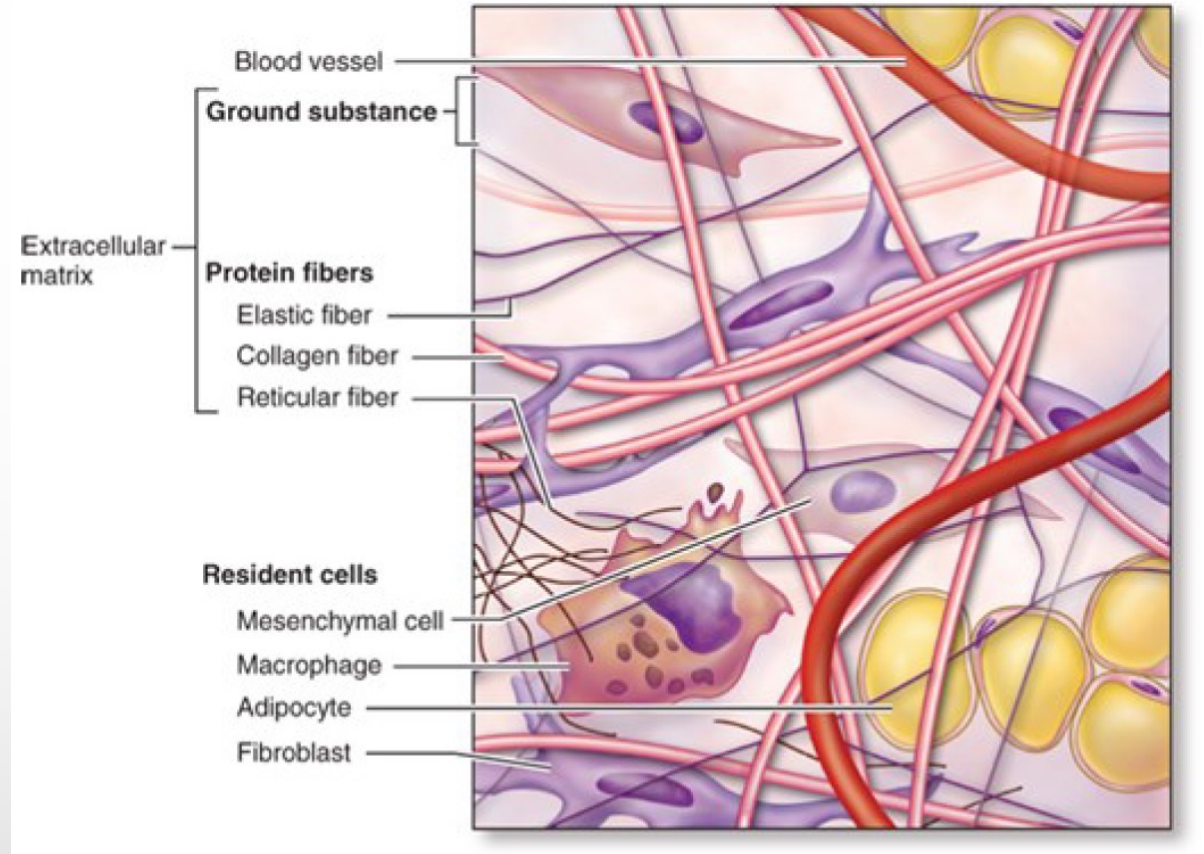
The interstitial fluid of connective tissue gives metabolic support to cells as the medium for diffusion of nutrients and waste products.

# Components

- Cells
- Fibers
- Ground substance

## Ground substance

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



# 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

# General Features

Originates from the mesoderm (Except some parts of the head and neck).

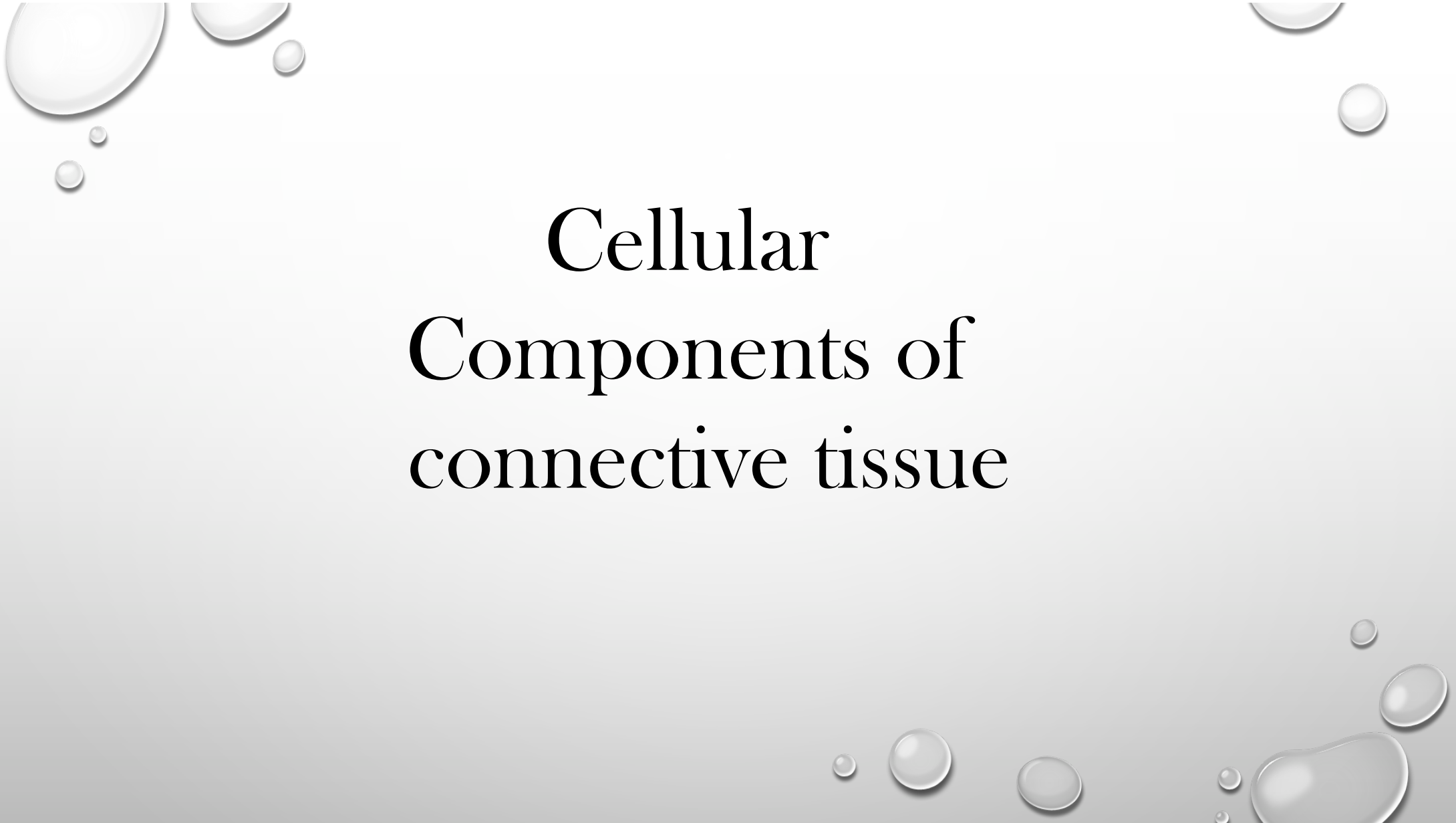
Composed of cells (fixed and wandering), fibres and ground substance.

Variable vascularity.

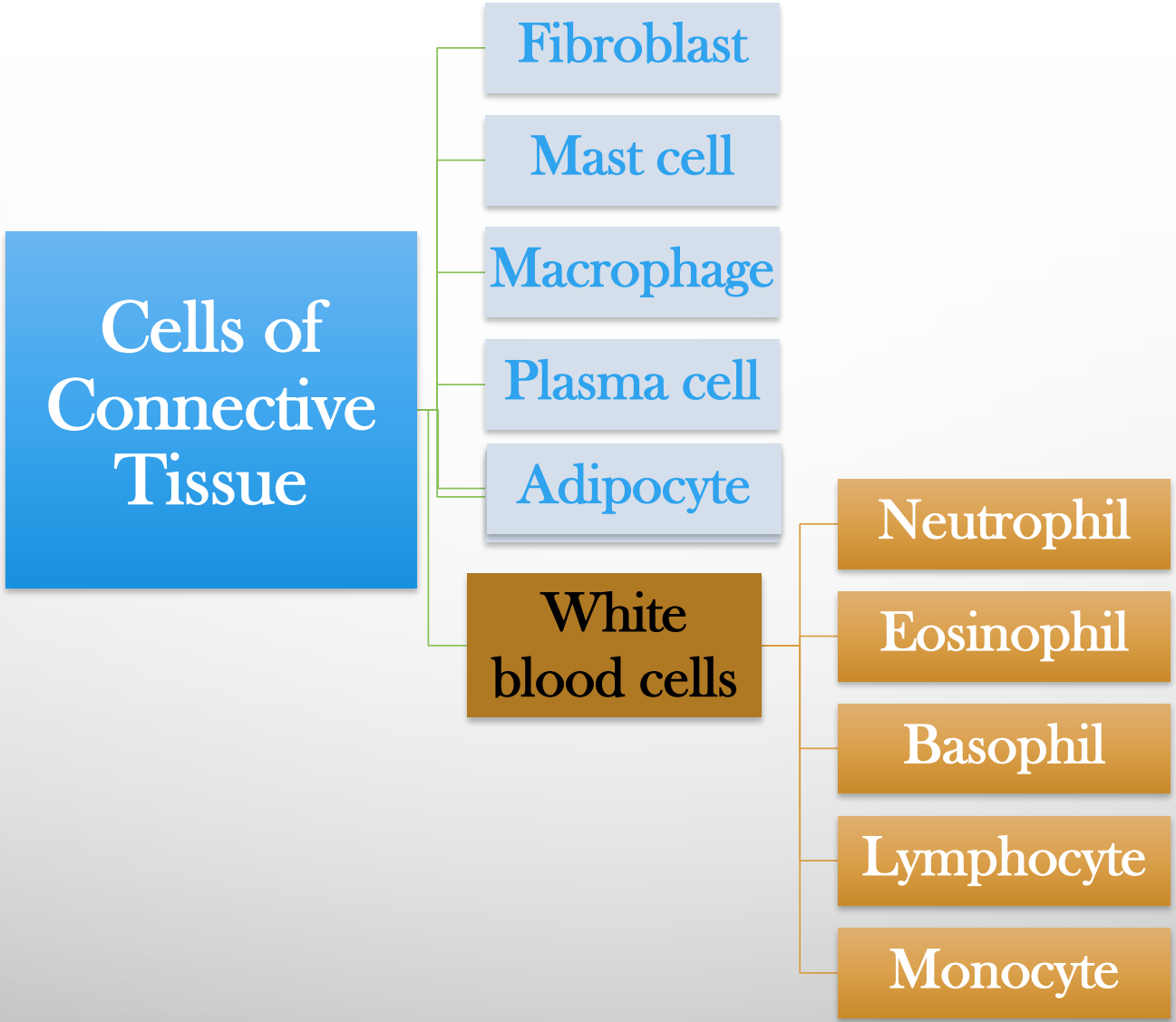
Variable regenerative power.

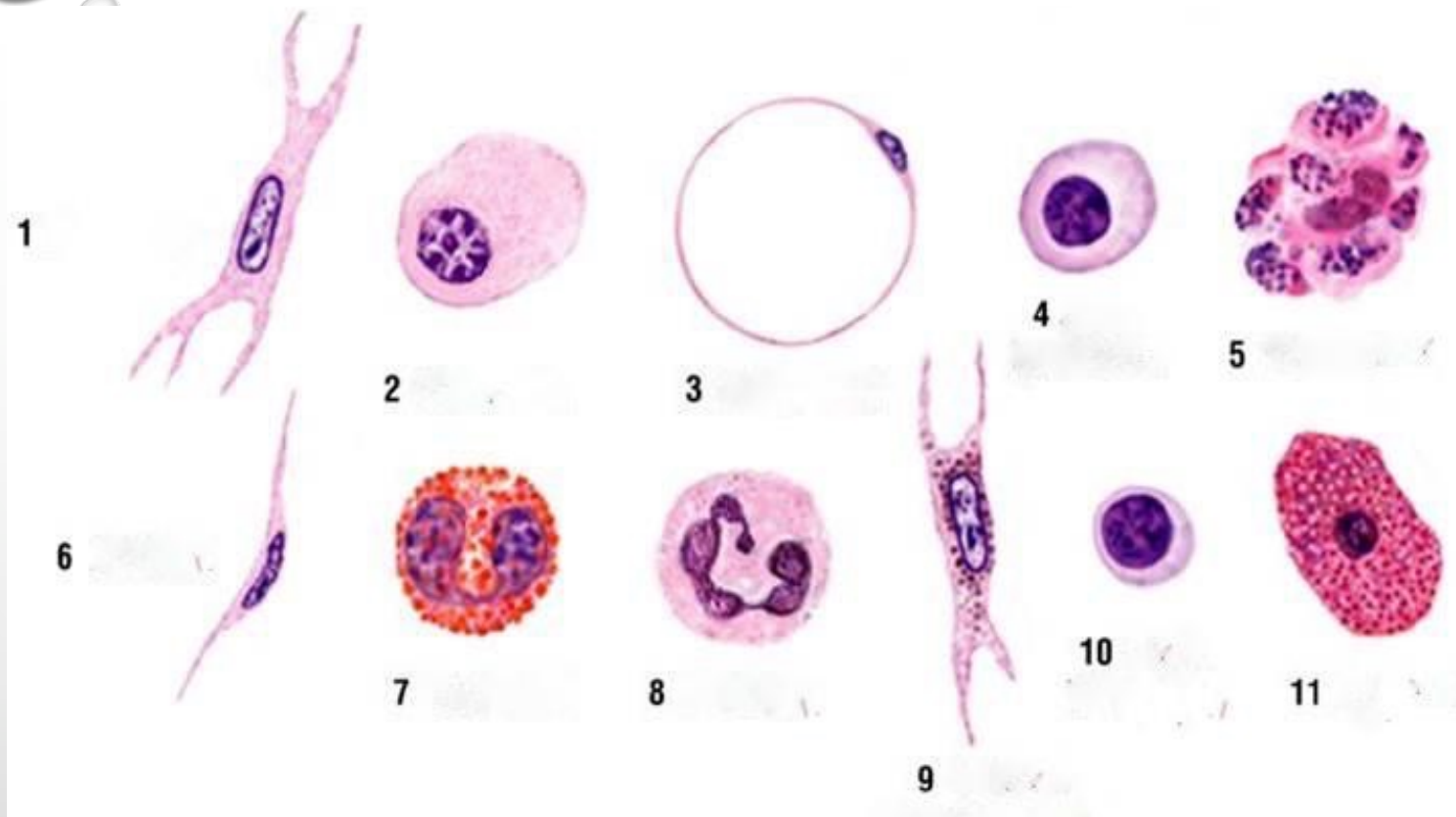
# Functions

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.

The slide features a light gray background with a subtle gradient. In the top-left and bottom-right corners, there are clusters of realistic, 3D-rendered water droplets of various sizes, some overlapping. The text is centered in a black, serif font.

# Cellular Components of connective tissue





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



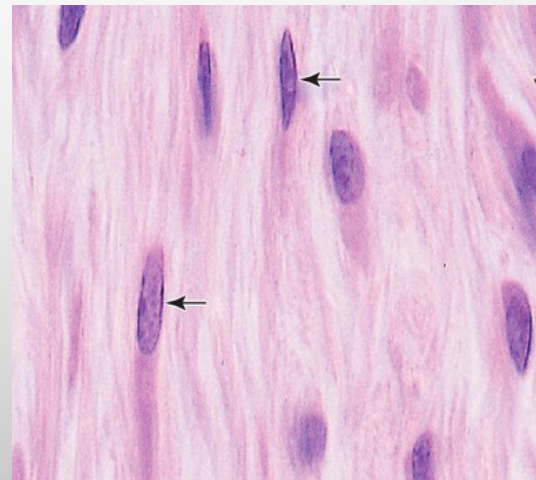
## Connective tissue cells

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

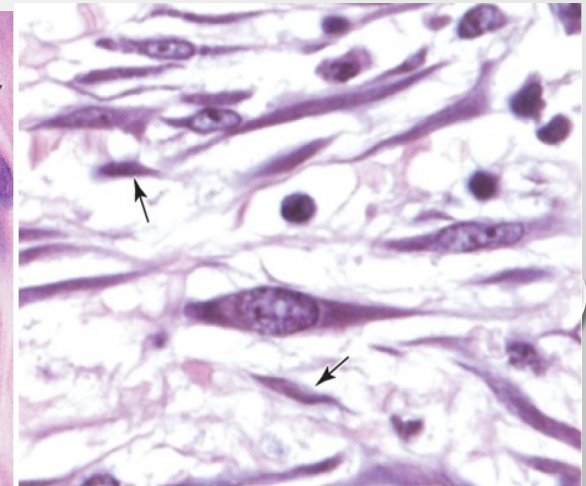
# Fibroblast

- 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**



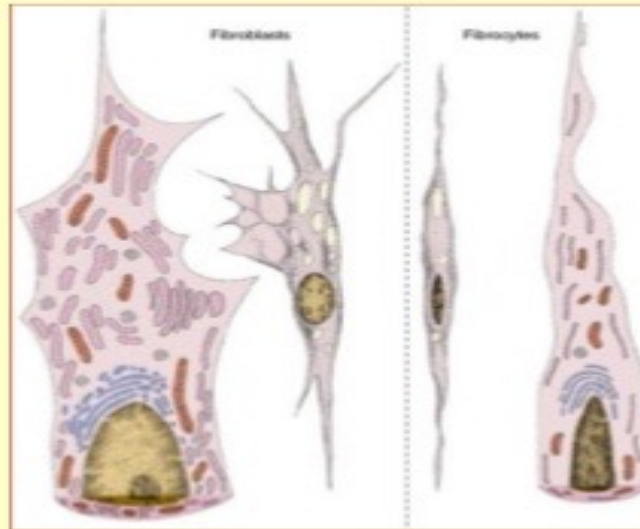
**Fibrocyte**



## Fibroblasts \_ Fibrocytes

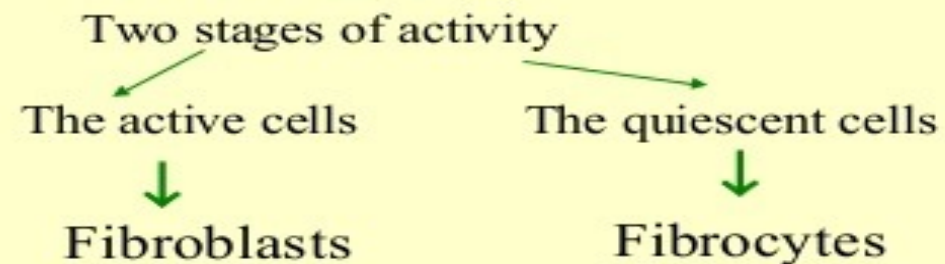
### ✓ Fibroblasts

- 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

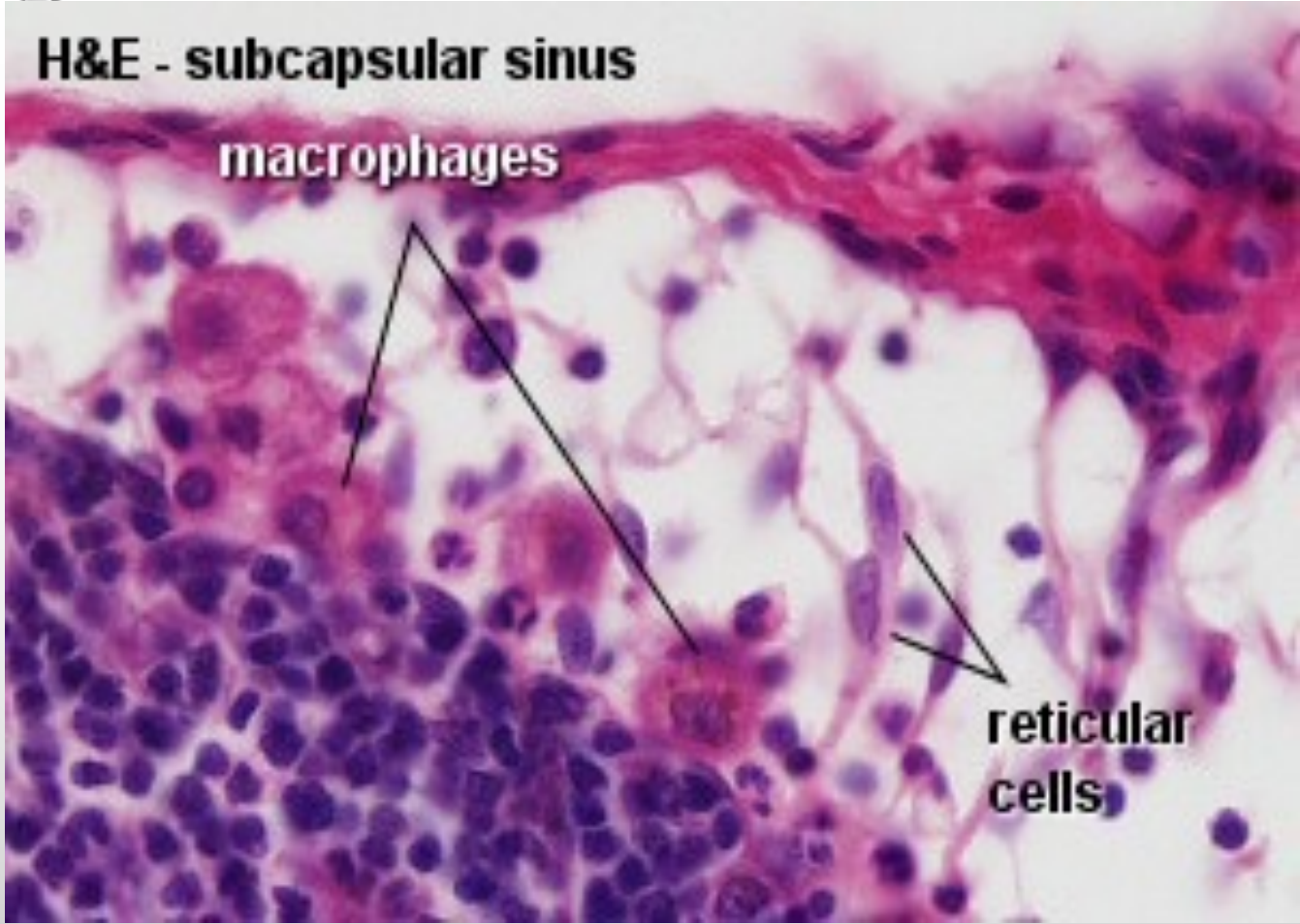


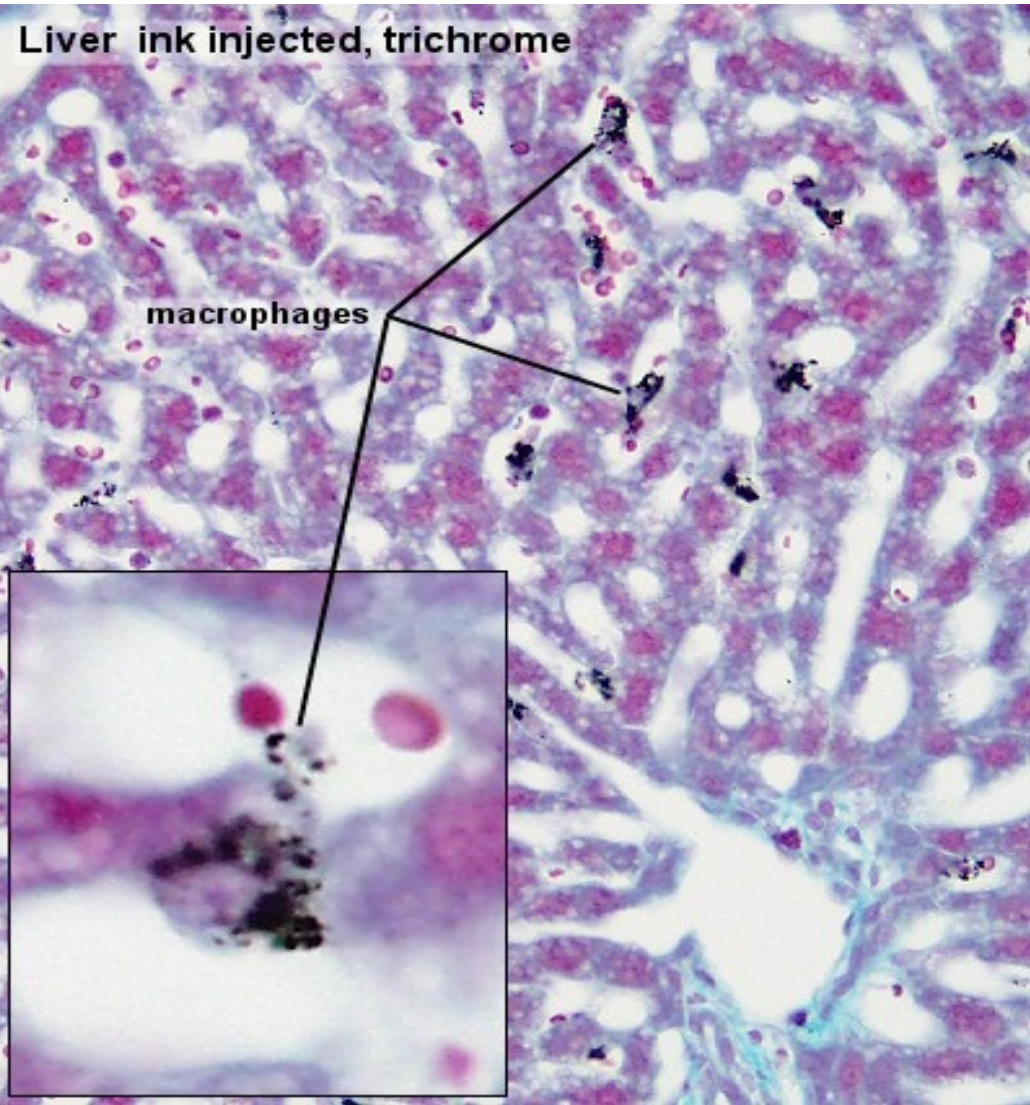
# Macrophage

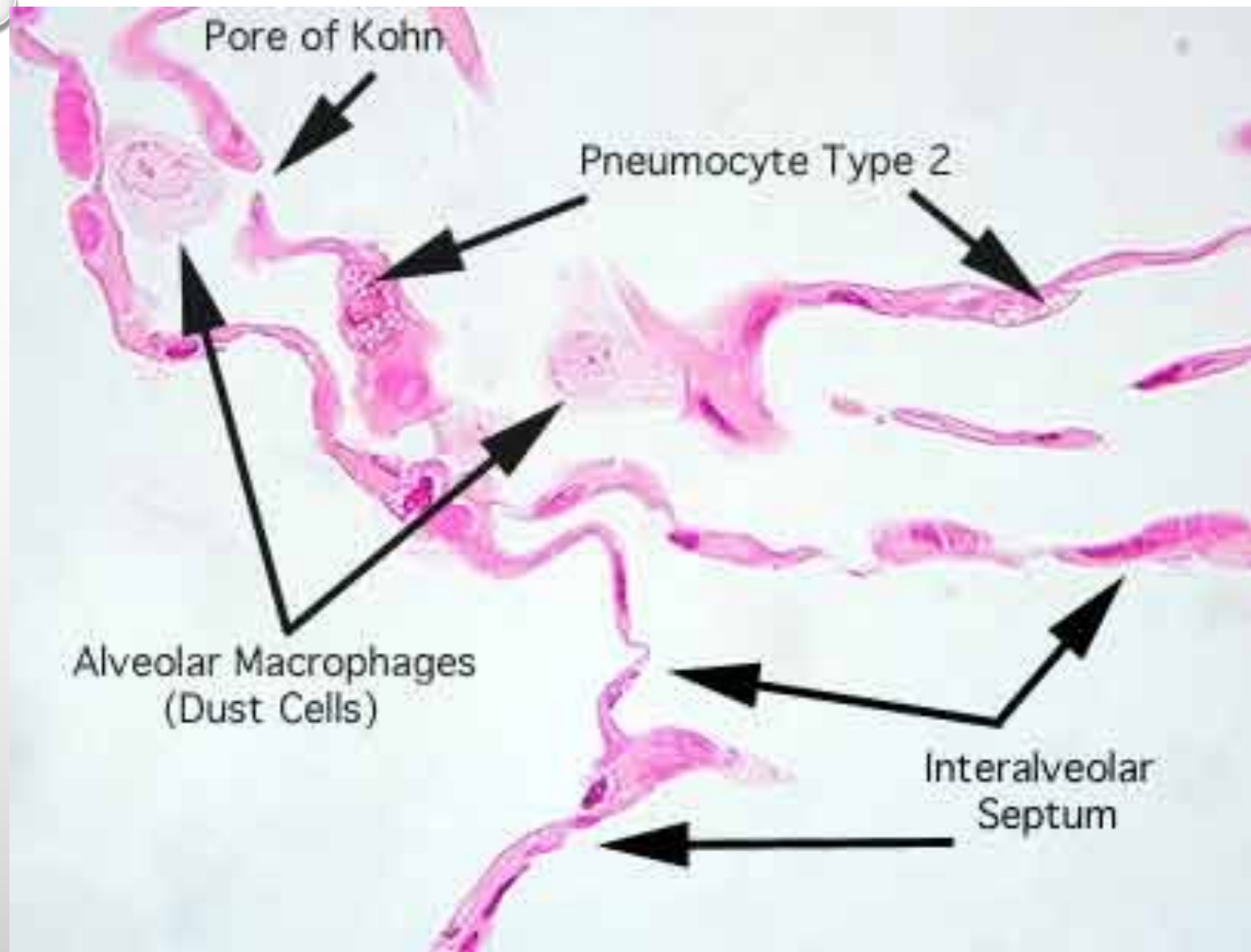
- Macrophages have highly developed phagocytic ability and specialize in turnover of protein fibers and removal of apoptotic cells, tissue debris, or other particulate material
- Being especially abundant at sites of inflammation.
- Size and shape vary considerably, corresponding to their state of functional activity.
- A typical macrophage measures between 10 and 30  $\mu\text{m}$  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







Pore of Kohn

Pneumocyte Type 2

Alveolar Macrophages  
(Dust Cells)

Interalveolar  
Septum



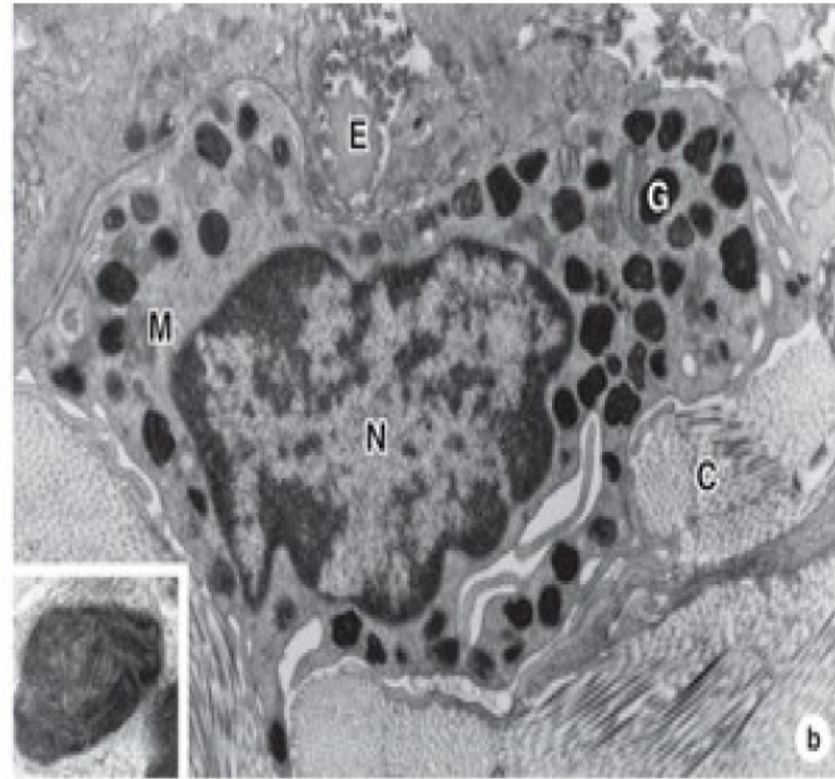
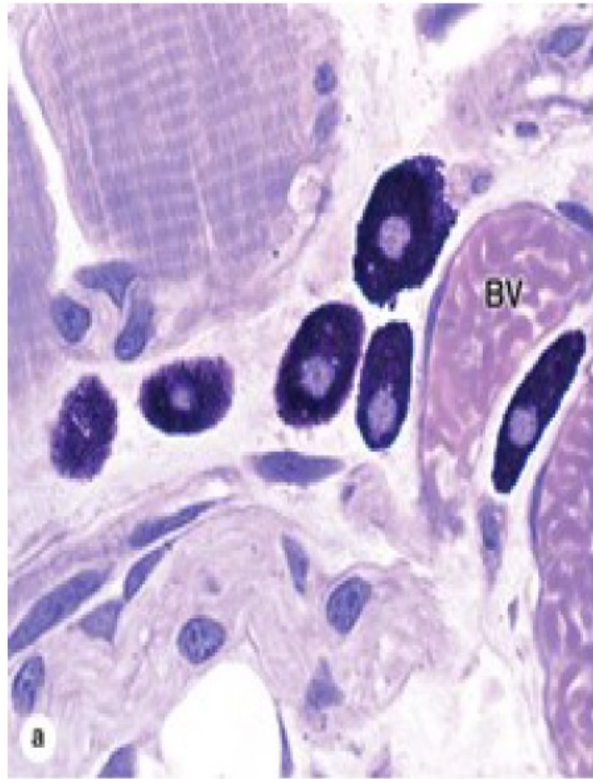
# Mast Cell

- Mast cells are oval or irregularly shaped cells of connective tissue,
- Between 7 and 20  $\mu\text{m}$  in diameter, filled with basophilic secretory granules that often obscure the central nucleus
- Granules are electron dense and of variable size, ranging from 0.3 to 2.0  $\mu\text{m}$  in diameter.
- 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, which promotes increased vascular permeability and smooth muscle contraction
  3. Serine proteases, which activate various mediators of inflammation
  4. Eosinophil and neutrophil chemotactic factors, which attract those leukocytes
  5. Cytokines, polypeptides directing activities of leukocytes and other cells of the immune system
  6. Phospholipid precursors, which are converted to prostaglandins, leukotrienes, and other important lipid mediators of the inflammatory

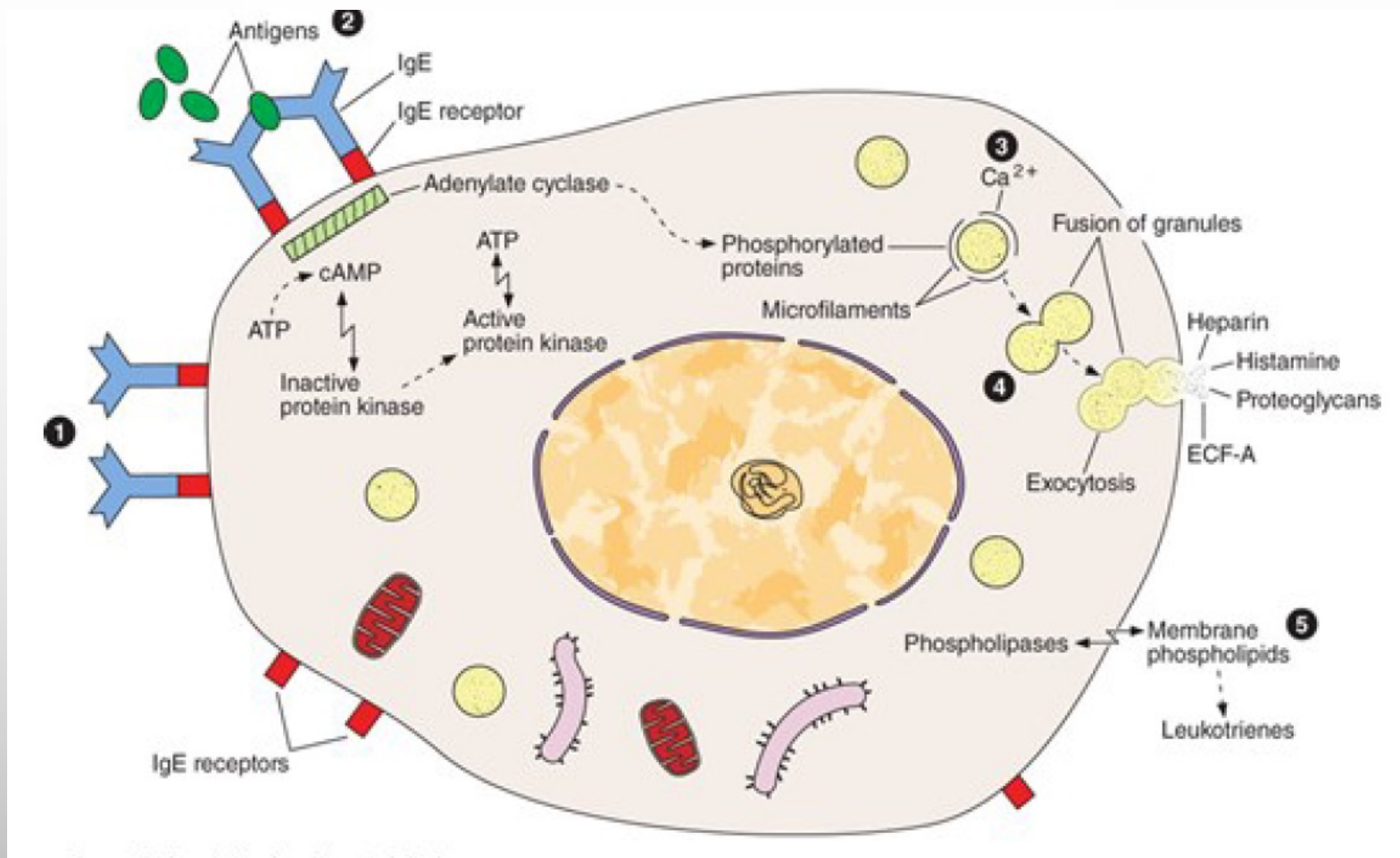
# Mast Cell

- Mast cells are especially numerous near small blood vessels in skin and mesenteries (perivascular mast cells) and in the tissue that lines digestive and respiratory tracts (mucosal mast cells).
- These major locations suggest that mast cells place themselves strategically to function as sentinels detecting invasion by microorganisms.
- Release of certain chemical mediators stored in mast cells promotes the allergic reactions known as immediate hypersensitivity reactions because they occur within a few minutes after the appearance of an antigen in an individual previously sensitized to that antigen.
- The first exposure to an antigen (allergen), such as bee venom, causes antibody-producing cells to produce an immunoglobulin of the ige class that binds avidly to receptors on the surface of mast cells.
- Upon a second exposure to the antigen, it reacts with the ige on the mast cells, triggering rapid release of histamine, leukotrienes, chemokines, and heparin from the mast cell granules that can produce the sudden onset of the allergic reaction.

# MAST CELL

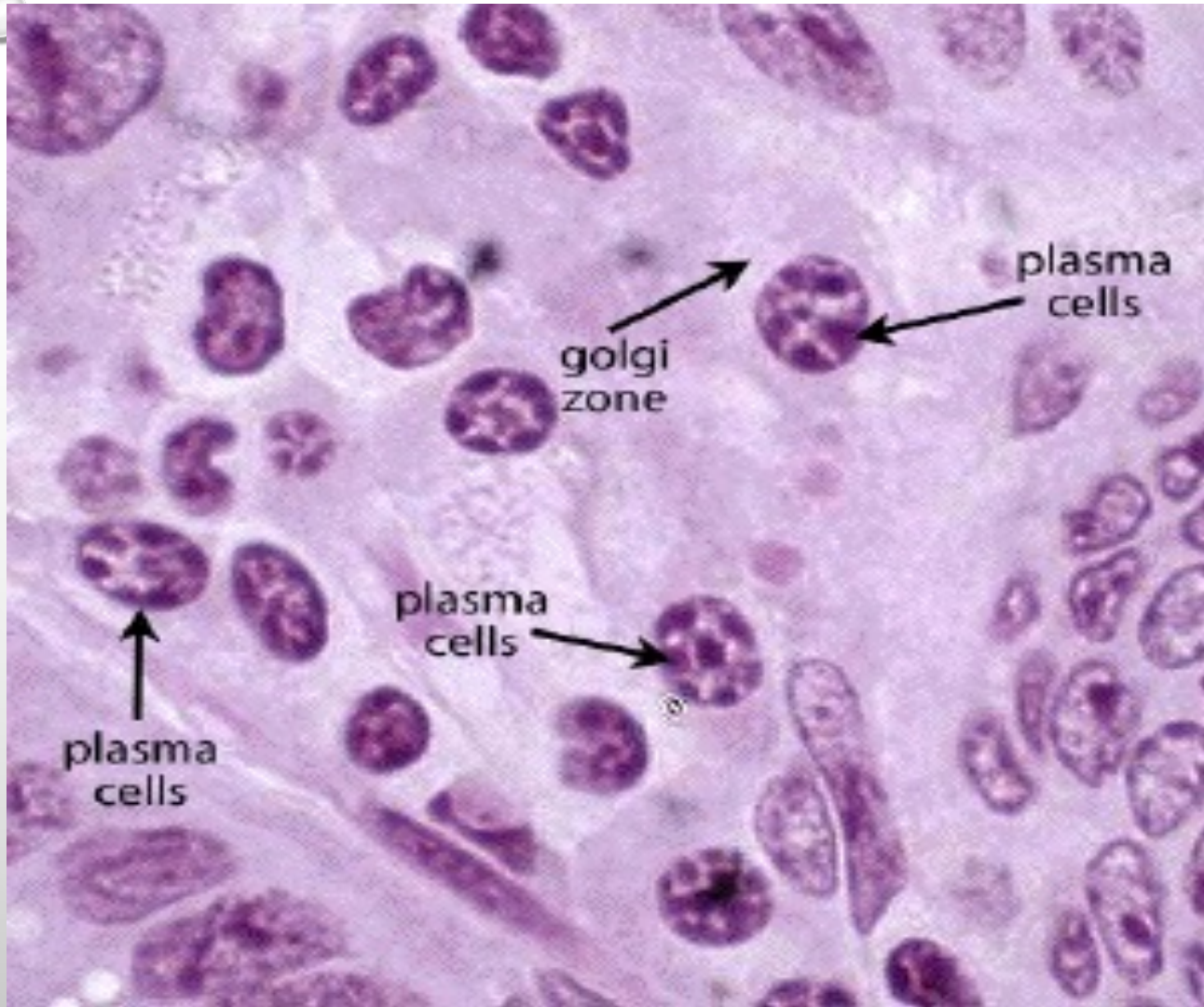


# MAST CELLS



# Plasma Cell

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



plasma cells


golgi zone

plasma cells

plasma cells




# Adipose Cells

- Or fat cells, are found in the connective tissue of many organs.
  - These large, mesenchymally 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.
- 



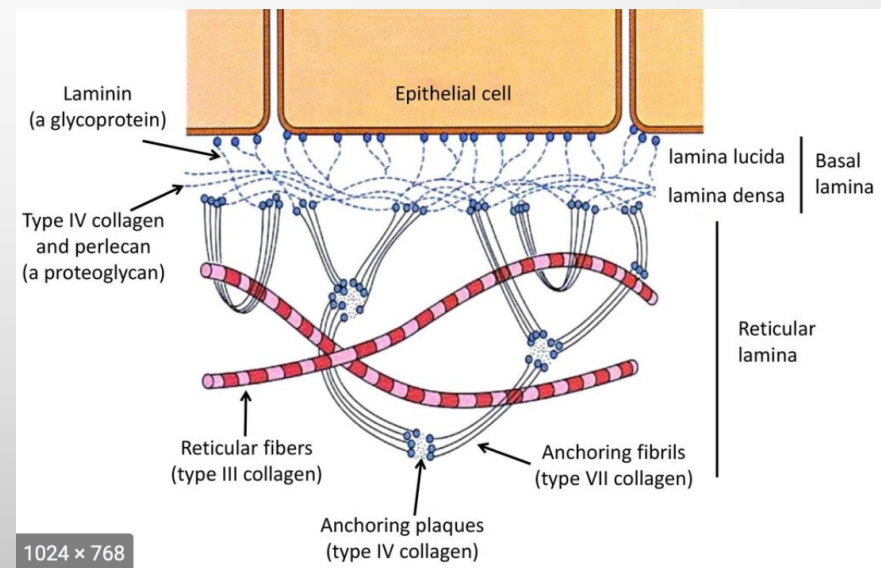
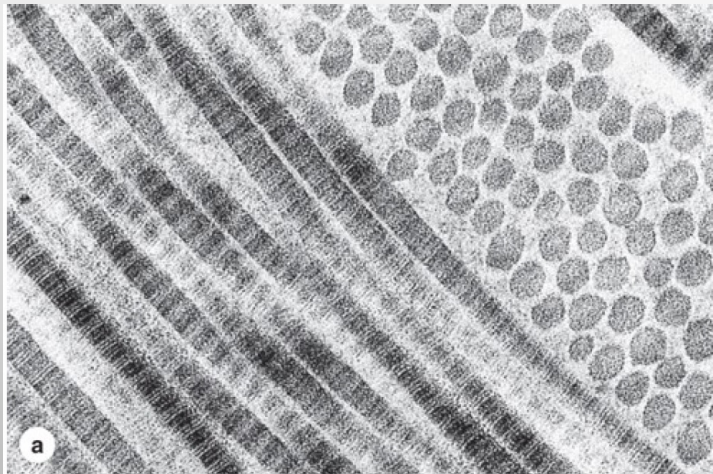
# Connective Tissue Fibers/Collagen

- 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

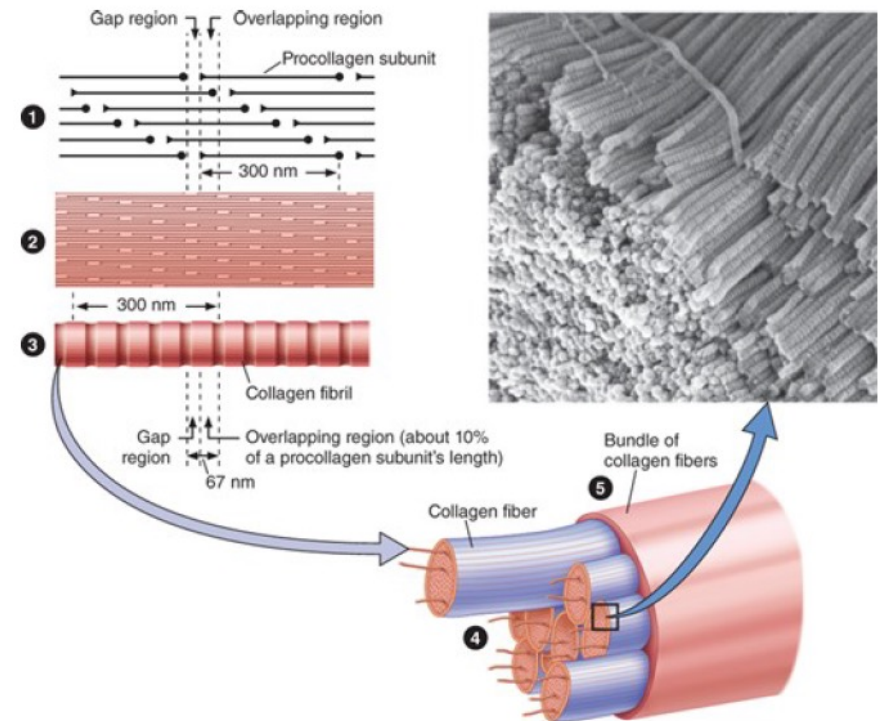
- **Fibrillar collagens**, notably collagen types I, II, and III. Form structures such as tendons, organ capsules, and dermis.
- **Network or sheet-forming collagens** such as type IV collagen have subunits produced by epithelial cells and are major structural of external laminae and all epithelial basal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

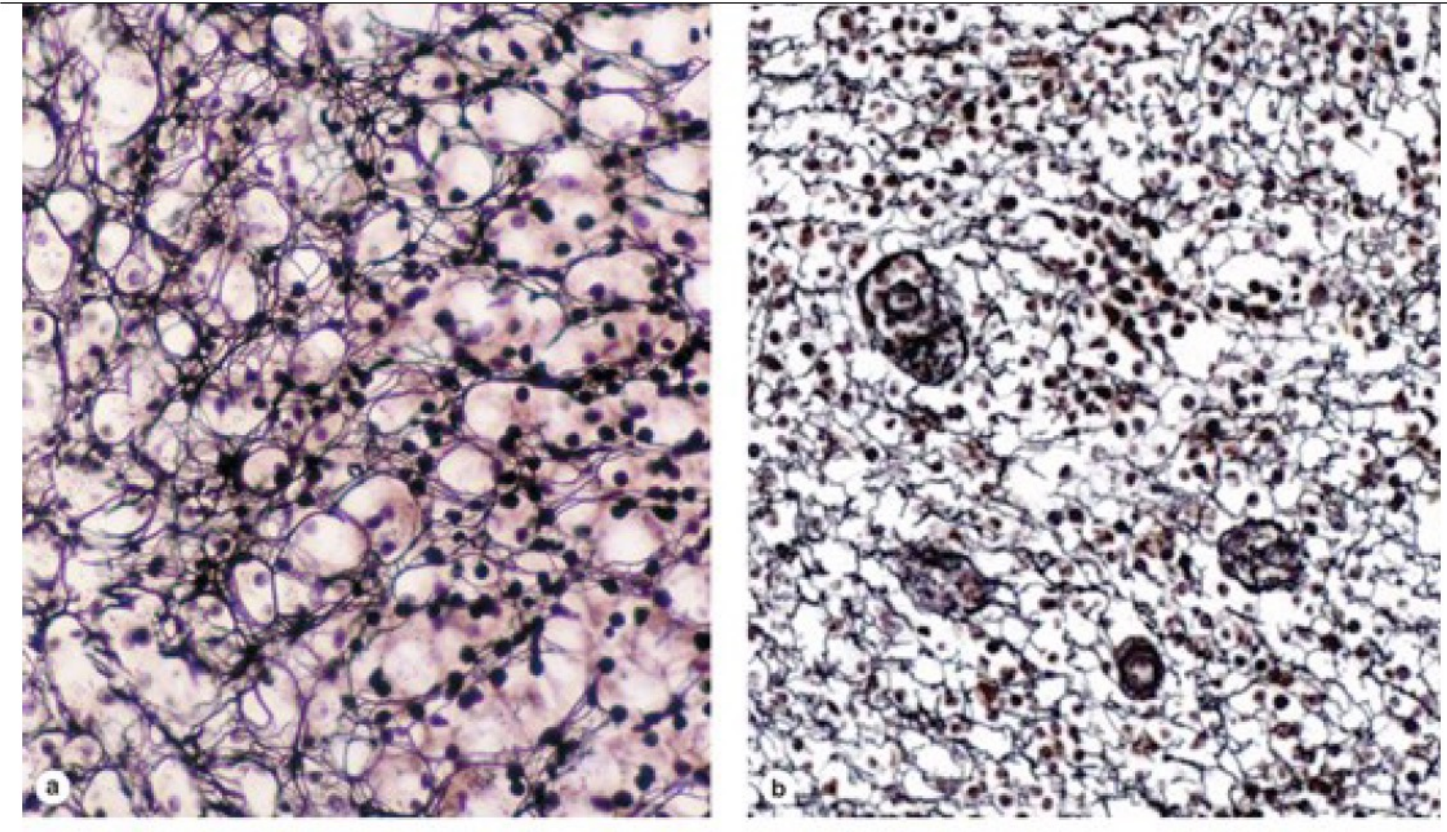
Assembly of type I collagen.



# 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

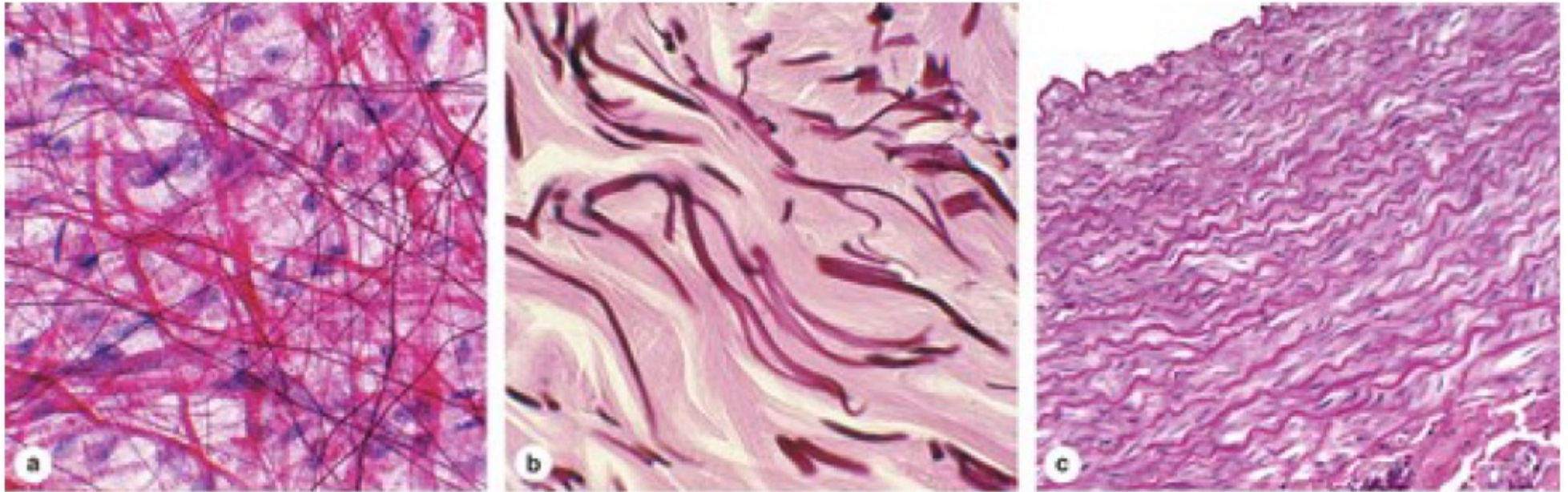


Lymph nodes-  
silver stain

# 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.

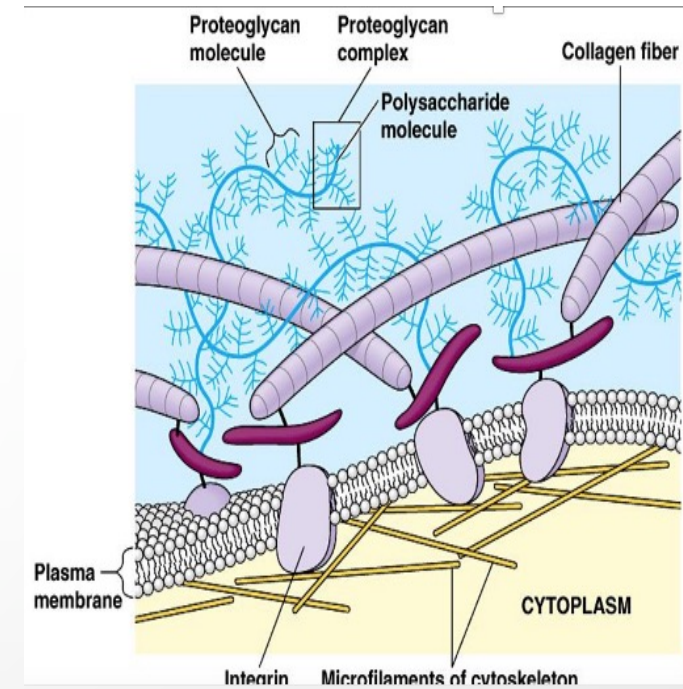
# Connective Tissue Fibers/Elastic



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

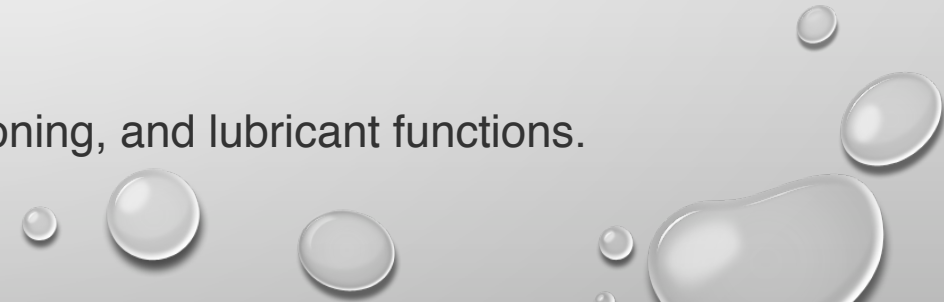
# Ground Substance

- 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, ground substance
- Allows diffusion of small molecules and,
- Because it is viscous---lubricant and a barrier to the penetration of invaders.





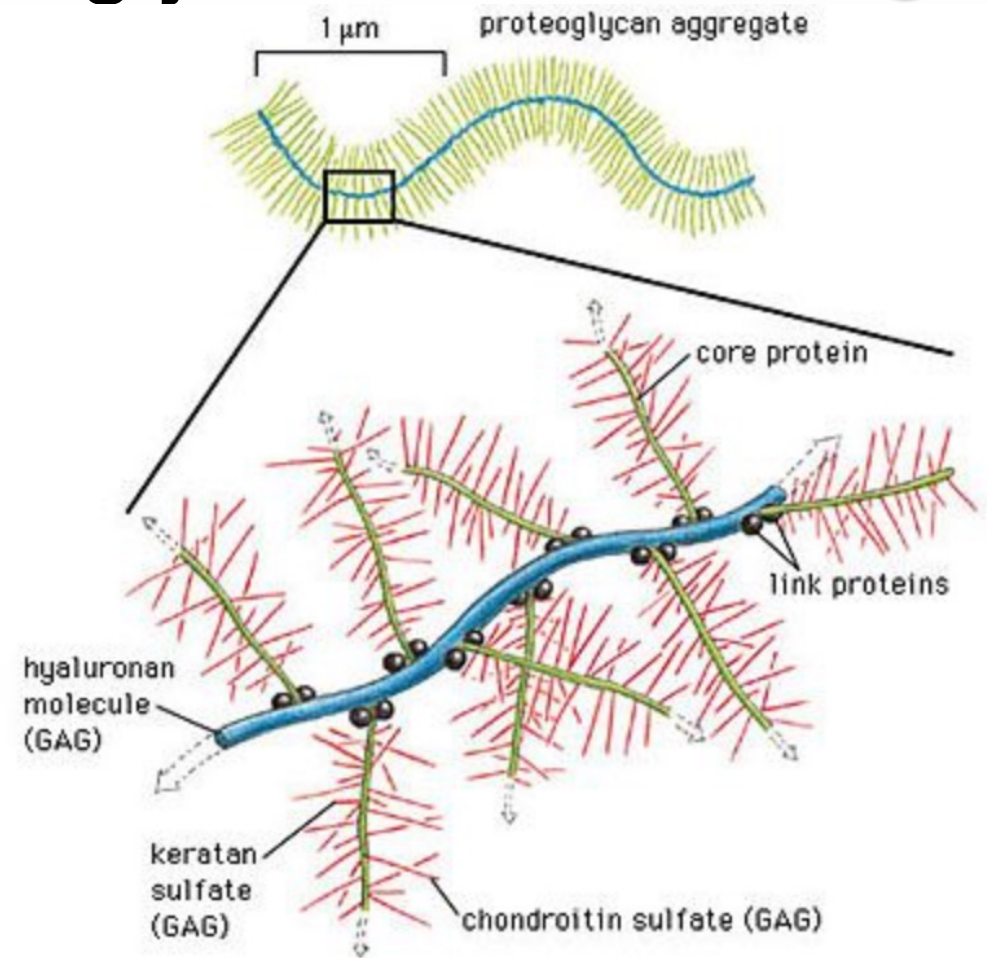
# GAGs

- 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).
  - 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

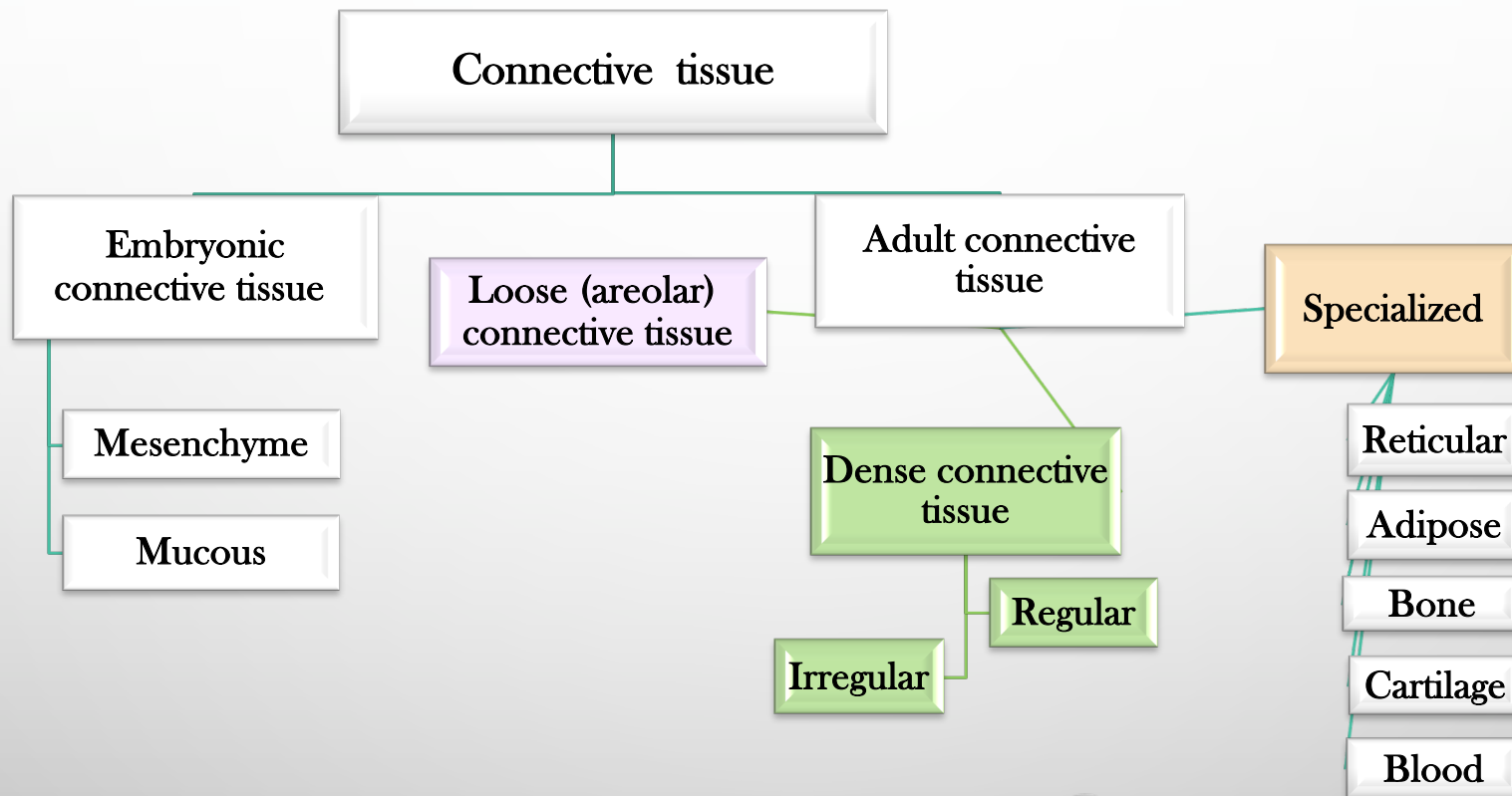
- Hyaluronic acid
- Chondroitin 4-sulfate
- Chondroitin 6-sulfate
- Dermatan sulfate
- Heparan sulfate
- Heparin
- Keratan sulfate



# 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

	General Organization	Major Functions	Examples
<b>Embryonic Connective Tissues</b>			
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

# Classification-Adult

	General Organization	Major Functions	Examples
<b>Connective Tissue Proper</b>			
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

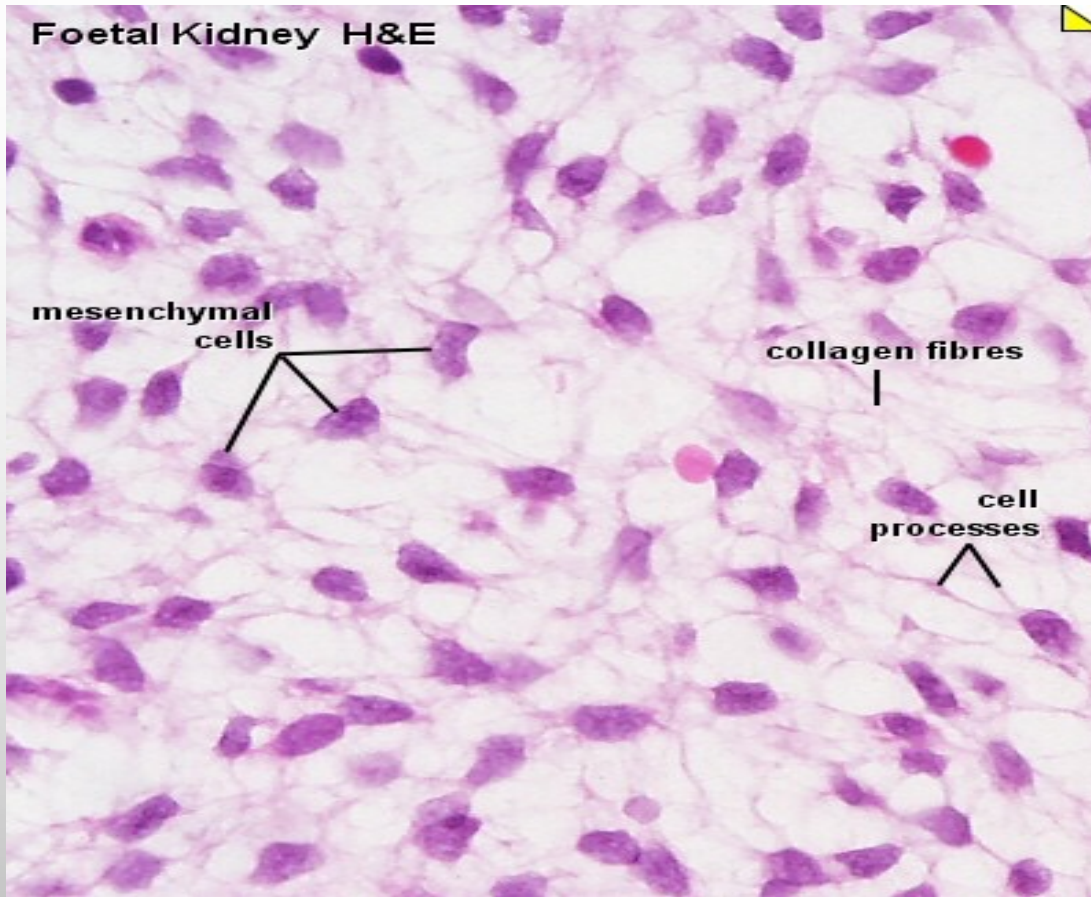
	General Organization	Major Functions	Examples
Reticular connective tissue (see Chapter 14)	Delicate network of reticulin/collagen III with attached fibroblasts (reticular cells)	Supports blood-forming cells, many secretory cells, and lymphocytes in most lymphoid organs	Bone marrow, liver, pancreas, adrenal glands, all lymphoid organs except the thymus
Adipose Tissue (see Chapter 6)			
Cartilage (see Chapter 7)			
Bone (see Chapter 8)			
Blood (see Chapter 12)			

# Embryonic Connective Tissue

- Mesenchyme connective tissue
- Mucous connective tissue

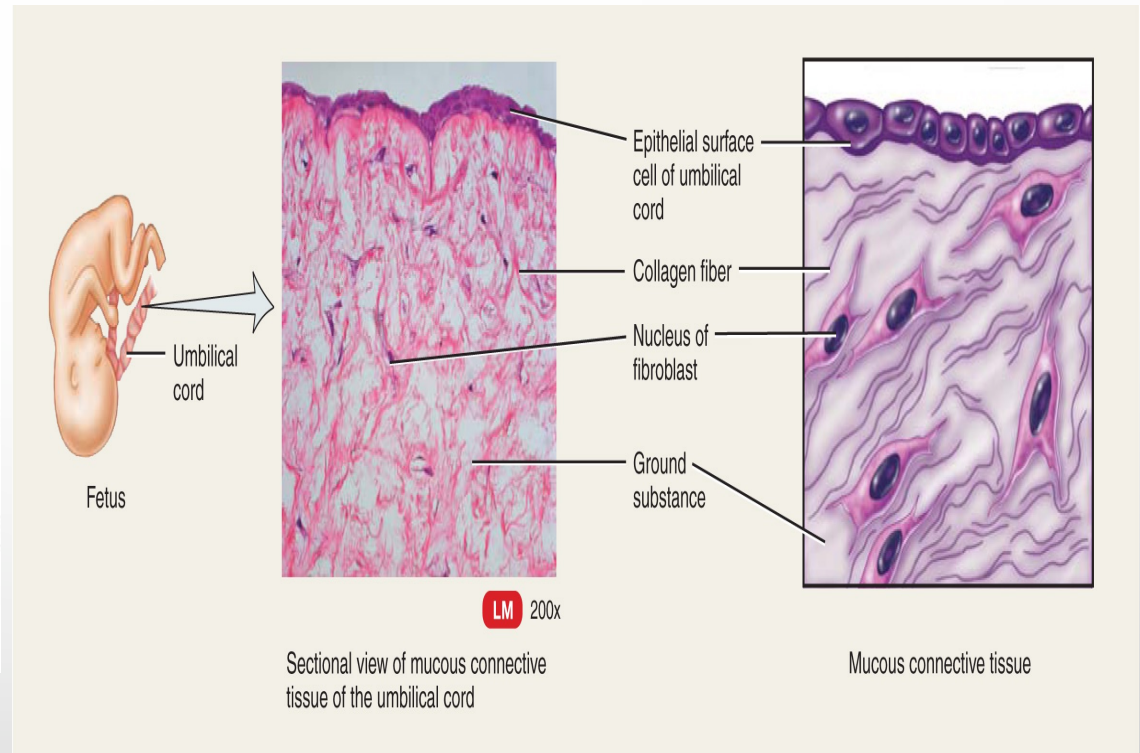
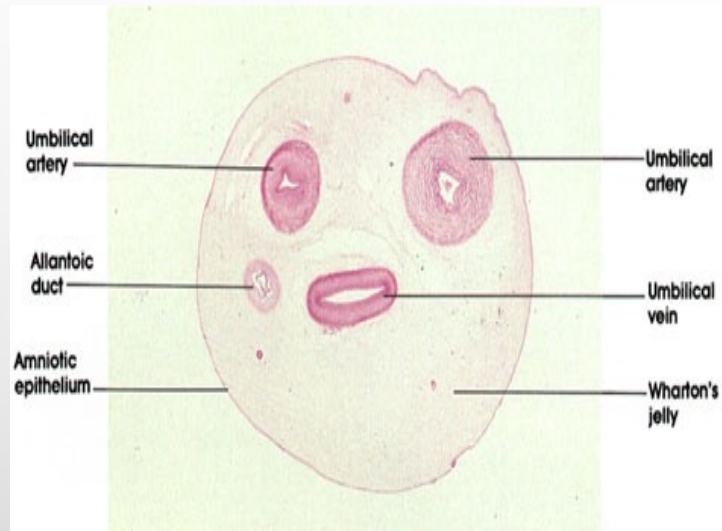
	General Organization	Major Functions	Examples
Mesenchyme	Sparse, undifferentiated cells, uniformly distributed in matrix with sparse collagen fibers	Contains stem/progenitor cells for all adult connective tissue cells	Mesodermal layer of early embryo
Mucoid (mucous) connective tissue	Random fibroblasts and collagen fibers in viscous matrix	Supports and cushions large blood vessels	Matrix of the fetal umbilical cord

# Mesenchyme



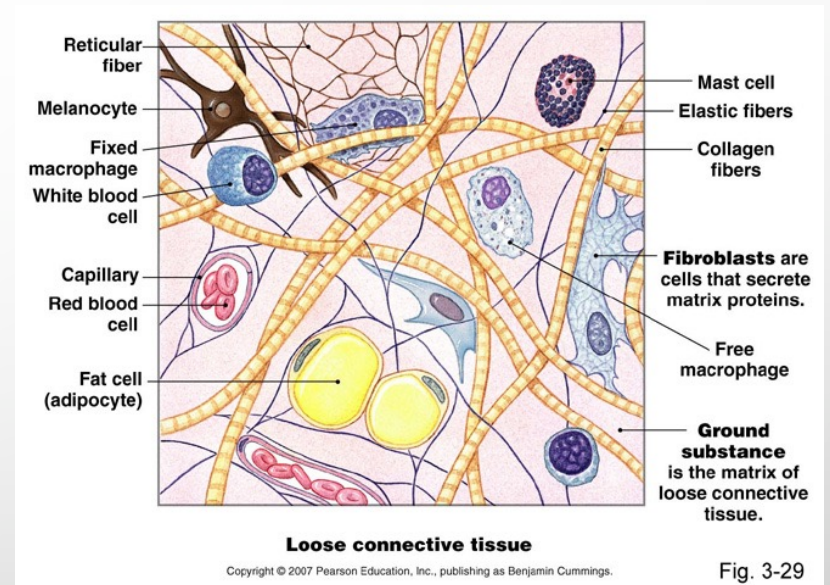


# Mucous Connective Tissue



# 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





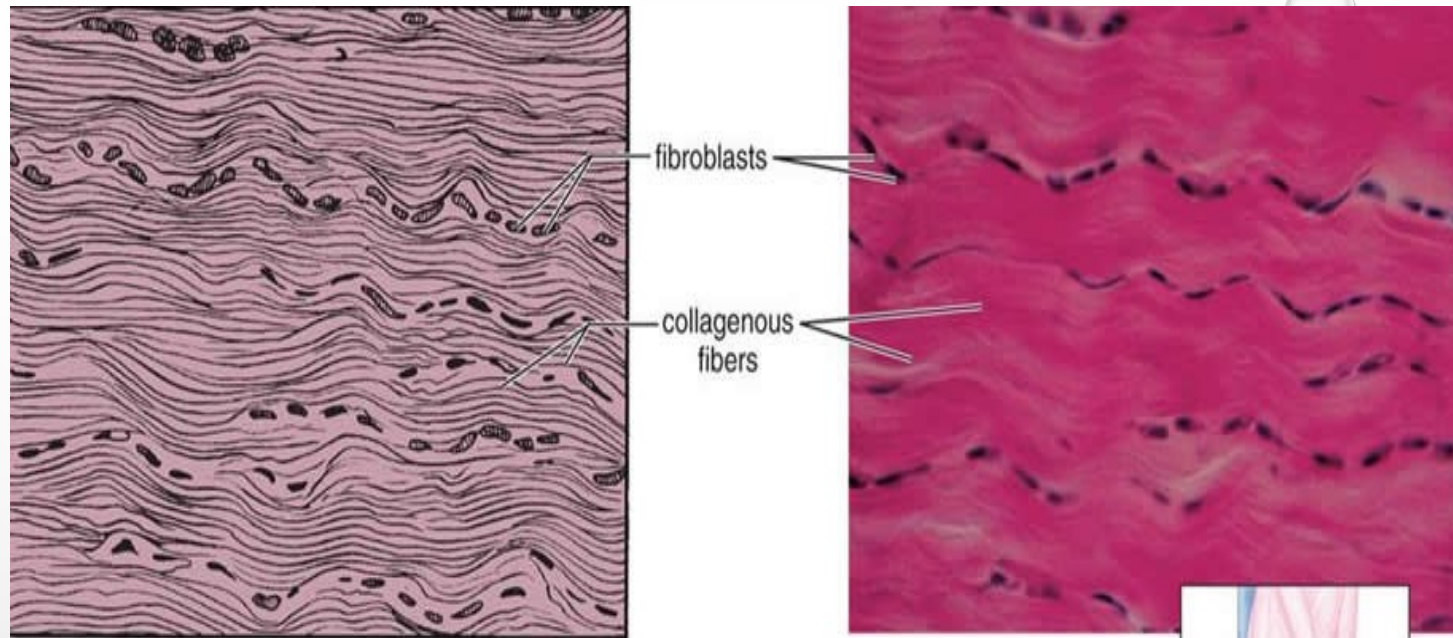
# Dense Connective Tissue

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

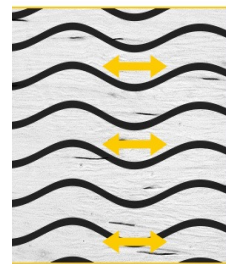
- a. Dense regular connective tissue  
Tendons and ligaments
  
  - b. Dense irregular connective tissue  
Dermis of skin
- 

# Dense Regular Connective Tissue

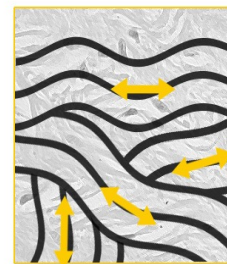
- Consists of bundles of collagen fibers and fibroblasts.
- Forms tendons, ligaments.
- Function = provide strong attachment between various structures.



Direction of Dense Connective Tissue Fibers



Dense Regular



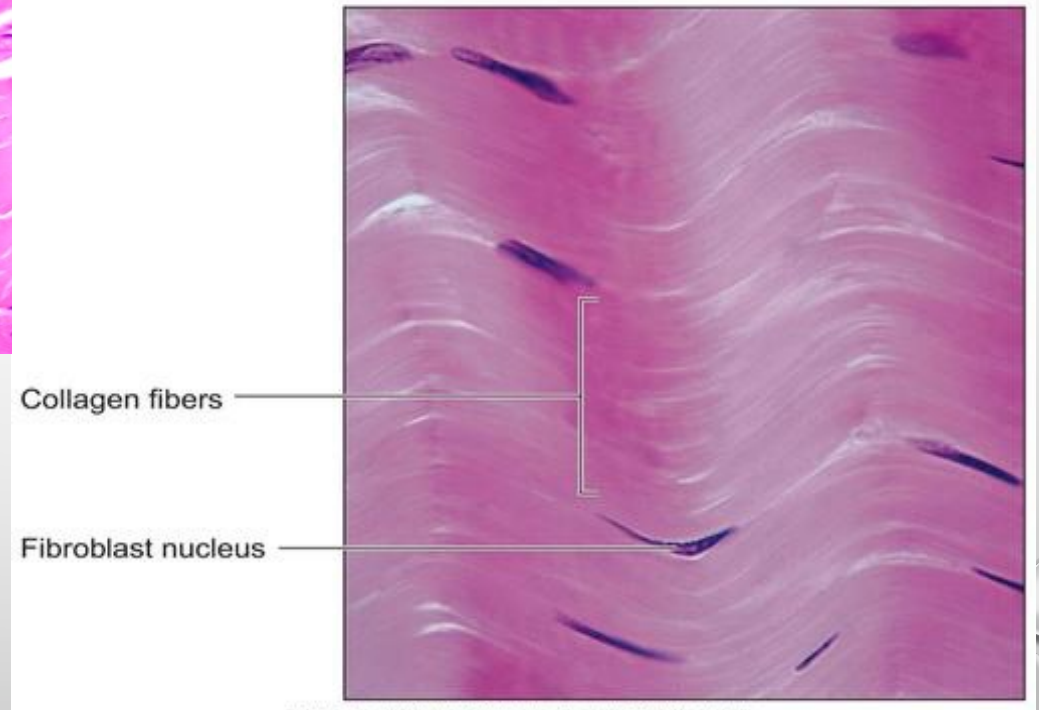
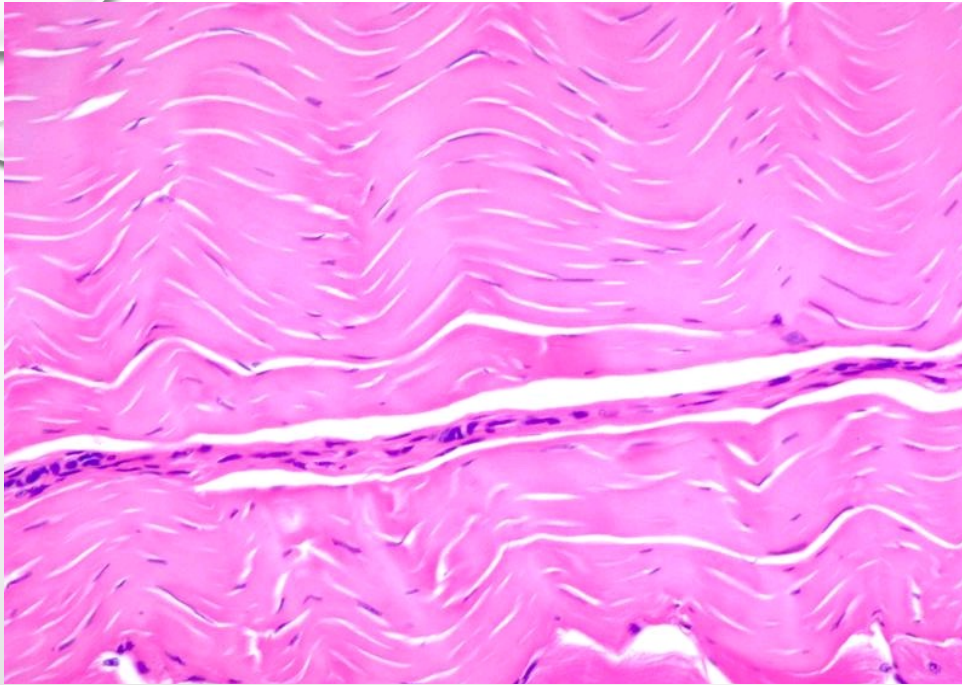
Dense Irregular

Connective Tissue

Tendons; ligaments

binds organs together





Collagen fibers

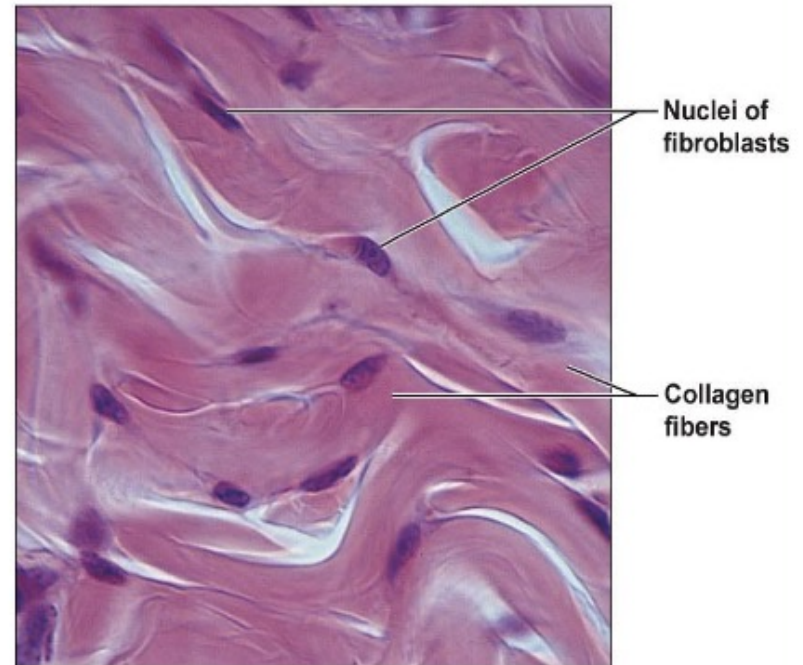
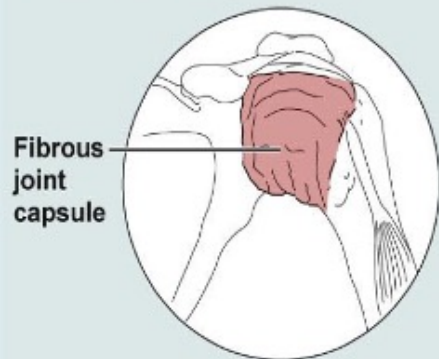
Fibroblast nucleus

# Dense Irregular Connective Tissue

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

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

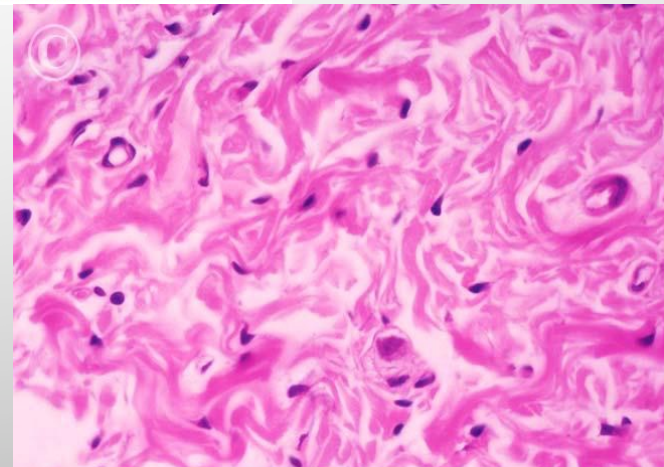
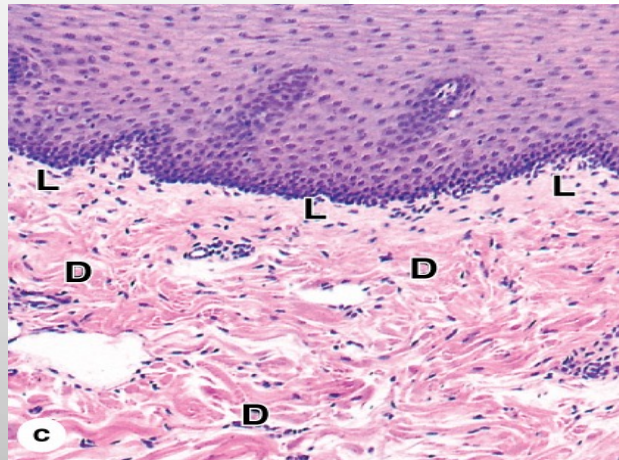
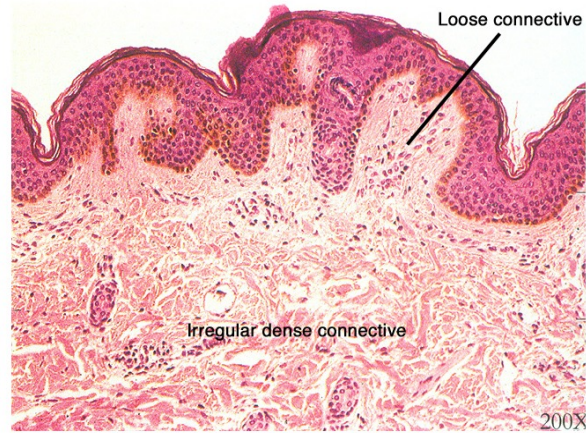
**Location:** Fibrous capsules of organs and of joints; dermis of the skin; submucosa of digestive tract.



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

# Dense Irregular CT

- Consists Of Randomly-arranged Collagen Fibers And A Few Fibroblasts.
- Found In Dermis Of Skin
- Function = Provide Strength



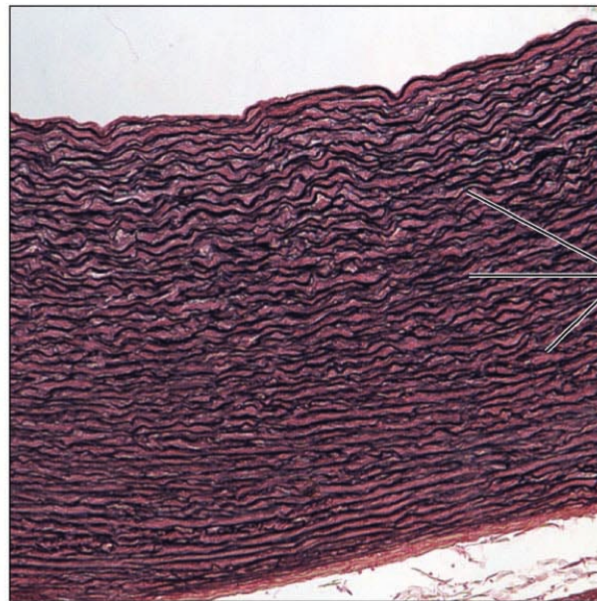
# Elastic Connective Tissue

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

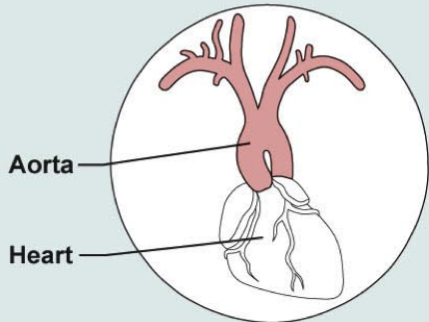
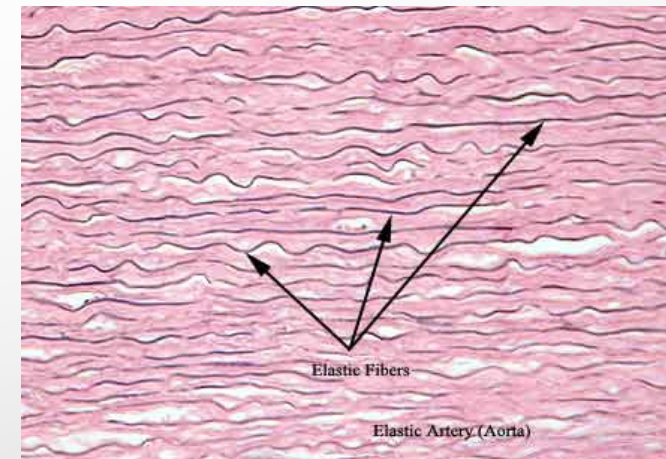
**Description:** Dense regular connective tissue containing a high proportion of elastic fibers.

**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.



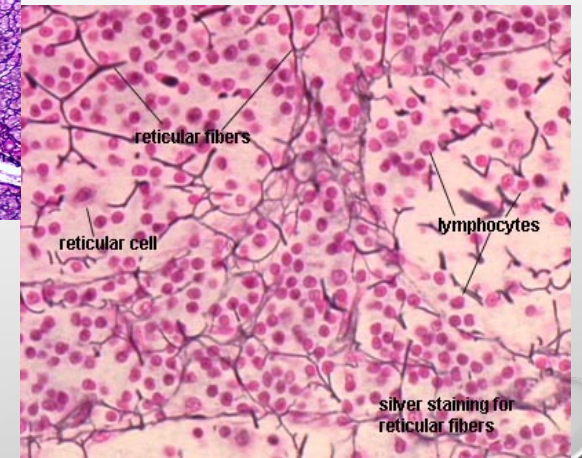
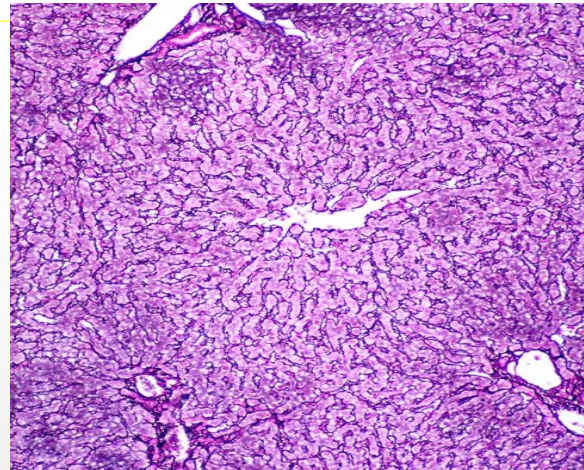
**Photomicrograph:** Elastic connective tissue in the wall of the aorta (85 $\times$ ).





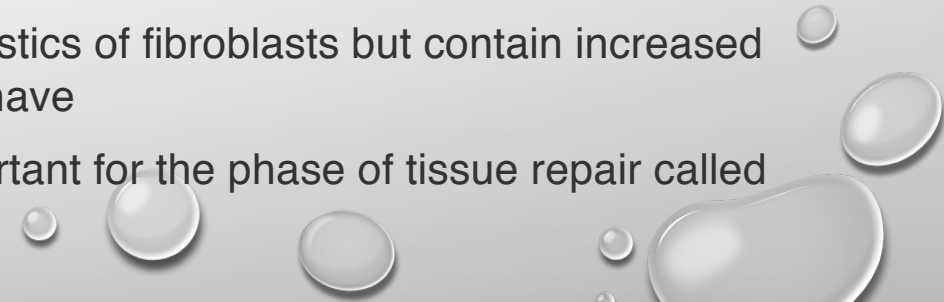
# RETICULAR CT

- 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

- The regenerative capacity of connective tissue is clearly observed in organs damaged by ischemia, inflammation, or traumatic injury.
  - Spaces left after such injuries, especially in tissues whose cells divide poorly or not at all (eg, cardiac muscle), are filled by connective tissue, forming dense irregular scar tissue.
  - The healing of surgical incisions and other wounds depends on the reparative capacity of connective tissue, particularly on activity and growth of fibroblasts.
  - In some rapidly closing wounds, a cell called the myofibroblast, with features of both fibroblasts and smooth muscle cells, is also observed.
  - These cells have most of the morphologic characteristics of fibroblasts but contain increased amounts of actin microfilaments and myosin and behave
  - Much like smooth muscle cells. Their activity is important for the phase of tissue repair called wound contraction.
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# 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