

The connective tissue ground substance:

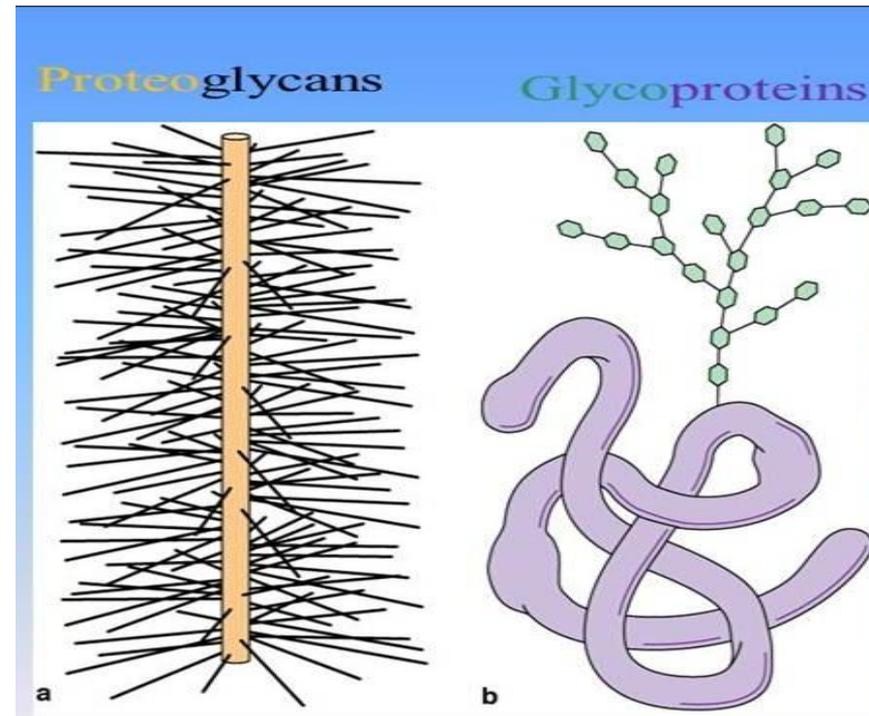
It is the material that fills the spaces between the cells and contains the fibers. It is composed of:

- **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.

- **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.

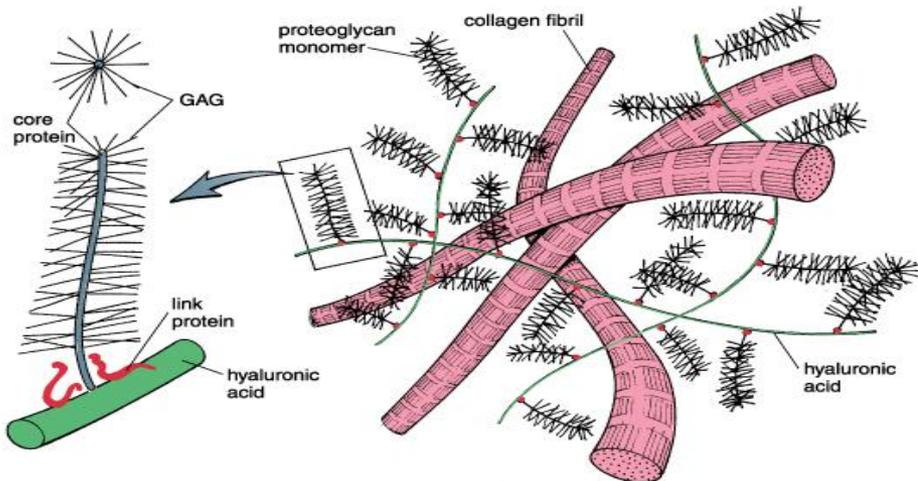
- **Adhesive glycoproteins** e.g. **fibronectin** and **laminin**. They serve mainly as connective tissue glue that allows connective tissue cells to bind themselves to matrix elements.



- **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=**Jelly like**



Function :

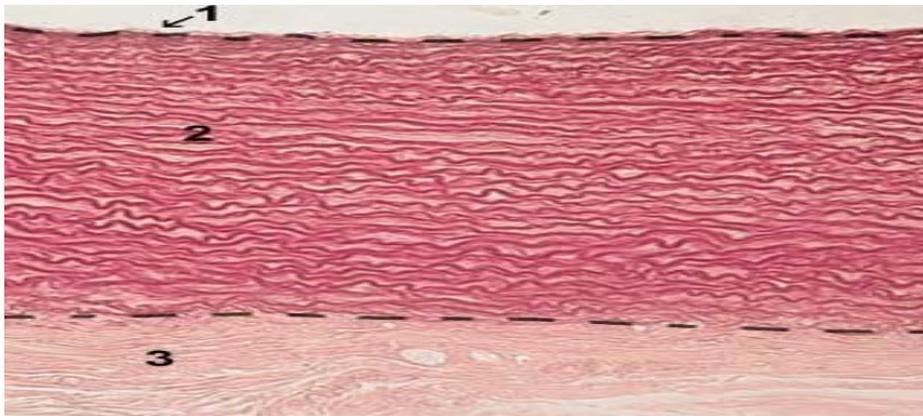
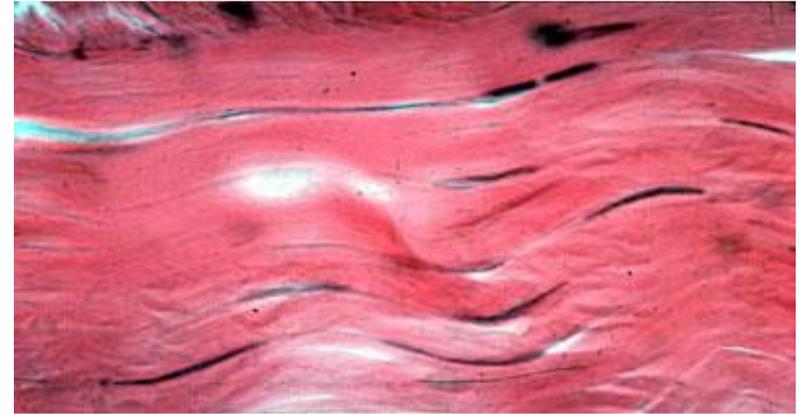
- The ground substance **holds large amounts of fluid** and functions as a medium through which nutrients and other dissolved substances can diffuse between the blood capillaries and the cells.
- Its gel state serves to **resist compression** and to act as a **lubricant**.
- It also acts as a **barrier**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

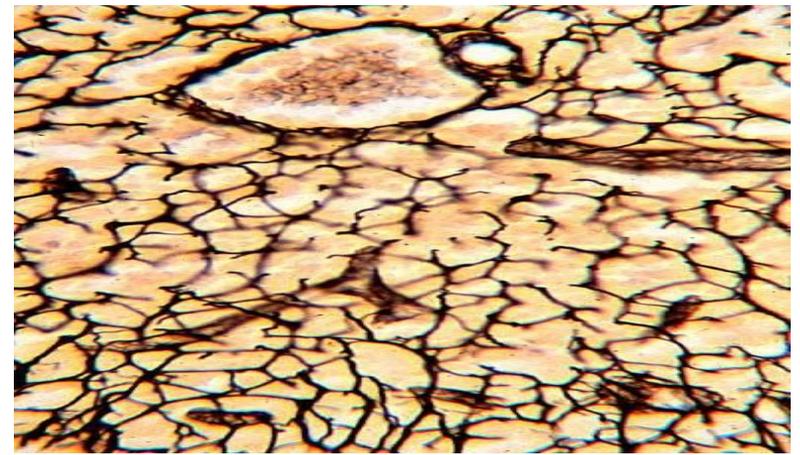
- The fibers of connective tissue provide support. They are embedded in connective tissue matrix. There are three types of CT fibers;

- ❖ collagen fibers,
- ❖ elastic fibers
- ❖ reticular fibers.

❖ collagen fibers,

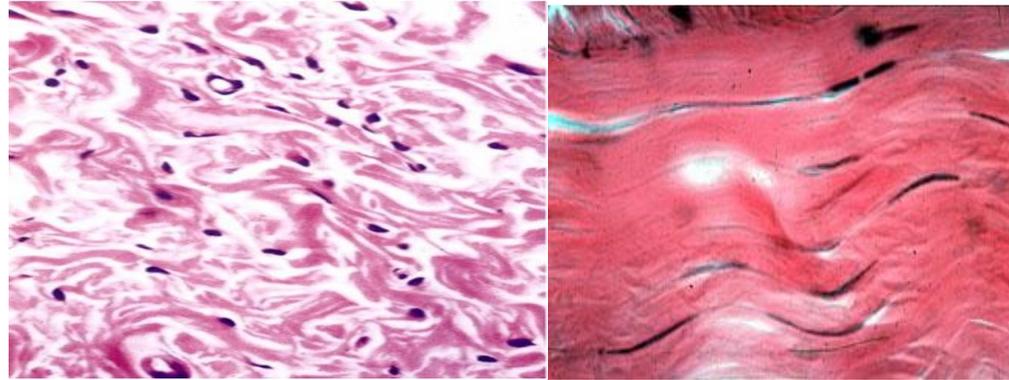


❖ elastic fibers



❖ 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 (eosinophilic), **blue** with Mallory's stain and **green** with Masson's trichrome stain.

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.

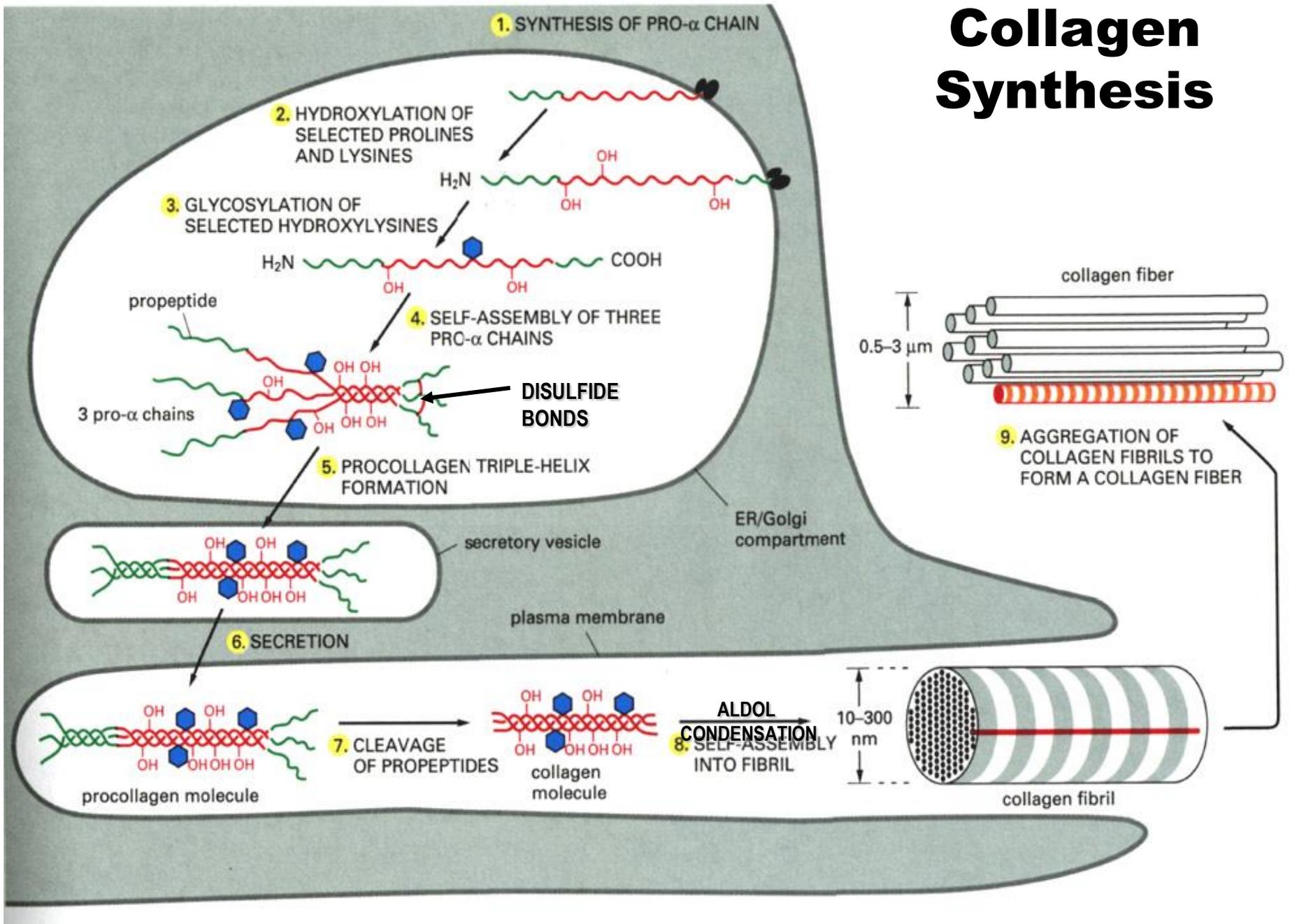
Types of collagen:

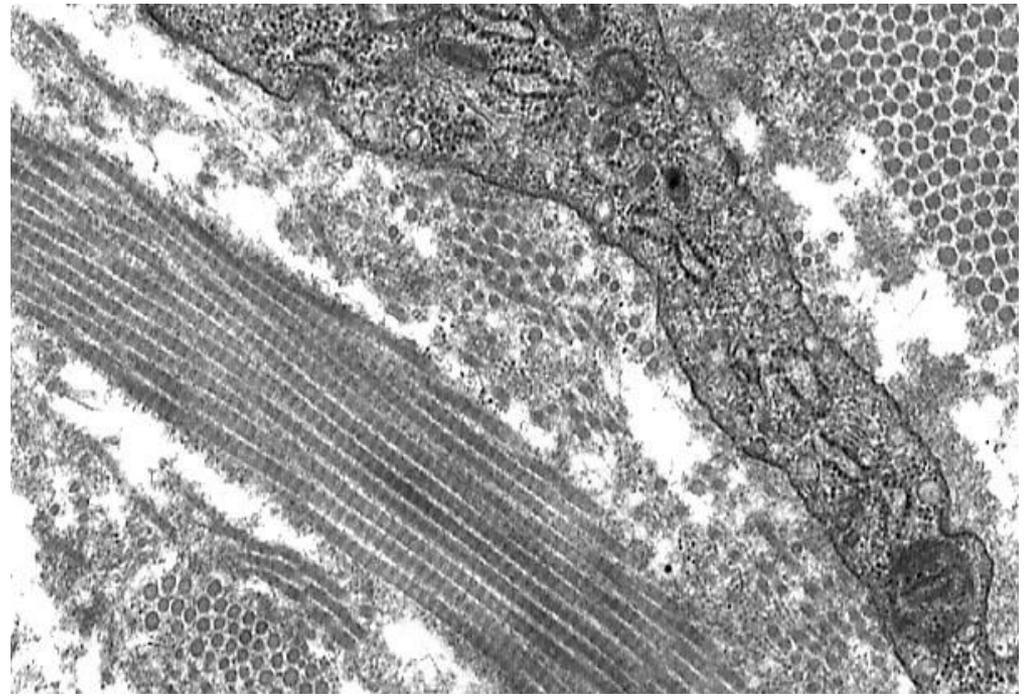
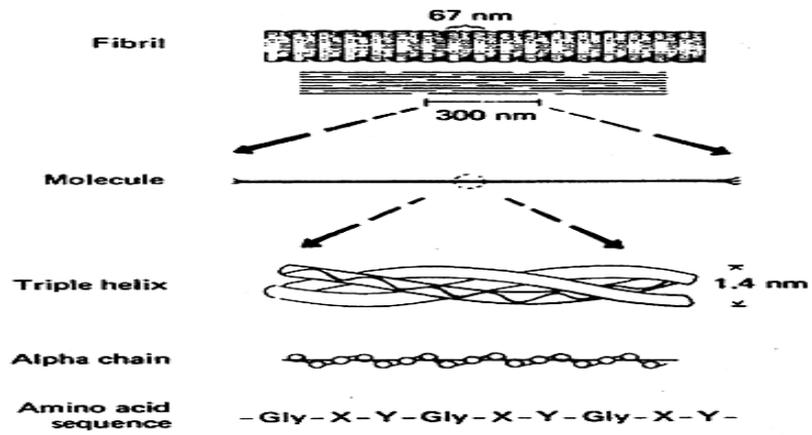
- More than **20 different types of collagen** fibers are known. They differ by their molecular composition, morphologic features, distribution in tissues and functions.

The major types of collagen are:

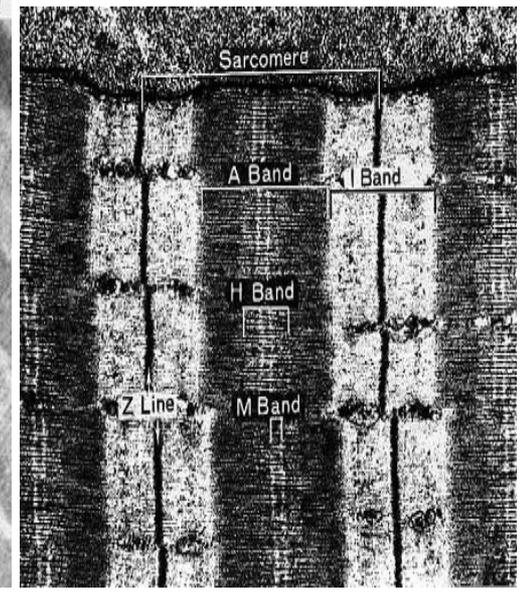
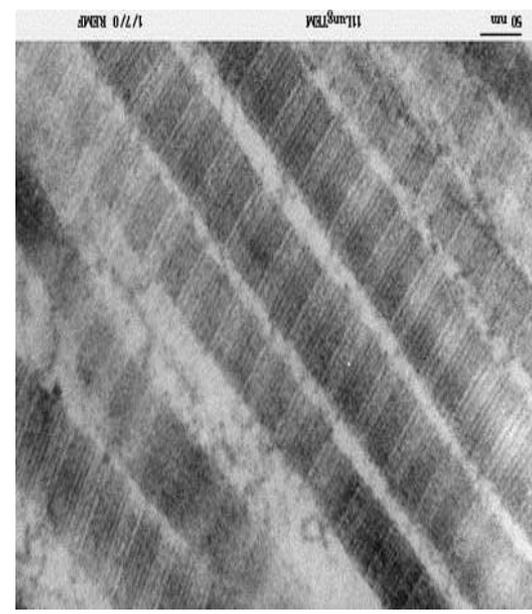
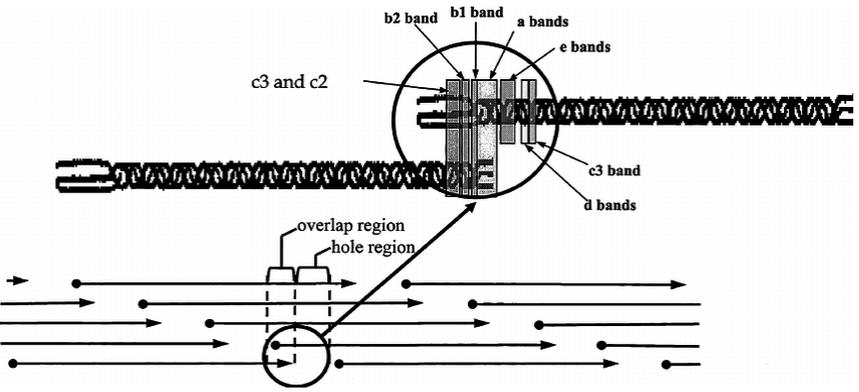
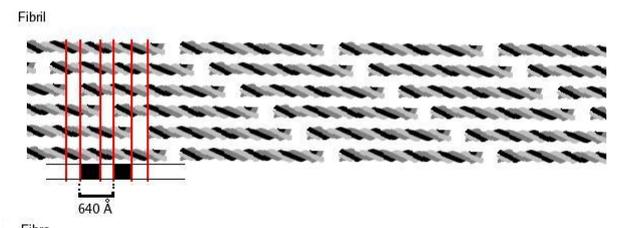
- Type I collagen fibers in connective tissue proper, and in fibrocartilage and bone matrix.
- Type II collagen fibrils in cartilage matrix (hyaline and elastic).
- Type III collagen fibers form the reticular fibers.
- Type IV in basement membrane.
- Type VII in basement membrane.

Collagen Synthesis

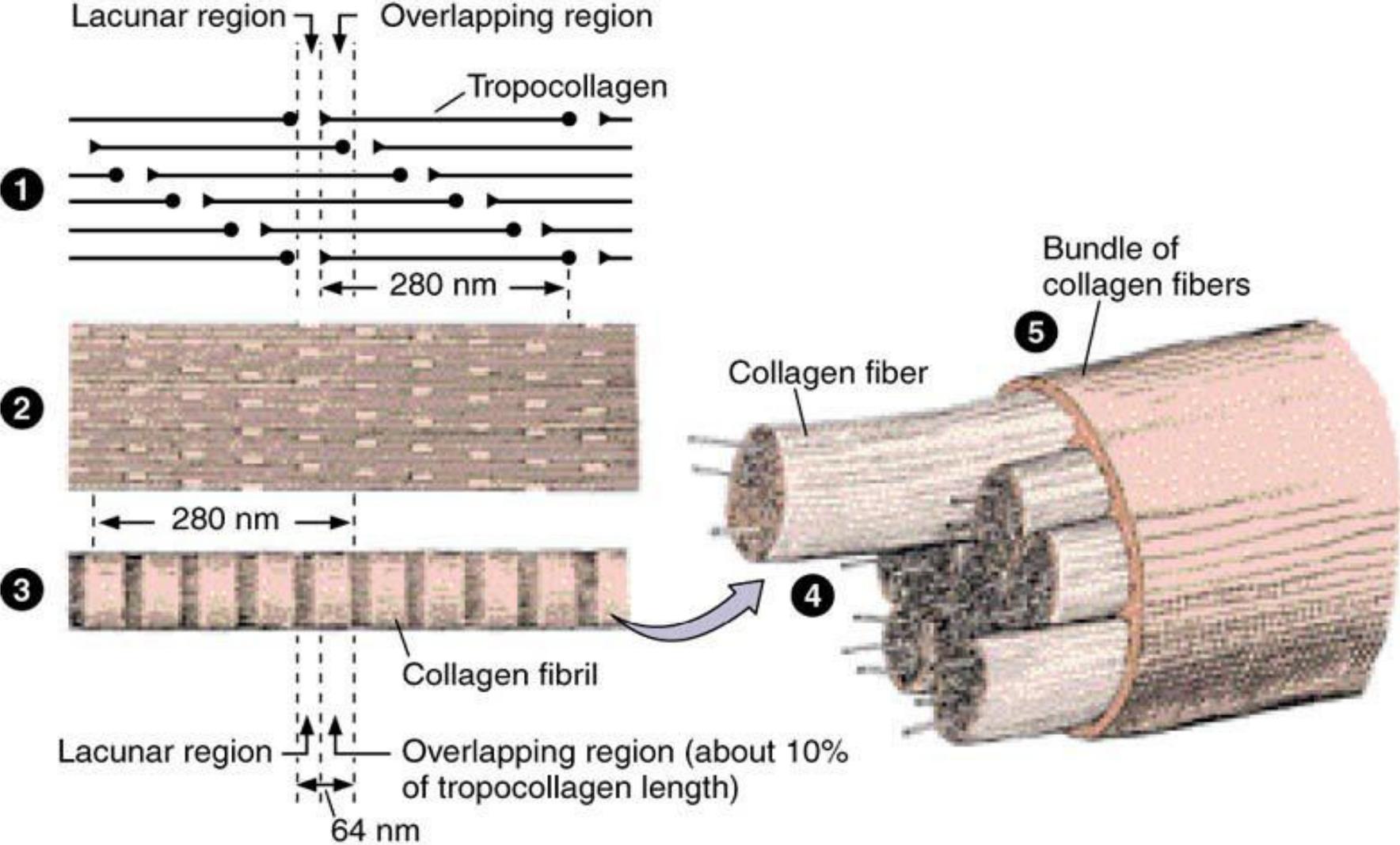




Synthesis of collagen



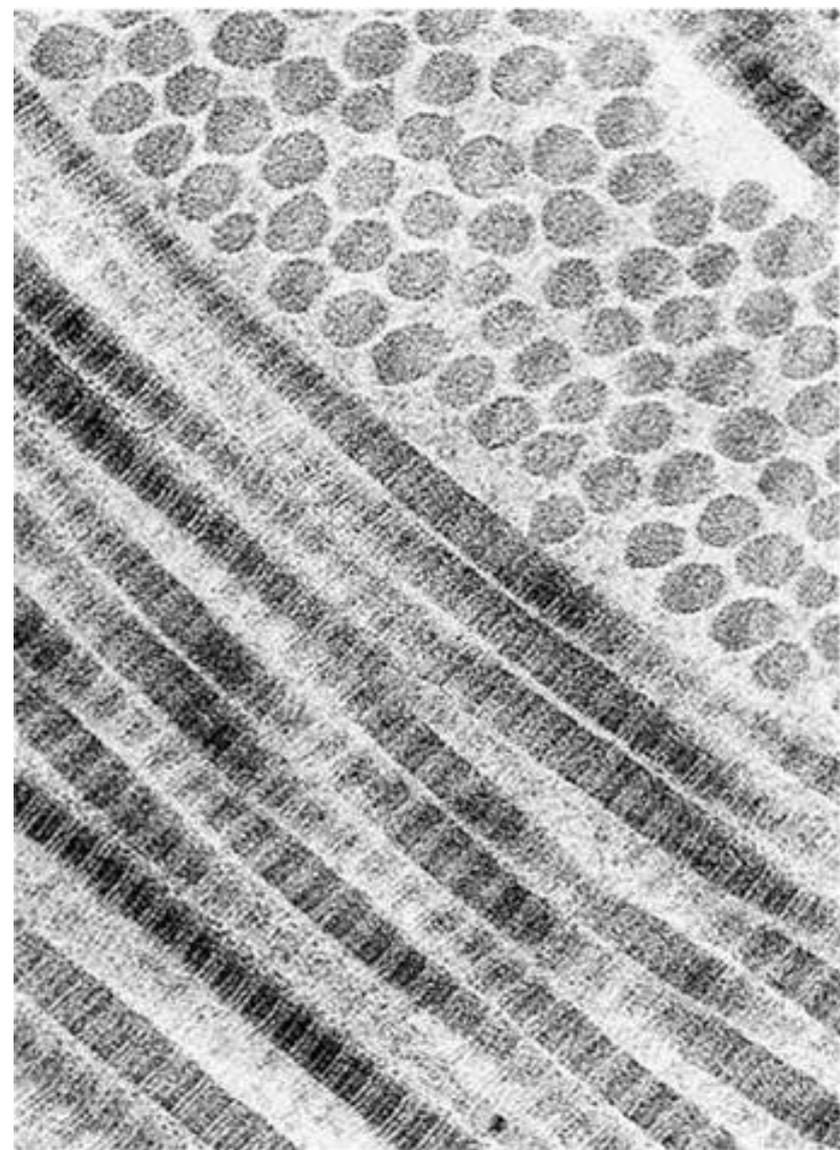
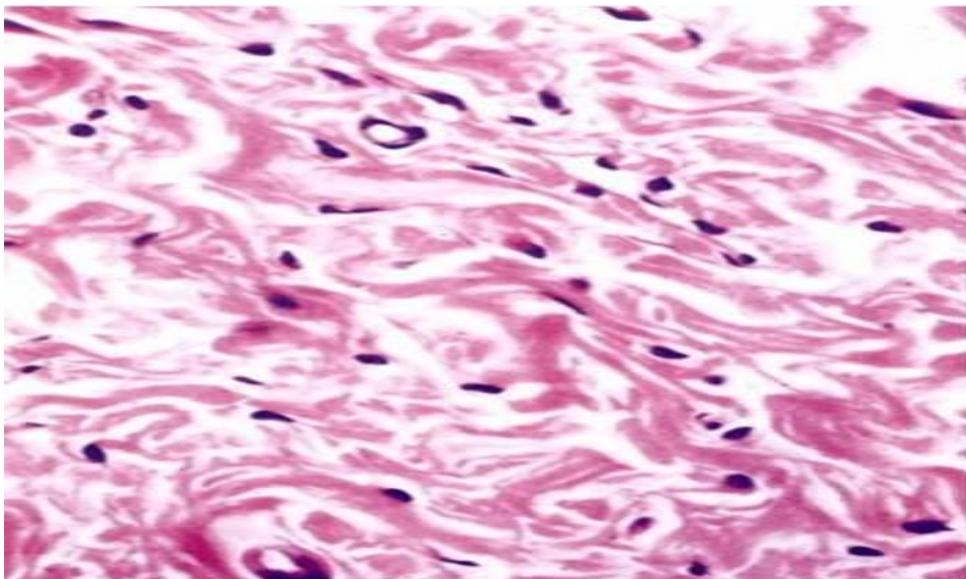
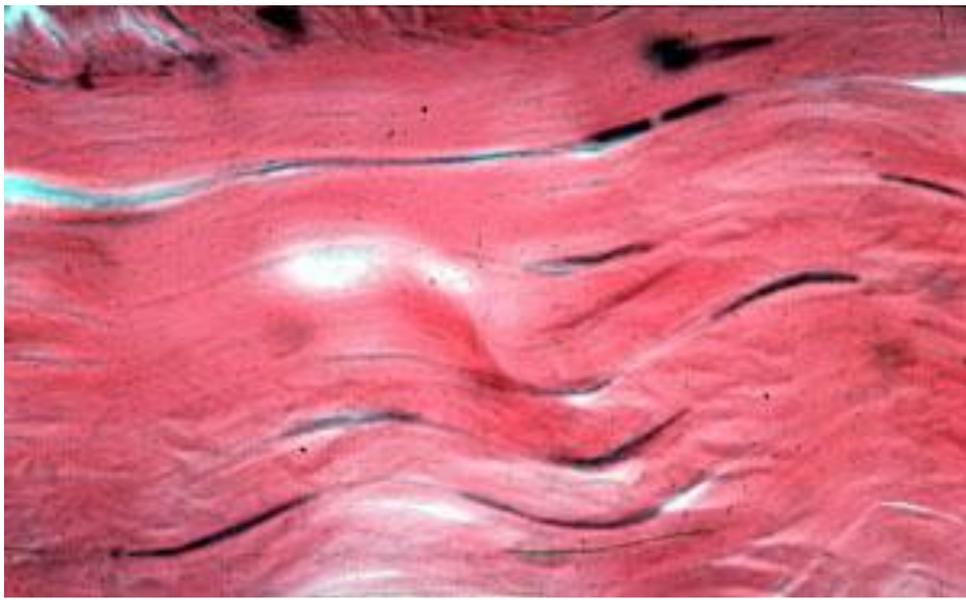
Assembly of collagen fiber bundles



H & E

Collagen Fibers

EM

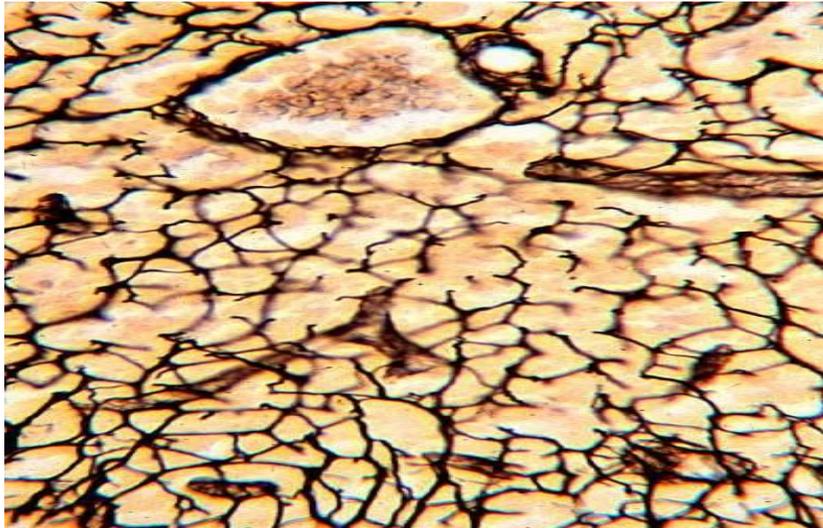
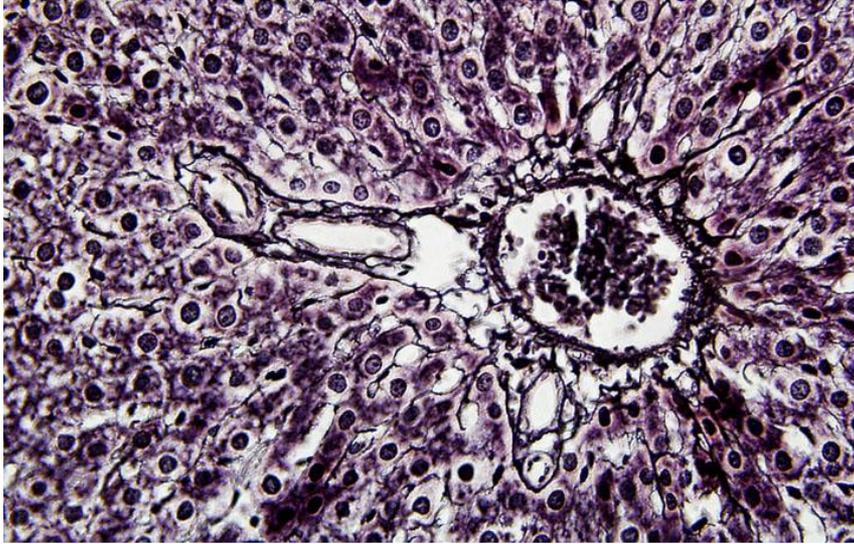


Major Collagen Fiber Types (out of at least 20)

According to the chemical composition of collagen molecules

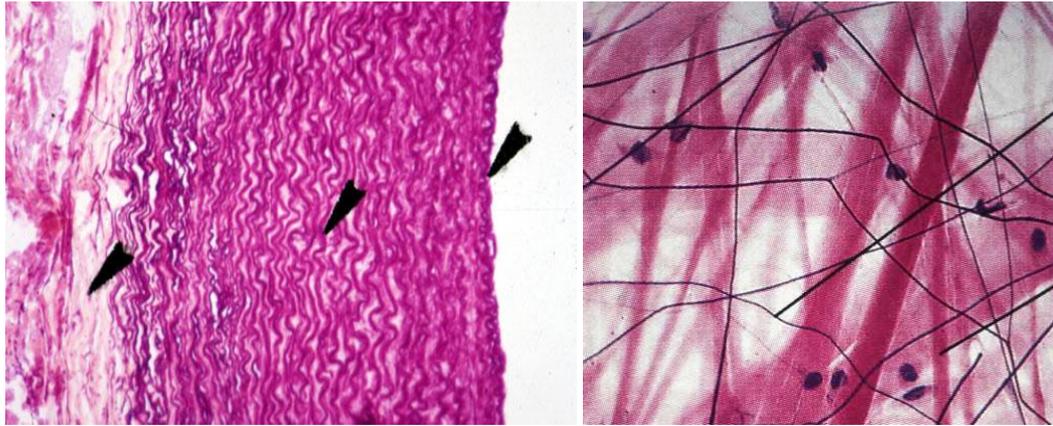
Collagen Type	Tissues	Function
Fibril-forming collagens (these are visible)		
I (most abundant)	Skin, tendon, bone, dentin	Resistance to tension
II	Cartilage, vitreous of eye	Resistance to pressure
III (reticulin)	Skin, muscle, blood vessels, liver, etc.	Structural framework and stability
Network-forming collagens		
IV	All basement membranes	Support and filtration
Anchoring filament collagens		
VII	Epithelia	Epidermis to basal lamina

Reticular (Reticulin) Fibers



- **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** impregnation to visualize.
- **Thinner than type I collagen** (Type III fibrils are 30-40 nm diameter; type I fibrils are ~200 nm diameter)
- made by **reticular cells (specialized fibroblasts)** and **vascular smooth muscle cells**

Elastic fibers



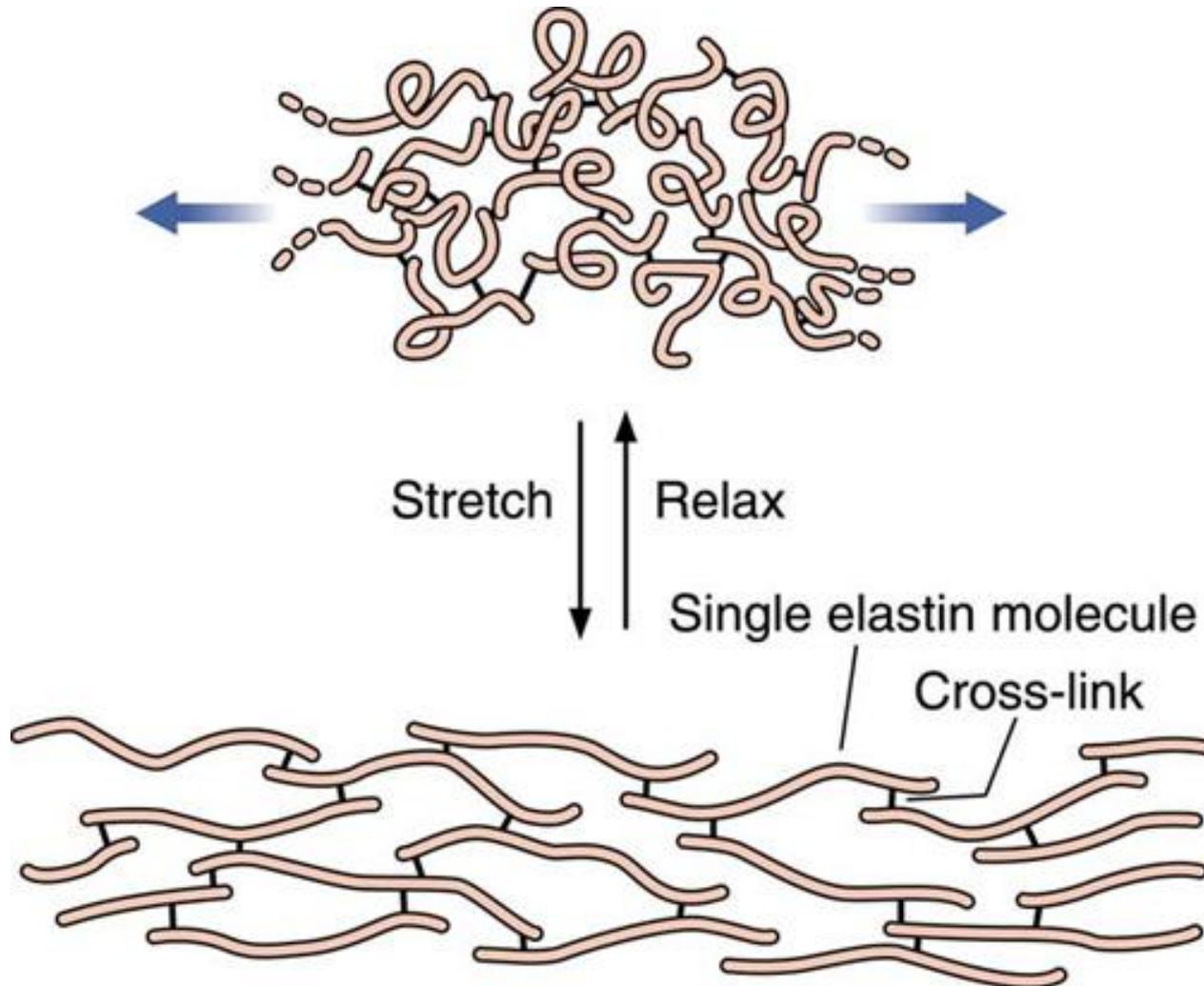
Characters:

- 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**.

Histological features:

- 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 color.

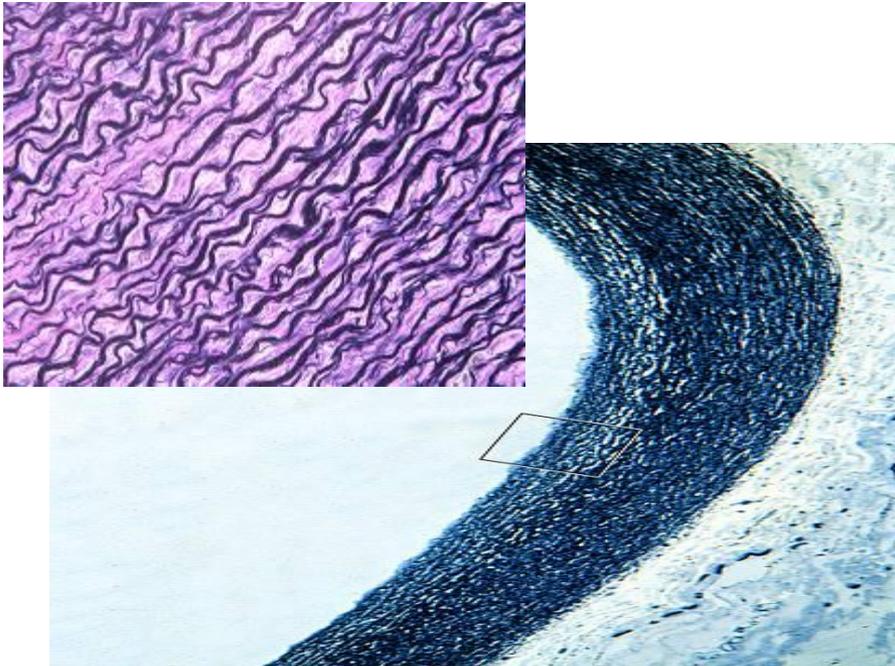
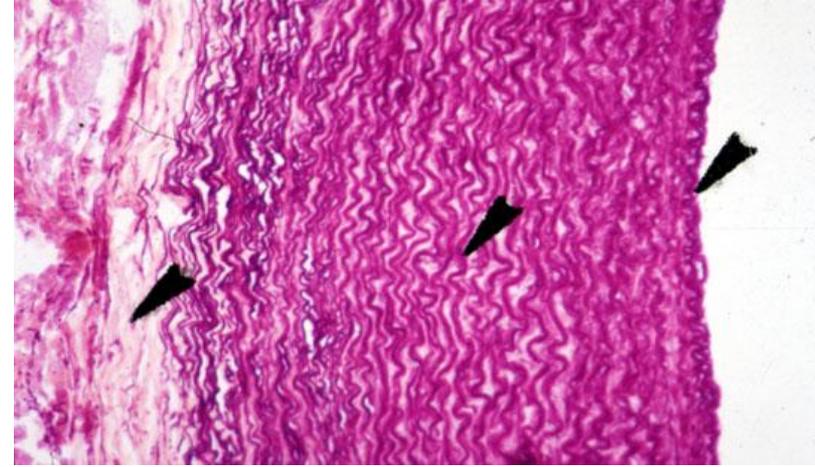
Network of elastin molecules can stretch and recoil like a rubber band

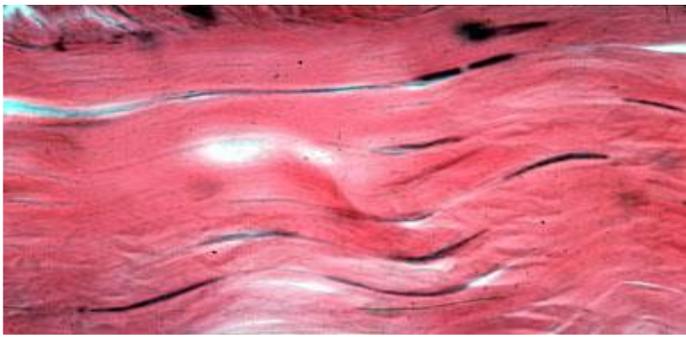


Elastic Fibers

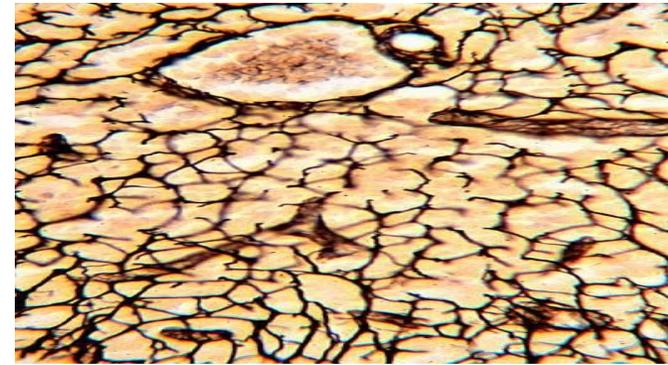
Elastic fibers (yellow fibers): can be stretched to one and one-half times their length, but recoil to their initial length when released. Fresh elastic fibers appear yellow and are also called **yellow fibers**.

Stain : H&E , Orcein , VVG





Fibers

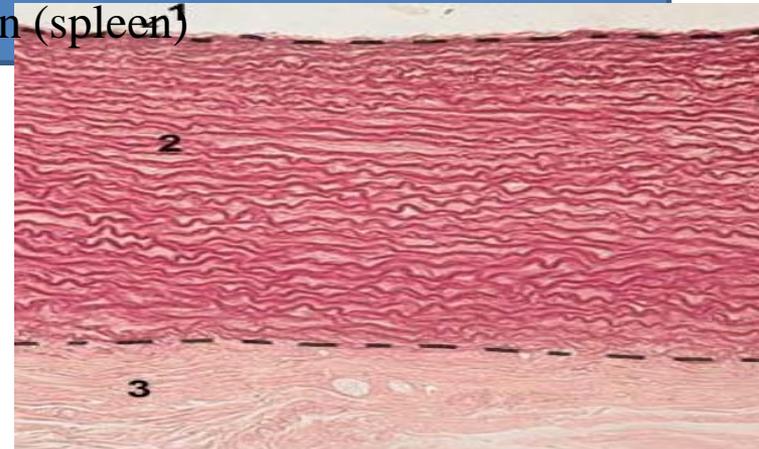


- The most **numerous**
- White if in great number (**white fibers**)
- **Strong and flexible**
- Fibers do not branch but bundles can do
- Formed of **collagen protein**
- Stain pink with eosin
- Types of Collagen Fibres

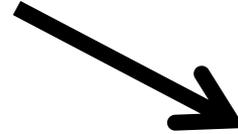
- **Thin branching**
- **Not** stained by H&E
- Stained dark brown with **silver stain**
- Consist of type **III collagen**
- Supportive function

- 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.

Highly cellular organ → support
Site : liver , bone marrow , lymphatic organ (spleen)



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

Undifferentiated Mesenchymal Cell

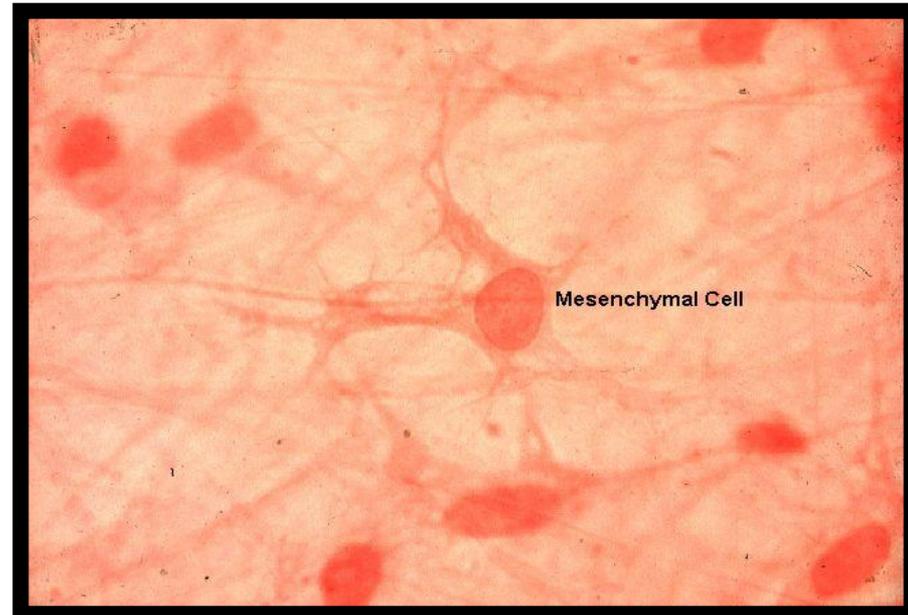
Histological features:

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

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

L.M.

The most important thing in a cell that will differentiate or divide is its nucleus



Highly active

Fibroblasts

Basophilic because cytoplasm has lots of aminoacids

they are the most common cells in CT.

Histological features:

- By LM, fibroblast is a spindle-shaped branching cell, with deeply basophilic cytoplasm and large euchromatic nucleus with prominent nucleolus.
- By EM, its cytoplasm contains abundant rough endoplasmic reticulum and well-developed Golgi complex.

Because it's protein secreator

Function:

- Fibroblasts, indicated by the suffix “blast” (means “forming”), are **active protein-synthesizing cells** that secrete the ground substance and the fibers of the matrix.

Fibrocytes

Less active

- After they synthesize the matrix, they become quiescent and are called fibrocytes. They assume their less active mode, indicated by the suffix “cyte”.
- are smaller cells with fewer processes than the fibroblasts. *By LM*, the cell has a small elongate, heterochromatic nucleus and an eosinophilic cytoplasm. *By 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

the most common type

▪ **Origin : from UDMC**

▪ **2 types**

Young fibroblast= active

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

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

mature (Fibrocytes)

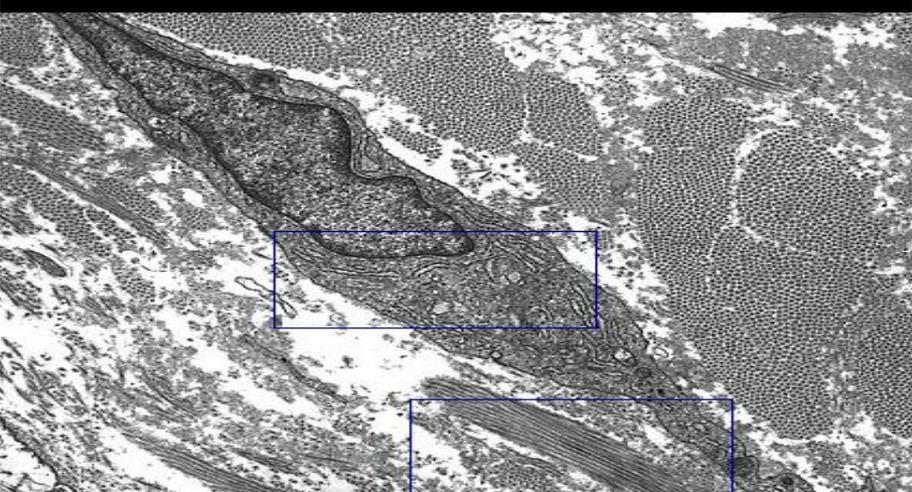
▪ **inactive**

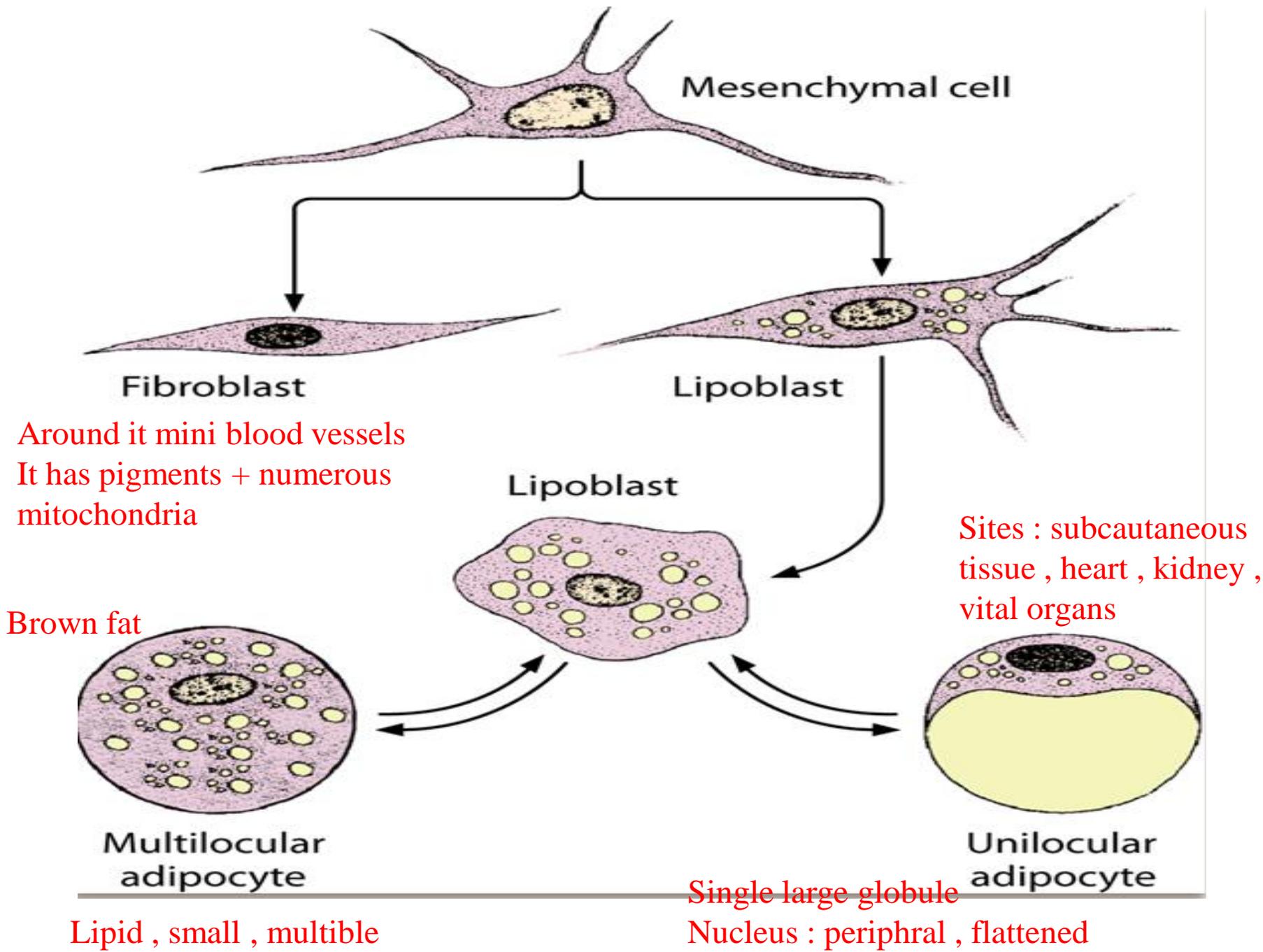
- Small in size
- Fusiform smaller
- oval central **darker** nucleus
- acidophilic cytoplasm

Fibroblasts



Fibrocytes





*Around it mini blood vessels
It has pigments + numerous mitochondria*

Brown fat

Sites : subcutaneous tissue , heart , kidney , vital organs

Lipid , small , multible

*Single large globule
Nucleus : peripheral , flattened*

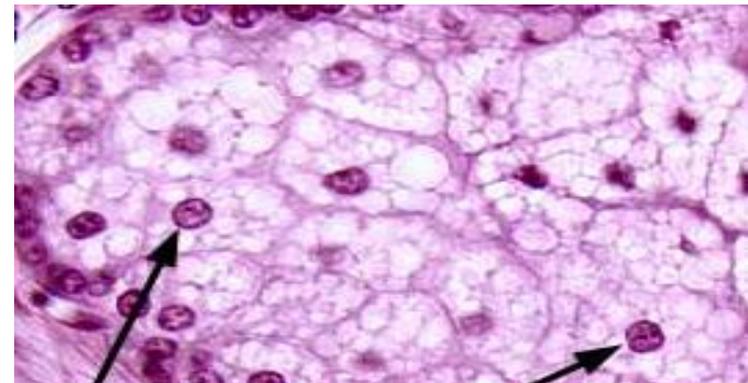
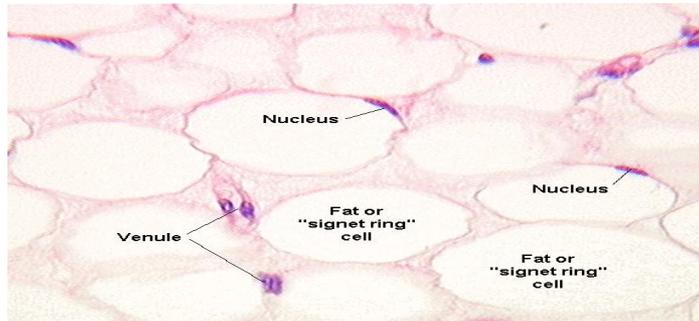
Fat Cell=Adipocytes= fixed cells

Histological features:

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

- The **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.

Fat dissolves
when
staining with
H&E



Adipocytes

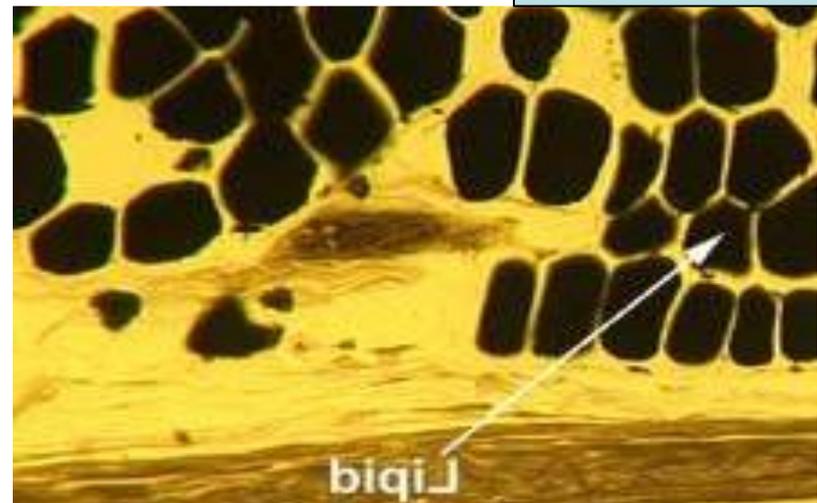
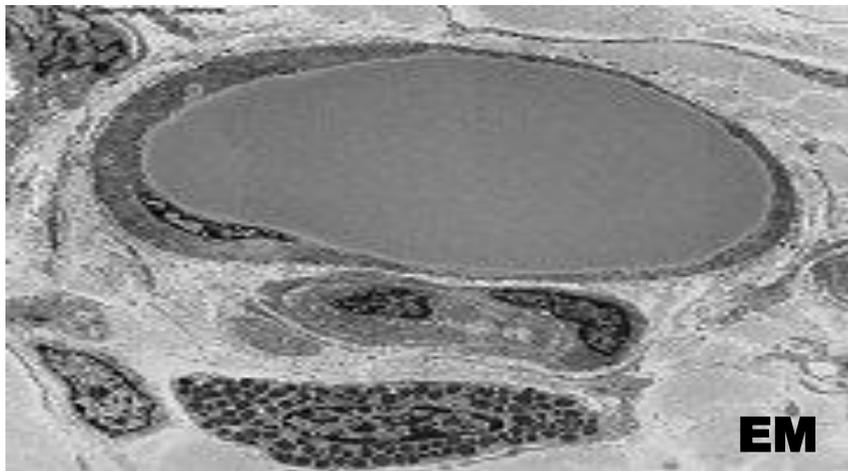
- **Origin : UDMC**
- large, spherical or polyhedral
- The flattened nucleus
- The cytoplasm only forms a very narrow rim around a large central lipid droplet.
- Single or several lipid droplets
- Adipocytes are long-lived cells. Their number is determined by the number of preadipocytes generated during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

Lipid storage/mobilisation is under:
• nervous (sympathetic) hormonal (insulin) control.

• **Function :**

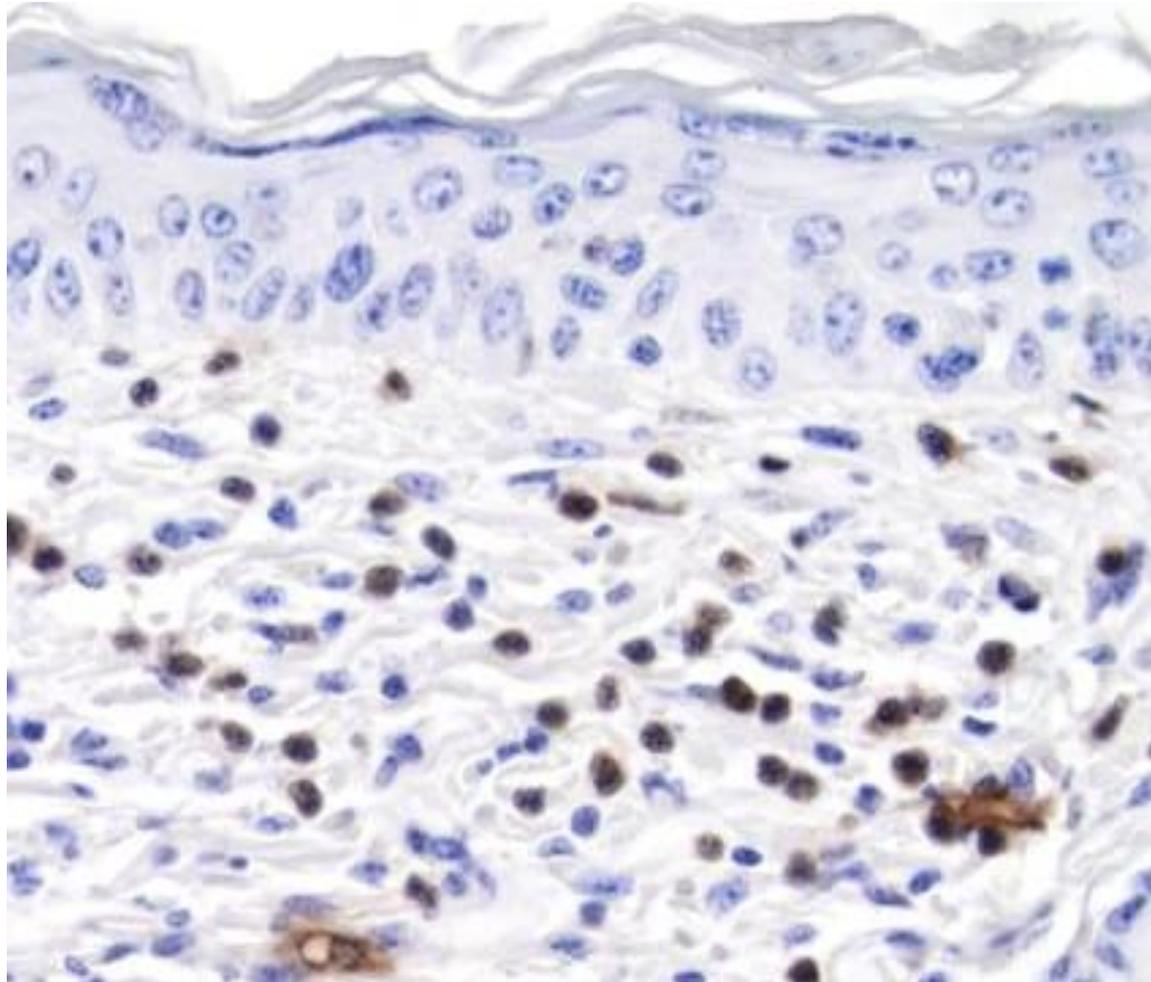
- Storage of lipid
- Production of energy
- endocrine function - they secrete the protein **leptin** which regulate appetite with feedback about the bodies fat reserves.

Osmic acid



Pigment Cells= fixed cells

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



Mast Cells

• **Origin:** from haemopoietic 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

▪ (**Metachromatic** staining)

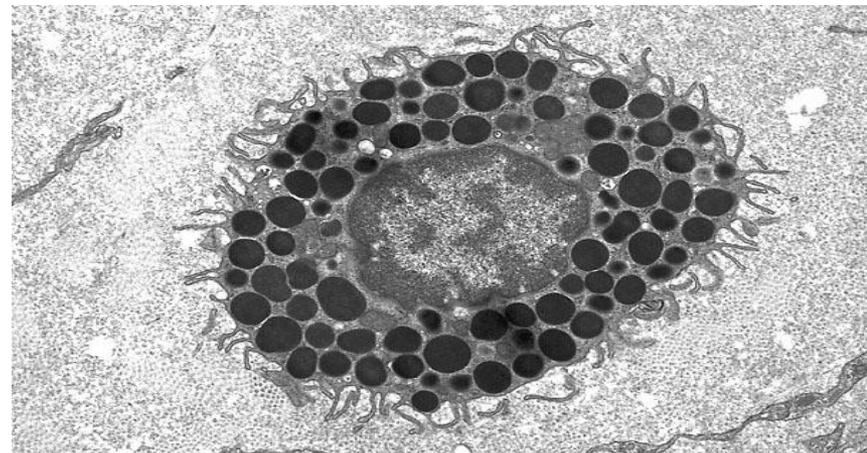
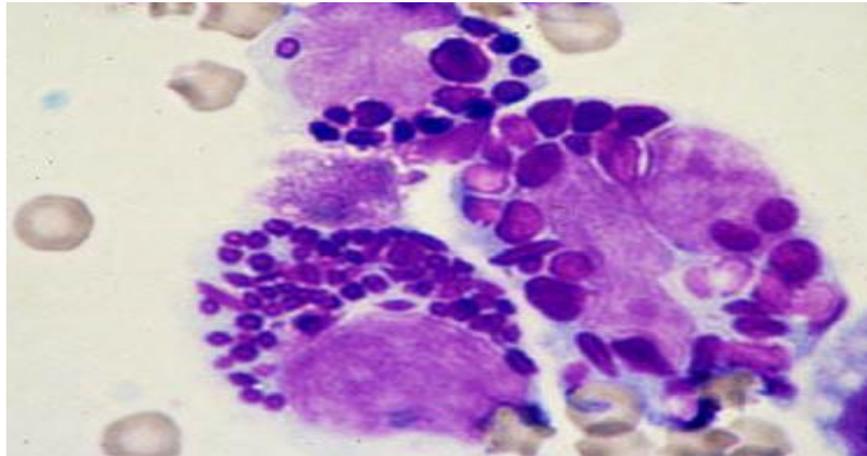
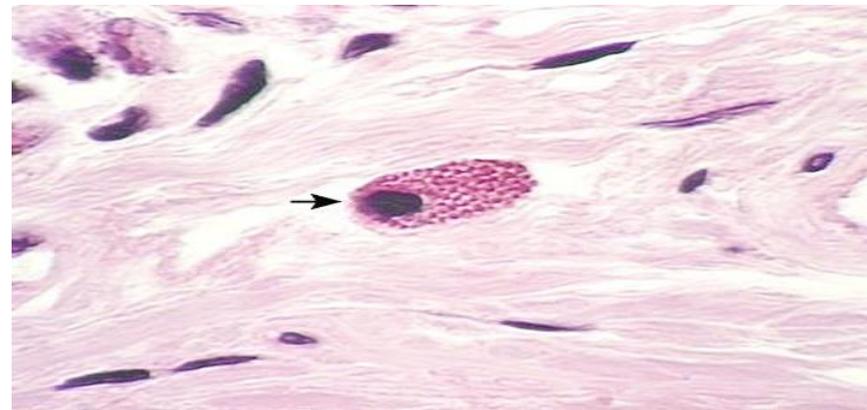
when stained with **toluidine blue**, the granules bind the dye and change its color to **red**.

Function :

secretion of histamine and heparin

↓
Allergy

↓
coagulation



Mast Cells

Histological features:

- By 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.

Because of heparin sulfate

- *By EM*, their cytoplasm contains numerous secretory granules.

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

Lactic shock :

1- mast cells : stimulated while allergy the excrete all granules in one time

2- histamine : when granules excrete once it makes peripheral vasodilatation thus hypotension

- ***White blood cells (leukocytes)***: they include neutrophils, eosinophils, basophils, monocytes and lymphocytes.
- RBCs live only in blood stream , if it go out from it , phathological circulation (extravasated)
- ***Macrophages***: they are derived from the monocytes that migrate from bloodstream into CT.
- ***Histological features***: they are large, irregular cells with eccentric kidney-shaped nucleus. The cytoplasm shows numerous lysosomes.
- **Function:**
- They are phagocytic cells; macrophages engulf a broad variety of foreign materials including bacteria, dead cells and dust particles.
- Monocyte's name according to its site :
Connective tissue (histocyte,tissue macrophage) / liver (kofercell) / bone (osteoclast)
Brain (microglia)

Macrophages= Histocytes

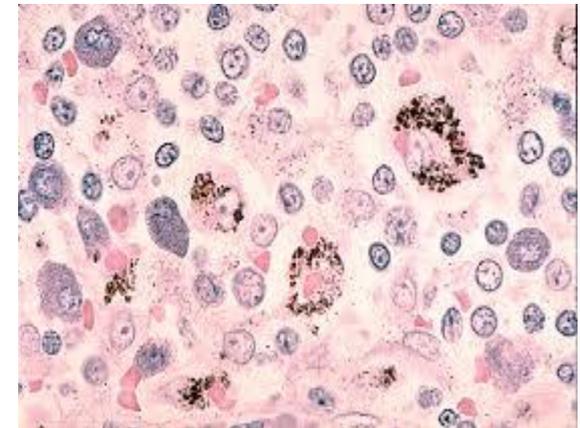
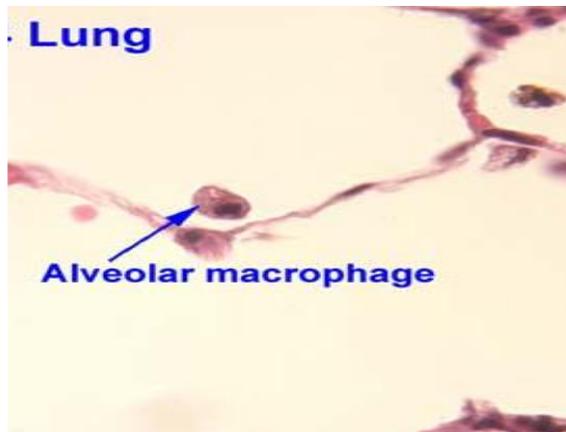
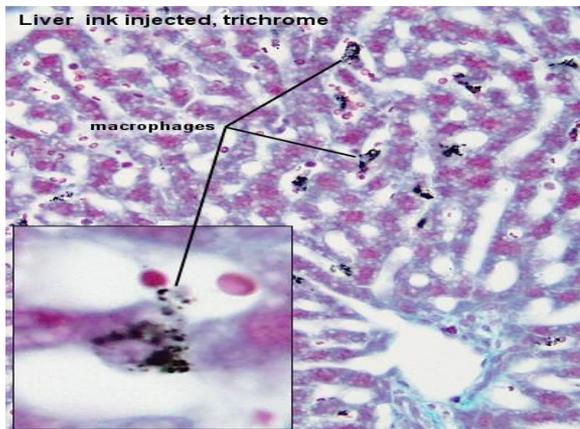
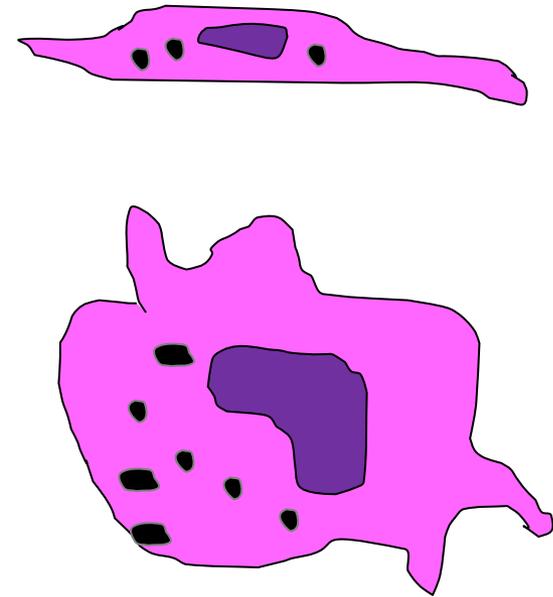
Origin : From **blood monocytes**

Three types:

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

Function : Phagocytosis

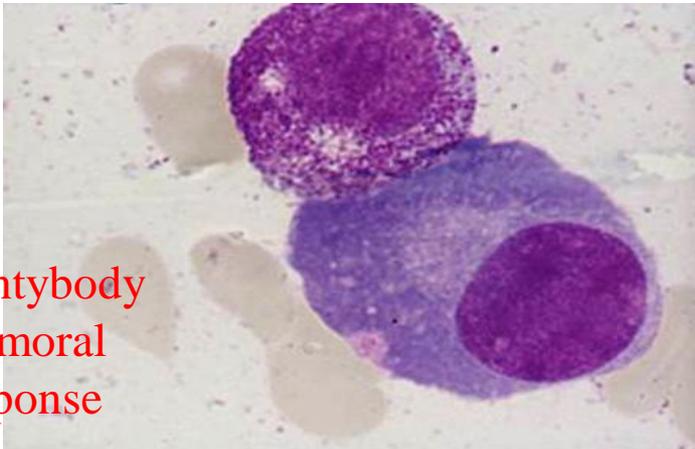
من انواع WBC
الها مدى للحياة
وبتعيش نص الوقت
في الدم والنص الثاني
بالخلايا وبكل مكان
الها اسم معين



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

Histological features:

- By 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.



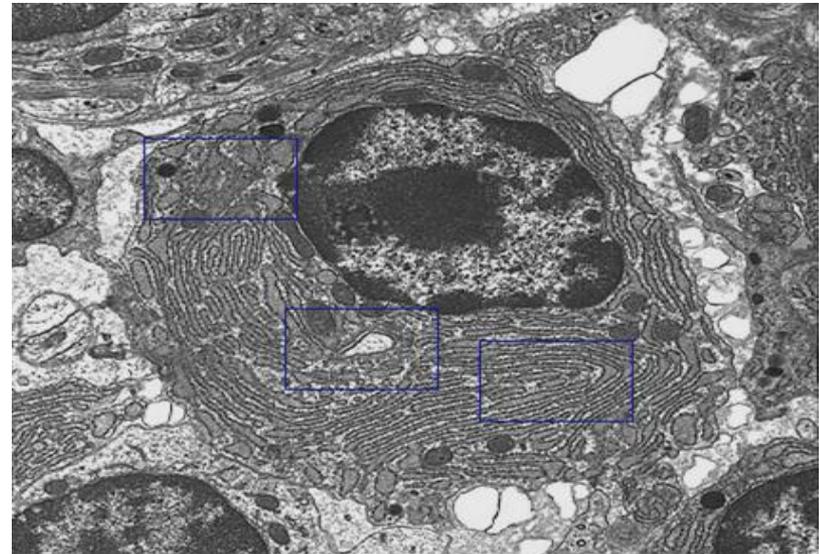
Antigene=antbody
reaction=humoral
immune response

Plasma Cells

Origin : activated B lymphocyte

- By EM, the cytoplasm shows closely-packed cisternae of rER together with large juxtannuclear Golgi complex. **Antibodies protein**

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



CLASSIFICATION OF CONNECTIVE TISSUE

I- Embryonic connective tissue

it includes:

- Mesenchymal CT.
- Muroid CT.

III- Specialized connective tissue;

it includes:

- Cartilage.
- Bone.
- Blood.

Classification depends on the proportion of **cells to fibers**, and on the **arrangement**, and the **types of fibers**.

Three categories can be defined:

II- Connective tissue proper:

it includes:

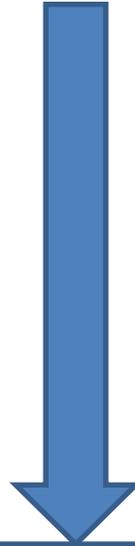
- Loose areolar connective tissue.
- Dense irregular connective tissue
- Dense regular connective tissue.
- Elastic connective tissue.
- Reticular connective tissue.
- Adipose connection tissue.

Classification of C.T.

Depend on ground substance



- Embryonic C.T**
- Mucoid C.T.**



**Jelly like
C.T. Proper**

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



Modified types

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

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.

Mucoid CT

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

Histological structure: It consists of:

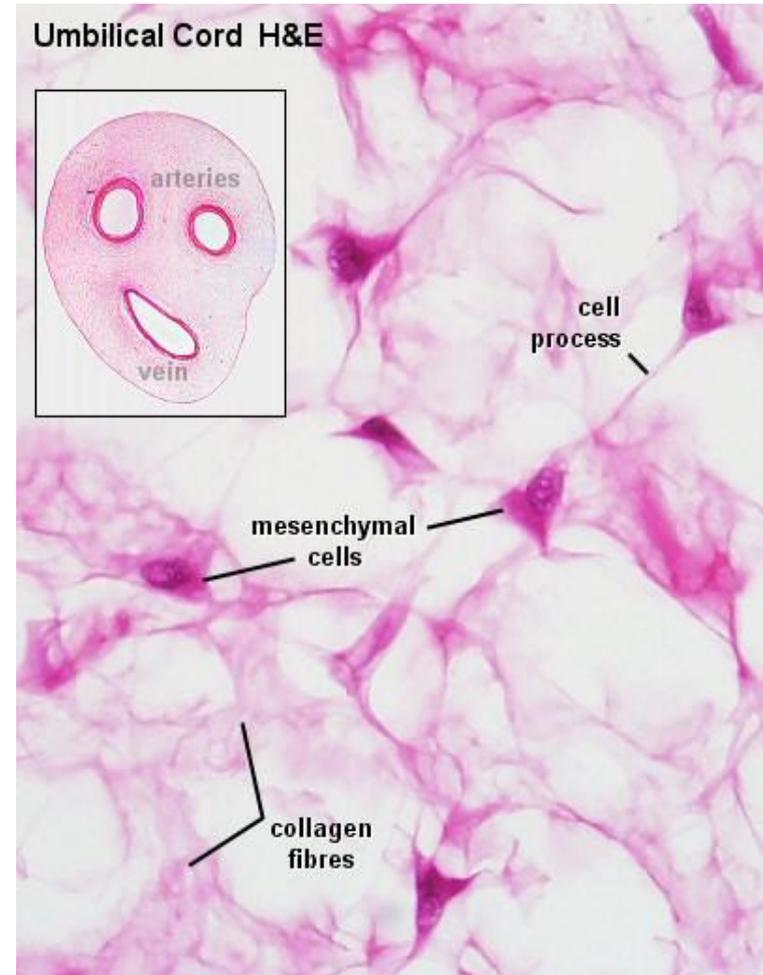
- ❑ Abundant ground substance (Wharton's jelly) composed mainly of hyaluronic acid. It appears homogeneous and basophilic.
- ❑ Spindle-shaped UMCs that are widely separated and fibroblasts.
- ❑ Unapparent fine collagen fibers that have the same refractive index as the matrix.

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 is 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 C.T.: 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:

Site: 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. It contains many small blood vessels coursing through this tissue.

- **Loose CT is found in the following 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.**

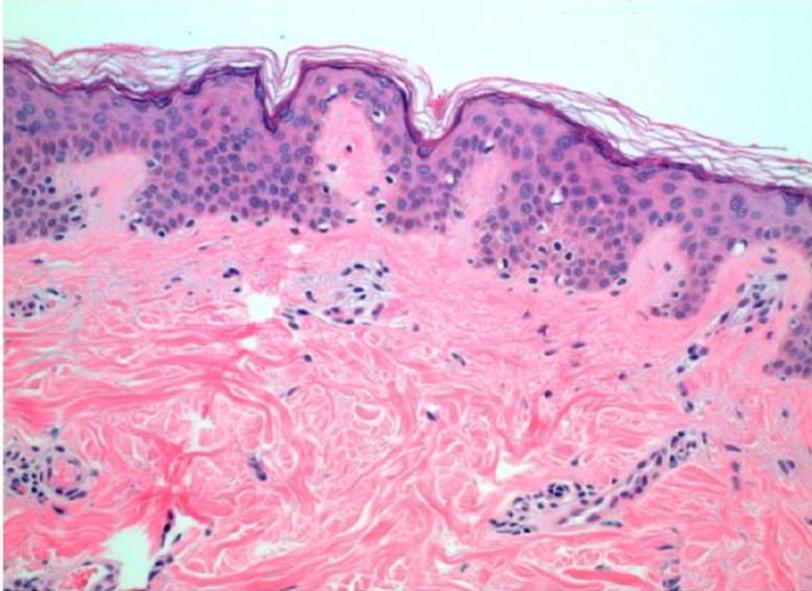
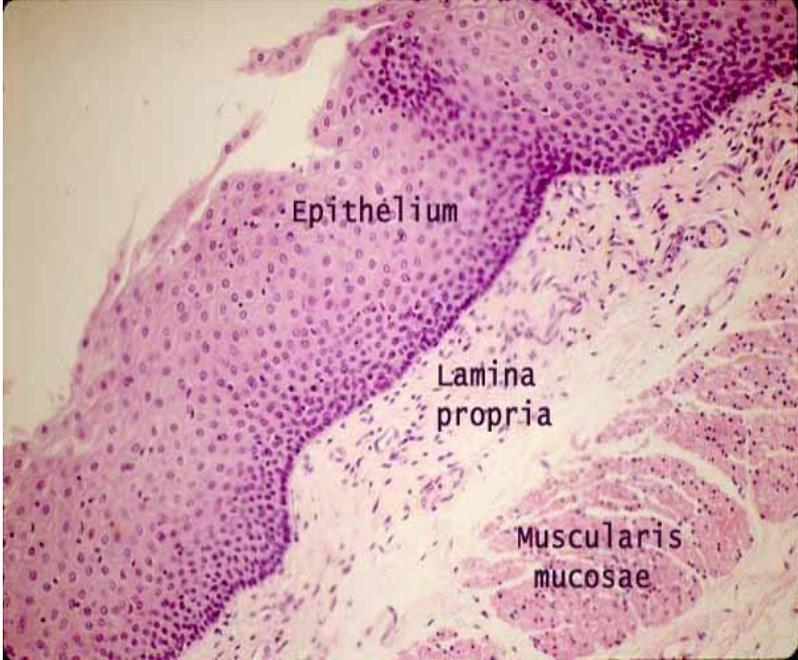
Histological structure

- **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.

Function:

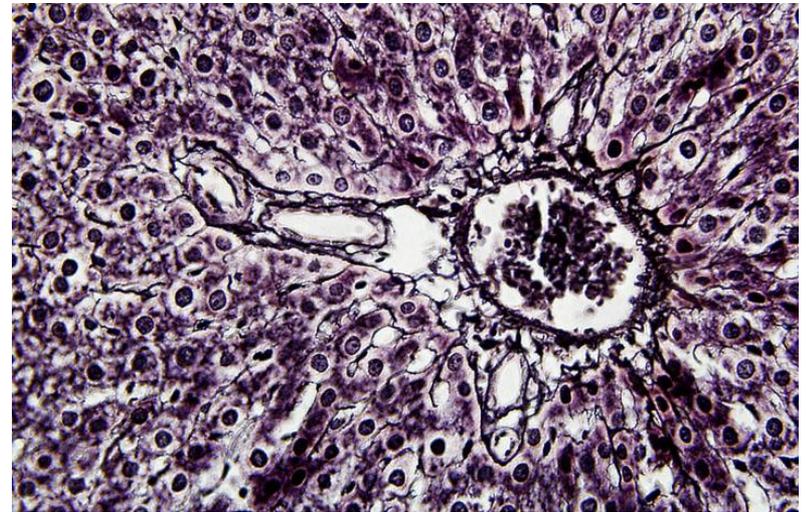
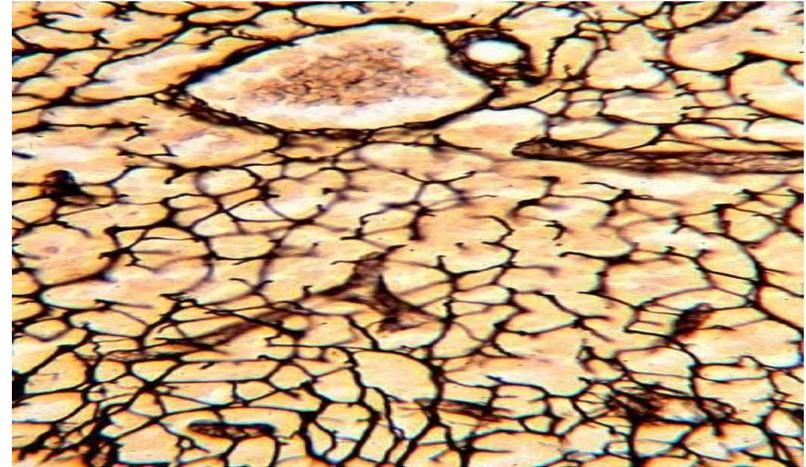
- a. Supports and binds other tissues (by its fibers).
- b. Holds body fluids and provide nutrition (by its ground substance).
- c. Defends against infection (by its white blood cells, plasma cells, mast cells and macrophages).

Loose Areolar C.T.



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 & function:** reticular tissue is limited to certain sites. It forms the supporting stroma for:
 - Hemopoietic tissue in the bone marrow.
 - Lymphoid tissue in lymph nodes and spleen.
 - Hepatocytes in liver.



Liver (silver stain)

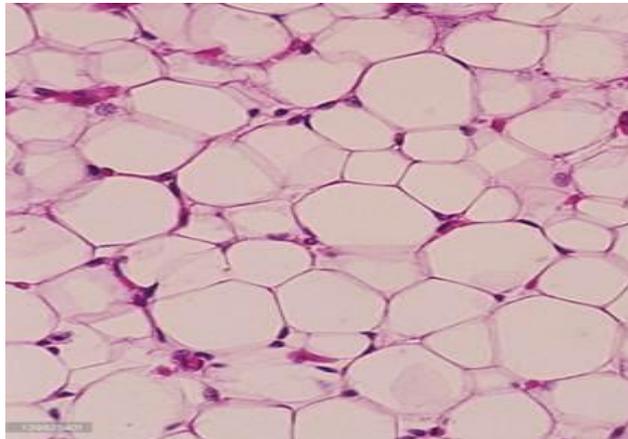
Adipose C.T.

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

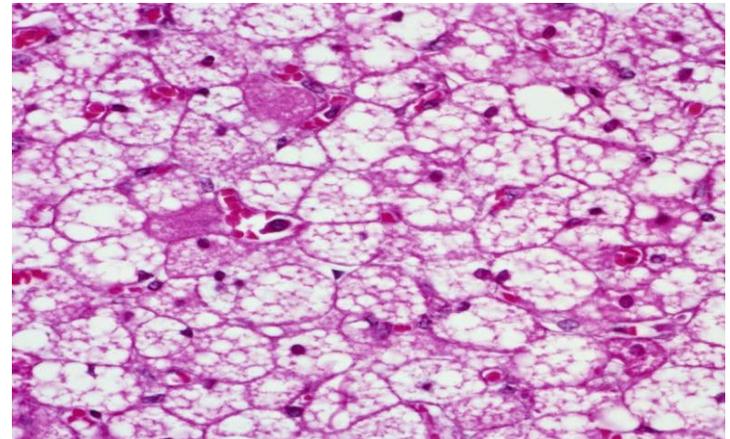


Multilocular adipose C.T. Brown fat

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

Sites:

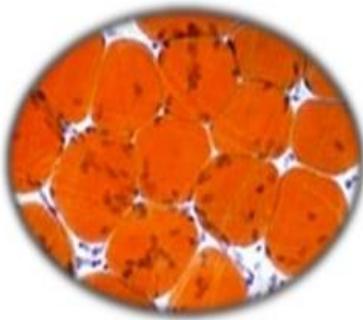
- Back & neck of newborn



Adipose C.T.

2. Lipid

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



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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.

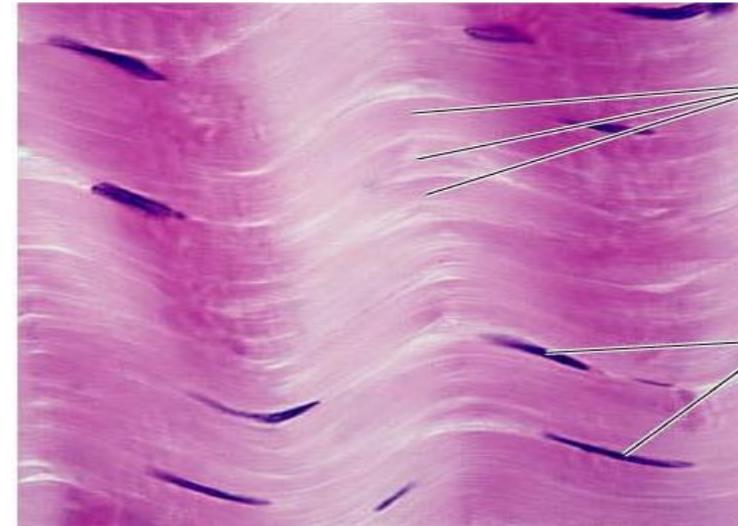
White Fibrous C.T.

Histological structure (Figure 84):

- 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.

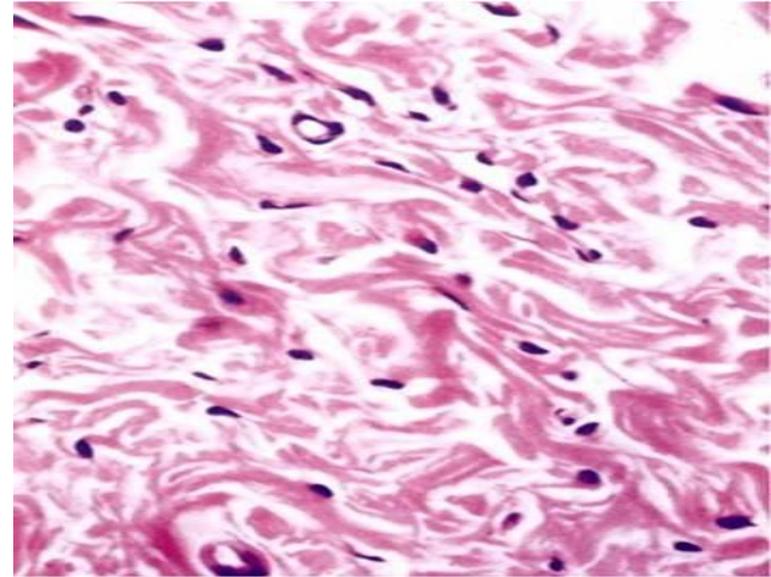
Sites & function:

- Unlike areolar CT, this tissue is poorly vascularized. This type of tissue forms white flexible structures with great resistance to pulling forces wherever it is exerted in a single direction. It is found in:
 - Tendons, which attach muscles to bones.
 - Ligaments, which bind bones together at joints.
 - **sclera of the eye**



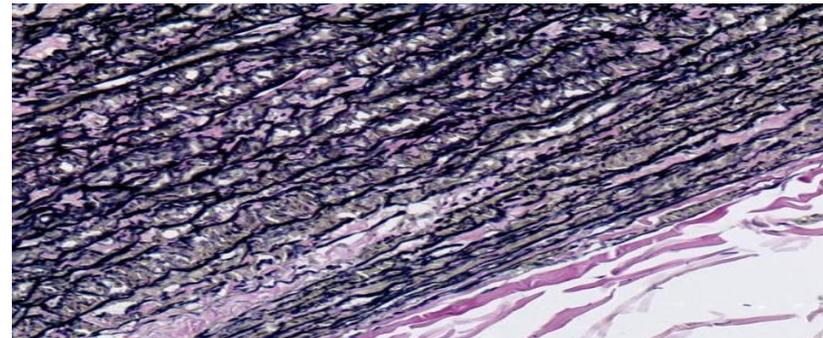
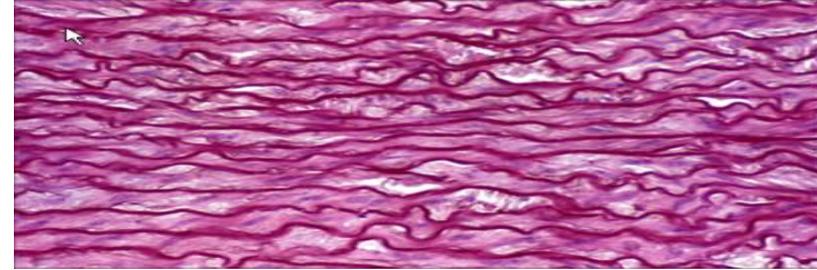
Dense Irregular CT:

- ***Histological structure:***
 - Thick bundles of collagen fibers arranged irregularly (running in more than one plane).
 - Little amount of ground substance with few fibroblasts.
- **Sites & function:** this type of tissue forms sheets in body areas where tension is exerted from many different directions.
- It is found in the ***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.



Elastic C.T.

- **Histological structure:** the elastic fibers predominate; they run in all directions, also they may form fenestrated membranes.
- **Site & function:** this tissue is present where flexibility and elastic recoil are needed; 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.



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. Binding, support and packaging:
2. Protection, defense and repair:
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. Transportation:
Blood is a connective tissue and it carries and delivers oxygen and nutrient to tissues.

7

CLASSIFICATION OF CONNECTIVE TISSUE PROPER

1. TYPES AND NUMBER OF CELLS
2. TYPES, NUMBERS AND ARRANGEMENT OF FIBERS
3. AMOUNT OF GROUND SUBSTANCE

CLASSES CONTENTS	CLASSES						
	MESENCHYME	MUCOID (Transitional)	LOOSE FECT	RETICULAR	ADIPOSE	DENSE FECT DS. IRREG. DS. REGUL.	
CELLS	MESENCHY- MAL	FIBROBLAST (primarily)	ALL TYPES: FIXED and WONDER. (highly cellular tiss.)	TWO TYPES: RETICULAR cells and (fixed) MACROPHS.	FAT CELLS and All others may be present	FEW: FIBROBL. and some MACROPH.	ONLY: FIBROBL. (between fibers)
FIBERS	NONE	Very fine COLLAGEN	COLLAGEN some ELASTIC & RETICULAR (Irregularly arranged)	RETICULAR	RETICULAR and COLLAGEN	Thick COLLAGEN (Irregularly arranged)	Parallel COLLAGEN in tendons & white ligaments and ELASTIC in yellow liga.
GROUND SUBSTANCE	AMORPHOUS, JELLY-LIKE						

Thank You