

# 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( found in the spaces between cells outside of blood vessels-part of ECF) 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(Matrix)

these cells (some is fixed and can always be seen in CT and others are seen depending on the physiological state of the tissues)

fibers differ in connective tissues by nature example: loose connective tissues have less amount of fibers

Ground substance → fillings between cells and fibers

Ground substance + Fibers = Matrix

# General Features

- Variable vascularity.

it's vascular but not all the time → for CT vascularity is reflected in regeneration unlike epithelium is Avascular with a good generation capacity → example on CT: bones are very well vascular while cartilage is Avascular → any damage in the bones can be healed immediately unlike cartilage

- Variable regenerative power. Depends on vascularity

# Functions

1. Structural framework for the body. → bones, and associated cartilage
2. Transportation of fluids and dissolved substances → blood
3. Protection of delicate organs. → Gland and kidney surrounded by capsule
4. Supports, surrounds, and connects other tissues. → like ligaments and fascia
5. Storage of energy in the form of lipids. → (adipose tissues)
6. Defend the body against microorganisms. → White blood cell

# 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 a few amount of cytoplasm**---- with their scant cytoplasm extended as two or more thin cytoplasmic processes
- The location and amount of such cells depend on the stage of the embryo

# Origin

All the types of connective tissue arise from mesenchyme(with different differentiation pathways)

Application :

Mesenchyme cells are used frequently in stem cell applications and (stemness: the ability to differentiate to something more advanced )  
Embryo → comes from fertilized ovum and gives rise to many cells which differentiate to create more specialized cells

**More differentiation=more specialized**

Until it reaches its final differentiation which won't give rise to new cells → example: bone cells

*The paragraph from the textbook on stem cells :  
Medical application page 96*

Some cells in mesenchyme are multipotent stem cells potentially useful in regenerative medicine after grafting to replace damaged tissue in certain patients. Mesenchyme-like cells remain present in some adult connective tissues, including that of tooth pulp and some adipose tissue, and are being investigated as possible sources of stem cells for therapeutic repair and organ regeneration.

**Note: adipose tissues are used because they are rich in fat which causes the least complications when used in such applications**

# Components

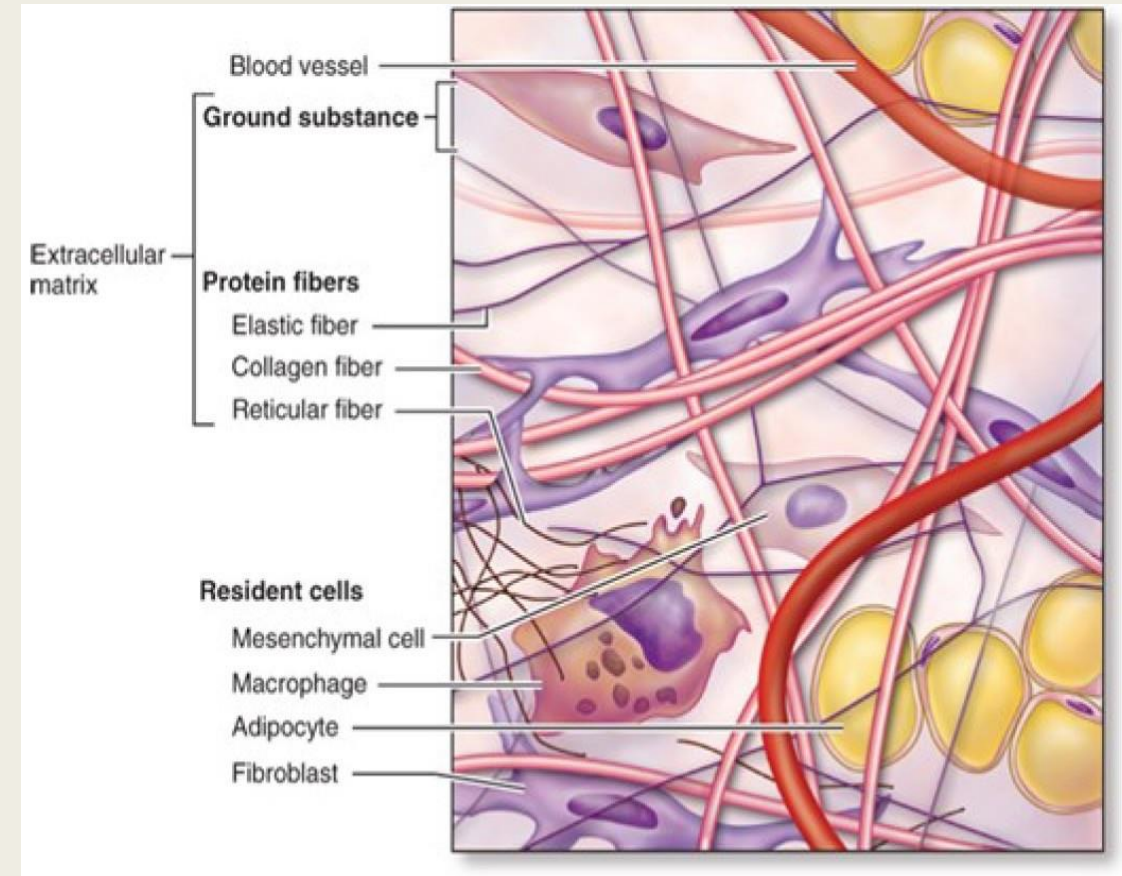
- Cells
- Fibers
- Ground substance

Matrix → significantly differs between different types of CT

## Ground substance

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

It differ bas on the type of connective tissues



It's the mother of connective tissue which means this cell is the one in charge of synthesizing and secreting fibers and ground substance and is present in all types of connective tissues

# Cells of Connective Tissue

- Fibroblast
- Mast cell
- Macrophage
- Plasma cell
- Adipocyte

Those are the one that we usually see in connective tissue

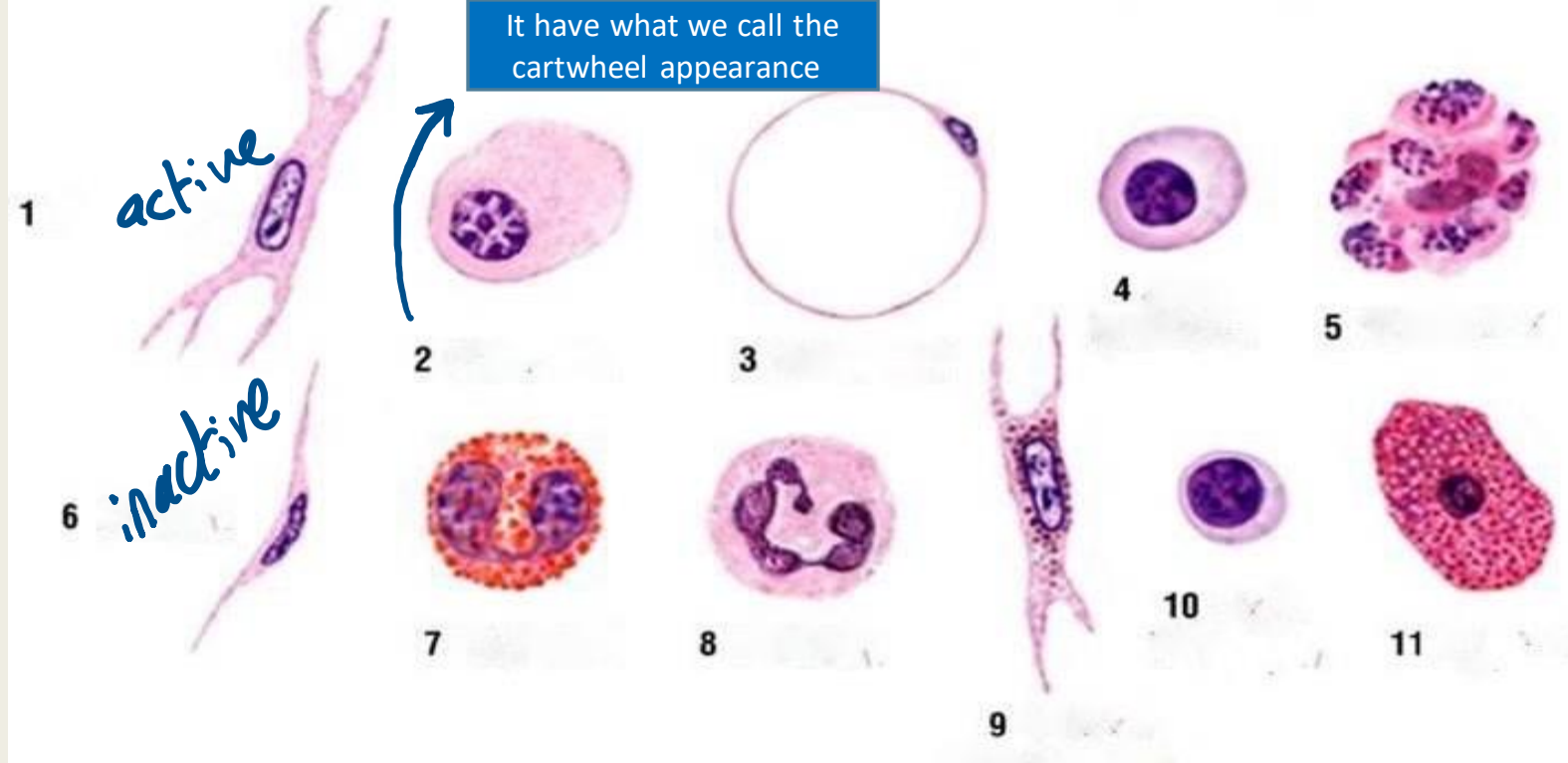
## White blood cells

- Neutrophil
- Eosinophil
- Basophil
- Lymphocyte
- Monocyte

Those are the one that we usually see in case of that we have infection or an inflammation ( which mean there's an immune reaction in the tissue)

When you are stung the antigens in the saliva of insthey will elicit this immune reaction so you will note that there is redness and swelling, this is the work of mast cell

How can we recognize active form from in active form cells?  
By the size of the nucleus and the amount of cytoplasm and the amount of processes (يلي) processes  
بتكون طالعاه من الخليه



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

Relatively large in comparison to other types of white blood cells

# 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                                                                                                                                  |

It's first line responders, it's emergency cell

First line responders are seen if we have infections and will take over the fight until more specialized cells appear

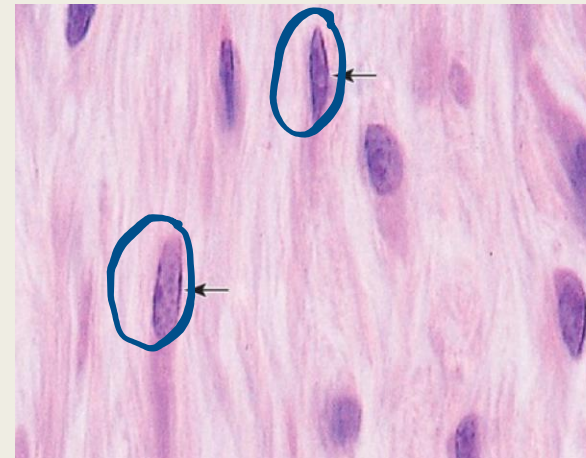
# Fibroblast

- 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.
  - Important for regeneration and repair
- why it's present in all CT

برضو لاحظوا  
the amount of  
cytoplasm  
around the  
nucleus

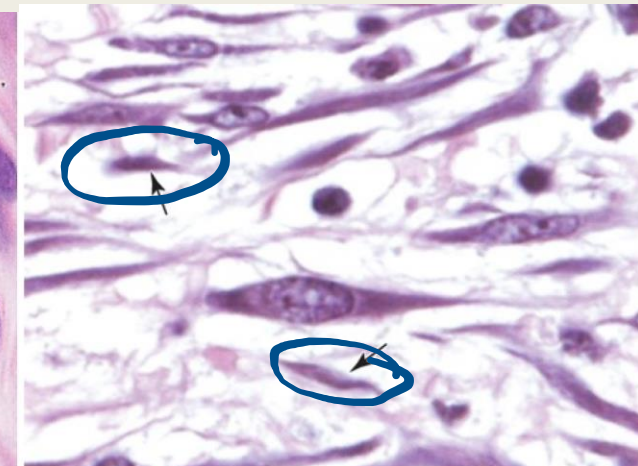
Euchromatic when the genetic material is free, accessible so we can easily get copies and messengers RNA which will go to the cytoplasm so we can translate this into proteins

## Fibroblast



Heterochromatic, the chromatin will clump on itself and it will be highly folded versus the chromatin in the fibroblast. transcriptionally silent

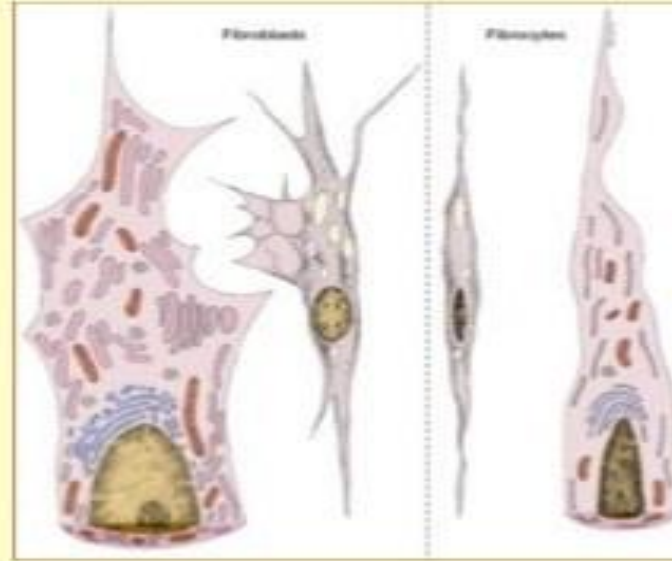
## Fibrocyte



## Fibroblasts \_ Fibrocytes

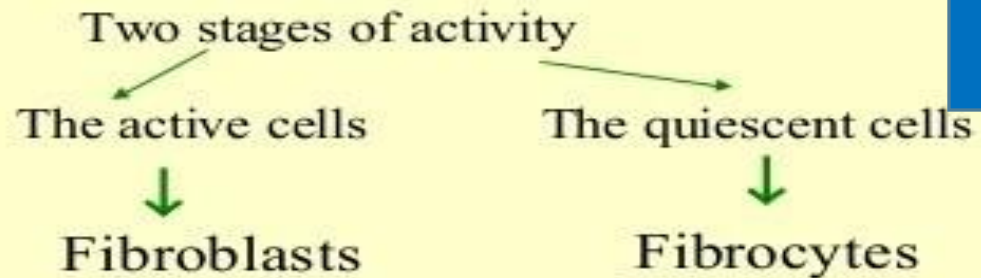
### ✓ Fibroblasts

- 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



Fibroblast has many processes as it can actively move between the other elements of the tissues

Fibrocytes can reverse into the active form(fibroblast) if needed → it's not a dead cell but a dormant sleeping cell

This also applies to bone and cartilage :  
Bone : osteoblast and osteocyte  
Cartilage : Chondroblasts and chondrocyte

Rich in RER as it's in charge of synthesizing and releasing proteins

# Macrophage

When they are in the blood they called monocytes ,  
when they are in connective tissue they called  
macrophages and when it leaves it acquire new  
features(different shape and function)

Those are white blood cells but they have left the blood and  
resided somewhere else ( موجودين تقريبا في كل مكان بجسمنا )

لما تنتقل الخلية monocytes من الدم وتروح لهاي الأماكن رح يصير لها بعض  
التغيرات رح تظل immune related function ولكن بطريقة مختلفه



- 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.

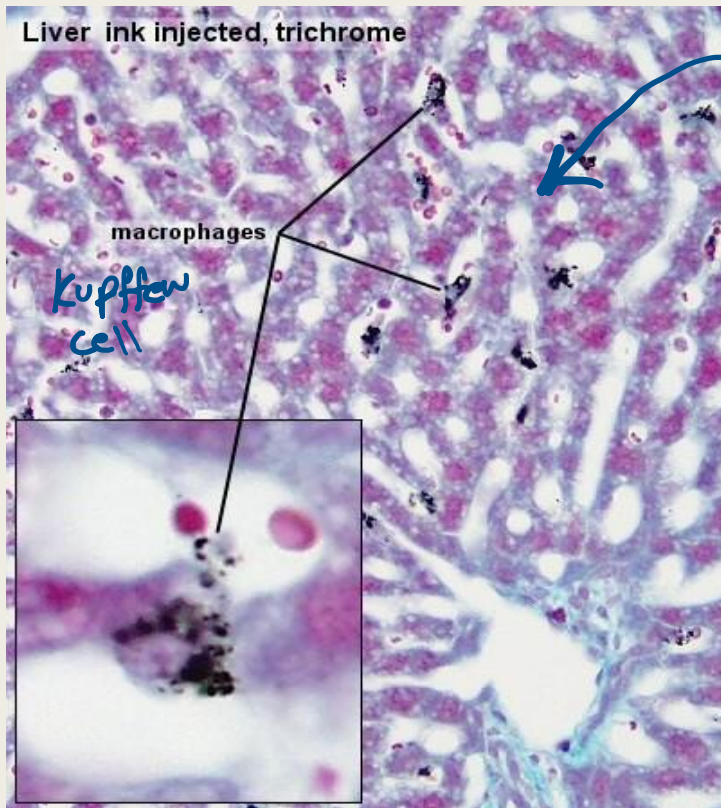
# Mononuclear phagocyte system → precursor is monocyte

| 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                                                                                                                |

Bones are in a constant state of remodeling

not immune related function , in this process we help liberate calcium and pump it back into the blood so we can restore the calcium level

Will see many nuclei inside the cytoplasm



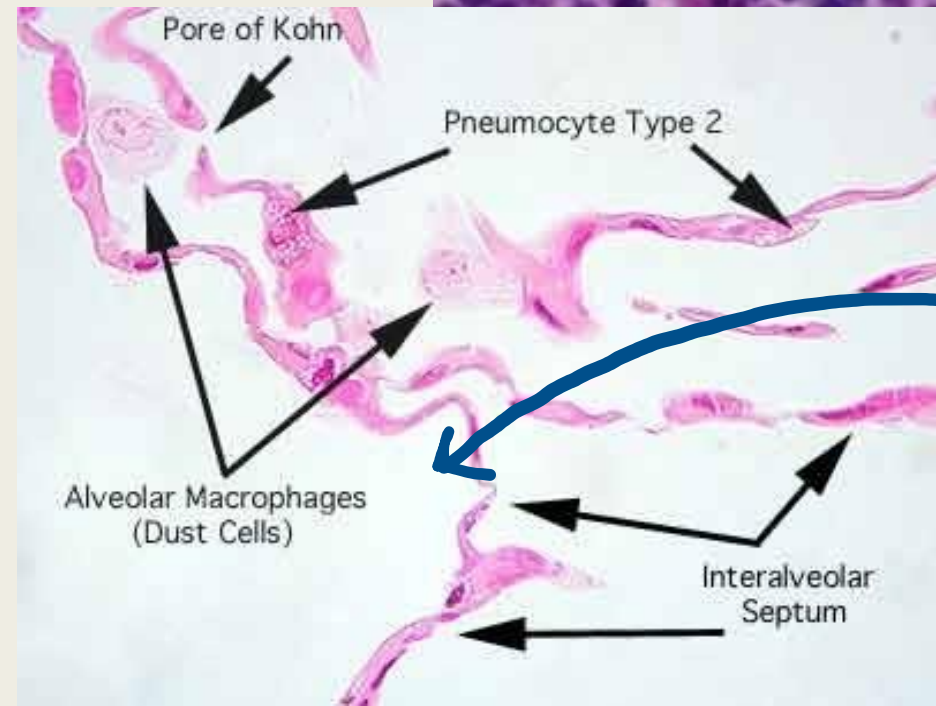
When anything runs in the blood and needs to be picked up, they will pick it and store it

H&E - subcapsular sinus

Relatively large



كيف قدرنا نلاقي هذه الخلايا وعرفنا مواقعهم  
We give an animal (mouse) ink ?  
and the blood will circulate , the blood will reach the liver where there is macrophages, and they will recognize the ink as foreign material so they will engulf it and bring it inside



We can see inside the lungs ( they engulf the particles that we inhale) to clean the interior of the lungs

# Mast Cell

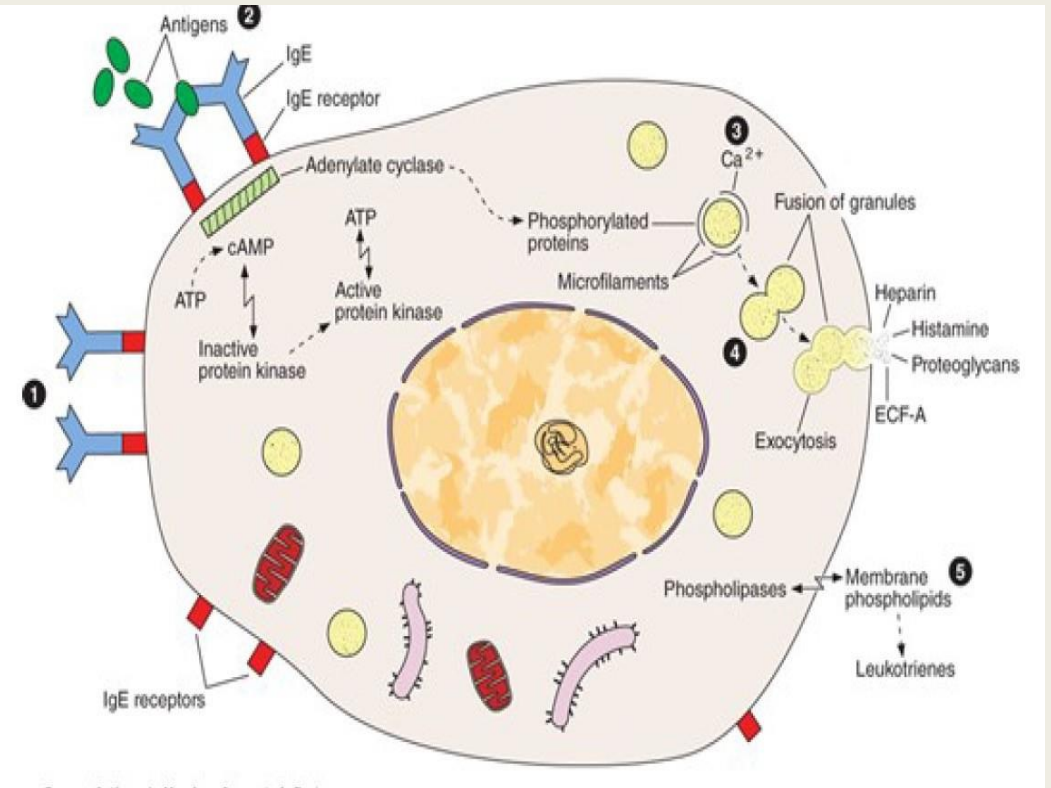
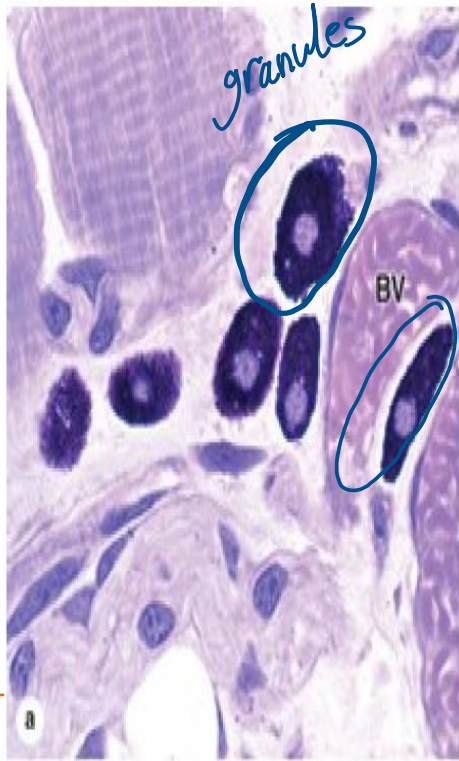
Resident cells → seen regularly in CT and vary in amount → more mast cells means that there is an immune reaction

- 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.

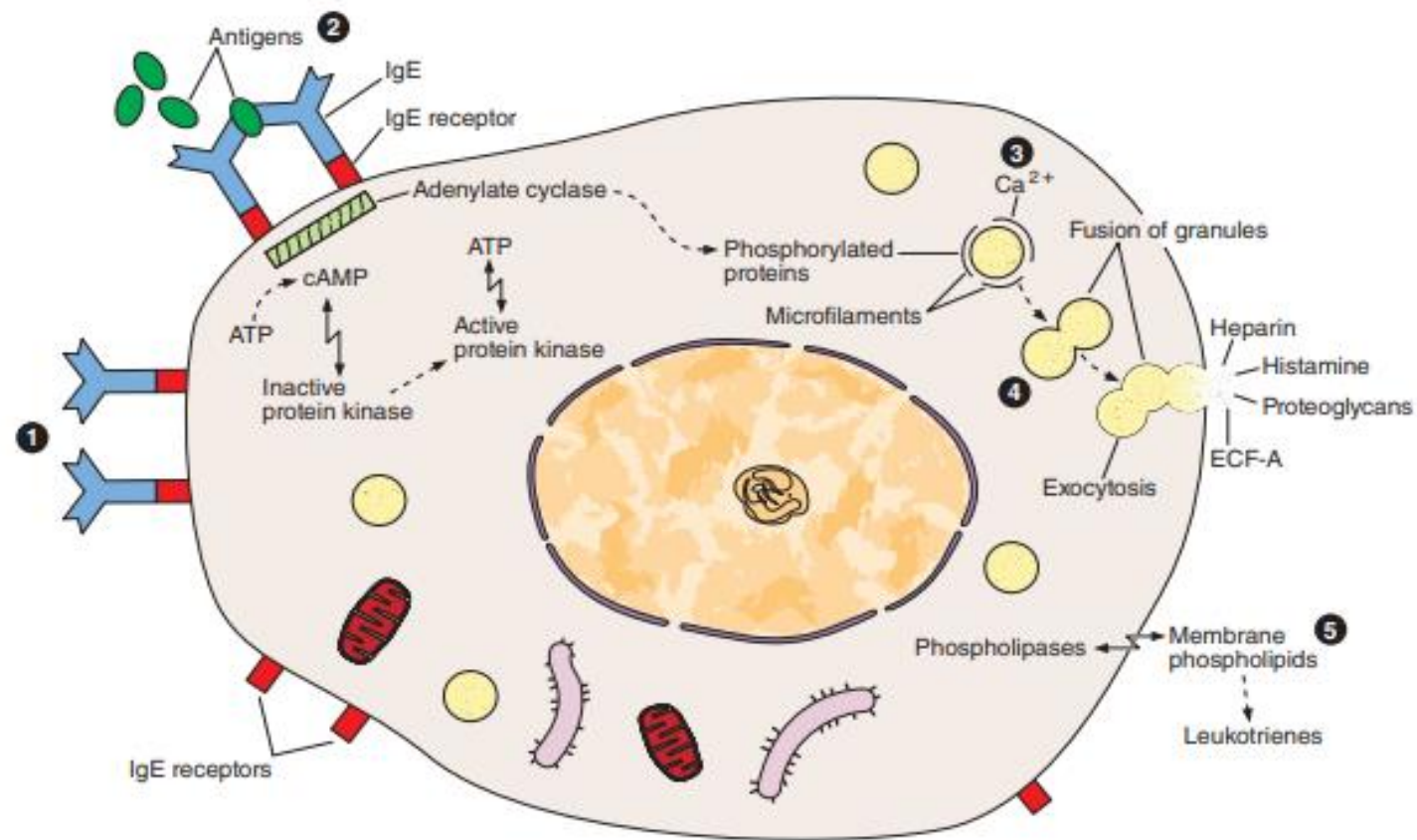
Blood vessels they are usually not permeable, when we have lots of histamine that make the capillaries more leaky, so when it's bigger the blood that's coming will be more — more red in the region — the temperature will rise — the size of stung will be bigger

# Mast cell

TEM



Toluidine blue → cells are filled with granules containing bioactive material and this stain recognises these granules



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 Cell

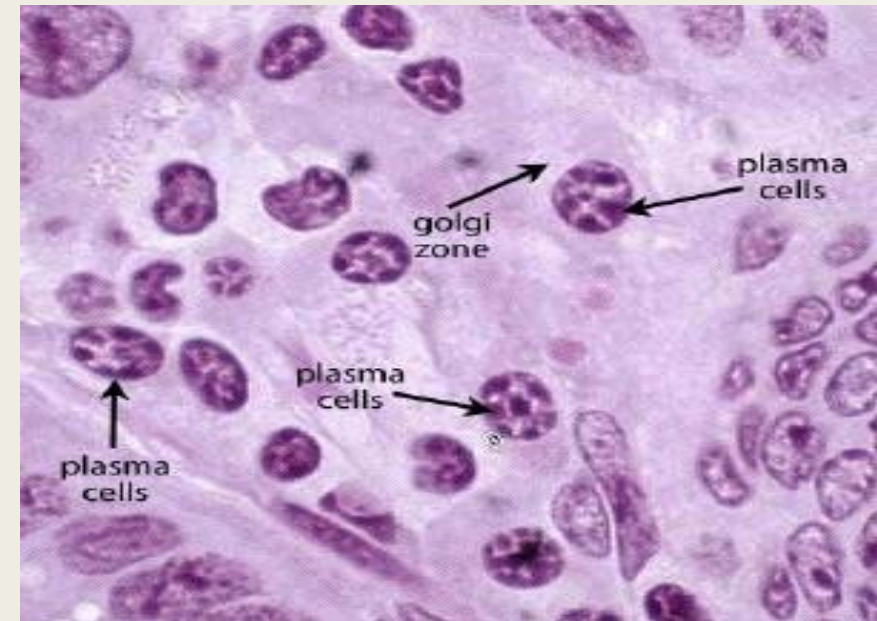
In the blood we have cell that's called lymphocytes and they are two major family: B lymphocytes and T lymphocytes

- 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

When they encounter a pathogen part of them eventually will store code for this pathogen will give us plasma cell and another one memory cell

The base of immunization, if we encounter this pathogen in the future They will alert the human Body and then they can fight that antigen quite easily

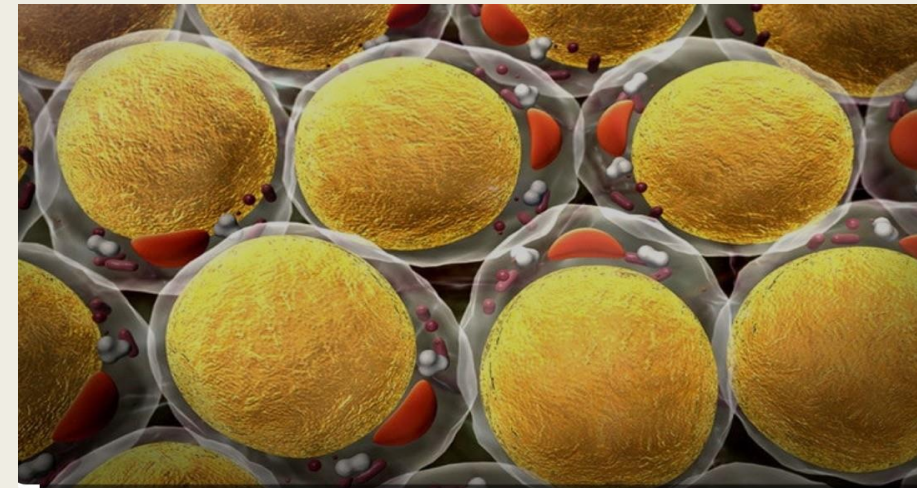
مقارنة مع الام ( B lymphocyte it's small ) طيب ليش ال plasma كبيره ؟  
because those are antibody secreting so the need golgi , ribosomes so I need a good amount of cytoplasm



# Adipose Cells

Usually they are found in the glands

- 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.
- **Appear as rings with empty white space because after undergoing tissue processing fat will be dissolved leaving an empty white space with flattened nuclei**



# Connective tissue Fibers/Collagen

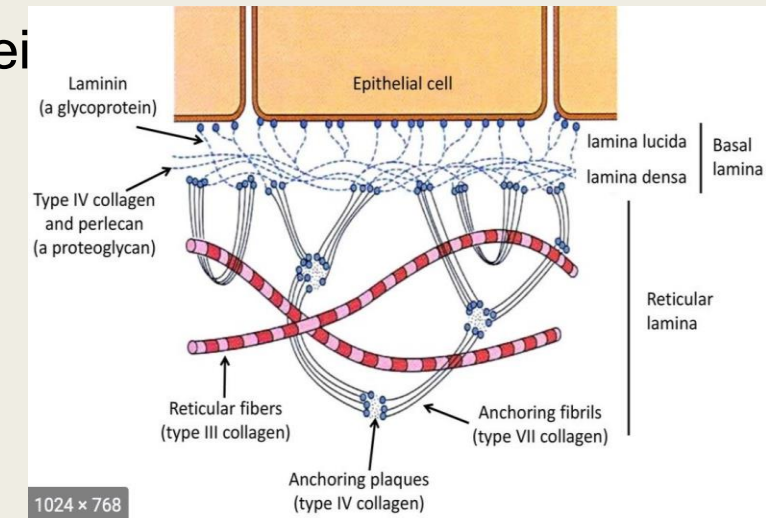
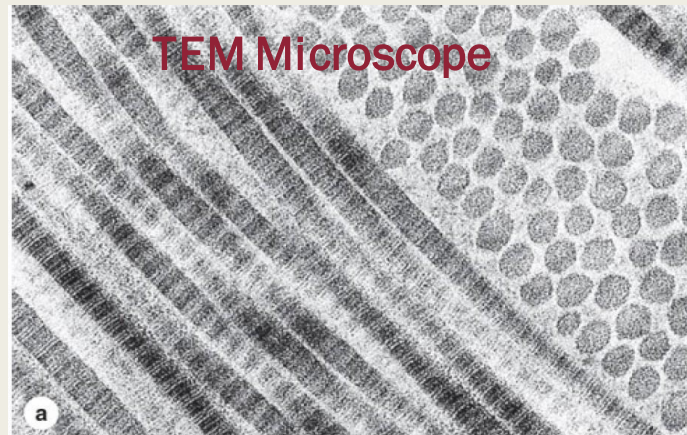
- Form various extracellular fibers, sheets, and networks.
- Extremely strong and resistant to normal shearing and tearing forces. Which make it a great candidate for structure like ligaments which hold bones together
- Collagen is a key element of all connective tissues, as well as epithelial basement 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.
- offers different functions and features and each is special on its own

# Collagen types

28 types are classified into 3 types

- **Fibrillar collagens**, notably collagen types I, II, and III. Form structures such as tendons, organ capsules, and dermis . extremely strong in structural tendons and capsules where protection and resistance is offered
- **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. In the basal lamina support epithelium
- **Linking/anchoring** collagens are short. Smaller can link different proteins type 7 and 9

Shows cross section and longitudinally image of fibers  
Dark and light regions  
Striations in collagen fibers

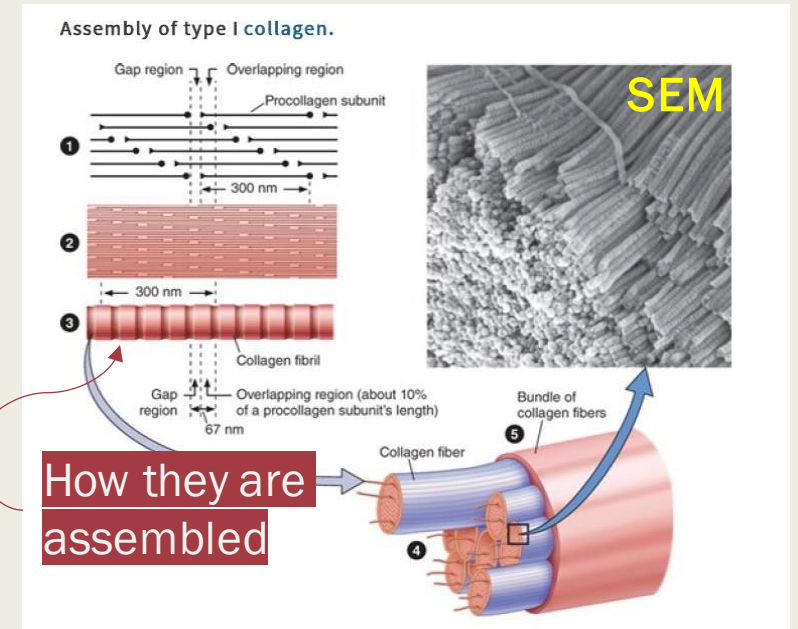


# Collagen Assembly

1. Rodlike triple-helix collagen molecules, each 300-nm long, self-assemble in a highly organized, lengthwise arrangement of overlapping regions. **procollagen** are tiny subunits and self assemble to longer structures called collagen fibrils and there is a smaller gap between them

2. The regular, overlapping arrangement of subunits continues as large collagen fibrils are assembled. **lighter** region is due to overlapping and can only be seen through an **electron microscope**

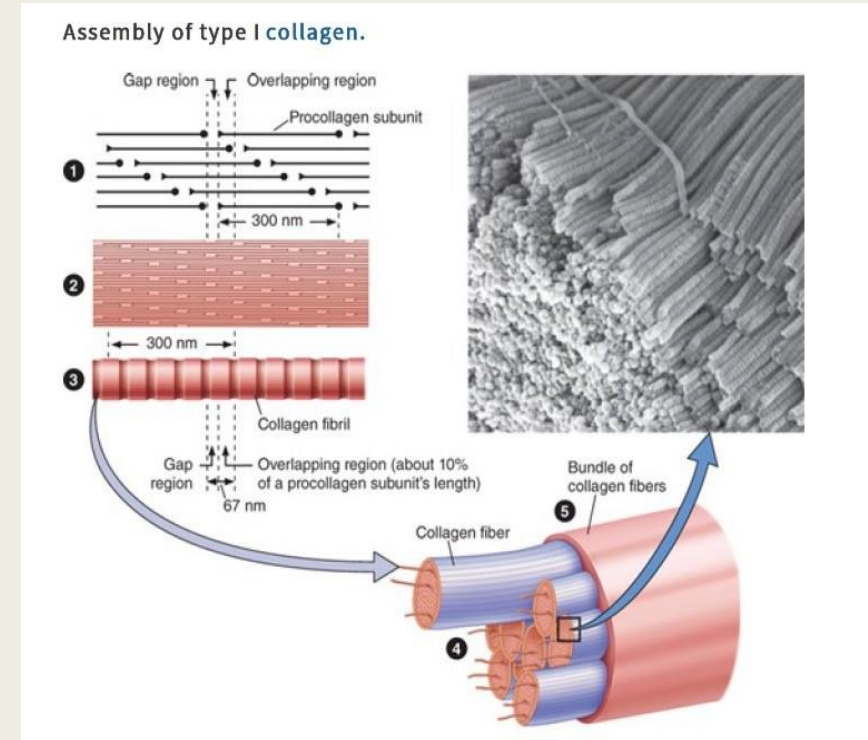
3. Further assembly to larger structure fibers → **further** assembled to mega structure called collagen bundles from fibers (can be seen in tendons and dermis)



Collagen type I from tiny units → bundles present in tendons capsules and dermis that support the epidermis

# Collagen Assembly

1. Units fibrils fibers bundles
2. Can't be visualized through light microscope
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

Collagen type 3

- Found in delicate(organs)→(endocrine glands ,bone marrow and liver) connective tissue of many organs, notably in the immune system. best location to study it→ liver--3D structure that can protect and house the liver cells→ which are called Hepatocytes
- 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.
- 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
- 1&2 can be stained with H&E and trichrome easily
- 3→Can't be visualized with H&E → must use silver salts →darkish fine lines under LM .PAS can be used because these fibers are rich with sugars→10% of their structure unlike other collagen types

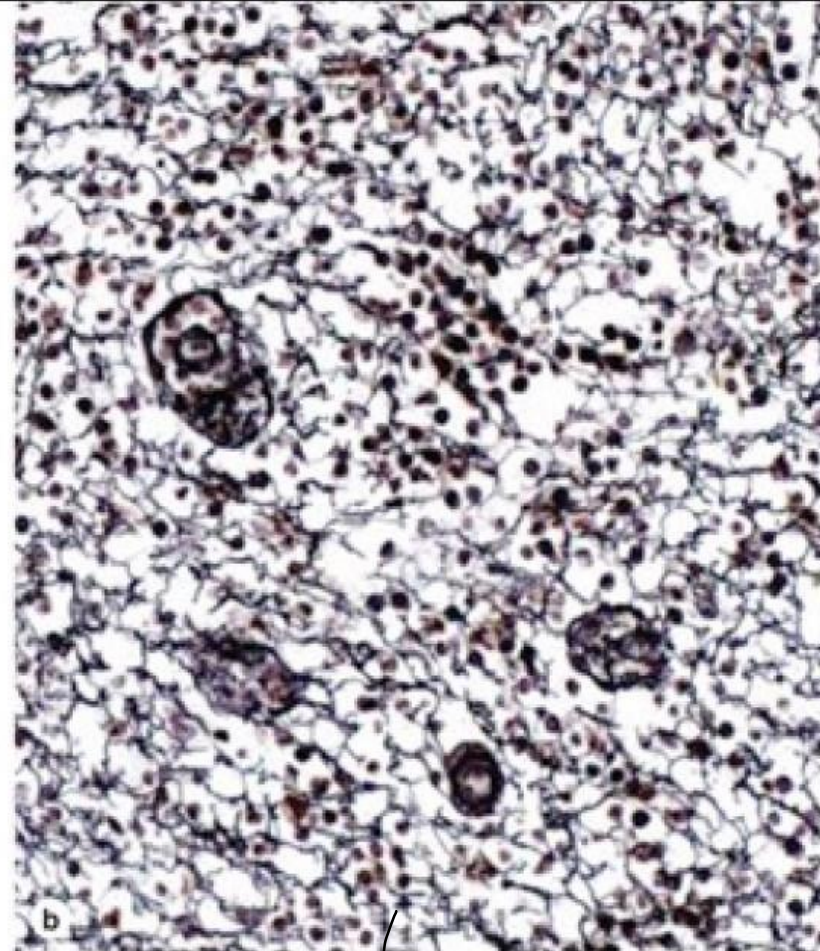
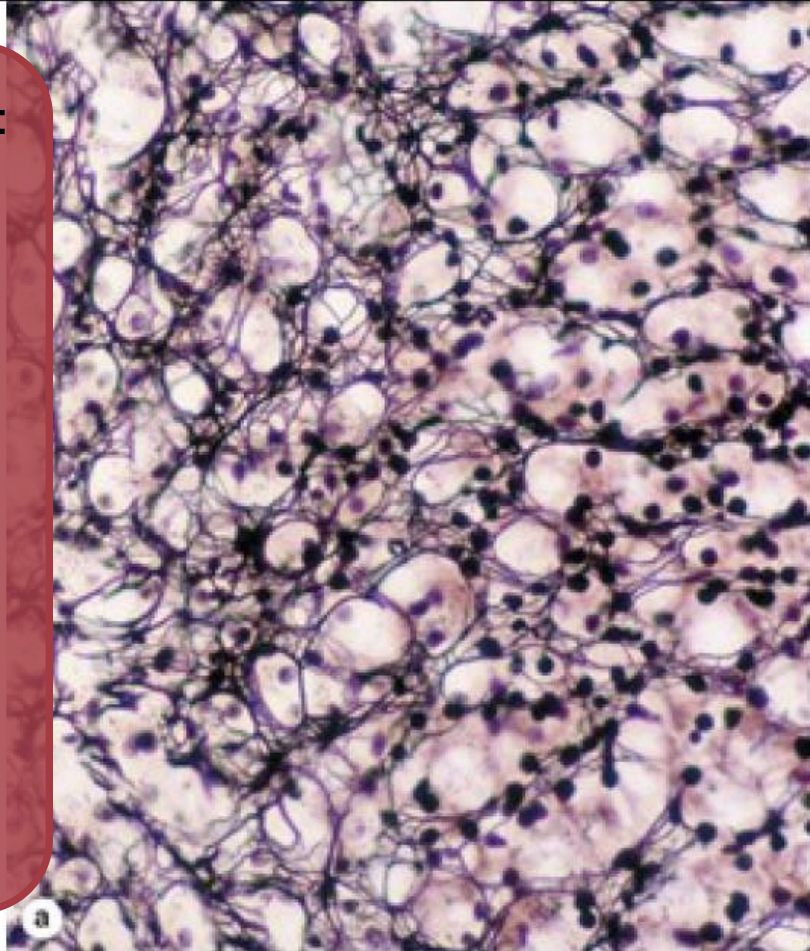
# Reticular Fibers

Lymph nodes rich with reticular fibers – silver stain

Silver salt stains :  
-Dark dots nuclei

-Fine blackish irregular structures → reticular fibers

-They create tiny compartments to support the interior delicate cells

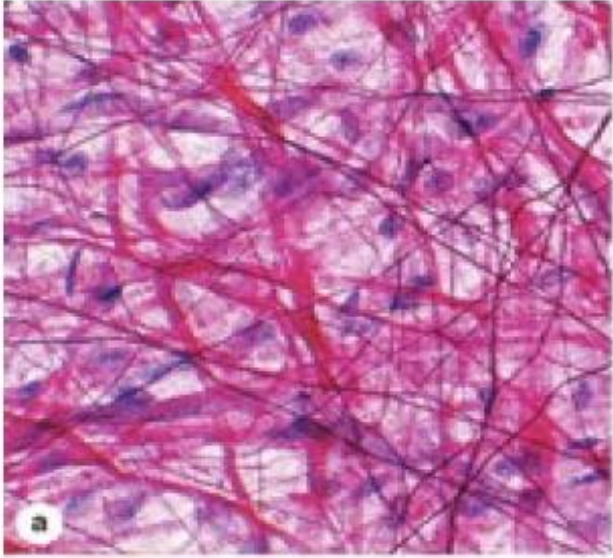


More magnified

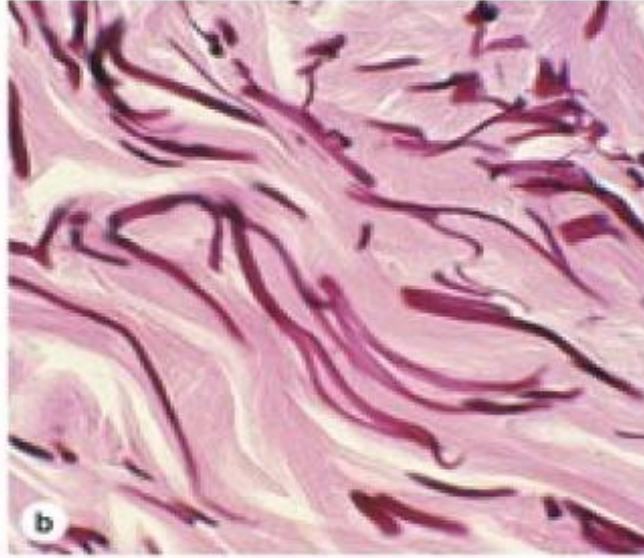
# Connective tissue Fibers/Elastic

- 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 → rely on them enable them to stretch to accommodate incoming blood from heart, 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. will give a maroon red color
- Dermis → second layer → skin undergoes a lot of stretching and pulling forces → present of elastic fibers is important and it's rich with collagen and elastic fibers
- Stain poorly with H&E unless there is a good amount of them.
- Unique → we can stretch them to a specific limit and they recall back to normal length and shape → recoil
- Seen in structures where stretching is needed such as lungs that increase their volume with inhaling

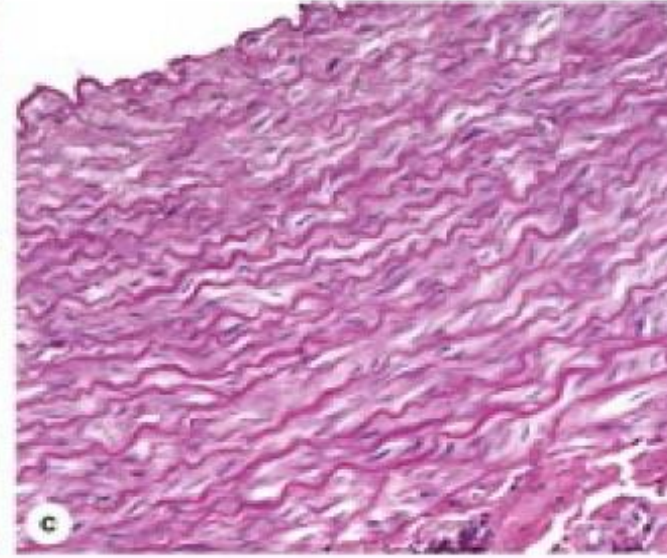
# Connective tissue Fibers/Elastic



A- Hematoxylin and orcein).



B-Aldehyde fuchsin).  
Can identify elastic fibers

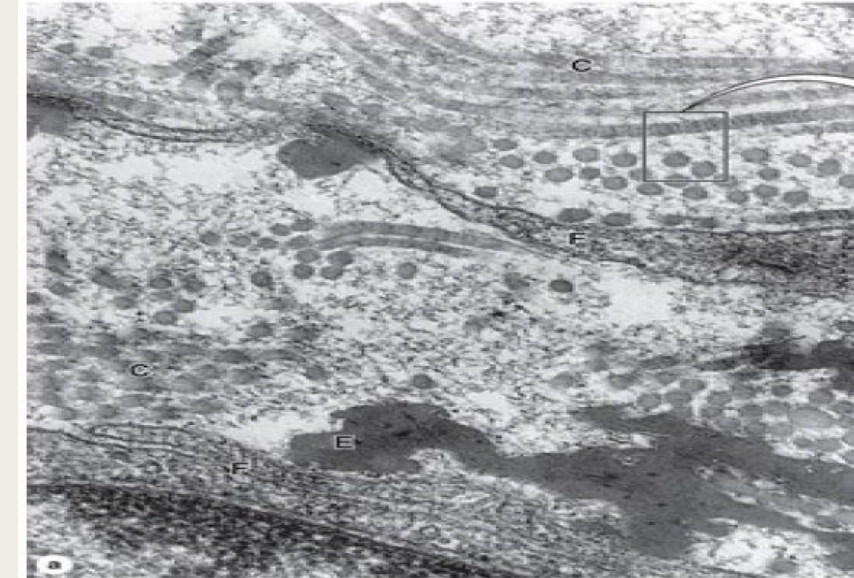
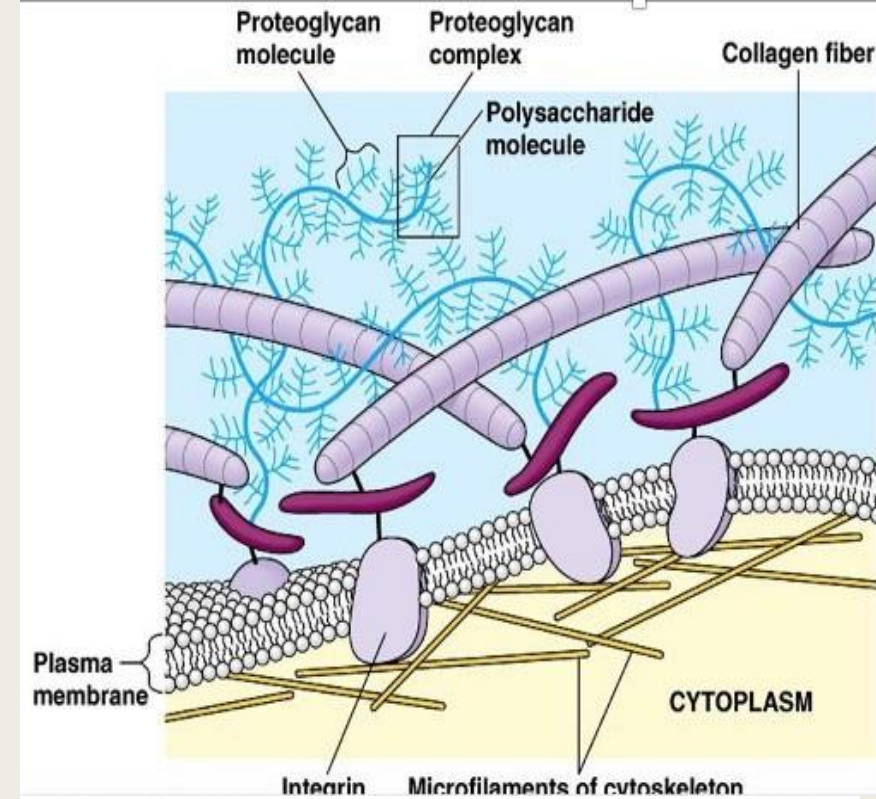


C- H&E

Part of the wall  
Wavy dark pinkish structures → elastic lamina  
Luckily good amount stacked together they show more color in contrast of collagen and smooth muscles

# 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.



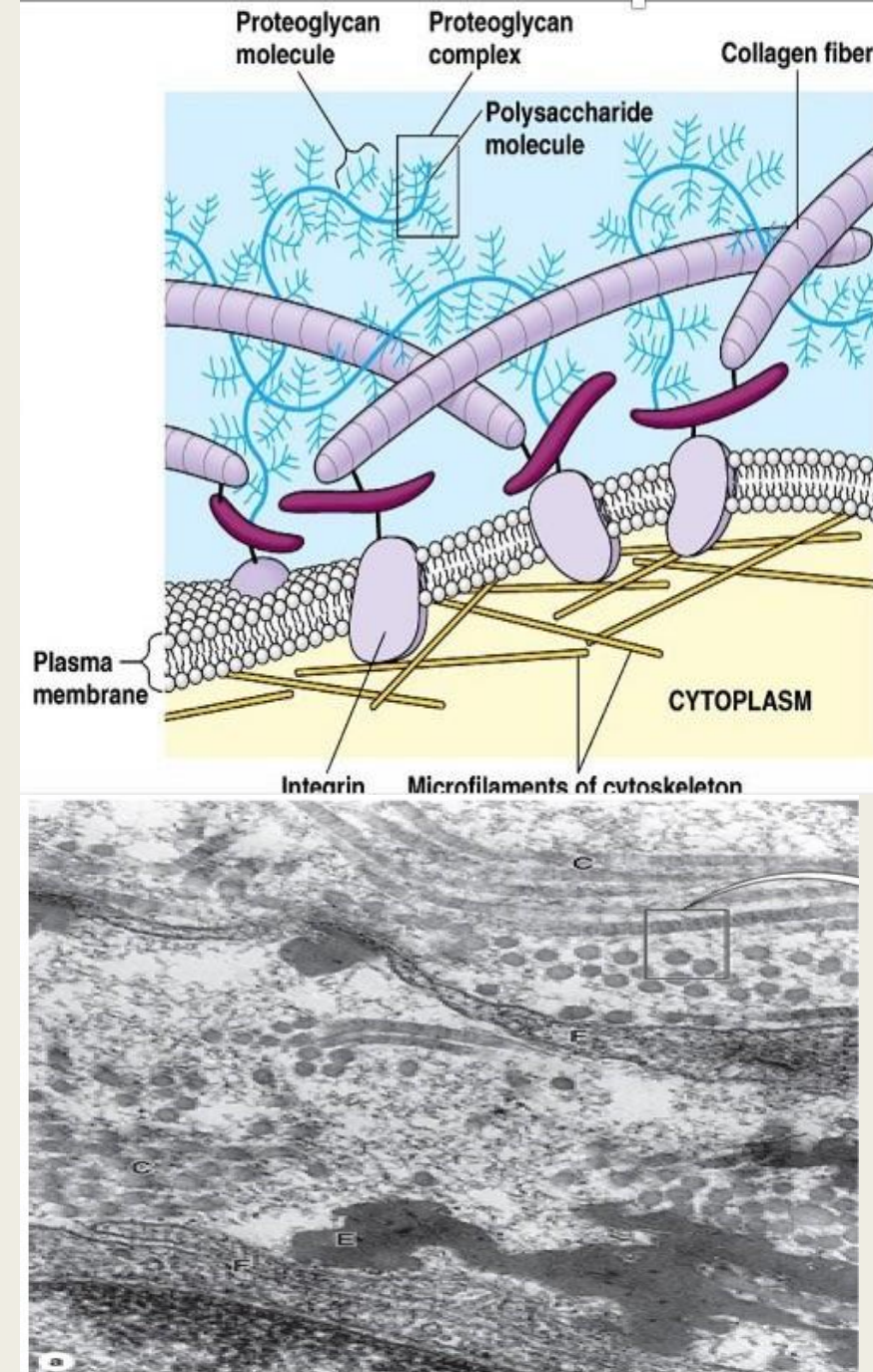
# Ground Substance

Filling between fibers and cells → a specific composition depending on type of connective tissue

Semi fluid → high hydration → rich with sulfate in some locations and negative charge carried on their molecules

lubrication in specific location such as umbilical cord → provide protection to blood vessels and allow diffusion → vascularization → facilitate diffusion of nutrients

Viscous → movement of microorganisms → Halts their ability to do more destruction



# 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). umbilical cord have a good amount of this acid → where nature of the anterior comes from

GAG → glucose and aminoglycans  
Depending on the type of sugar there will be different types of GAGs

# 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.
- Cartilage matrix is basophilic → stained with hematoxylin

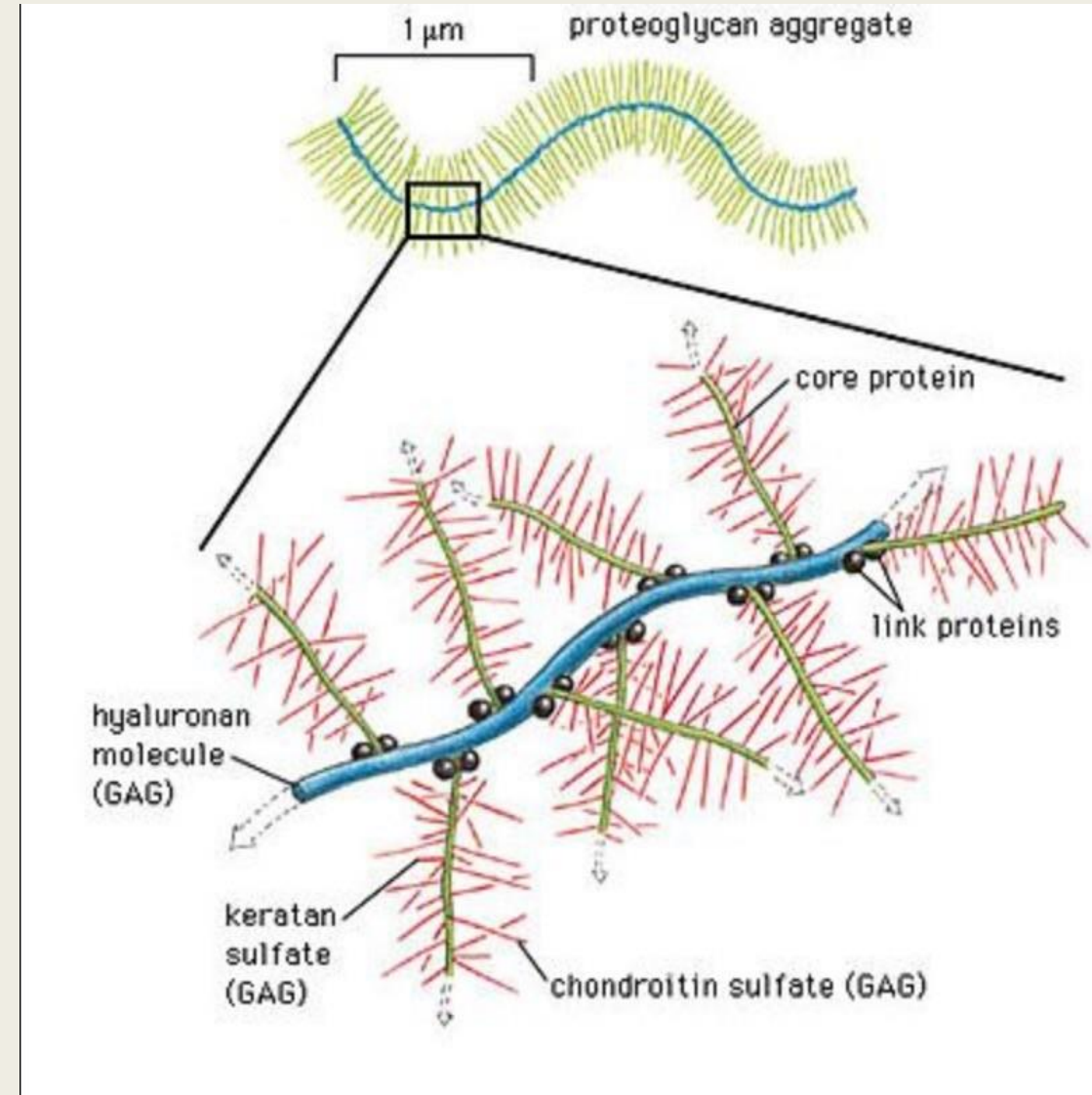
# GAGs

| 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                                                                      |

# GAGs that form proteoglycans

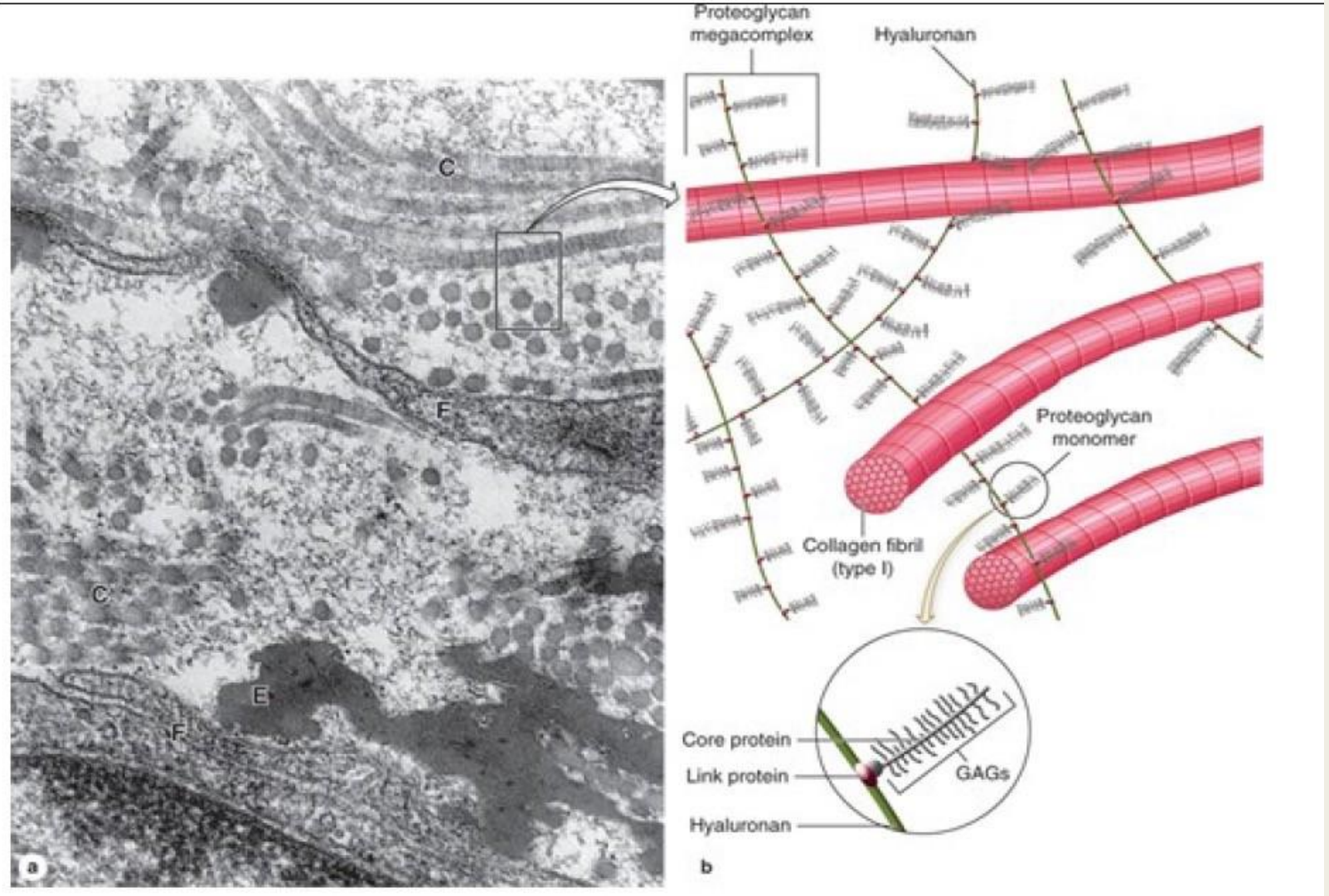
- Hyaluronic acid
- Chondroitin 4-sulfate
- Chondroitin 6-sulfate
- Dermatan sulfate
- Heparan sulfate
- Heparin
- Keratan sulfate

Diagram → is a proteoglycan aggregate  
After expanding it :  
Hyaluronic → backbone for smaller structures  
And these smaller structures have a core protein  
Which binds to many GAGs  
Type of GAGs → depend on the type of tissue  
Cartilage → Chondroitin sulfate  
Core protein is linked to link protein



## TEM

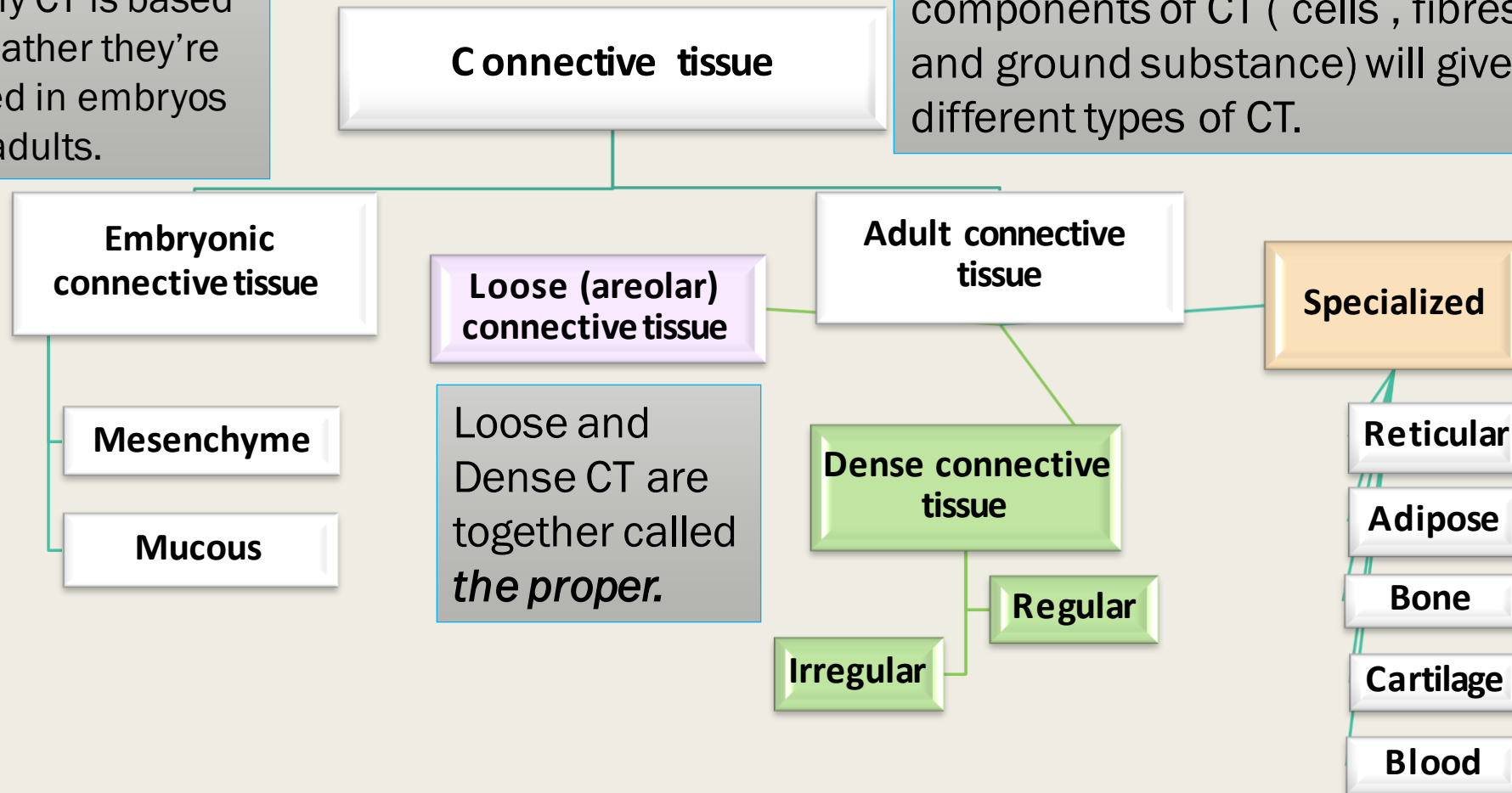
Rounded perfect structures  
are cross sectional  
collagen fibers Also  
longitudinal collagen fibers  
More irregular structure →  
elastic fibers  
More in the relaxed form  
would appear different  
flexed  
Tiny greyish → ground  
substance



# Classification Of Connective Tissue

The first factor to classify CT is based on whether they're located in embryos or in adults.

Different composition of the three components of CT ( cells , fibres and ground substance) will give us different types of CT.



The main component of Dense CT is fibres. It's divided into reg. and irreg. depending on the arrangement and the alignment of it's fibres.

# 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 |

Mesenchymal cells are undifferentiated in embryos , to differentiate in adults to fibroblasts, osteoblasts, chondroblasts , etc.

Mesenchyme is the source of various types of CT .  
It's presented in the early stages of embryos, distributed in the matrix that contain a little amount of fibres, a good amount of ground substance , a good amount of hyaluronan.

Mucoid is existed in the uterus and will be delivered with the born baby.

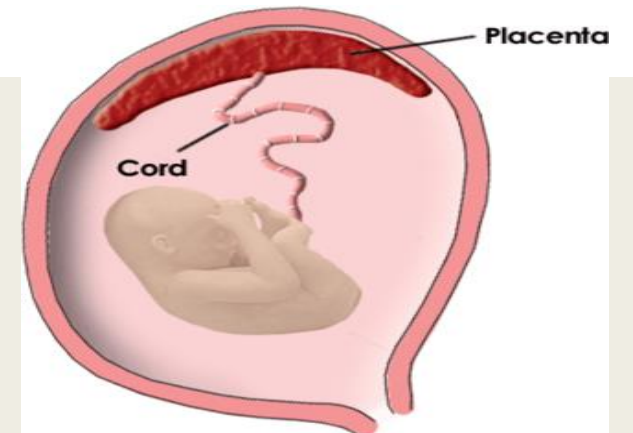
# Further information about the umbilical cord (mentioned in the lecture)

The umbilical cord is attached to the **placenta** of the mother, the placenta is a temporary organ that develops during pregnancy attached to the lining of the uterus.

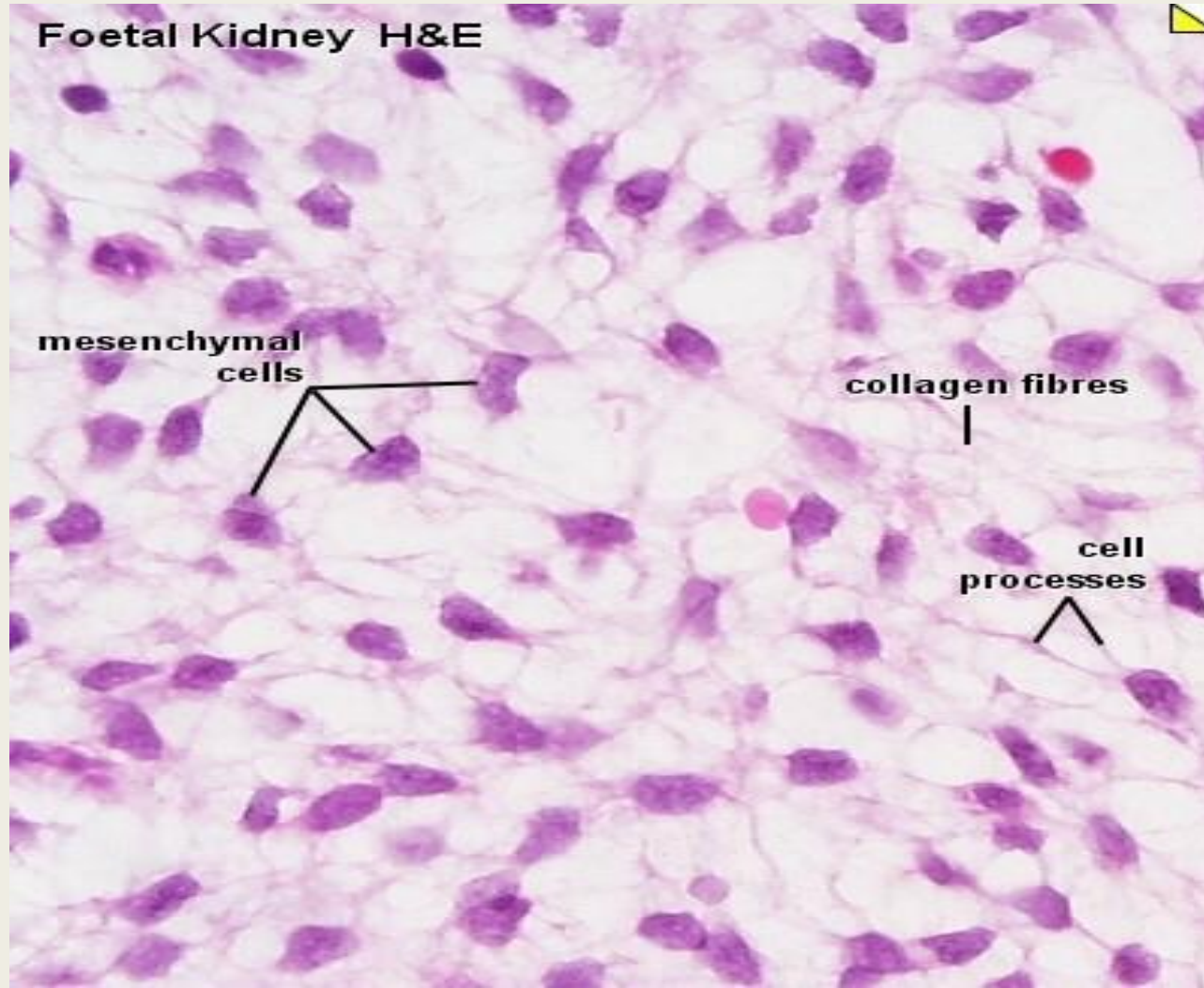
This placenta is where the embryo gets the nutrients and gases from the mother, and sends the waste products to the mother as well.

The umbilical cord contains a few number of stem cells, some fibroblasts, collagen fibres and ground substance.

After the born of the baby, we can extract the stem cells from the umbilical cord and store them for the baby , this is easier than extracting them from an adult person, using them for treatment which is in rise.

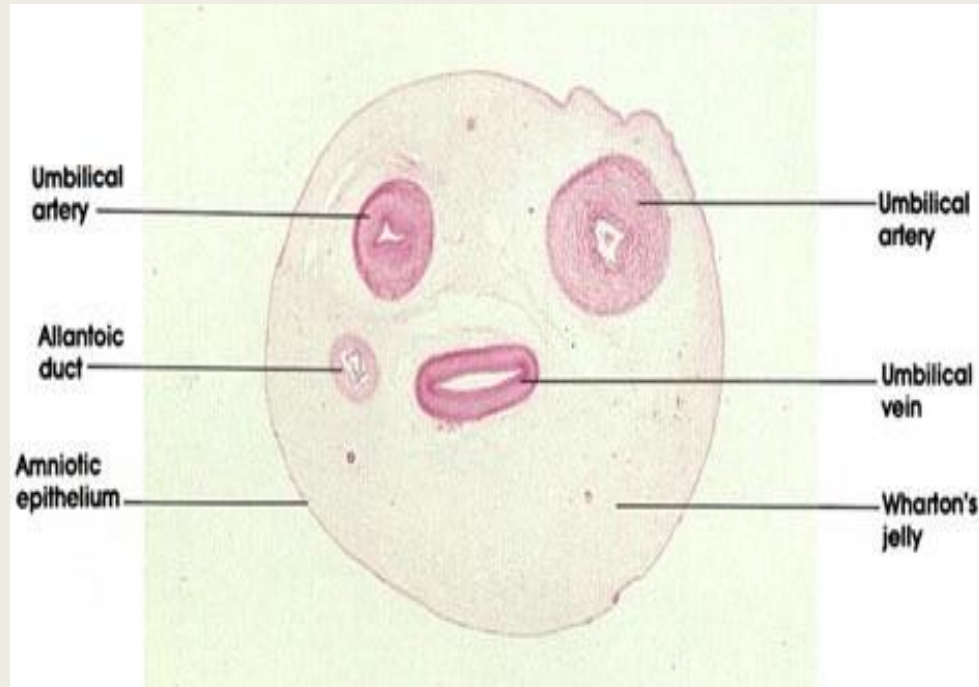


# Mesenchyme

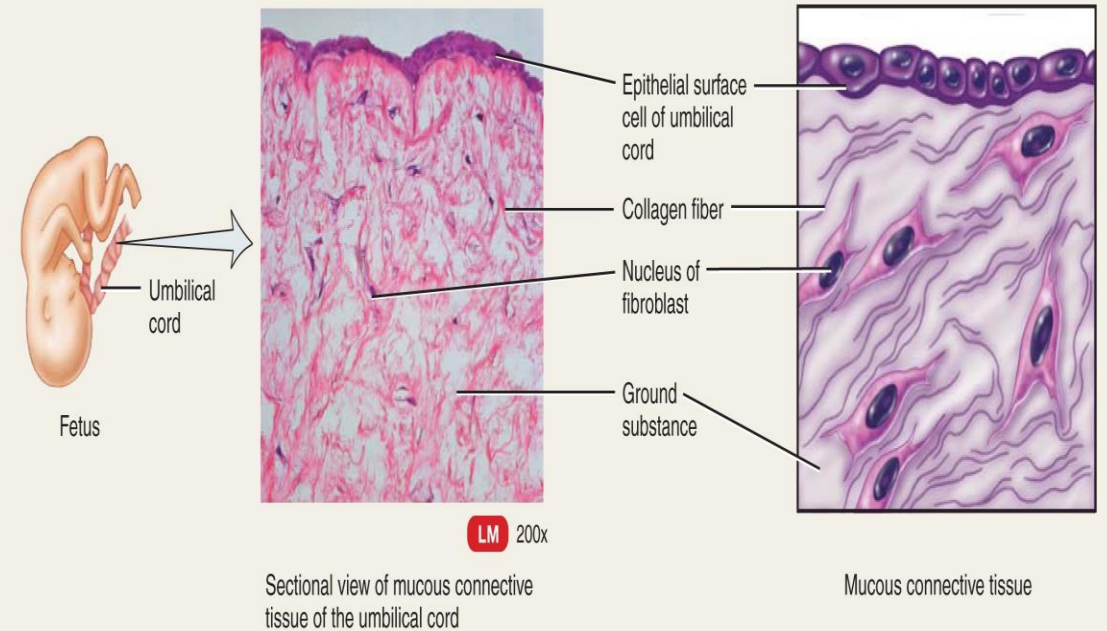


In this Mesenchyme , there are evenly distributed collagen fibres, mesenchymal cells and an empty space which is actually the ground substance.

# Mucous Connective Tissue



This is a H&E cross section of the umbilical cord, it shows two arteries with thicker wall and smaller lumen, one vein with thinner wall and larger lumen.



Mucoid CT is running in between, filling all spaces, surrounding, protecting, cushioning the cord from any damage that could lead to its blockage.

# Classification-Adult CT

We have Loose CT in blood vessels, immune cells and under epithelium. In epithelium, the Loose CT contains ground substance that's responsible to the delivery of nutrients from the blood vessels in the CT to the overlying epithelium.

|                                   | 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                    |

On the extreme ends , we have Dense CT that contains a large amount of collagen fibres. Collagen fibres have a high tensile force and it's compared to steel to show how tough this tissue is. So , Dense CT is one of the **strongest** tissues in our bodies.

# Pay Attention !

Dense regular



Parallel fibres

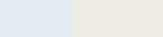


Offers a tensile force in unidirection

Dense irregular



Not arranged fibres



Offers a tensile force in different directions, so it can protect the organ from any pressure applied to it.

Ligaments are regular CT , so collagen fibres with huge amount are running parallel to each other, they connect bones together.

Tendons are located at the ends of the bones to connect them with muscles.

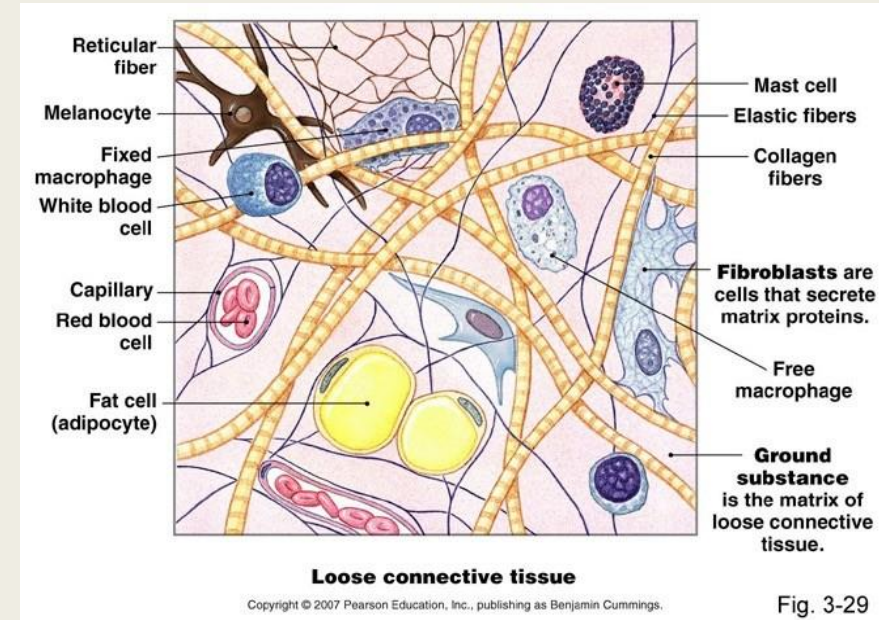
|                                              | General Organization                                                                   | Major Functions                                                                             | Examples                                                            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

Reticular CT is collagen type three , and fibroblasts with more specialty that we call them **reticular cells (they produce those reticular cells).**

This tissue is distributed in a large amount, and it makes small spaces to support delicate cells and small vessels and nerves.

# 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

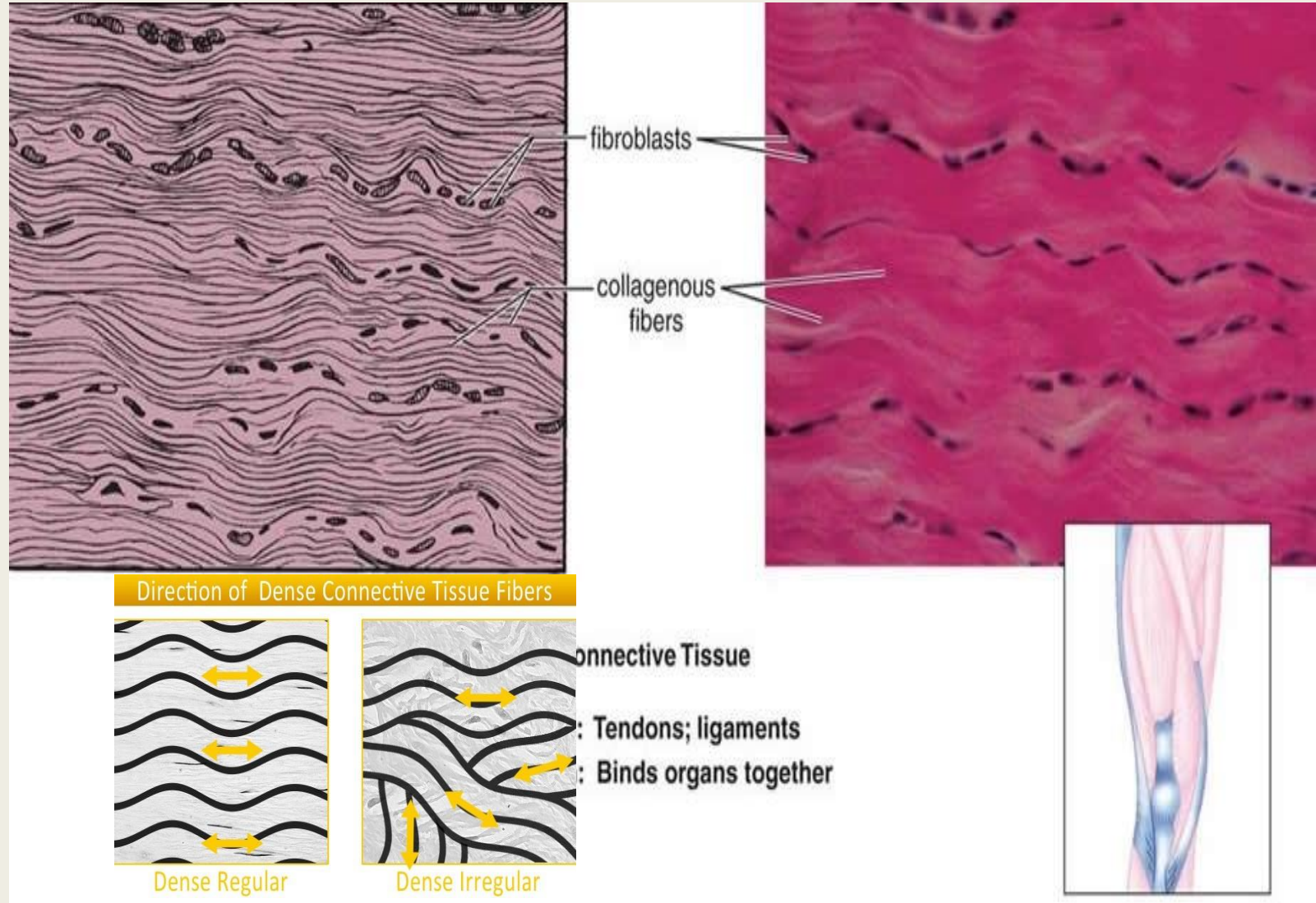
Contains more numerous and thicker fibers and far fewer cells than loose CT.

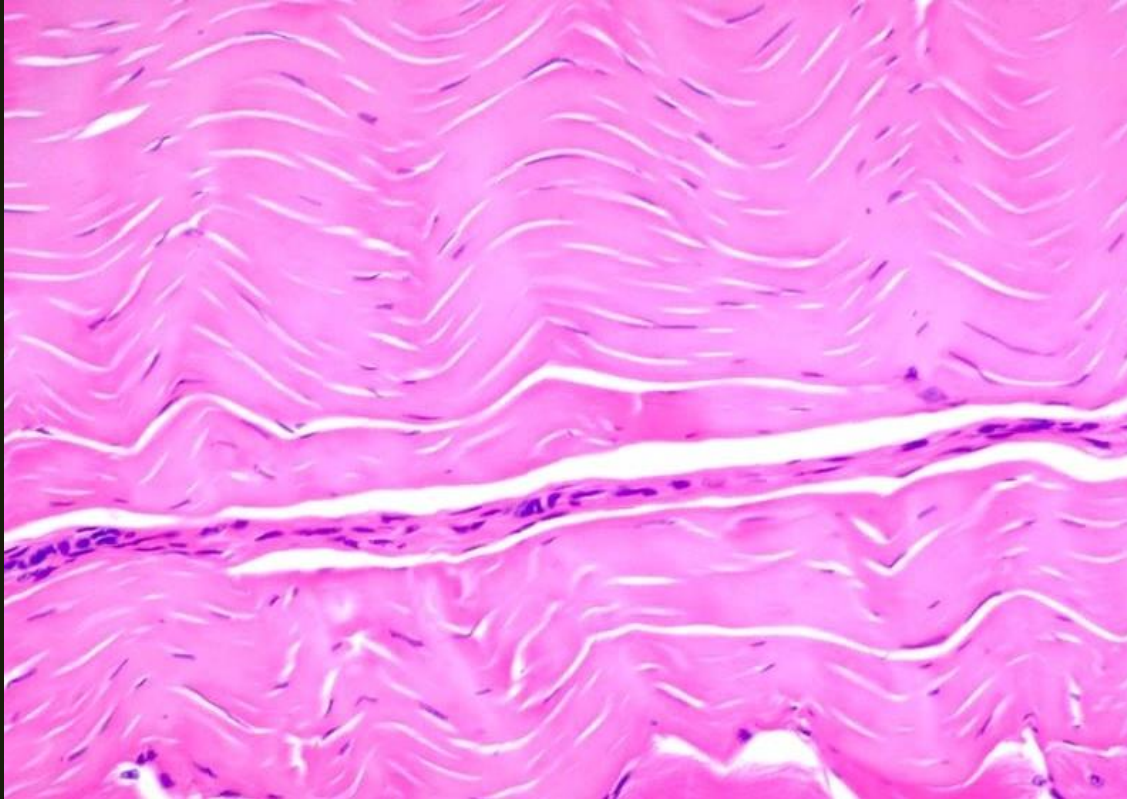
- a. Dense regular connective tissue   Tendons and ligaments
- b. Dense irregular connective tissue   Dermis of skin

# Dense Regular Connective Tissue

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

Those fibres are more aligned around one axis .  
Usually fibroblasts are in between forming rows.

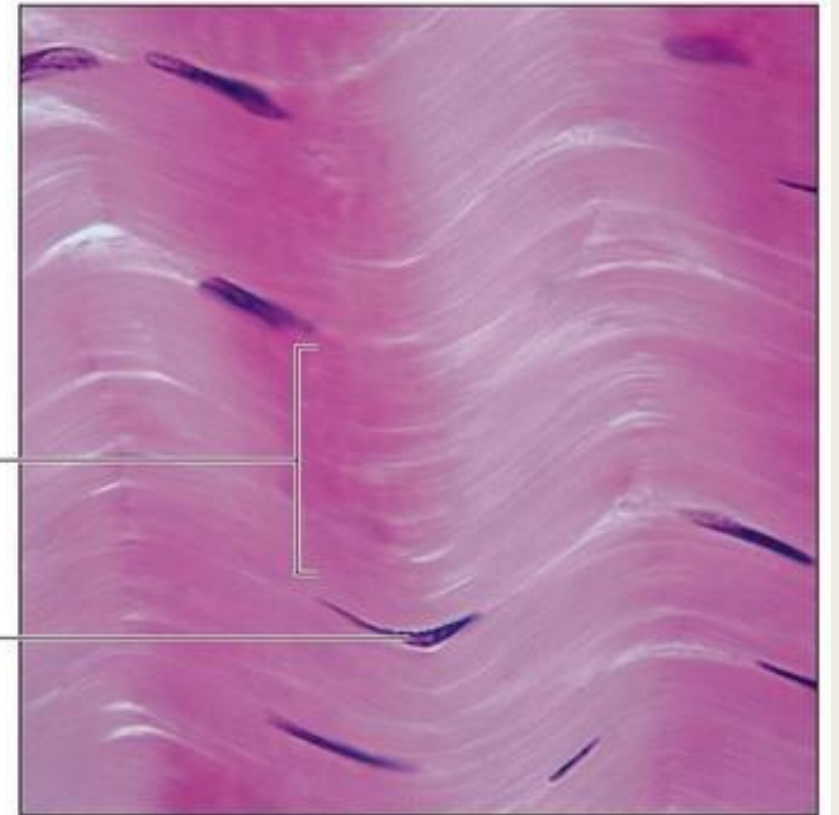




H&E dense regular image  
taken by the light  
microscope.

Collagen fibers

Fibroblast nucleus



# 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

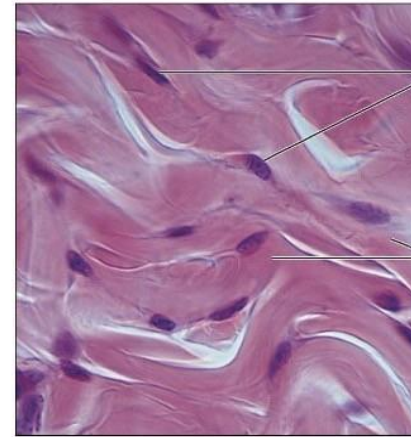
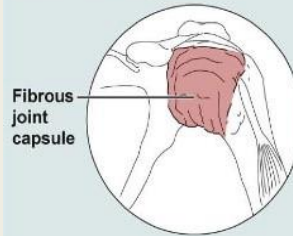
Capsules are sheets of CT surround two bones isolating the joint between them.

A section through the epidermis. Nuclei in purple, Collagen fibres in pink, with no alignment.

**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.

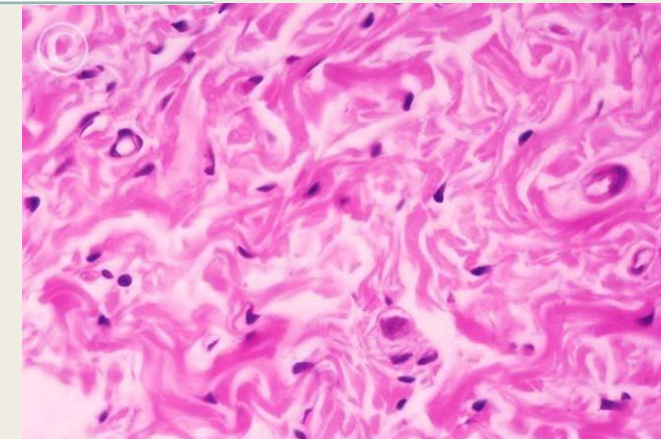
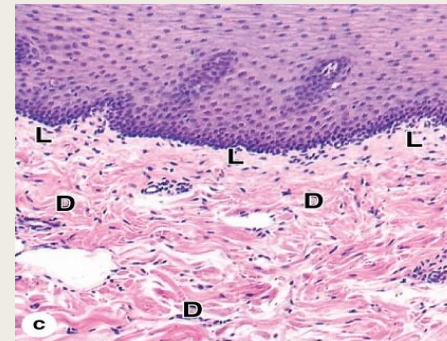
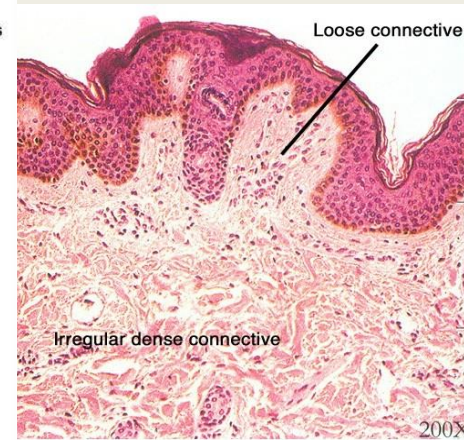
**Location:** Fibrous capsules of organs and of joints; dermis of the skin; submucosa of digestive tract.



Nuclei of fibroblasts

Collagen fibers

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



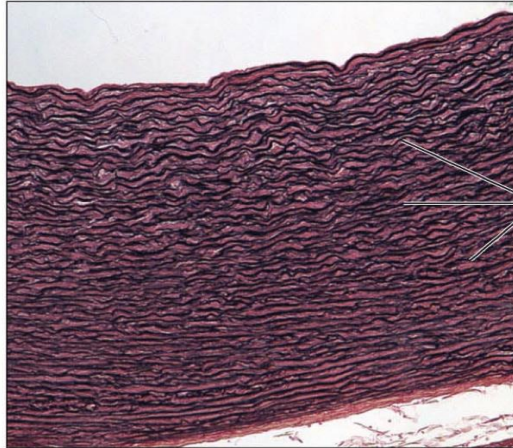
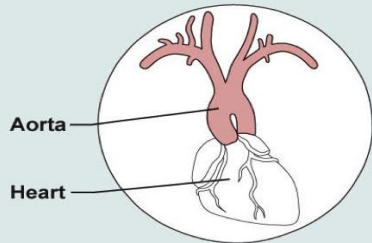
# Elastic Connective tissue

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

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

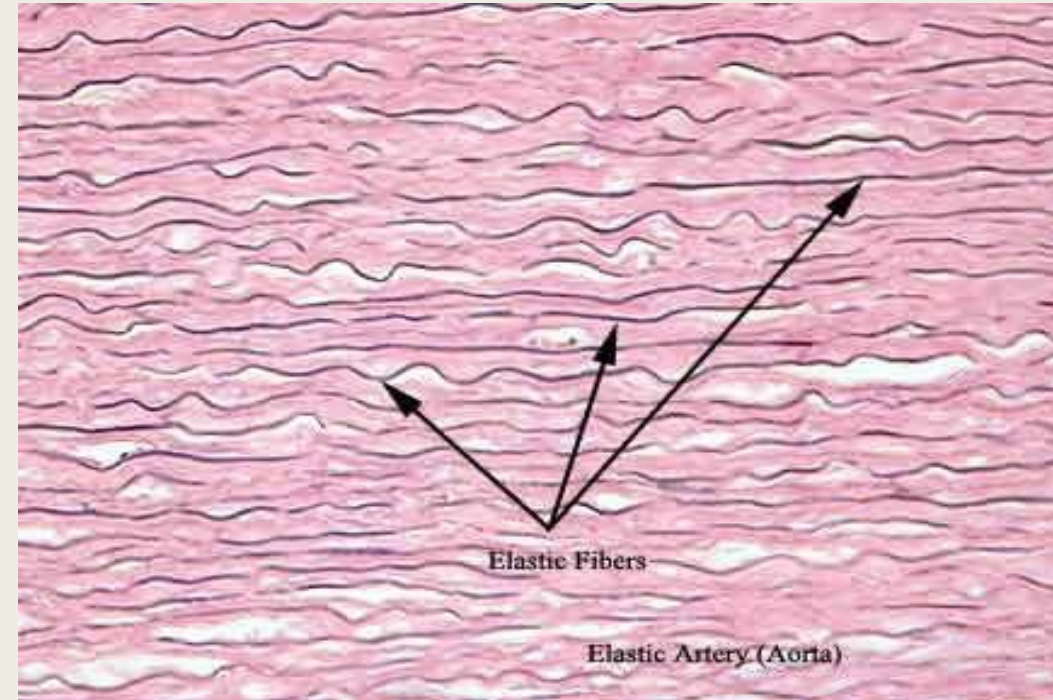
**Function:** Allows recoil of tissue following stretching; maintains pulsatile flow of blood through arteries; aids passive recoil of lungs following inspiration.

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



Elastic fibers

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



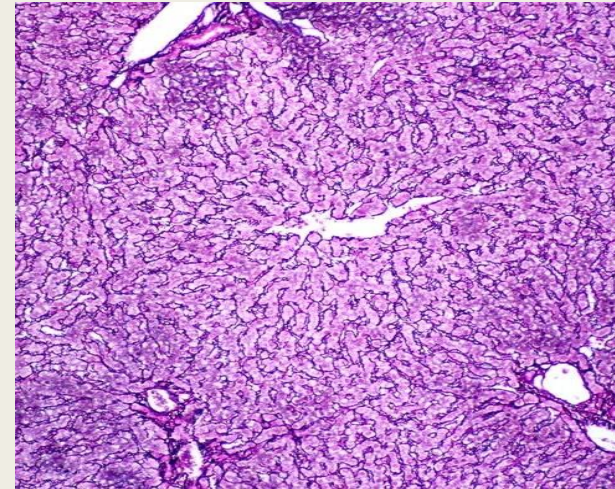
Elastic fibres tend to run parallel to each other, one good location for them is the aorta, the largest blood vessel that emerges from the left ventricle of the heart (البُطَيْن الأيسر), carrying the blood to the rest of the body.

Elastic CT allows a slight stretching to the wall of the aorta.

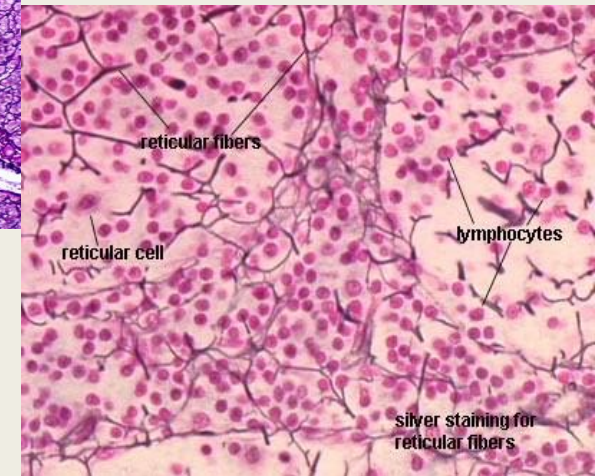
Elastic CT cannot be seen very well using H&E stain, so we use special stain like (orcein) to visualise them and distinguish them from neighbouring collagen fibres.

# 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.



This is a section through a lymphoid organ , tiny rows of reticular fibres supporting lymphoid cells , those reticular fibres can be distinguished as they are larger than lymphocytes which have small nuclei.



This is a section from the liver , reticular fibres surround and support hepatocells which are responsible to the work of the liver.

# 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 |