

HISTOLOGY SHEET

Doctor 2021 -mercy- | medicine | MU

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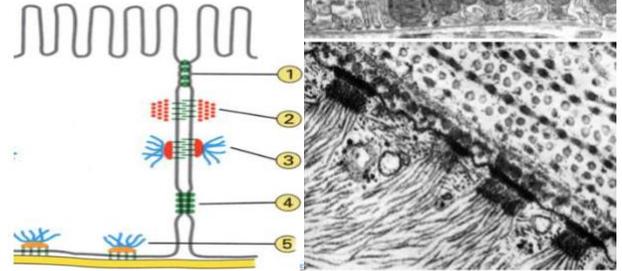
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DOCTOR

Dr. ferdous star

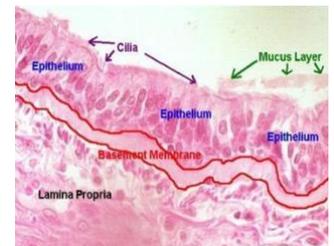
Basal modifications

- Basement membrane
- Basal infolding The kidney make filtration 180 L/day but we get rid of proximally 1.5-2 L/day that's because basal infoldings on reabsorption kidney tubes ,but this mechanism needs an energy so I need numerous large mitochondria
- Hemidesmosome
Desmosome : it is between two cells
Hemidesmosome: It is Between epithelium tissue and connective tissue
... In junction Normal space (20-30) complete fusion between two membrane (tight and anchoring)

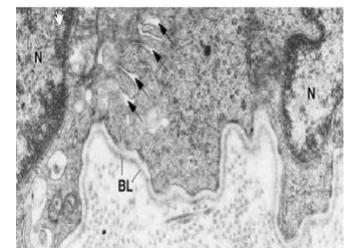


Basement membrane

Between connective tissue and epithelium tissue there is basement membrane , this basement membrane makes a modification (hemidesmosome) so the cells are attached to the underlying connective tissue.



- Thin extracellular layer having two parts:
- Basal lamina (From epithelium tissue
- and It has a collagen IV that causes dense): type IV collagen + laminin
- Produced by epithelial cell
- Reticular lamina from connective tissue : Type VII collagen (Anchoring fiber attaches under connective tissue with epithelium tissue) + type III collagen (reticular F)
- Secreted by C.T. cells



If there a cancer and I want to determine if it dangerous or not ,I will check if cell's cancer passes the connective tissue or not , if passes it's dangerous because the connective tissue very rich of blood vessels

Function :

1. Attach epithelium to C.T.

2. Separate epithelium from other tissue
3. Regulate (filter) substances passing from C.T. to epithelium
4. Guide during tissue regeneration

...Basal infolding : there is folding inside the cell (to increase the surface of area) like that found in kidney transport which is active transport

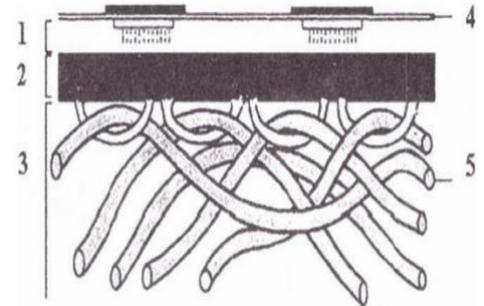
Basal lamina. Basement membrane

The **basal lamina** connects the epithelium and subjacent connective tissue.

With electron microscope the basal lamina consists of 2 layers: inner **lamina lucida** (thin amorphous layer of glycoprotein) and Outer **lamina densa** (thick network of collagen fibrils). Outside the basal lamina is associated with the **reticular lamina**; it consists of delicate reticular fibres.

Schematic diagram of the basement membrane.

1. lamina lucida,
2. lamina densa,
3. reticular lamina,
4. plasmolemma of the basal surface of the epitheliocytes,
5. collagen fibers



CLINICAL APPLICATION

Basement Membranes and Diabetes

In untreated cases of diabetes mellitus (type 1 or type 2 diabetes), the basement membranes of the epithelial lining of capillaries thicken over time. This thickening is caused by increased amounts of glucose, present in high concentrations in diabetics, binding to the proteins of the basement membrane. This process is referred to as increased glycosylation of the basement membrane. Thickening is especially evident in the capillaries in the kidneys and retina of the eye, which can become nonfunctional. For this reason, kidney failure and blindness are major symptoms of advanced diabetes.

Basement Membranes and cancer

When cancer cells penetrate the basement the cells spread and metastasis

CONNECTIVE TISSUE

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.) EC : ground space fiber > Which separates cells from each other(
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.



most CT are highly vascularized, while others are poorly vascularized. However, cartilages are not vascular .

Generally, CT is source of nutrition for ET(ET is avascular).

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

general features of CT :

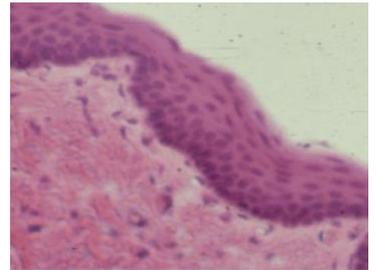
1-few cell, widely separated .

2- cells differ in their types and function.

3- there is ground substance and fiber between the cell.

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 (3 embryonic layer)
- Function: covering or secretion (glands)



Connective T

- Cells: few, widely separated, different types
- Intercellular substance abundant
- fibers are present in the ground substance
- substance
- Blood vessels: rich
- Origin: mesodermal
- Function: support, defiance and nutrition protection



Extracellular Matrix (ECM) (the protein in middle and GAG on peripheral)

Ground Substance ((ECM < Ground Substance Fiber))

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 (why? Because it comes from blood through exudate (إفراز) from blood vessel)

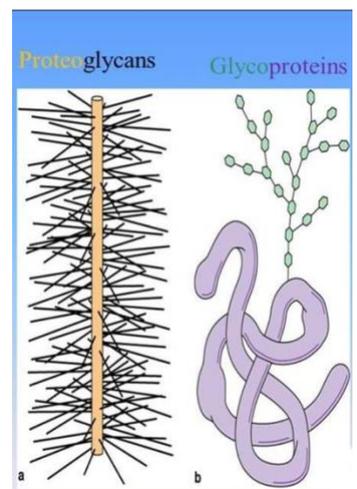
Edema is accumulation of tissue fluid (pathology)

2. Proteoglycans

3. Multiadhesive glycoproteins

4. Glycosaminoglycans (GAG)

the protein in side and the GAG on another side



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.

Adhesive glycoproteins e.g. **fibronectin** and **laminin** (adhesion between fiber and ground substance). They serve mainly as connective tissue glue that allows connective tissue cells to bind themselves to matrix elements.

!! Difference between laminin and Lamin: lamin is found on the inner surface of inner nuclear membrane, its function is to attach chromatin with nuclear.

Carbohydrates and protein always act as adhesion, which makes the cell membranes held together.

!!!Cell coat that surrounds the cell is carbohydrate is attached with protein and lipids, It serves weak adhesion.... On the other hand, the cell junction adhesion is strong.

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

Glycosaminoglycans (GAG) (hydrophilic)

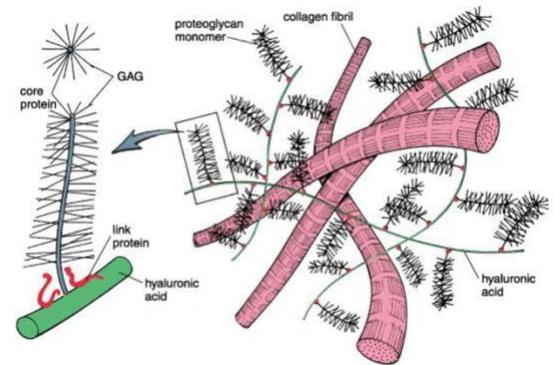
- linear (unbranched) polysaccharides, e.g. heparan sulfate, chondroitin sulfate, keratan sulfate, hyaluronic acid
- attract sodium & **hold water** (the Sodium takes the water with it)
- very hydrophilic due to abundant negative charges.
- except for hyaluronic acid, are usually bound covalently to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

Any thing you want to do adhesion should have protein, if it has carbohydrates the adhesion will be weak while the adhesion in cell junction strong and the

carbohydrates help in sometimes (If you have adhesions, their should be proteins as the major unit and the carbohydrates as assistant (مساعد)

Function:

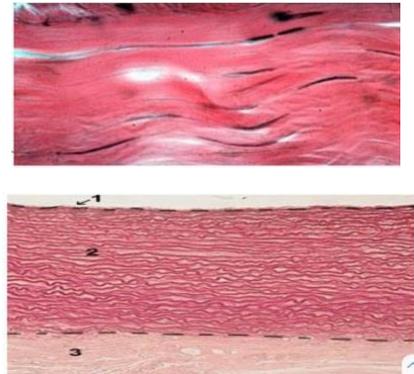
- The ground substance **holds large amounts of fluid** and functions as a medium through which nutrients and other dissolved
- substances can diffuse between the blood capillaries and the cells. CT is rich with interstitial fluid, in addition it has high ability to absorb fluids, subsequently (و بالتالي) dissolving fats and other substances, and working as transporter for nutrients.
- Its gel state serves to **resist compression** and to act as a **lubricant**. (shock absorption)
- 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.
- Nutrition because it is full with carbohydrates and water and protein.
- Can absorb sodium and water with him, which leads to the product of tissue fluids.



Some virulent bacteria can penetrate the ground substance. If it can penetrate it, it will spread the infection, so that's why it is a barrier.

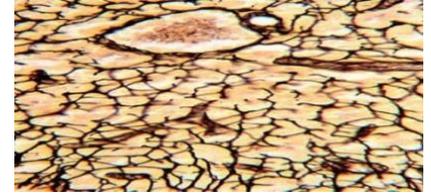
Connective tissue fibers

- They are embedded in connective tissue matrix.
- The fibers of connective tissue provide support.
- There are three types of CT fibers;
 - ❖ collagen fibers, the most available
 - ❖ elastic fibers (it stretching and elasticity)



❖ **reticular fibers.** (as network)

actually, there are two types not three because reticular fiber is a type of collagen 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(**in naked eye with out stain**), collagen fibers have a glistening white appearance; they are therefore also called **white fibers.** because **Without dye(stain), it is white.**

Histological features:

- In longitudinal section, collagen fibers appear as cylindrical structures that run in **wavy bundles**

*single fiber=unbranched . // bundle fiber=branched , as a wave in shape.

*the white fibers run as bundle not single .

- The individual fibers do not branch while the **bundles** of fibers often do.
- They stain pink with H&E

The cell that makes ground substance and fibers are called fibroblasts

Fibroblasts are considered as protein secreting cells

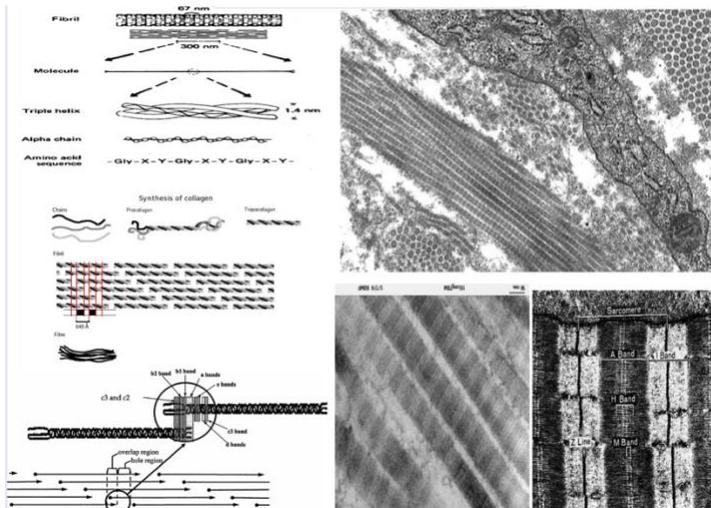
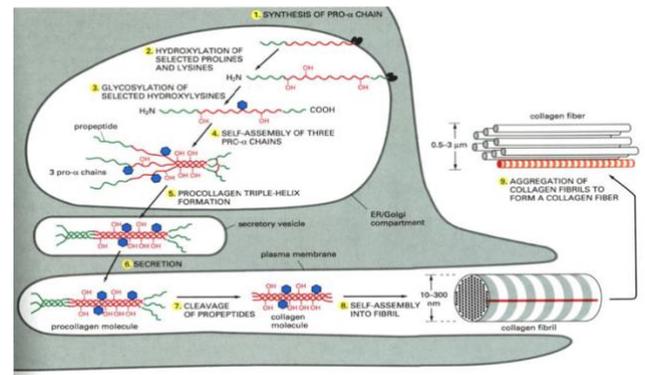
Protein secreting cell is rich with:

- Ribosome, rough endoplasmic reticulum

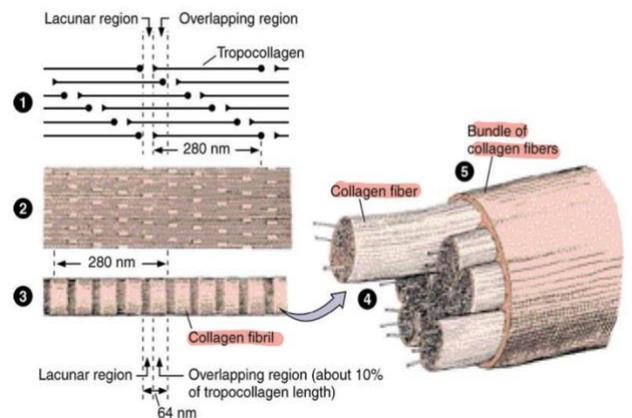
Lipid secreting cell has a lot of smooth endoplasmic reticulum

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.
- Fiber and ground substances is protein in nature so that the cell is secreting protein cell
- Secreting protein cell have ribosome and RER(most AVAILABEL)
- Secreting lipid cell have SER
- Collagen fibrils in turn are further assembled into collagen fibers which may be bundled together into the thick collagen bundles.



Assembly of collagen fiber bundles



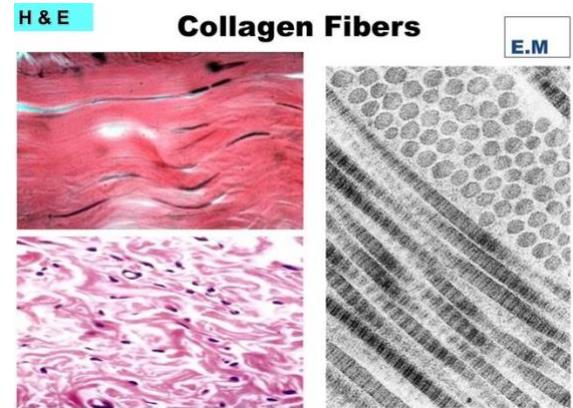
Major Collagen Fiber Types (out of at least 20)

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. **(white fiber)**
- 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
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, VII	All basement membranes	Support and filtration

Polarity: apical, basal, lateral

basal infoldings hemidesmosomes basement membrane

(full with IV, VII type)/(support and filtration).

type I collagen : as bundle /// pink color with H&E stain.

type II collagen : very thin fiber /// refractive index as refractive ground substance, so it is not seen\\\ found in bone and cartilage.

type III collagen : there are two types of fibers in CT not three because reticular fiber is type of collagen fiber. It is usually found in tissues rich with cells, as it works as structural framework.

* type IV&VII (4&7) collagen : It doesn't appear as if it doesn't exist

RETICULAR (RETICULIN) FIBERS (NOT STAINED BY H&E STAIN)

Histological features: (thin , as network)

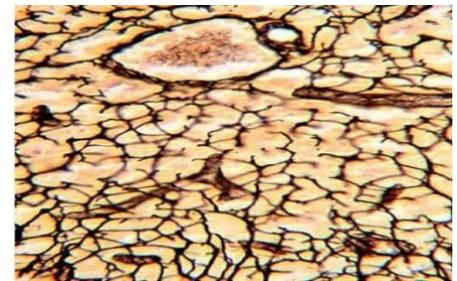
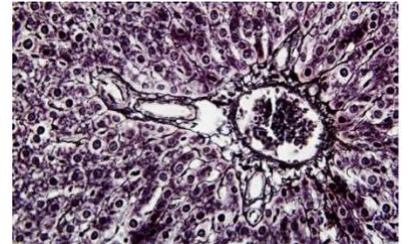
- **Form a delicate supporting framework** for highly cellular tissues (endocrine glands, lymph nodes, liver, bone marrow, spleen, smooth muscle) **to make support**

- **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)

- made by **reticular cells** (specialized fibroblasts) and vascular smooth muscle cells



With silver (Ag) stain gives brown color

Elastic Fibers

- Have elasticity. If you stretched it Elastic Fibers and let it go  it will recoil.

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.

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. (elastic proteins with each others make yellow color in fresh state (fresh state=non-stain!!!))

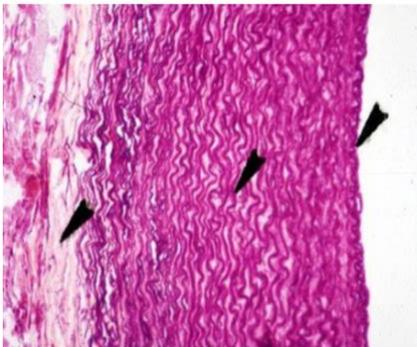
- They are found where greater elasticity is needed present in large amounts in ligaments, lung, skin, bladder, and walls of blood vessels + vagina +large elastic artery (aorta)..
- Elastic fibers may exist in two different forms:
- Individual long and thin fibers that branch in the extracellular matrix.
- In the wall of large blood vessels they form fenestrated parallel sheets
- They stain weakly with H&E.

Special staining 1-) collagen type I : stained with H&E stain and give pink color.
 2-) reticular fiber stained with silver stain and give brown color
 3-) elastic fiber stain with 3 type of stain (H&E / orcein / VVG) and H&E give pale pink, with **orcein stain**(Brick-red = black-red = not bright- red) gives a brick-red color to elastic fibers, while staining with **V.VG stain** gives them a dark violet color. (dark violet color Or black color).

if collagen fibers :

- -run as bundle = branched
- -run as individual= non-branched

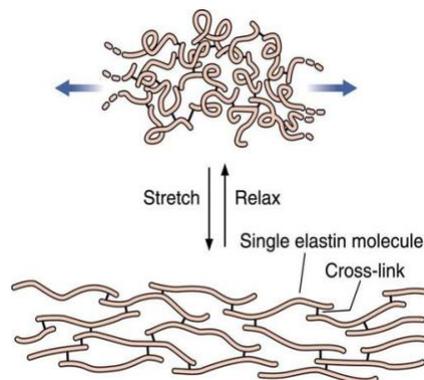
Elastic fibers



bundle of Collagen type I



bundle of Collagen type I



Reticular fibers are not stained by H&E, instead they are stained by silver dye to be seen. Although, it is already existed, H&E can't distinguish (يميز) them.

The elastic fiber ranged in two form :

1- Corrugated elastic fenestrated fiber.

membrane e.g.g large blood vessel.

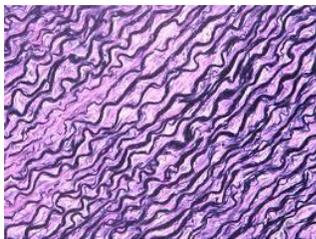
2- Thin branching

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

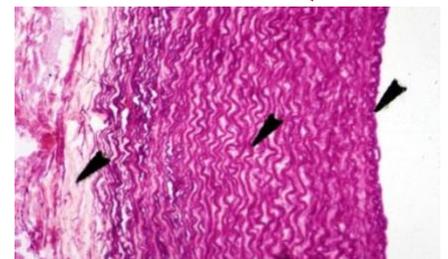


Dark violet by VVG stain



black

Break red by orcein



H&E

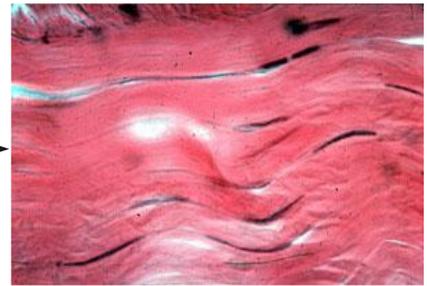


Fibers There are 20 types of collagen

Description of the type I collagen

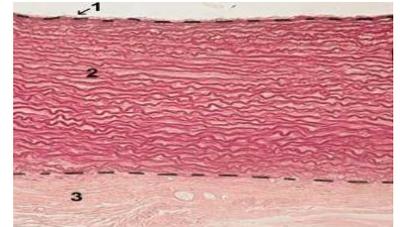
- The most numerous
- White if in great number (white fibers)

- Strong and flexible
- Fibers do not branch but bundles can do
- Formed of collagen protein
- Stain pink with eosin
- Types of Collagen Fibres



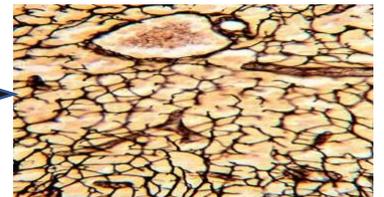
Description of elastic fiber

- 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.



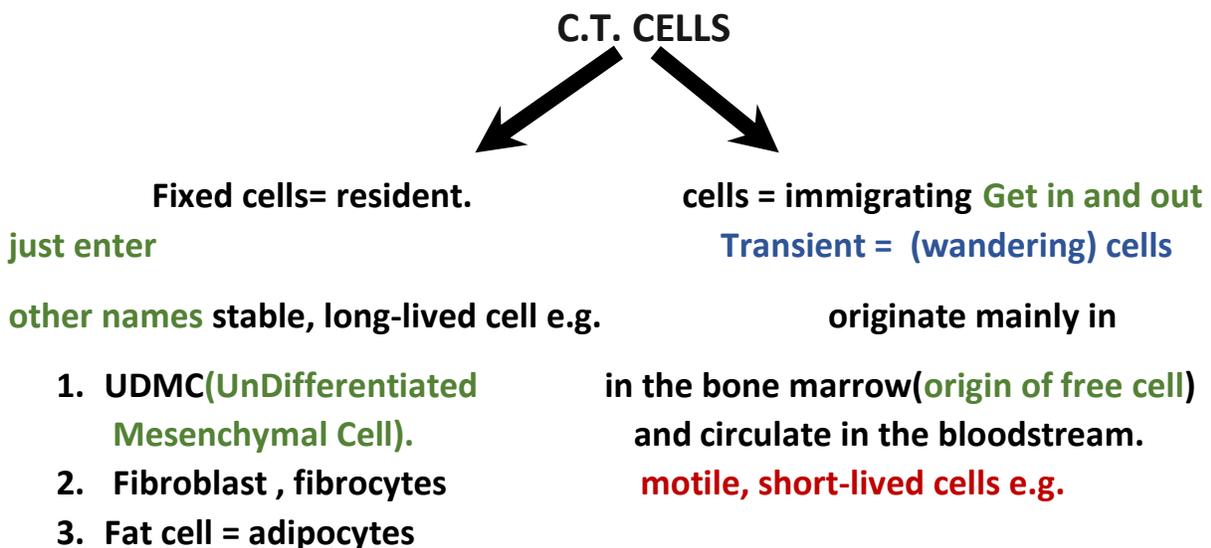
Description of reticular fiber

- Thin branching (fiber)= **reticulum**
- **Not** stained by H&E
- Stained dark brown with silver stain
- Consist of type III collagen
- Supportive function in **places that highly cellular.**



Collagen type III is reticulum

Silver stain is specific for reticulum fiber



- Adipo =fat/ cyte =cell.
 4. Pigment cell.

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

Each type of CT has a specific functions.

Fixed cells

1. Undifferentiated Mesenchymal Cell

- 1-mother cell(stem cell)
- 2-has active nucleus (rich with euchromatin)
- 3-origin of fixed cell just

Histological features:

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

Function: 1-Prolifration increase their number= 2-
 Differentiation---> has specific function
 they are adult stem cells that can divide and differentiate into
 many types of CT cells.

The most important thing to describe the cell is the nucleus, and I
 must write that the nucleus is the most important thing in this cell

Prominent euchromatin active that means (active chromatin with
 active nucleus)

Every type you need to know about: 1- origin 2- function3- specific
 characteristics 4- description

2. Fibroblasts

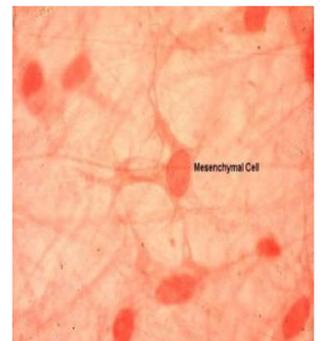
- 1- blast cell = -highly active cell -produce fiber& ground substance .
- 2- protein in nature (protein secreting cell) active cell =
 basophilic ,,,
 cytoplasm

- The most common type
- Origin : from UDMC

Cell:

Origin
 Characters
 Function

L.M.



2 types

Young active = fibroblast

- Large in size
- Fusiform with processes
- oval central paler nucleus
- **Basophilic** cytoplasm = numerous rER **Basophilic** because it is full with ribosomes and rER. And because it is protein secreting Cell.

Mature = fibrocytes

(quiescent) Quiet = do nothing, But when needed it becomes active

mature (Fibrocytes) :inactive

- Small in size inactive cell = acidophilic cytoplasm
- Fusiform smaller
- oval central **darker** nucleus (because it inactive)
- acidophilic cytoplasm. Light Microscope

Acidophilic because it hasn't much of ribosomes

Fibroblast= cell in connective tissue

Chondroblast= cell in cartilage

osteoblast= cell in bone

Young active = fibroblast

Highly active cell . +Nucleus and nucleolus appear. +large in size.

Mature = fibrocytes small in size.

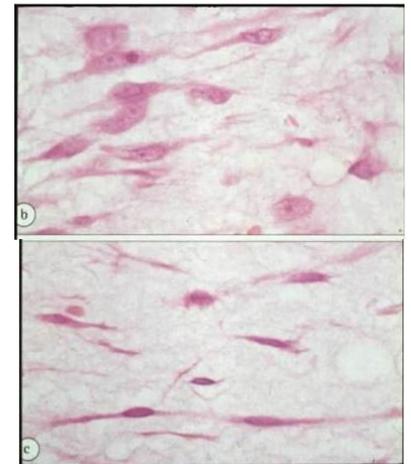
Fibroblasts

Any cell has blast will be highly active cell

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.



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
- . if the CT damaged or injured (wounded) ,it will be active to helping the fibrocytes in the healing(maintenance).

Fibrocytes (it's as a reserve maintenance (store inactive and if necessary it's be active))

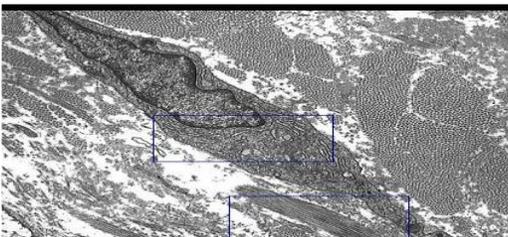
After they synthesize the matrix, they become quiescent and are called fibrocytes. They assume their less active mode, indicated by the suffix "cyte". • are smaller cells with fewer processes than the fibroblasts. By LM, the cell has a small elongate, heterochromatic nucleus and an eosinophilic cytoplasm.

- 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.

In general it is less active but if the CT damaged or injured ,it will be active to helping in the healing.

Fibroblasts E.M.



- 1- The cytoplasm is full of organelles. 2-Larg.
- 3-The white dots are collagen fiber.
3. Adipocytes=**fat cell**

Fibrocytes E.M

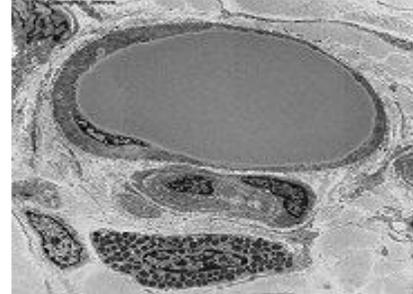


Its shape is polyhedral when the cell is overcrowded.(the polyhedral is irregular in shape).

Its shape is spherical when the cell is farther away from the other.

Origin : **UDMC**

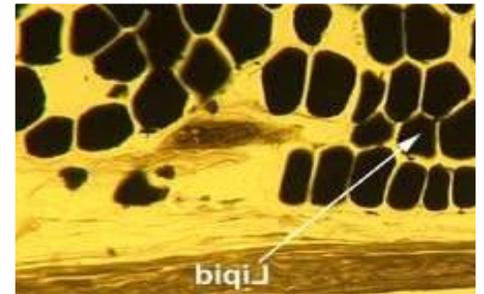
- large, spherical or polyhedral
- The flattened nucleus
- The cytoplasm only forms a very narrow rim around a large central lipid droplet.
- Single or several lipid droplets
- Adipocytes are long-lived cells. Their number is determined by the number of preadipocytes generated during foetal and early postnatal development.
- Lipid storage/mobilisation is under: •nervous (sympathetic) , hormonal (insulin) control.



Function :

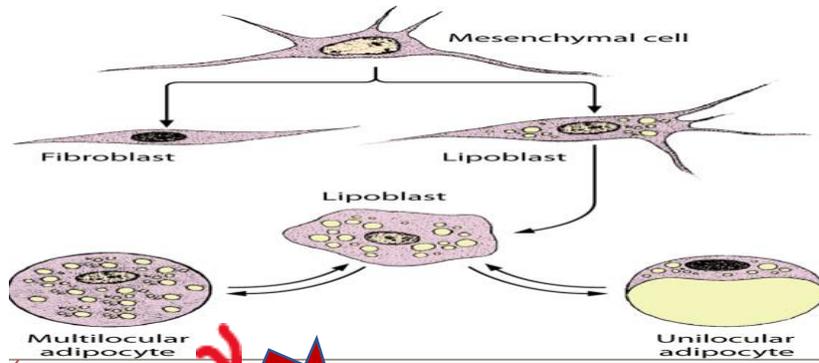
Osmic acid

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



If there is a different/disturbance in protein leptin (hormone), it will lead to obesity.

Fat Cell=Adipocytes= fixed cells



It has central rounded nucleus). It has multiple of small lipid droplet

Multilocular are just found in new born specifically in the back of neck of shoulder that's why the new born doesn't have a lot of fat but as a person gets older, it is altered (تحول) into unilocular and reduce its number

...unilocular has a large single globule of lipid , it's found in the skin (subcutaneous) Gives shape , protection to the body , store lipid and release hormones (leptons hormone) it means that's work as gland

... Has a flat nucleus on peripheral thin rate of cytoplasm.

...This cell, the nucleus can move to become compressed on peripheral to finally become flatend nucleus

Histological features:

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

● **unilocular adipocytes** Found in subcutaneous tissue

It's a large in size

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 function of unilocular :

- 1- makes the shape of the body
- 2- works as insulation and protection
- 3- storage the lipid
- 4- gives energy
- 5- has endocrine function :secrets lipitin hormone
- 6- responsible of the distribution of fat and gives the shape of this distribution in female or male

● **multilocular adipocytes** are polygonal and smaller than the unilocular adipocytes.(make bushing for the nucleus on the edge of the cell, and the nucleus looks like flat and the fat doesn't appear in H&E because of that the cell appears as empty)

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

4. Pigment Cells= fixed cells

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

(There is a part of the brain called Substantia nigra .)

The pigment cells in the skin are called melanocytes .

Any part contains melanocytes has a specific color.

Any place where exist pigment cells give a color because they store the pigment melanin.

