

# CONNECTIVE TISSUE

- The connective tissue (CT) is found everywhere in the body.
- It is the most abundant and widely-distributed tissue by its several types.

## Structural elements of connective tissue:

it is made up of

- ❑ **cells**
- ❑ **Extracellular matrix** which in turn has 2 elements the
  - **ground substance**
  - **CT fibers.**



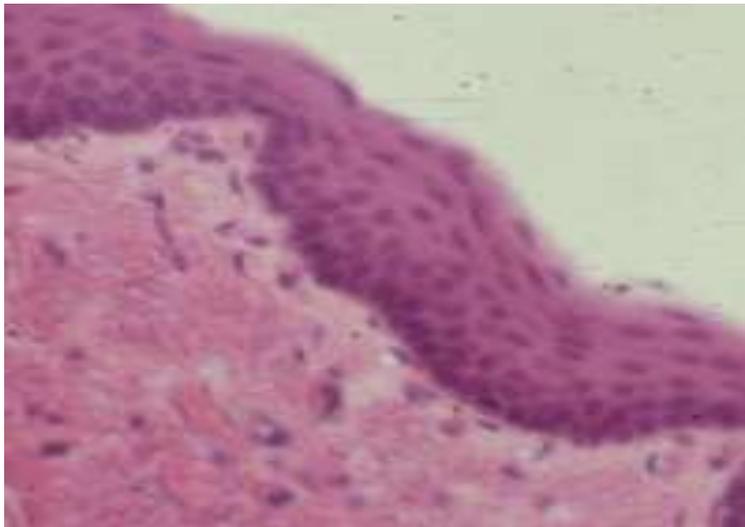
## Common characteristics of CT:

1. **Common origin:** all types of connective tissues arise from the mesenchyme = (**mesoderm**)
2. **Several types of cells:** they are widely-separated and immersed in an abundant intercellular substance (extracellular matrix) formed by these cells.
3. **Extracellular matrix:** where as all other tissues are composed mainly of cells, connective tissue is **formed of abundant non-living extracellular matrix**, which separates the living cells of the tissue.
4. **Variable degrees of vascularity:** some types of connective tissue have a rich supply of blood vessels, other is poorly-vascularized e.g. dense CT and cartilage is avascular.



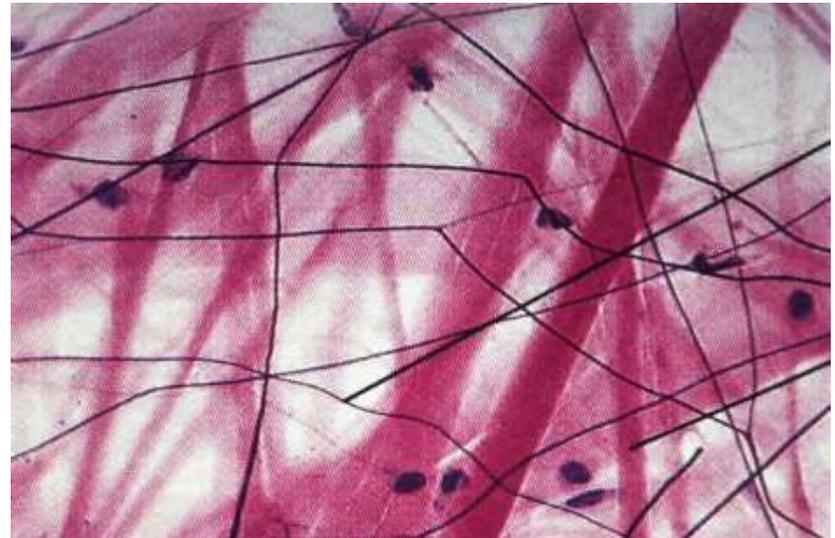
## Epithelium T

- ❑ **Cells:** closely aggregated, of the same type and shape
- ❑ **Intercellular substance:** very little
- ❑ **No fibers:** in the ground substance
- ❑ **Blood vessels:** Avascular
- ❑ **Origin:** ectodermal, endodermal, mesodermal
- ❑ **Function:** covering or secretion (glands)



## Connective T

- ❑ **Cells:** few, widely separated, different types
- ❑ **Intercellular substance:** abundant
- ❑ **Fibers :** are present in the ground substance
- ❑ **Blood vessels:** rich
- ❑ **Origin:** mesodermal
- ❑ **Function:** support, defence and nutrition



# Extracellular Matrix (ECM)

## Fibers

## Ground Substance

It is the material that fills the spaces between the cells and contains the fibers. It is composed of:

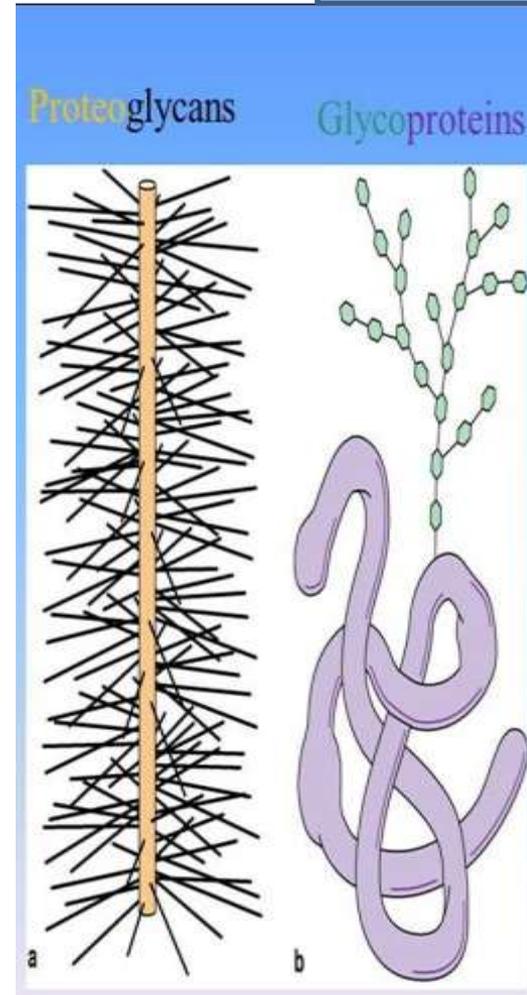
1. **Tissue fluid:** Similar to blood plasma
2. **Adhesive glycoproteins**
3. **Proteoglycans**
4. **Glycosaminoglycans (GAG)**

1. **Interstitial tissue fluid:** formed of plasma proteins of low molecular weight that escape through the capillary wall as a result of the hydrostatic pressure.

**Edema:** is an increase in the quantity of the tissue fluid due to loss of the equilibrium between the tissue fluids entering and leaving the matrix of CT.

2. **Adhesive glycoproteins** e.g. **fibronectin** and **laminin**.

They serve mainly as connective tissue glue that allows connective tissue cells to bind themselves to matrix elements.



### 3. Proteoglycans

consist of a protein core to which glycosaminoglycans (GAGs) are attached. The strand-like GAGs are large, negatively-charged polysaccharides that extend from the core protein like the fibers of a bottle brush. GAGs are like chondroitin sulfate and keratan sulfate.

- The proteoglycans tend to form huge **proteoglycan aggregates** with hyaluronic acid that trap water, forming a substance that varies from a fluid to a viscous gel

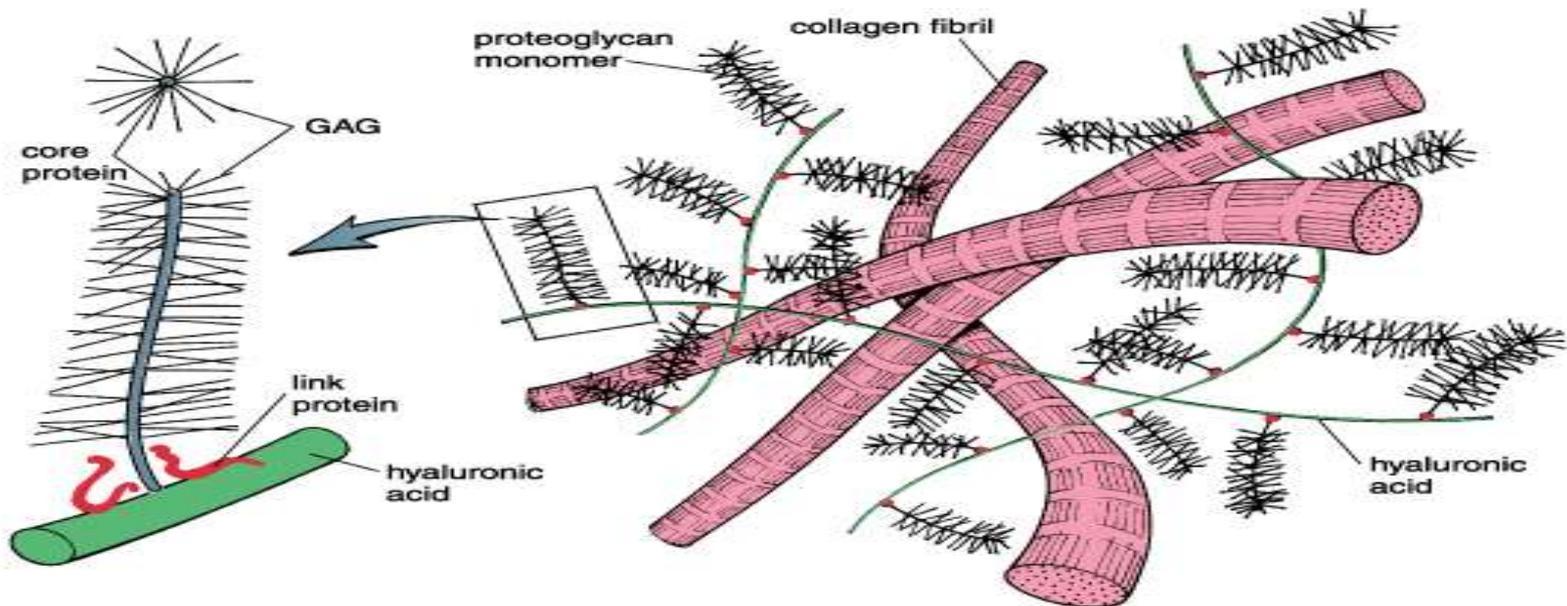
### 4. Glycosaminoglycans (GAG)

- linear (unbranched) polysaccharides, e.g. heparan sulfate, chondroitin sulfate, keratan sulfate, hyaluronic acid
- attract sodium & **hold water**
- very hydrophilic due to abundant negative charges.
- except for hyaluronic acid, are usually bound covalently to protein core as part of a **proteoglycan**

## Function :

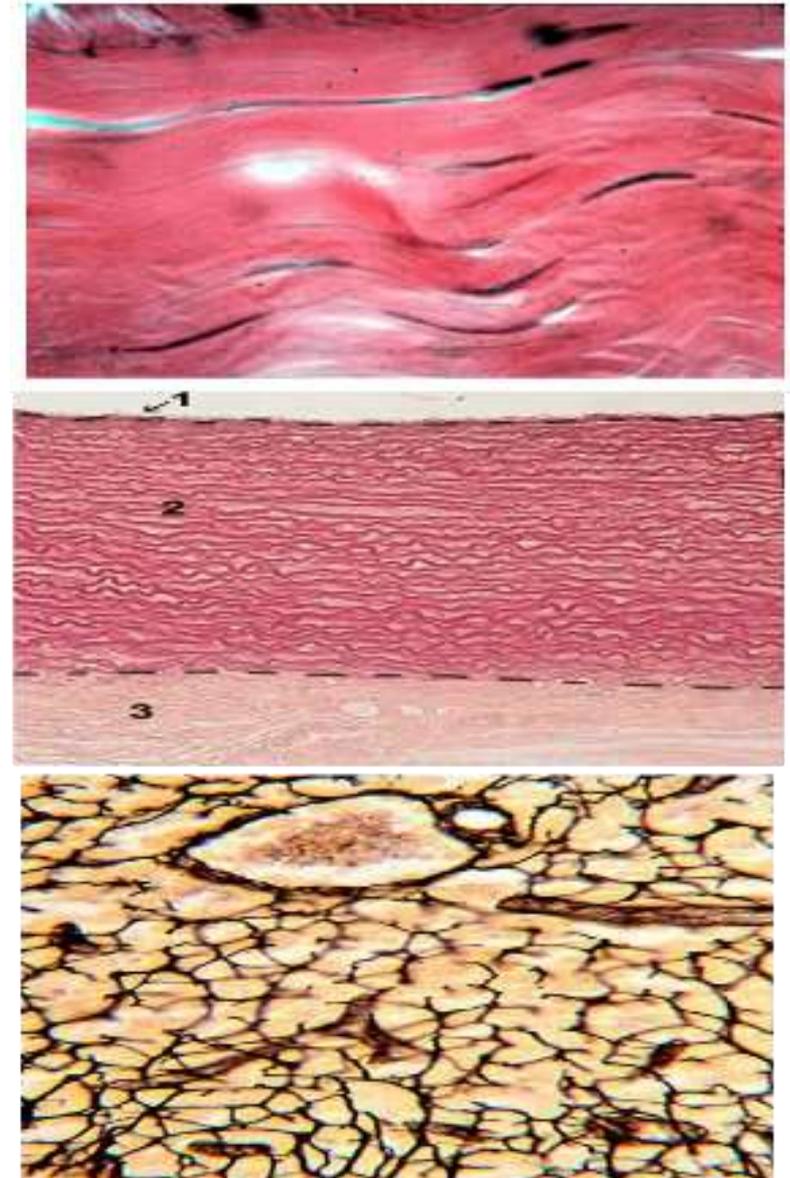
- The ground substance holds large amounts of fluid and functions as a medium through which nutrients and other dissolved substances can diffuse between the blood capillaries and the cells.
- Its gel state serves to resist compression and to act as a lubricant.
- It also acts as a barrier to bacterial penetration.

Some virulent bacteria can secrete the enzyme hyaluronidase that hydrolyzes the ground substance and facilitates bacterial invasion to CT.



# Connective tissue fibers

- They are embedded in connective tissue matrix.
- The fibers of connective tissue provide support.
- There are three types of CT fibers:
  - ❖ Collagen fibers,
  - ❖ Elastic fibers
  - ❖ Reticular fibers.



# Collagen fibers= (white fibers)



## Characters:

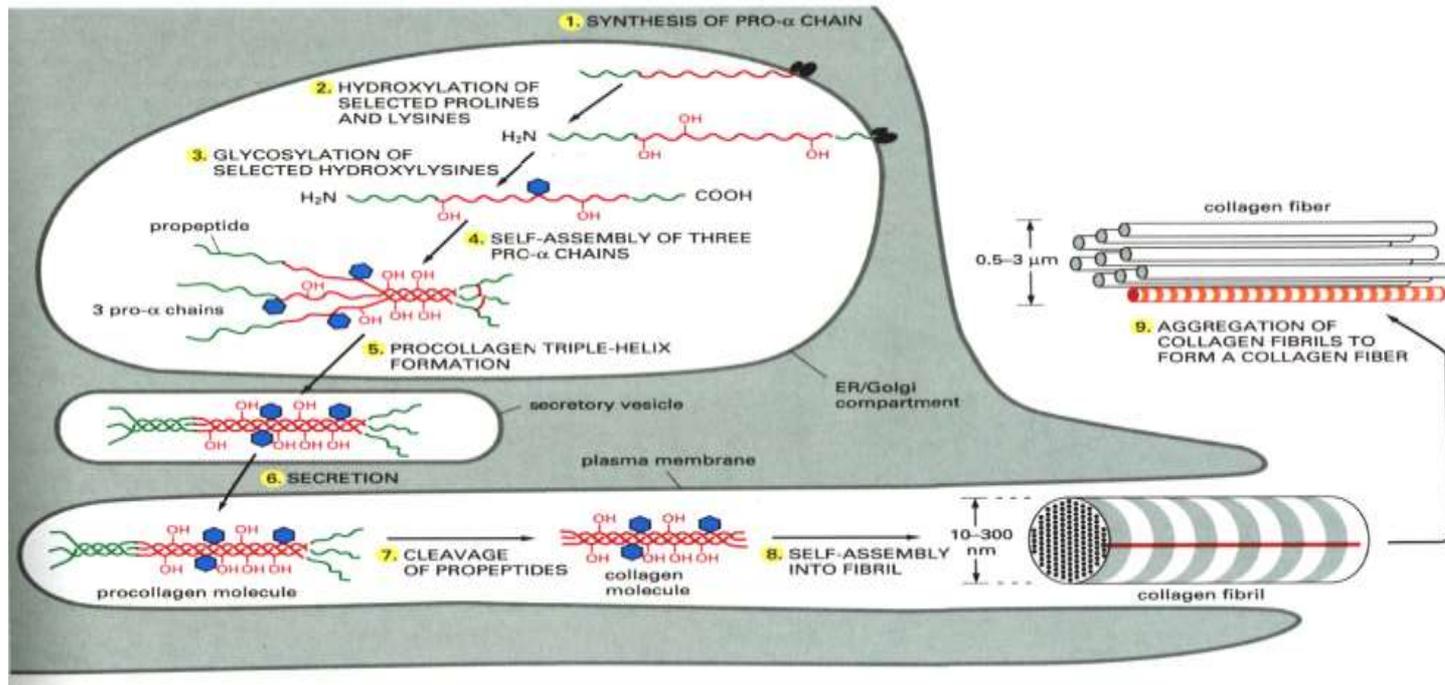
- Collagen fibers are the most abundant CT fibers.
- They are the strongest and provide **high tensile strength** (that is the ability to resist longitudinal stress). Stress test shows that collagen fibers are stronger than steel fibers of the same size.
- In fresh state, collagen fibers have a glistening white appearance; they are therefore also called **white fibers**.

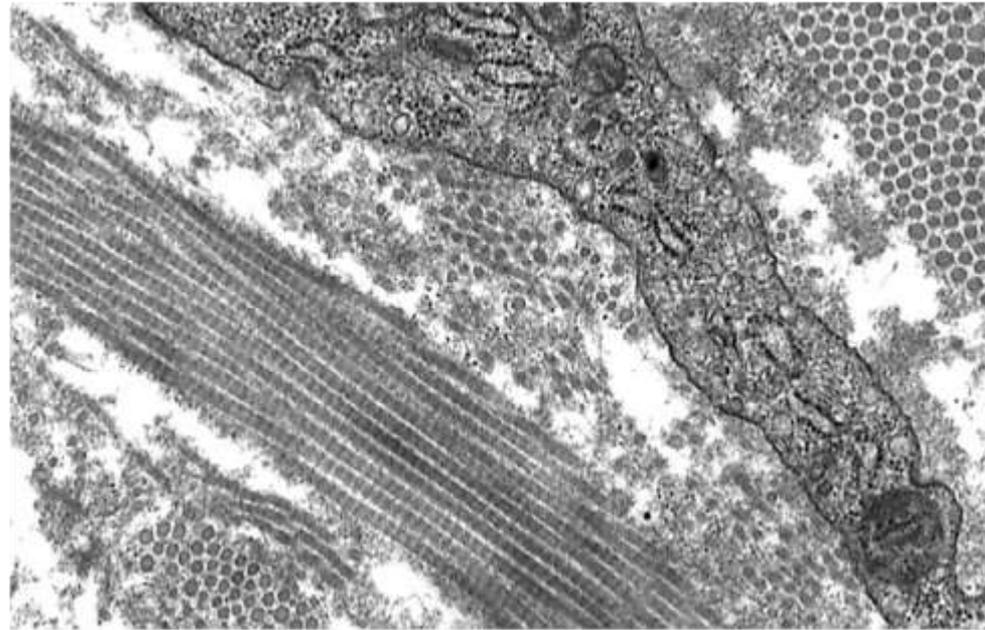
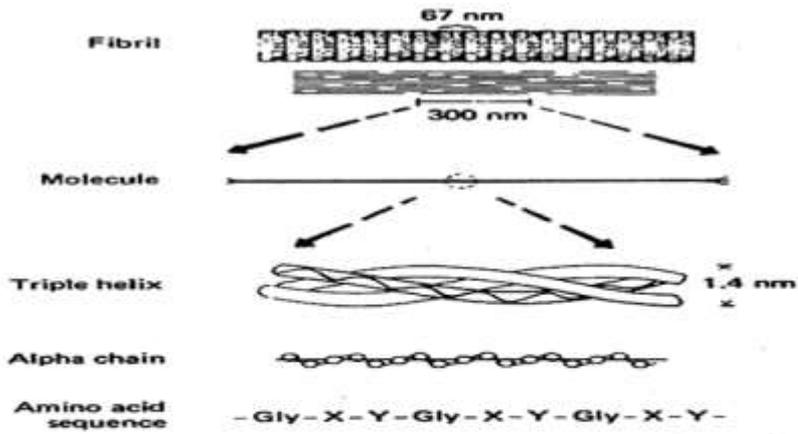
## Histological features:

- In longitudinal section, collagen fibers appear as cylindrical structures that run in **wavy bundles**
- The individual fibers do not branch while the **bundles** of fibers often do.
- They stain pink with H&E

## Synthesis of collagen:

- ❑ Procollagen, a precursor of collagen protein is formed inside the fibroblasts then it is released by exocytosis into the extracellular space.
- ❑ Procollagen is cleaved to form collagen molecules which assemble spontaneously into collagen fibrils.
- ❑ Collagen fibrils in turn are further assembled into collagen fibers which may be bundled together into the thick collagen bundles.

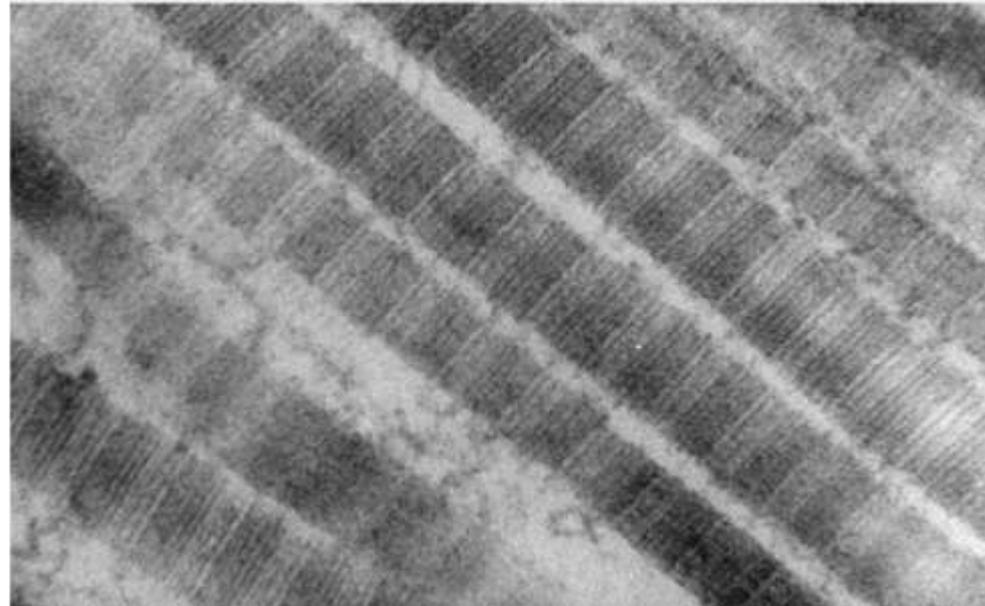
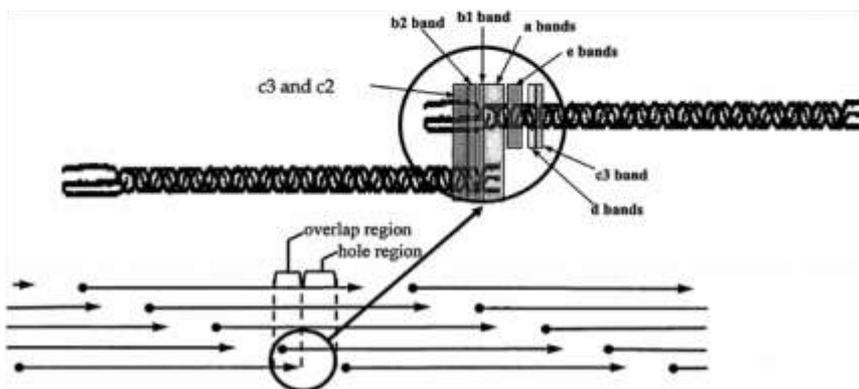
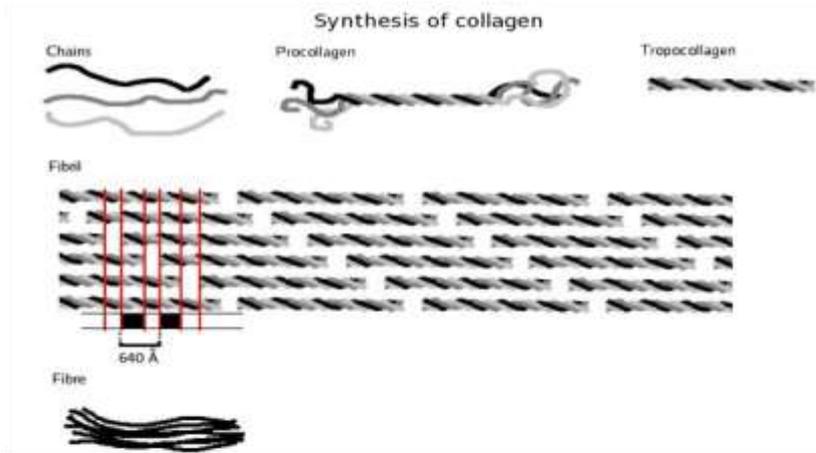




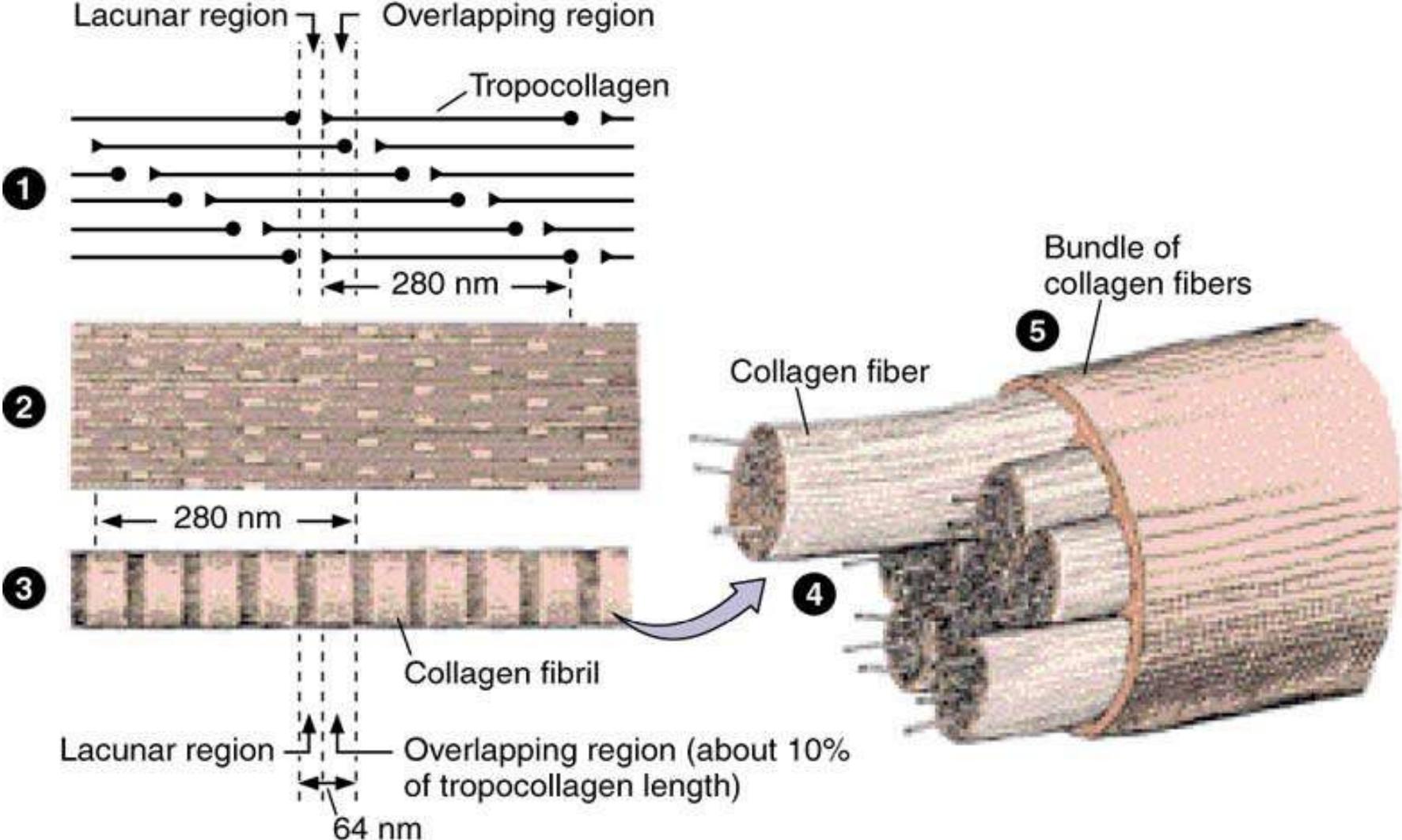
1/7/0 RMPF

1111111111

50 nm



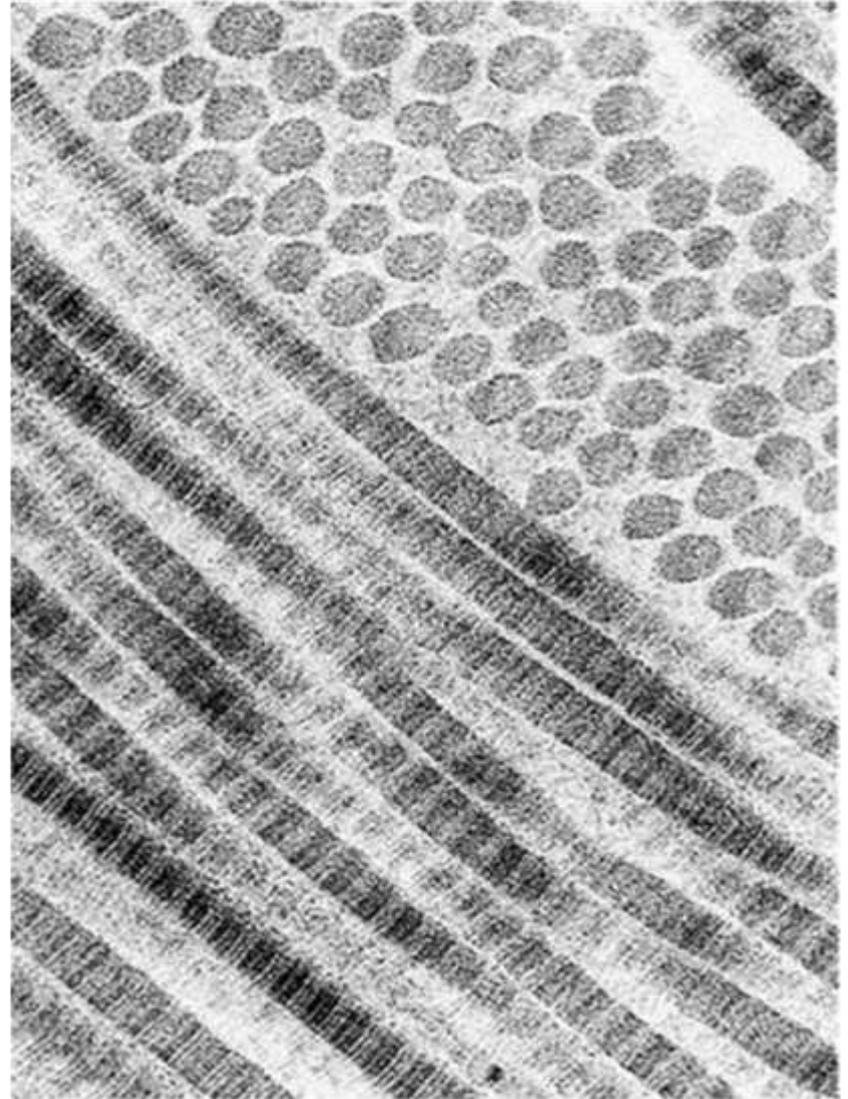
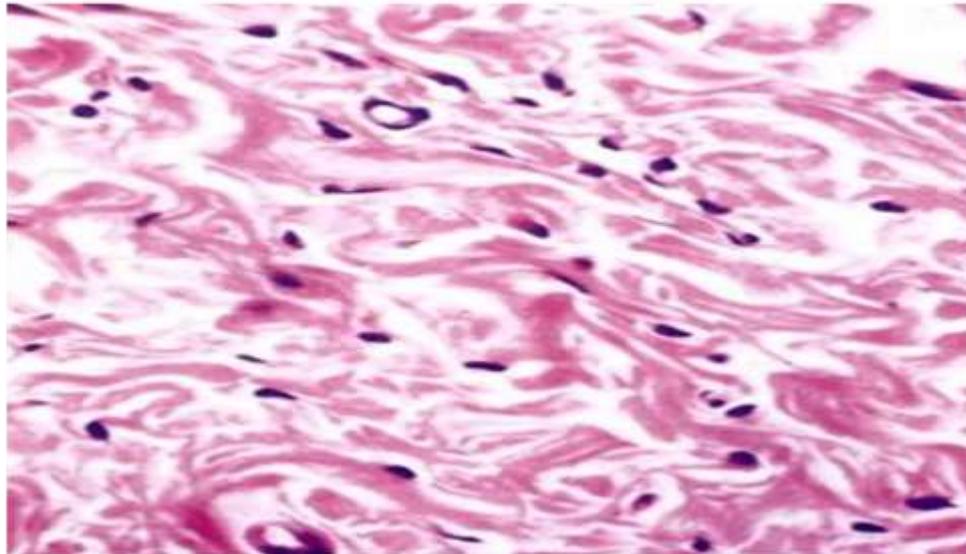
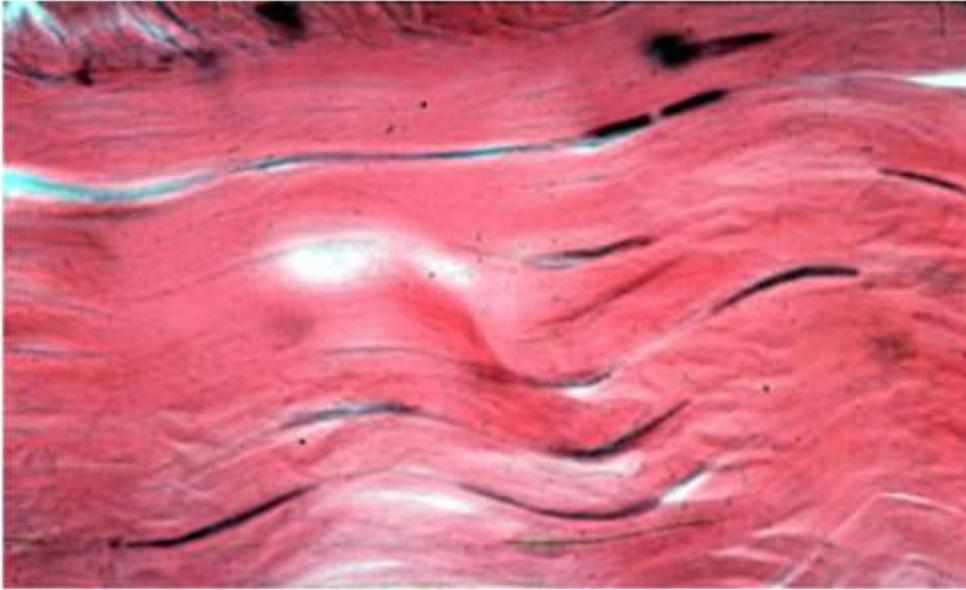
# Assembly of collagen fiber bundles



**H & E**

# Collagen Fibers

**E.M**



# Major types of Collagen Fiber

According to the chemical composition of collagen molecules

## Types of collagen:

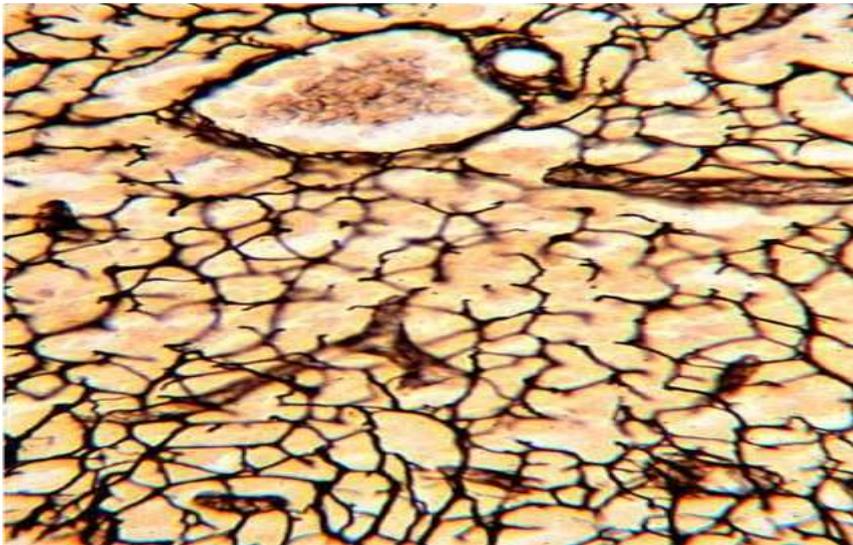
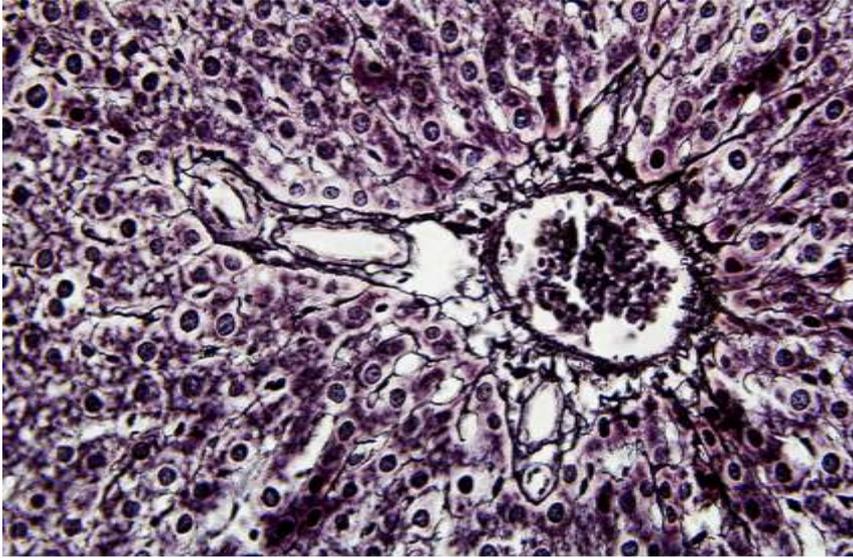
More than 20 different types of collagen fibers are known. They differ by their molecular composition, morphologic features, distribution in tissues and functions.

The major types of collagen are:

- Type I collagen fibers in connective tissue proper, and in fibrocartilage and bone matrix.
- Type II collagen fibrils in cartilage matrix (hyaline and elastic).
- Type III collagen fibers form the reticular fibers.
- Type IV, VII in basement membrane.

Collagen Type	Tissues	Function
I (most abundant)	Skin, tendon, bone, dentin	Resistance to tension
II	Cartilage , vitreous of eye	Resistance to pressure
III (reticulin)	Skin , muscle, blood vessels, liver, etc.	Structural framework and stability
IV, VII	All basement membranes	Support and filtration

# Reticular Fibers



## Histological features:

❑ **Form a delicate supporting framework** for highly cellular tissues (endocrine glands, lymph nodes, liver, bone marrow, spleen, smooth muscle).

❑ **Composed mainly of Type III collagen**, with a carbohydrate moiety that reduces  $Ag^+$  to metallic silver = **argyrophilic**.

❑ **Special stain:** silver stain

❑ **Thinner than type I collagen** (Type III fibrils are 30-40 nm diameter; type I fibrils are ~200 nm diameter)

❑ Formed by **reticular cells** (specialized fibroblasts) and vascular smooth muscle cells

# Elastic Fibers

## yellow fibers

**Elastic fibers** : can be stretched to one and one-half times their length, but recoil to their initial length when released.

Fresh elastic fibers appear yellow and are also called **yellow fibers**.

### Histological features:

➤ These fibers contain protein, elastin that allows them to stretch and recoil like rubber bands. Because the fresh elastic fibers appear yellow, they are called **the yellow fibers**.

➤ They are found where greater elasticity is needed **present in large amounts in ligaments, lung, skin, bladder, and walls of blood vessels**.

➤ Elastic fibers may exist in **two** different forms:

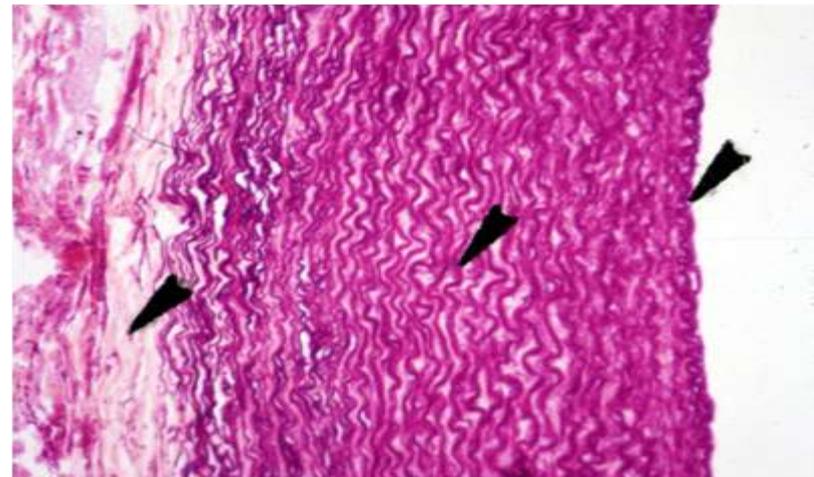
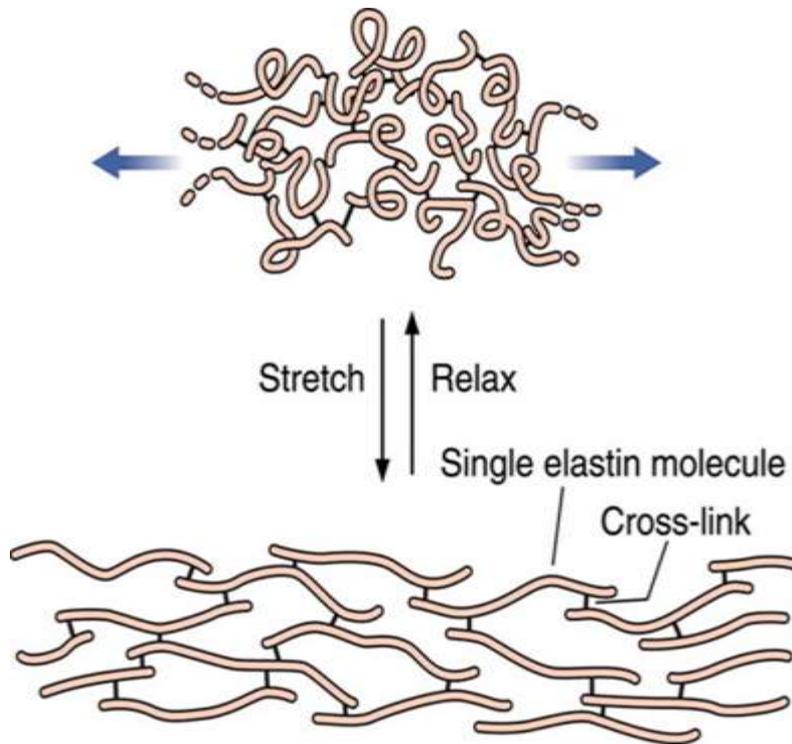
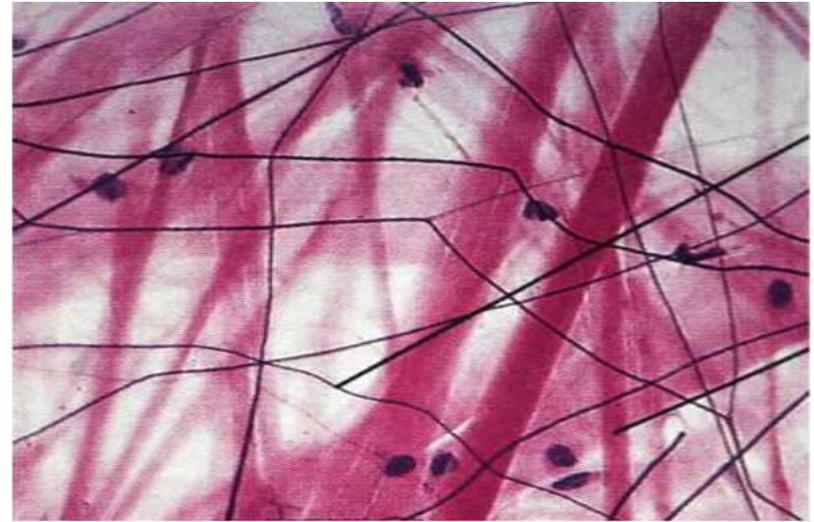
❖ Individual long and thin fibers that branch in the extracellular matrix.

❖ In the wall of large blood vessels they form fenestrated parallel sheets

➤ They stain weakly with H&E.

Special staining with **orcein stain** gives a brick-red color to elastic fibers, while staining with **V.VG stain** gives them a dark violet or black color.

# Elastic fibers

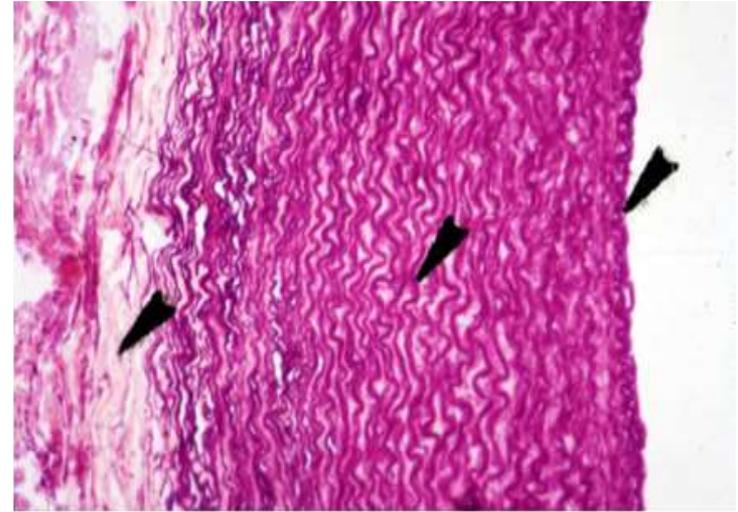


# Elastic Fibers

**Elastic fibers** (yellow fibers): can be stretched to one and one-half times their length, but recoil to their initial length when released.

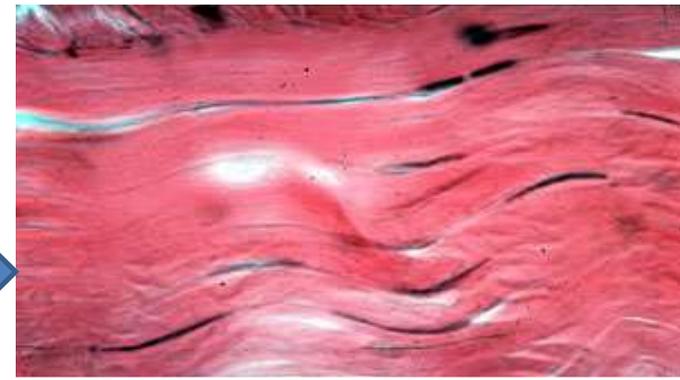
Fresh elastic fibers appear yellow and are also called yellow fibers.

Stain : H&E , Orcein , VVG

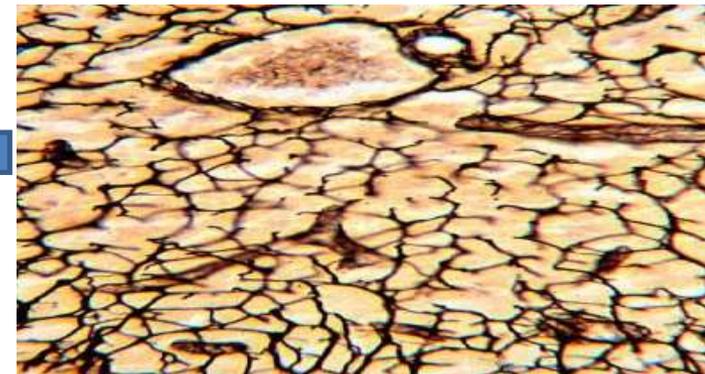
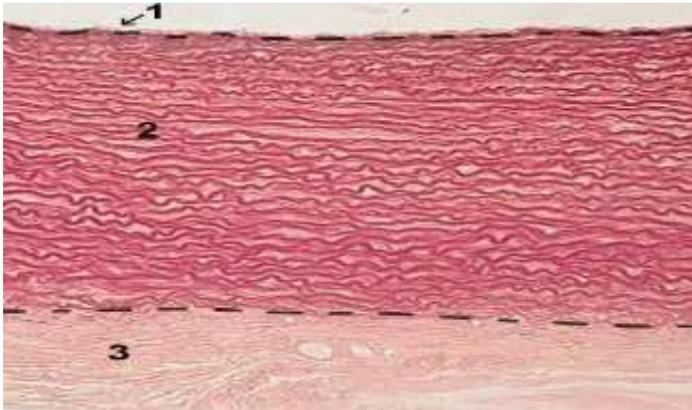


# Fibers

- The most numerous
- White if in great number (**white fibers**)
- Strong and flexible
- Fibers do not branch but bundles can do
- Formed of **collagen protein**
- Stain pink with eosin
- Types of Collagen Fibres



- Yellow if in great number (Yellow fibers)
- Elastic and stretchable
- Fibers can branch and unit
- Formed of **elastin protein**
- Stained weakly by H&E
- Stain brick red by orcein
- Stain dark violet with V.V.G stain.



- Thin branching
- Not stained by H&E
- Stained dark brown with silver stain
- Consist of type III collagen
- Supportive function

# C.T. CELLS



## **Fixed cells= resident**

□ stable, long-lived cell e.g.

1. UDMC
2. Fibroblast & fibrocytes
3. Fat cell = adipocytes
4. Pigment cell



## **Free cells = immigrating**

**Transient = (wandering) cells.**

Originate mainly in the bone marrow and circulate in the bloodstream.

□ **motile, short-lived cells e.g.**

1. Macrophages
2. Plasma cell
3. Mast cell
4. White blood cells=  
Leucocytes

# Fixed cells

## Undifferentiated Mesenchymal Cell

### Cell:

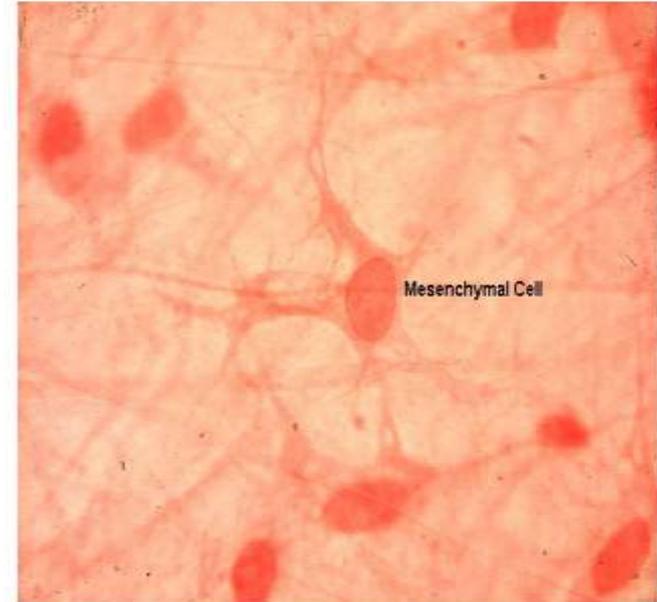
- Origin (stem cells)
- Characters
- Function

### L.M.:

- They are stellate cells with few processes.
- They have euchromatic nuclei (active)
- with faint basophilic cytoplasm.

### Function:

they are adult stem cells that can divide and differentiate into many types of CT cells.



# Fibroblasts

## 2 types

### ❑ Young = Fibroblasts

The most common type

- Origin : from UDMC

#### ❑ Young active = fibroblast

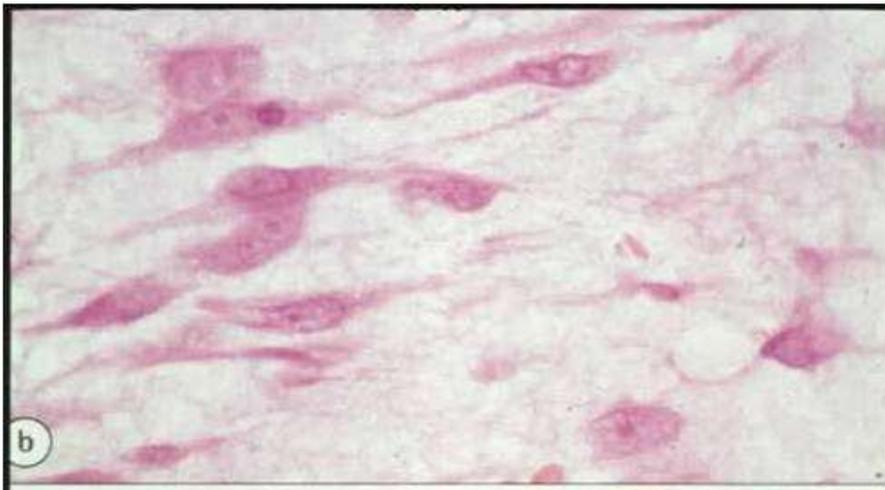
- Large in size
- Fusiform with processes
- oval central **paler** nucleus
- **Basophilic** cytoplasm = numerous rER

### ❑ Mature = fibrocytes

#### ❑ Mature = fibrocytes

mature (Fibrocytes) :inactive

- Small in size
- Fusiform smaller
- oval central **darker** nucleus
- acidophilic cytoplasm



# Fibroblasts

They are the most common cells in CT.

## LM:

fibroblast is a spindle-shaped branching cell, with deeply basophilic cytoplasm and large euchromatic nucleus with prominent nucleolus.

## EM:

its cytoplasm contains abundant rough endoplasmic reticulum and well-developed Golgi complex.

## Function:

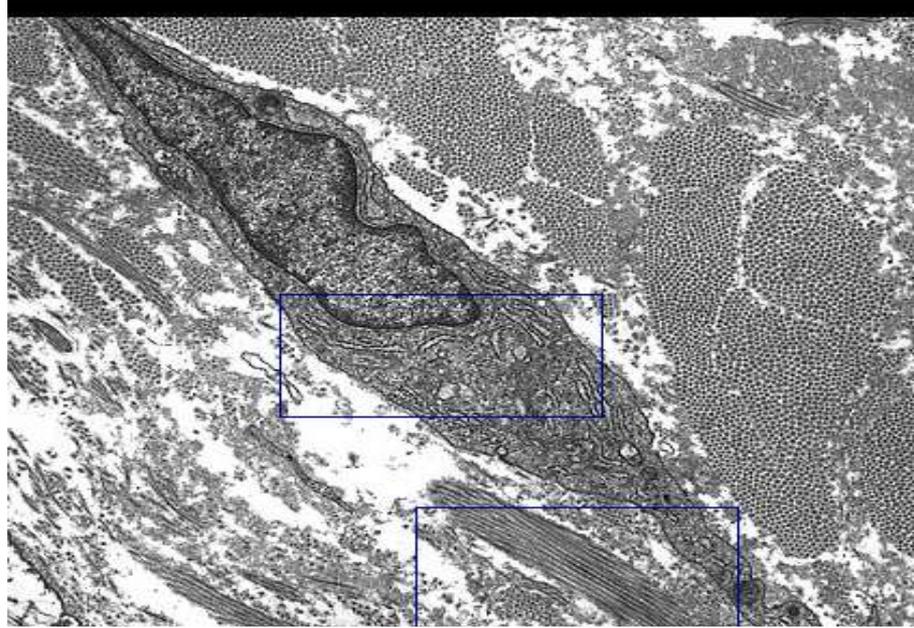
- ❑ Synthesize and secrete components of the ECM: fibers and ground substance.
- ❑ Synthesize growth factors.
- ❑ Rarely undergo cell division unless tissue is injured, which activates the quiescent cells.
- ❑ Play a major role in the process of wound healing and respond to an injury by proliferating and enhanced fiber formation.

# Fibrocytes

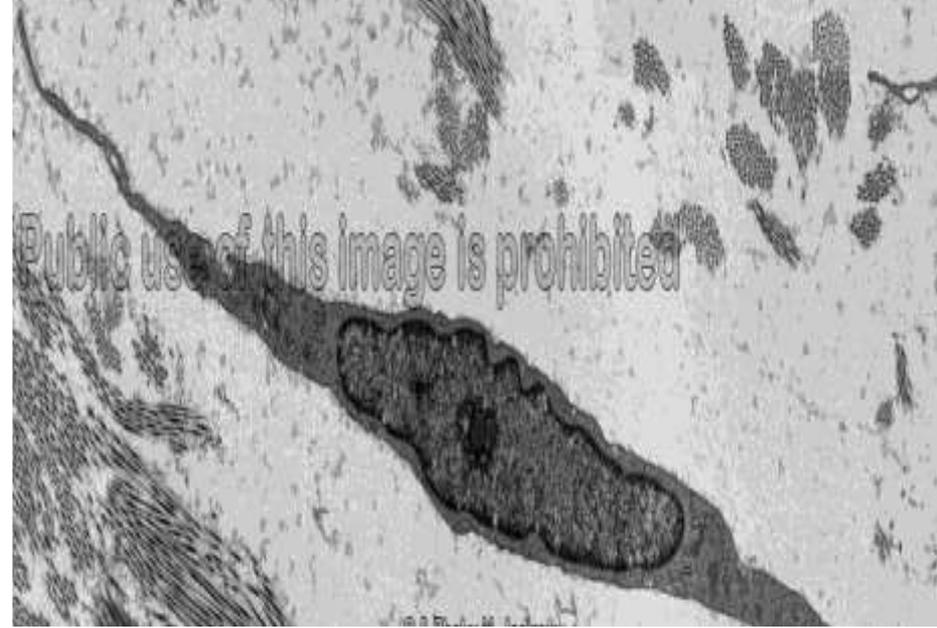
- After they synthesize the matrix, they become quiescent and are called fibrocytes.
- **LM:**  
smaller cells with fewer processes than the fibroblasts. Dark nucleus and an acidophilic cytoplasm.
- **EM:**  
they have fewer rER and small Golgi.

**Function:** maintenance of the CT matrix. However, if the matrix is injured, they can easily return to their more active state (fibroblast) to repair and regenerate the matrix.

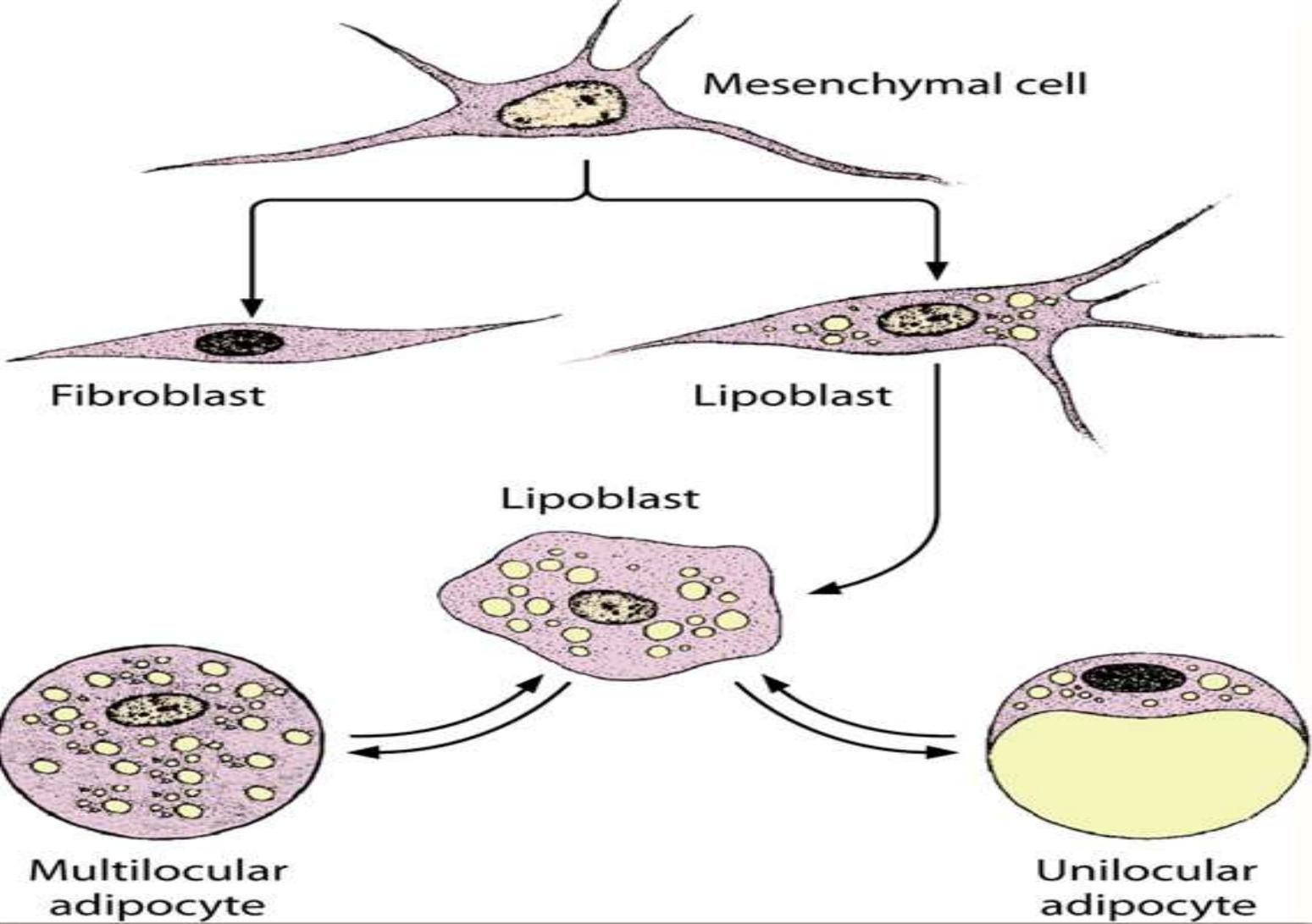
# Fibroblasts E.M



# Fibrocytes E.M



# Fat Cell=Adipocytes= fixed cells



# Adipocytes = Fat cell

Origin : **UDMC**

**LM:**

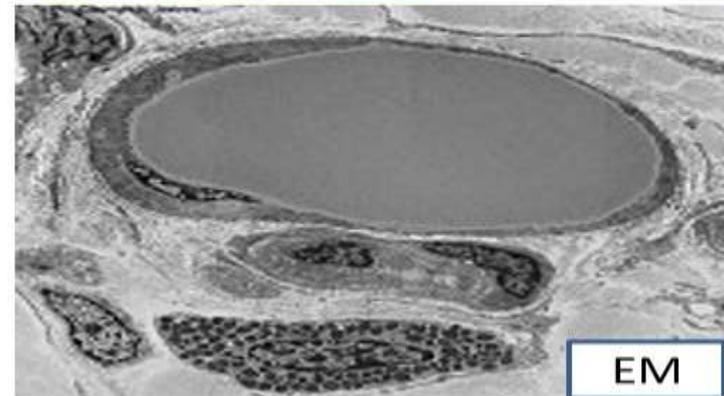
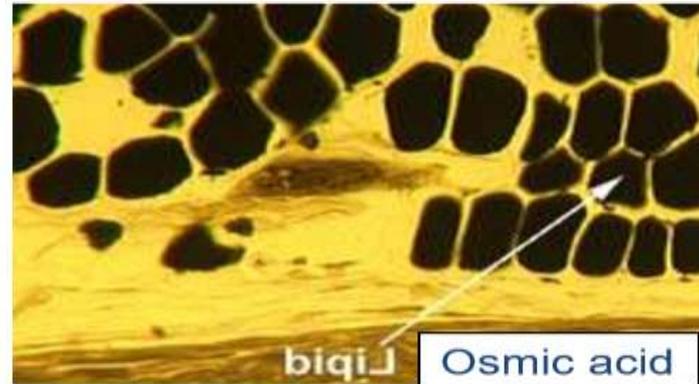
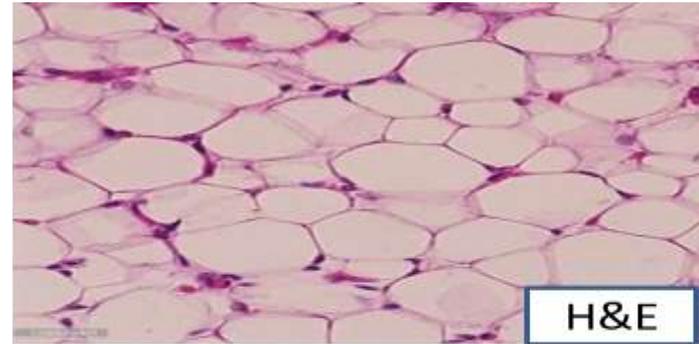
- large, spherical or polyhedral
- The flattened nucleus
- The cytoplasm only forms a very narrow rim around a large central lipid droplet.
- Single or several lipid droplets
- Adipocytes are long-lived cells. Their number is determined by the number of preadipocytes generated during foetal and early postnatal development.

Lipid storage/mobilisation is under:

- nervous (sympathetic) , hormonal (insulin) control.

**Function :**

- Storage of lipid
- Production of energy
- endocrine function - they secrete the protein **leptin** which regulate appetite with feedback about the bodies fat reserves.

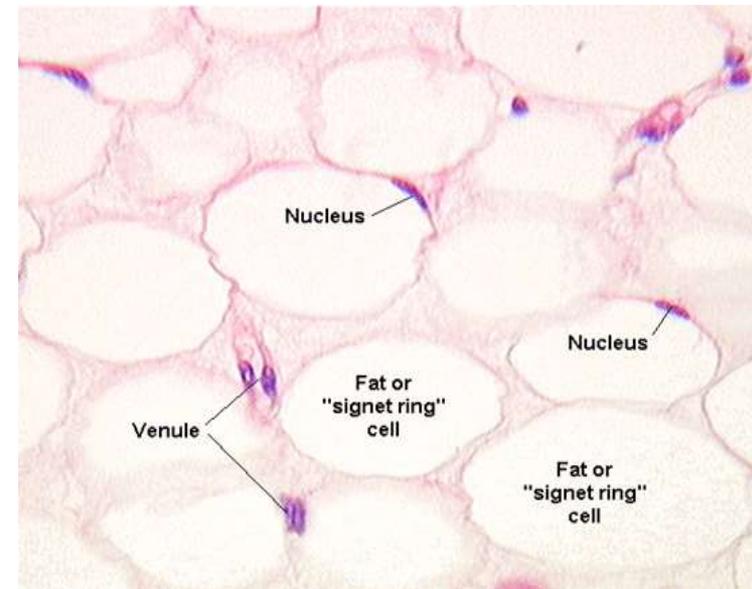


## Histological features:

They are large cells, spherical when single or polyhedral in shape when they are closely-grouped.

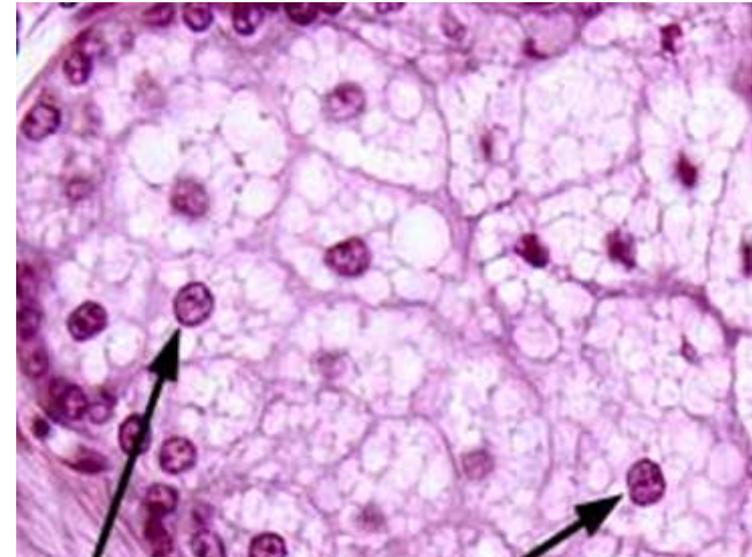
### ❑ Unilocular adipocytes

the cytoplasm is occupied by a single large lipid droplet that pushes the cytoplasm to a thin peripheral rim with peripheral flattened nucleus giving the “signet-ring” appearance.



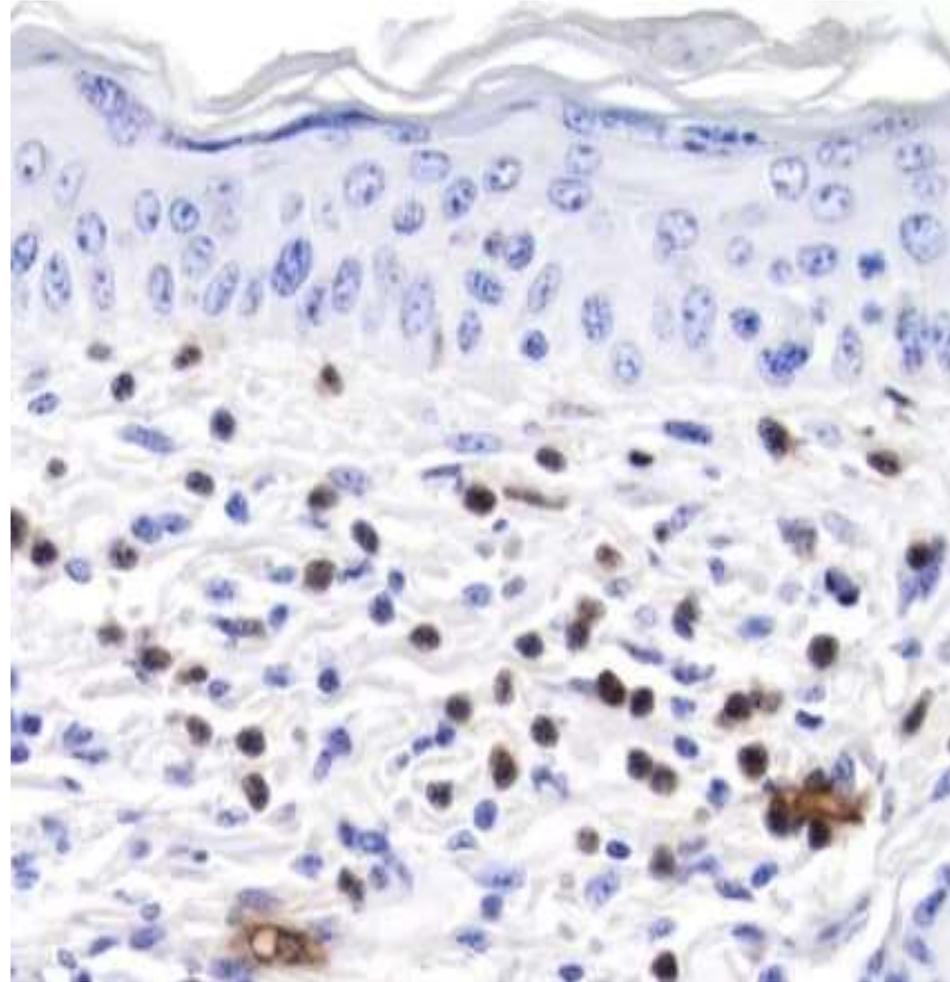
❑ **Multilocular adipocytes** are polygonal and smaller than the unilocular adipocytes.

Their cytoplasm contains a central rounded nucleus, numerous small lipid droplets and numerous mitochondria with abundant long cristae.



# Pigment Cells= fixed cells

- **Origin :UDMC**
  - branched cells
  - Contain pigment granules:  
Melanin (melanocytes)
- Function :**
- gives the color of skin and iris of the eye



# Free cells

## Mast Cells

**Origin:** from haemopoetic stem cell in B. M

**Two types:**

- **Connective tissue mast cells** are found in skin (dermis) and peritoneal cavity
- **mucosal mast cells** are in the mucosa of the digestive and respiratory tracts.
- ❑ Contain basophilic granules by H&E
  - (**Metachromatic** staining) By toluidine blue

when stained with **toluidine blue**, the granules bind the dye and change its color to **red**.

# Histological features:

## LM:

mast cell is a large CT cell. Its cytoplasm is full of basophilic granules that may obscure the nucleus. Its nucleus is rounded and central in position.

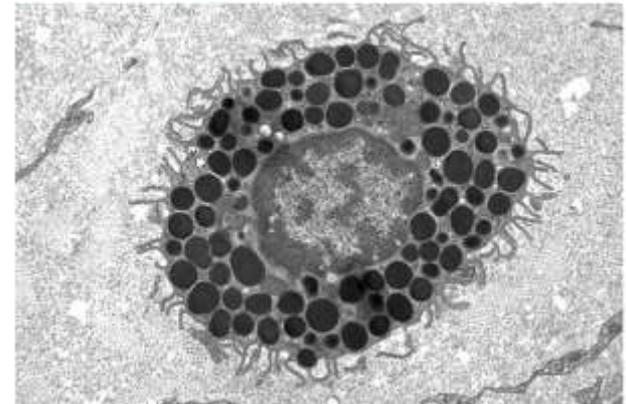
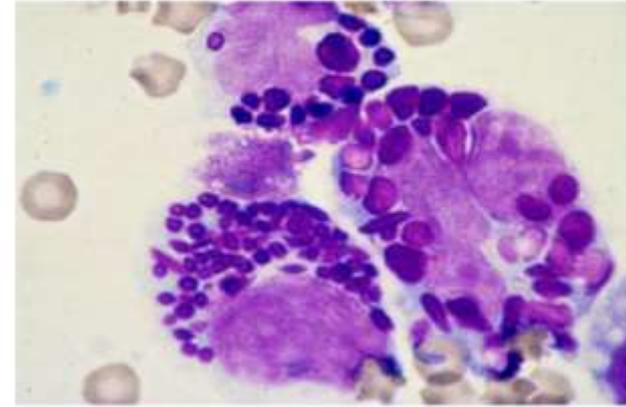
- A distinctive staining feature of mast cells is "**metachromasia**" which means that certain basic stains give to their granules a color other than that of the dye itself e.g. toluidine blue stain gives a purple color instead of blue, due to the chemical composition of the secretory granules.

## EM:

their cytoplasm contains numerous secretory granules.

## Function:

they initiate allergic and local inflammatory responses by release of their granules (degranulation) which contain; the anticoagulant **heparin** and **histamine** which promotes increased vascular permeability and smooth muscles contraction.



# Macrophages= Histiocytes

**Origin :** From **blood monocytes**

**Macrophages:** they are derived from the monocytes that migrate from bloodstream into CT.

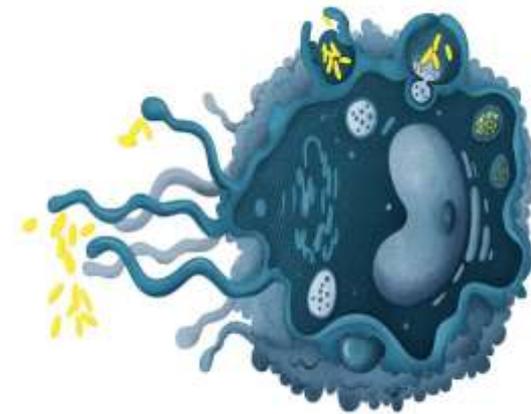
**Histological features:**

large, irregular cells with eccentric kidney-shaped nucleus.

The cytoplasm shows numerous lysosomes.

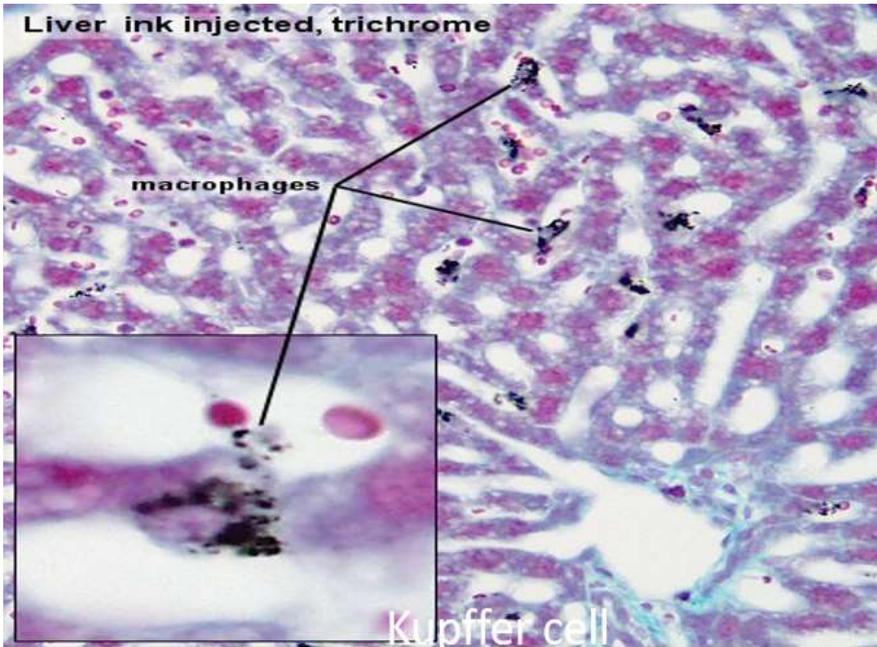
**Three types:**

- **Resident** :resting
- **Elicited**: moving to a stimulus
- **Activated**: active in phagocytosis:
  - pseudopodea
  - Kidney shaped eccentric nucleus-
  - large number of **lysosomes**

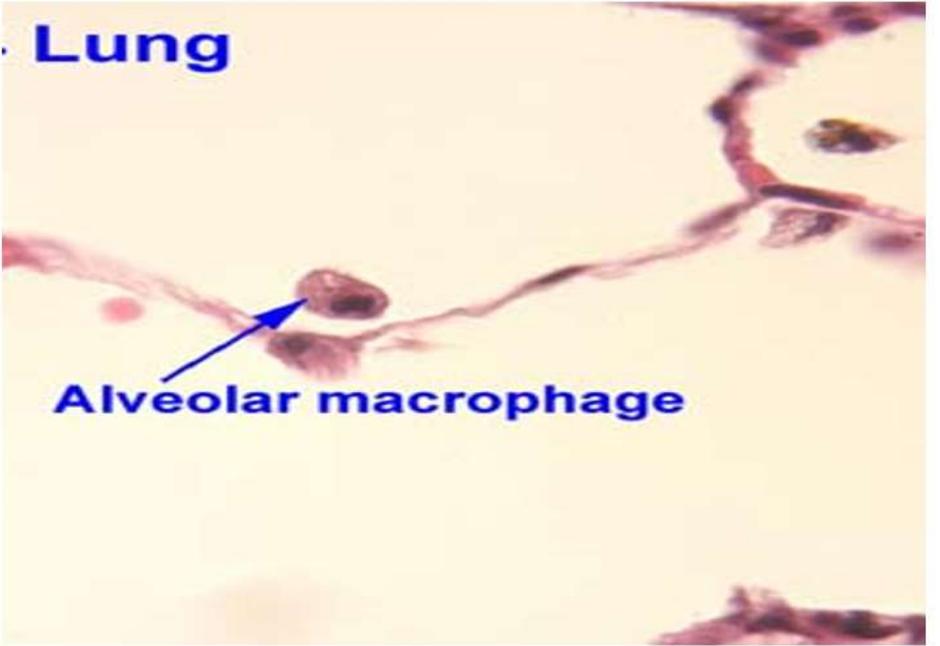
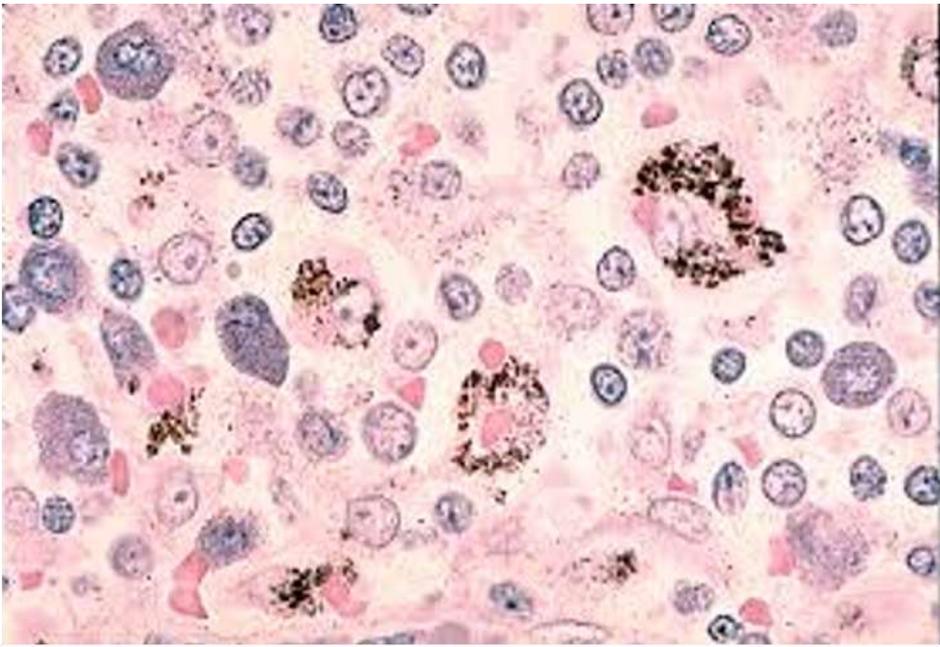


**Function :**

**Phagocytosis**, they are phagocytic cells; macrophages engulf a broad variety of foreign materials including bacteria, dead cells and dust particles.



**Kupffer cell in liver**



# Plasma Cells

**Origin :** they are derived from  
**B lymphocytes that enter the CT.**

## **Histological features:**

### **LM:**

they are large oval cells, with basophilic cytoplasm. The nucleus is spherical and eccentrically-placed. The chromatin of the nucleus is arranged giving the nucleus a **cart-wheel appearance**.

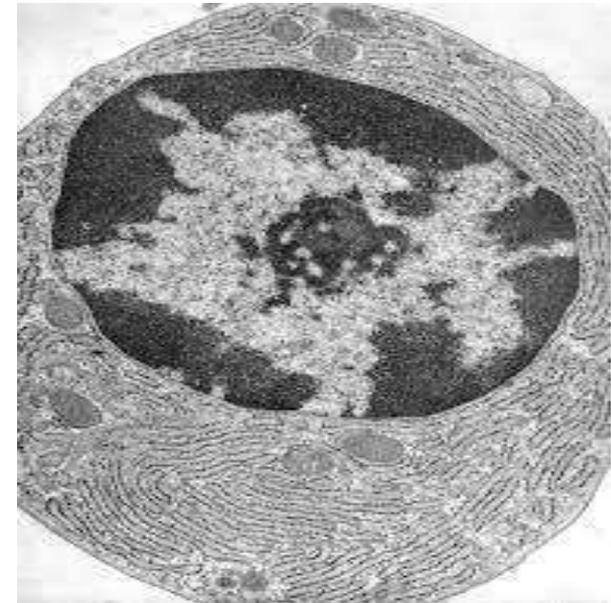
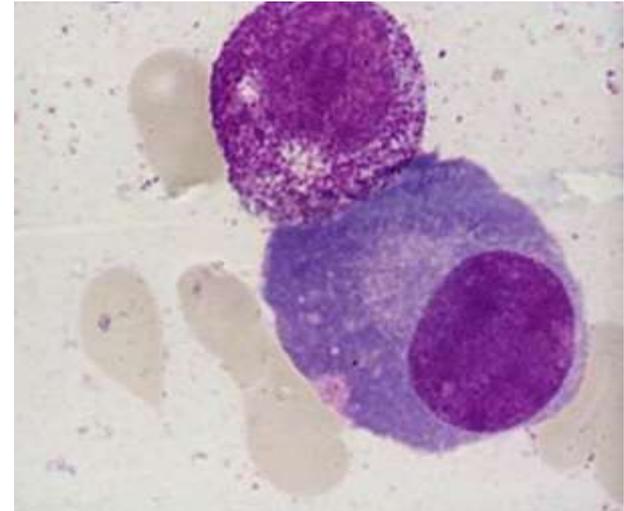
- The prominent juxtannuclear Golgi apparatus appears unstained "**negative Golgi image**" against the deeply-basophilic cytoplasm.

### **EM:**

The cytoplasm shows closely-packed cisternae of rER together with large juxtannuclear Golgi complex.

### **Function:**

they are responsible for synthesis of antibodies against bacteria and foreign proteins penetrating into the CT.



## **White blood cells (leukocytes)**

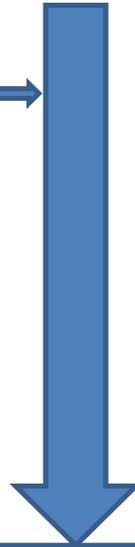
They include neutrophils, eosinophils, basophils, monocytes and lymphocytes.

# Classification of C.T.

Depend on ground substance



Jelly like



- Embryonic C.T
- Muroid C.T.

- C.T. Proper**
  - Loose C.T.
  - Dense C.T.

- Modified types**
  - ❖ Blood =fluid
  - ❖ Cartilage= firm
  - ❖ Bone = hard

# CLASSIFICATION OF CONNECTIVE TISSUE

Classification depends on the proportion of :

- cells to fibers
- Arrangement
- types of fibers.

**Three categories** can be defined:

## **❑ Connective tissue proper:**

it includes:

- ❑ Loose areolar connective tissue.
- ❑ Dense irregular connective tissue
- ❑ Dense regular connective tissue.
- ❑ Elastic connective tissue.
- ❑ Reticular connective tissue.
- ❑ Adipose connection tissue.

## **❑ Embryonic connective tissue**

it includes:

- Mesenchymal CT.
- Muroid CT.

## **❑ Specialized connective tissue:**

it includes:

- ❑ Cartilage.
- ❑ Bone.
- ❑ Blood.

# Embryonic connective tissue

## Mesenchymal CT

**Site:** it is found in embryo.

**Histological structure:**

**it consists of:**

- Undifferentiated mesenchymal cells (UMCs) with their processes come in contact with each other forming a network.
- A gel-like, amorphous ground substance.
- Scattered reticular fibers.

## Muroid CT

**Site:** it is found in the umbilical cord and pulp of growing teeth.

**Histological structure:**

It consists of:

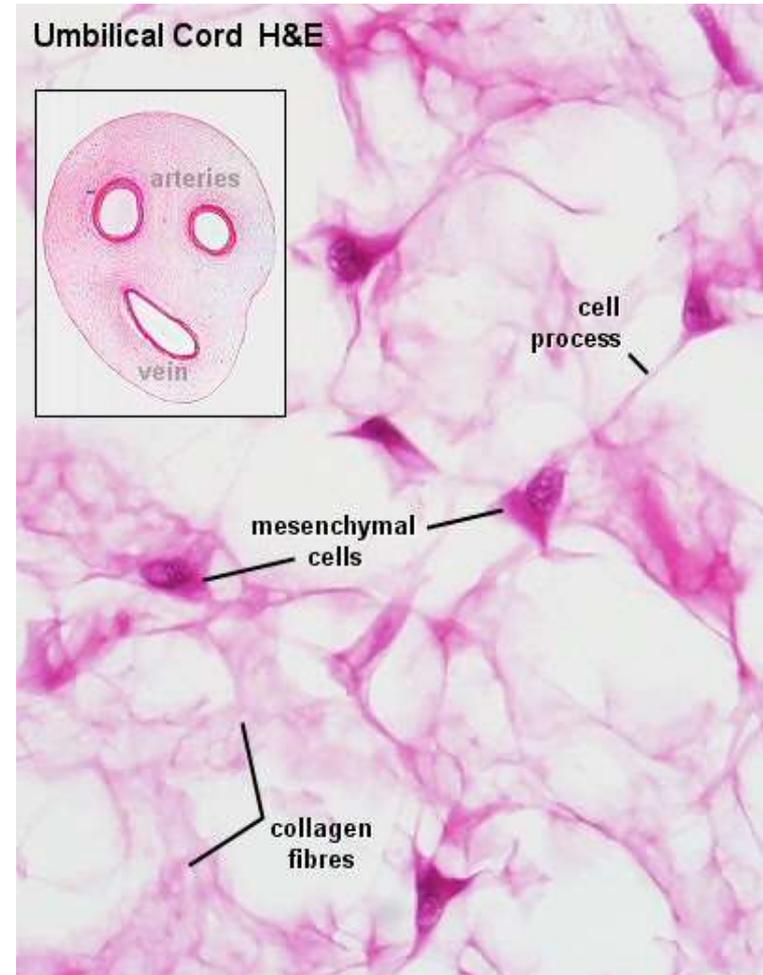
- ❑ Abundant ground substance (Wharton's jelly)
- ❑ Spindle-shaped UDMCs that are widely separated and fibroblasts.
- ❑ Unapparent fine collagen fibers that have the same refractive index as the matrix. (**Type II collagen**)

# Mucoid C.T.= Embryonic C.T

- **Mucoid connective tissue** (or **mucous tissue**) is a type of [connective tissue](#) found during [fetal](#) development.
- It is composed mainly of [ground substance](#) with few cells & fibers
- It is most easily found as a component of [Wharton's jelly](#).
- **Cells : UDMC, Fibroblasts**
- **Fibers : present but not apparent collagen type II**
- **Ground substance : Abundant**

## Sites:

- Mucous connective tissue forms the [umbilical cord](#).
- The [vitreous of the eyeball](#) is a similar tissue.



# Connective tissue proper

## Loose connective tissue:

relatively cell rich, soft .

It is also rich in vessels and nerves.

Loose connective tissue may occur in some special variants:

- **LACT:** connective tissue
- **Reticular:** connective tissue
- **Adipose:** tissue.

## Dense CT:

- connective tissues are completely dominated by fibres.
- They are subdivided according to the arrangement of the fibres in the tissue.

## Dense irregular:

connective tissue the fibres do not show a clear orientation within the tissue but instead form a densely woven three-dimensional network (dermis).

## Dense Regular

1. White fibrous C.T.
2. Elastic C.T.

# Connective tissue proper

## Loose areolar CT:

it is the most widely distributed connective tissue in the body.

It binds body parts together while allowing them to move freely over one another.

## Histological structure

- ❑ All types of fibers; collagen, elastic and a small proportion of the reticular fibers.
- ❑ All types of connective tissue cells with predominance of fibroblasts and macrophages.
- ❑ Good amount of ground substance.
- ❑ Highly vascular

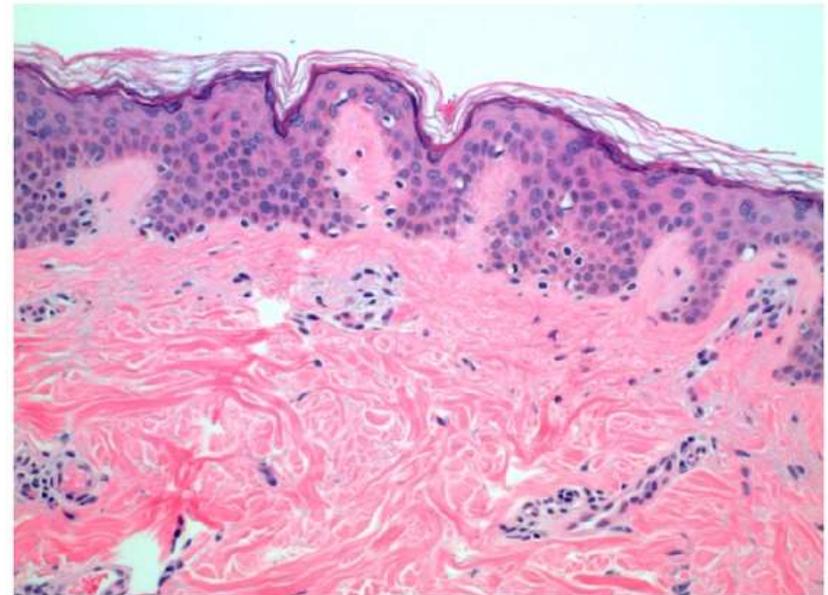
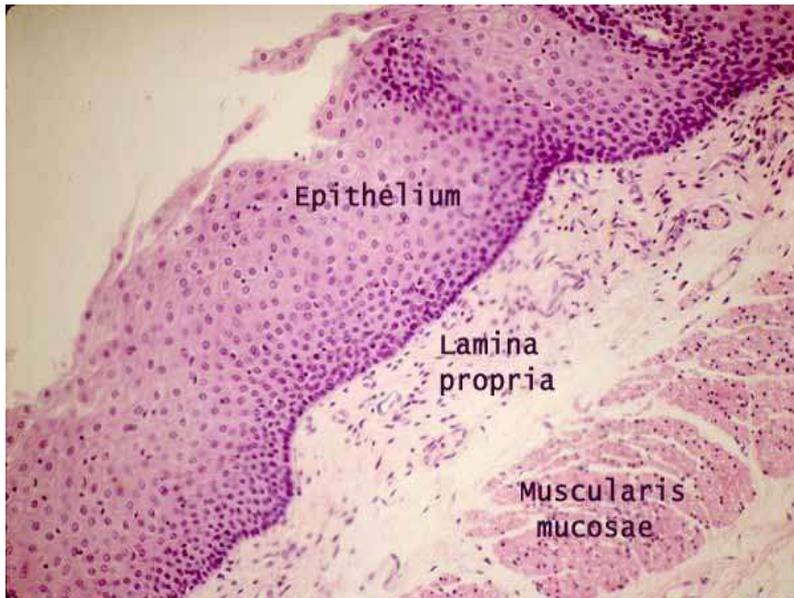
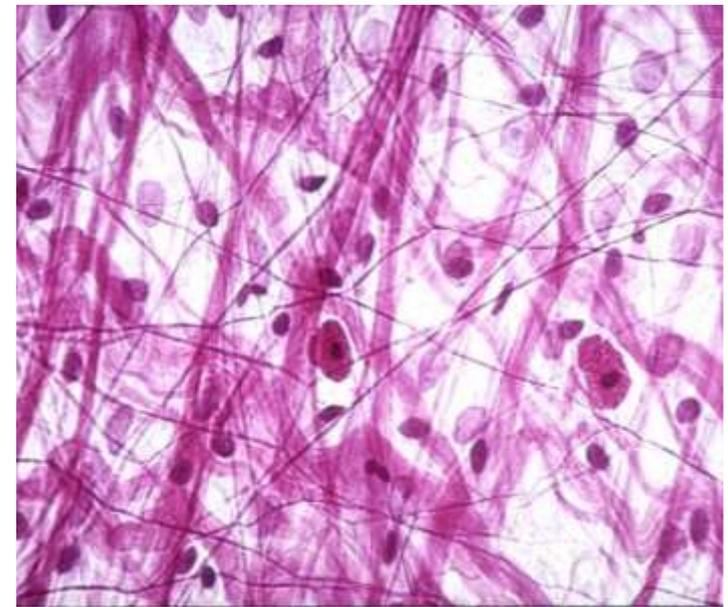
## sites:

- It is present beneath the epithelium in all mucous membranes forming the lamina propria.
- It forms the papillary layer of dermis which attaches the skin epidermis to underlying structures.
- It surrounds glands, small blood vessels, and nerves.

# Loose Areolar C.T.

## Function:

- Supports and binds other tissues (by its fibers).
- Holds body fluids and provide nutrition (by its ground substance).
- Defends against infection (by its white blood cells, plasma cells, mast cells and macrophages).



# Reticular CT:

## Histological structure:

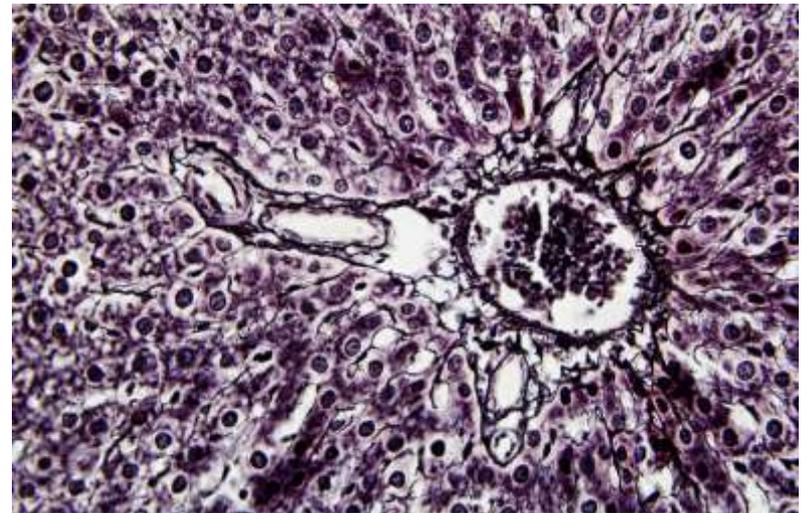
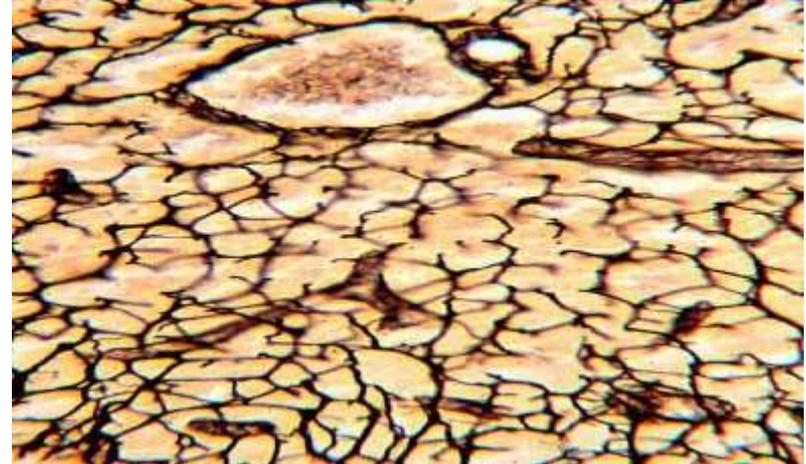
- Reticular fibers, forming a network.
- **Reticular cells**, these are the fibroblasts of reticular connective tissue, that synthesize the reticular fibers.

**Site :** reticular tissue is limited to certain sites

- Hemopoietic tissue in the bone marrow.
- Lymphoid tissue in lymph nodes and spleen.
- In the **liver**.

## Function

- It forms the supporting



**Liver (silver stain)**

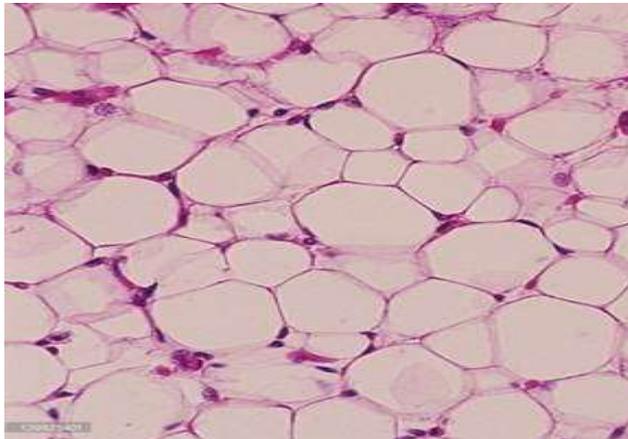
# Adipose C.T.

## Unilocular adipose C.T. Yellow fat

- Unilocular fat cells
- C.T. fibers: collagenous F.
- rich in blood supply
- Carotenoids

### Sites:

- Subcutaneous tissue
- Around vital organs

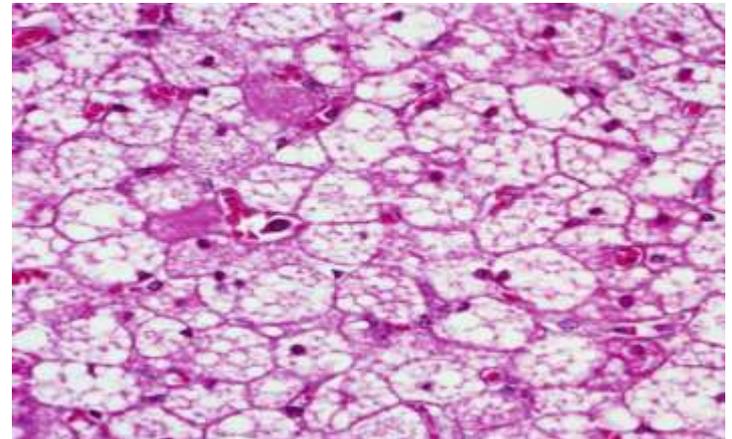


## Multilocular adipose C.T. Brown fat

- Multilocular fat cells
- C.T. fibers – collagenous F.
- rich in blood supply
- Many blood vessels , numerous mitochondria , cytochrome pigment

### Sites:

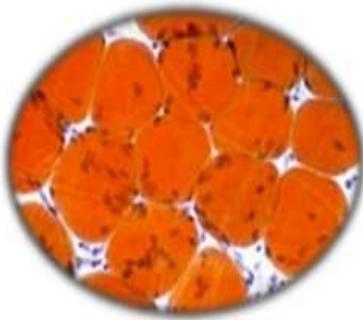
- Back & neck of newborn



# Adipose C.T.

## 2. Lipid

- **Frozen sections are used**
- **Sudan III** → **orange colour**
- **Sudan black** → **black colour**
- **Osmic acid** → **black colour**



[synthesismatters.blogspot.com.br](http://synthesismatters.blogspot.com.br)

## Function:

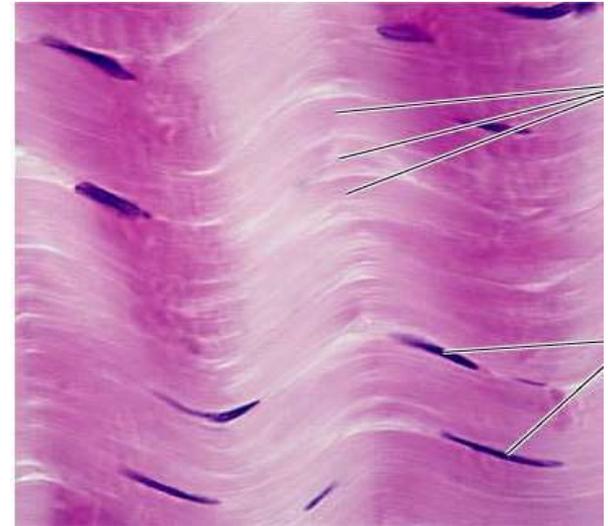
- Storage of energy in the form of triglycerides.
- Subcutaneous adipose tissue shapes the body.
- Pads of fatty tissue in palms and soles act as shock absorber.
- Thermal insulation of the body; due to the poor heat conduction of adipose tissue.
- Fixation of the vital organs as heart and kidney, thus keeping them in position.

# Dense regular C.T.

## White Fibrous C.T.

### Histological structure

- Closely-packed wavy bundles of collagen fibers running in the same direction and parallel to the direction of pull.
- Rows of fibroblasts (**tendon cells**) with flattened nuclei aligned between the collagen bundles.
- Little amount of ground substance.
- Unlike areolar CT this tissue is poorly vascularized.



### Sites

- It is found in:
- Tendons, which attach muscles to bones.
- Ligaments, which bind bones together at joints.
- sclera of the eye

### Function:

forms white flexible structures with great resistance to pulling forces wherever it is exerted in a single direction.

# Dense Irregular CT:

## Histological structure:

- Thick bundles of collagen fibers arranged irregularly (running in more than one plane).
- Little amount of ground substance with few fibroblasts.

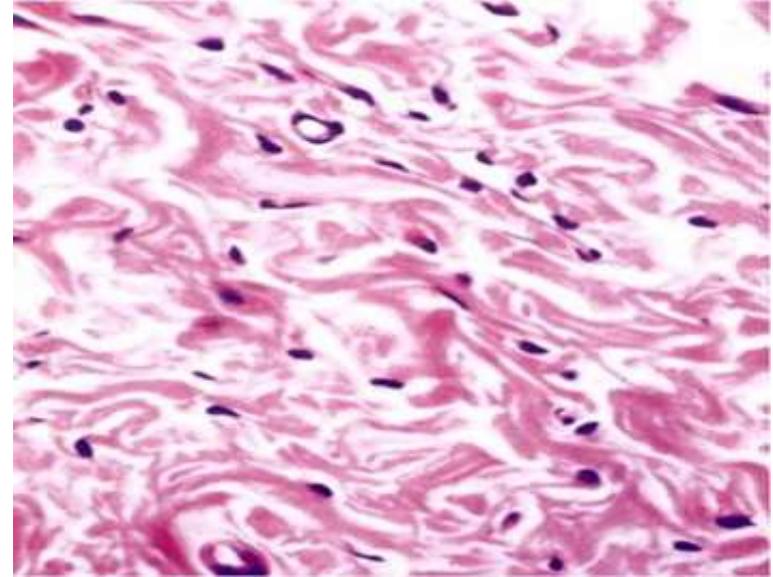
## Sites :

It is found in :

- reticular layer of dermis** of the skin.
- It forms the capsules of fibrous joints.
- It forms the capsules of body organs e.g. kidney, spleen, lymph nodes and liver.

## Function

forms sheets in body areas where tension is exerted from many different directions.



# Elastic C.T.

## Histological structure:

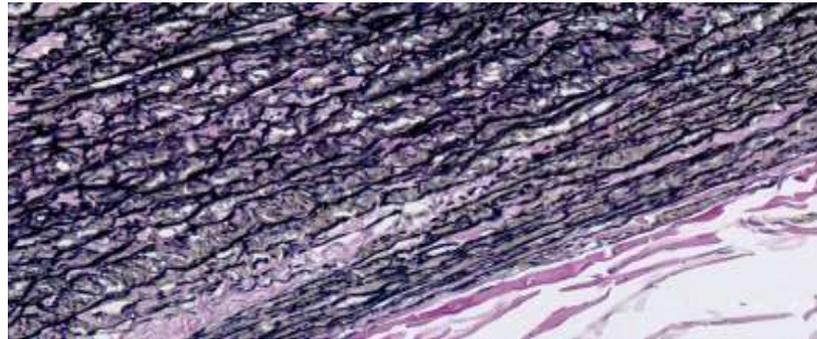
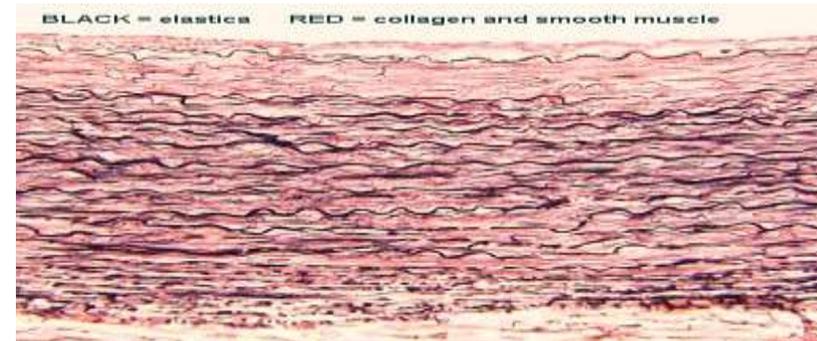
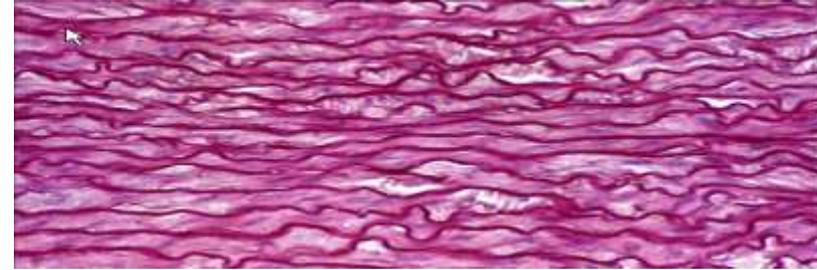
elastic fibers predominate; they run in all directions, also they may form fenestrated membranes.

## Site :

it is found in:

- Elastic laminae of arteries.
- True vocal cords.
- Few ligaments in the body are very elastic such as ligamenta flava and ligamenta nuchae connecting adjacent vertebrae.

**Function:** this tissue is present where flexibility and elastic recoil are needed



# CONNECTIVE TISSUE

- Connective tissues are the most abundant of the primary tissues.
- The cells of the connective tissues are far apart, separated by an abundant amount of extracellular material, also called extracellular matrix

## Function :

1. **Bind** together and provide **mechanical support** for other tissue (metabolic, defense, transport, storage)
2. Architectural **framework** of the body
3. Insulation:  
Fat cells or adipose tissue, is a connective tissue which not only cushions body organs but also insulates them and provides reserve energy fuel.
4. Nutrition
5. **Protection:** inflammatory response
6. Wound repair
7. Transportation:  
Blood is a connective tissue and it carries and delivers oxygen and nutrient to tissues.