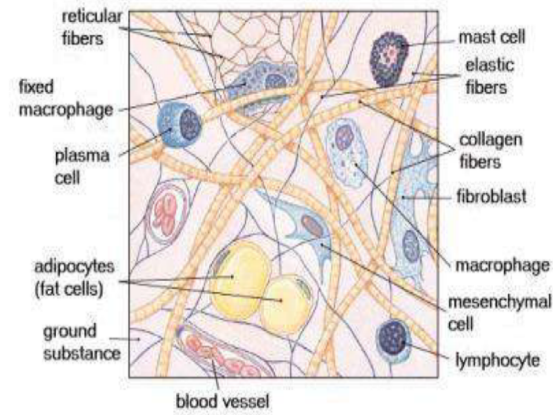


Connective tissue (CT) is a type of body tissue characterized by an abundant extracellular matrix within which are dispersed different types of cells and fibers.



Function:-

1. Provide and maintain form of organs.
2. Support different tissue and organ
3. connect and bind different body regions
4. Provide a medium for diffusion of nutrients and waste products and gas.

Cells of the CT are, usually, not regularly arranged.

could CT of cells The: من حيث مكان النشوء والبقاء

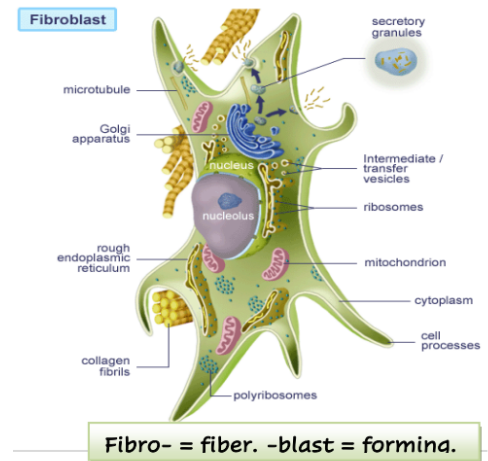
- Originate and remain in the CT all their lives (fibroblasts).
- Originate outside the CT and then come to the CT and remain in it for the rest of their long lives (cells mast)
- Originate outside the CT and then come to the CT and remain in it for a short period (neutrophils)

1) Fibroblasts

? Function : Synthesizes fibers and produces components of extracellular matrix.

? Active **?** Fibroblasts
inactive **?** Fibrocytes.

Rarely divide. Mitosis resumes when they're needed under influence of several growth factors



Fibroblasts:

- Abundant irregularly branched cytoplasm
- Large, pale-staining nucleus with prominent nucleolus
- Rich in RER (rough endoplasmic reticulum)
- Golgi apparatus well developed

Fibrocytes:

- Smaller than fibroblasts.
- Less cytoplasmic processes.
- Nucleus smaller and darker.
- Less RER.

Myofibroblasts: Fibroblast cells with contractile ability. Important in wound contraction

2(Macrophages and the Mononuclear phagocyte system

- o Monocytes form in the bone marrow.
- o Travel with blood and enter the connective tissues by passing through capillary walls.
- o Activated monocytes will form several types of phagocytic cells in tissues.
- o Macrophages in different tissues are given different names.

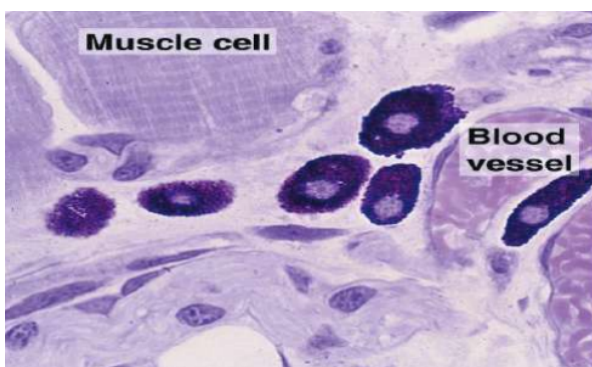
Functions of Macrophages:-

1. Phagocytosis (Microorganisms, neoplastic cells, dead cells, debris, and abnormal elements extracellular + tumor cells)
- 2) Destruction of red blood cells (metabolism of iron and hemoglobin).
3. Antigen presentation to lymphocytes
4. Release of cytokines and collagenase

3) Mast Cells

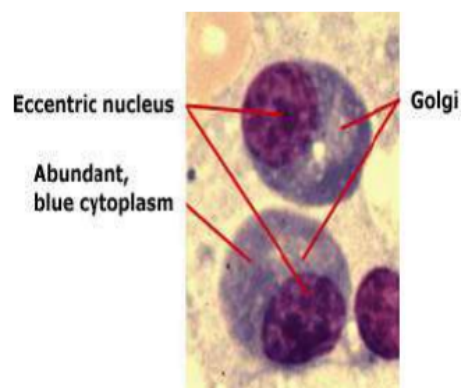
- ? Large, oval or round cells.
- ? Cytoplasm filled with basophilic secretory granules.
- ? Nucleus small, spherical and centrally located (may be obscured by granules).

Depending on what's contained in their secretory granules, they may change the blue color of basic dyes into a different color - metachromasia.



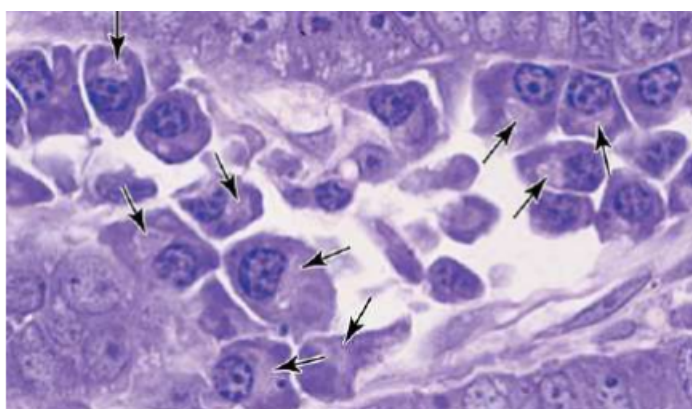
4(Plasma Cells

- ? Large, ovoid cells.
 - ? Basophilic cytoplasm because it's rich in RER (no secretory granules).
 - ? Golgi and centrioles occupy a juxtannuclear position and appear pale
 - ? Nucleus spherical and eccentric .
- Has dark peripheral regions alternating with lighter regions (clock-face appearance).
- ? Short life span (10-20 days).
 - .- Derived from B-Lymphocytes
 - ? Stimulated by several local factors



Function: production of Antibodies

Plasma cells. The cytoplasm is basophilic. Note the juxtannuclear pale area (arrows) and the clock-face appearance of the nucleus



Fibers of the Extracellular Matrix

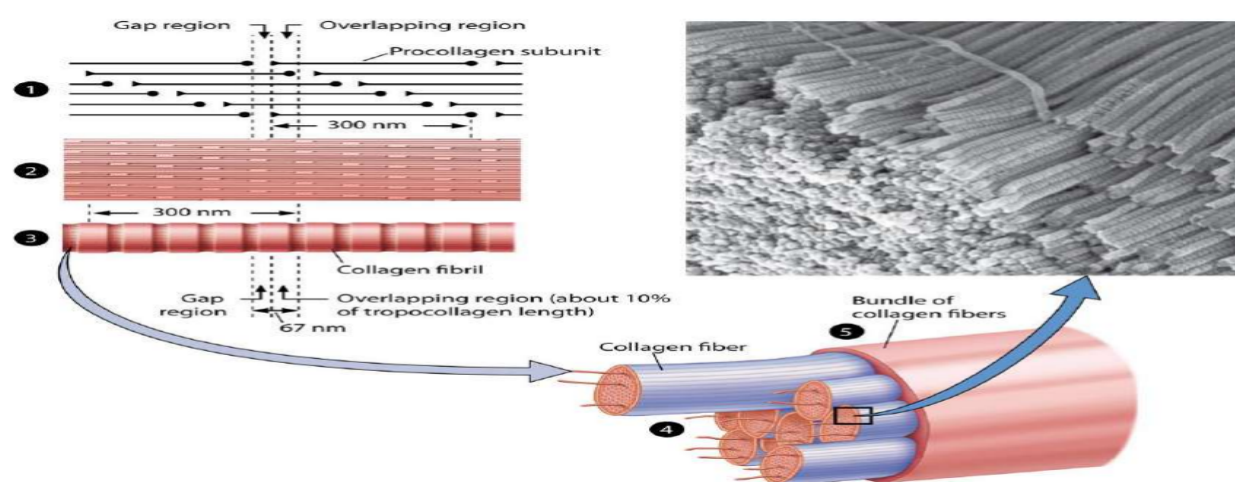
- Formed from proteins that polymerize into elongated structures. Repeating units of protein

- The 3 main types are:

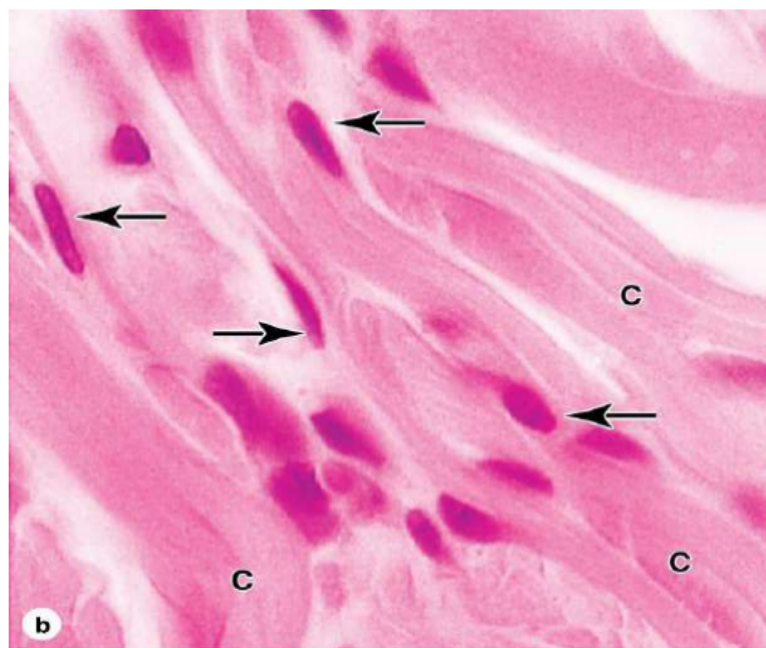
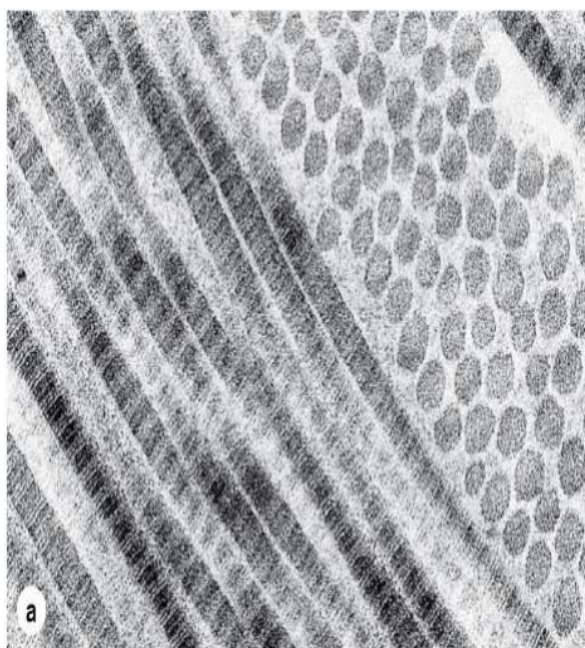
- 1) Collagen fibers (from protein Collagen)
- 2) Reticular fibers (from protein Collagen)
- 3) Elastic fibers (from protein Elastin)

1) Collagen Fibers { very common in the body/ most abundant }

- Present in different tissues: skin, bones, cartilage, basal lamina, ligaments, and tendons. They give them strength.
- Several types of collagen protein exists.
- Collagen turn-over is slow in some organs, like tendons where the collagen is stable. In the periodontal membrane(which holds the teeth in their sockets) collagen has a high turn-over rate.



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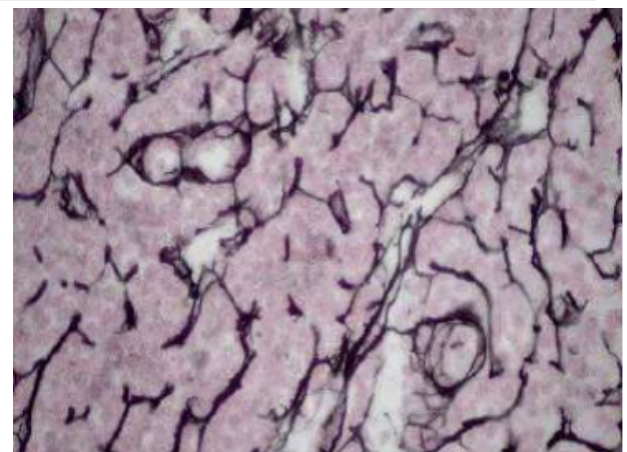
Collagen fibers as seen by TEM (a) and LM (b). Note the striation seen under the EM. Also note the pink color of the collagen fiber in (b). The arrows point to nuclei of fibroblast .

Collagen disease

Disease	Pathology	Notes
Osteogenesis imperfecta	Genetic defect in collagen synthesis	Affects all body. A severe condition. May result in spontaneous bone fracture.
Scurvy	Vitamin C deficiency (this vitamin is important for collagen synthesis)	Periodontal membrane is mostly affected and the teeth fall off
Sclerosis	Accumulation of collagen	Affects all body
Keloid	Accumulation of collagen	In skin wounds

2) Reticular Fibers { means network }

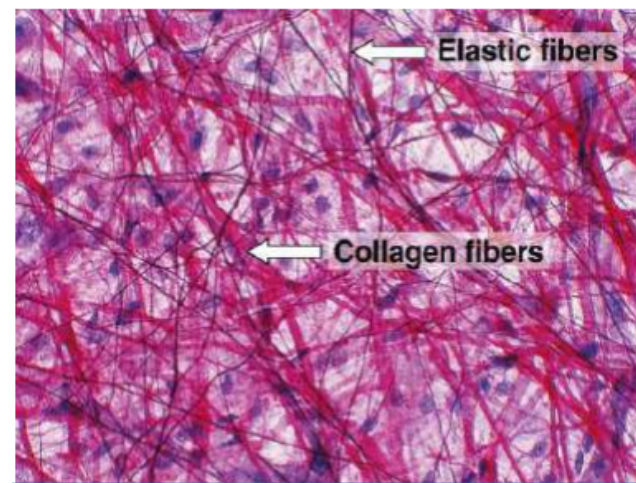
- [?] Formed by a type of collagen protein that is heavily glycosylated
- [?] Thinner than Collagen fibers.
- [?] Stain black with silver impregnation (argyrophilia).
- [?] Form a network of fibers that holds the parenchyma of several organs: liver, spleen, lymph nodes, bone marrow
- [?] Allow organs to stretch: arteries, uterus



Reticular fibers in lymph node (silver impregnation).

3) Elastic Fibers

- [?] Thinner than collagen fibers.
- [?] Forms a network dispersed between collagen bundles
- in organs subject to stretching and bending.
- Elastic fibers may form fenestrated sheets in the walls of large blood vessels called Elastic lamellae .
- [?] They provide Elasticity for the organ
- [?] They're synthesized by fibroblasts and smooth muscle cells.



Two stains were used to differentiate between collagen fibers (which are red/pink) and elastic fibers (which are darker in color).

Ground Substance

Is a highly hydrated, transparent شفاف, and viscous لزجة mixture of complex macromolecules that fills the spaces between the cells and the fibers in the connective tissue

- The Macromolecules are:

- 1) Glycosaminoglycans (GAG)
- 2) Proteoglycans
- 3) Glycoprotein

[?] The largest GAG is hyaluronic acid. This is the

only GAG synthesized on the cell membrane. Others are part of proteoglycans and are synthesized inside the cell.

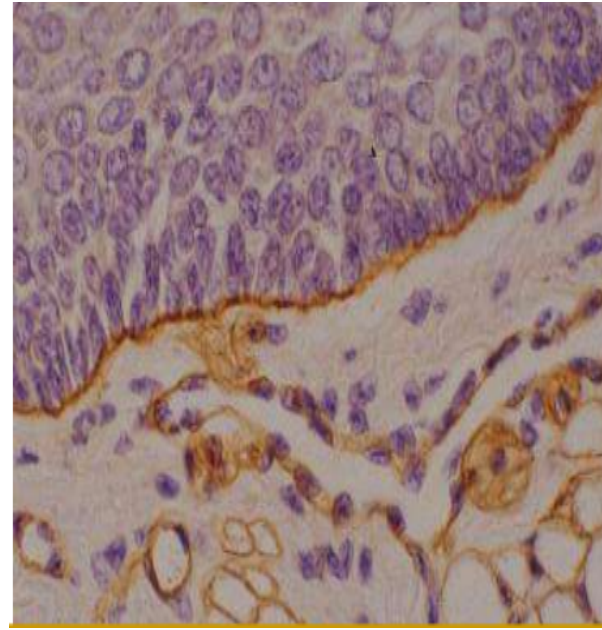
[?] Glycoproteins can bind to various components

of the ECM and the cell membrane. They're, therefore, called multiadhesive. They help keep the tissues together. Examples:

Laminin (in basal lamina)

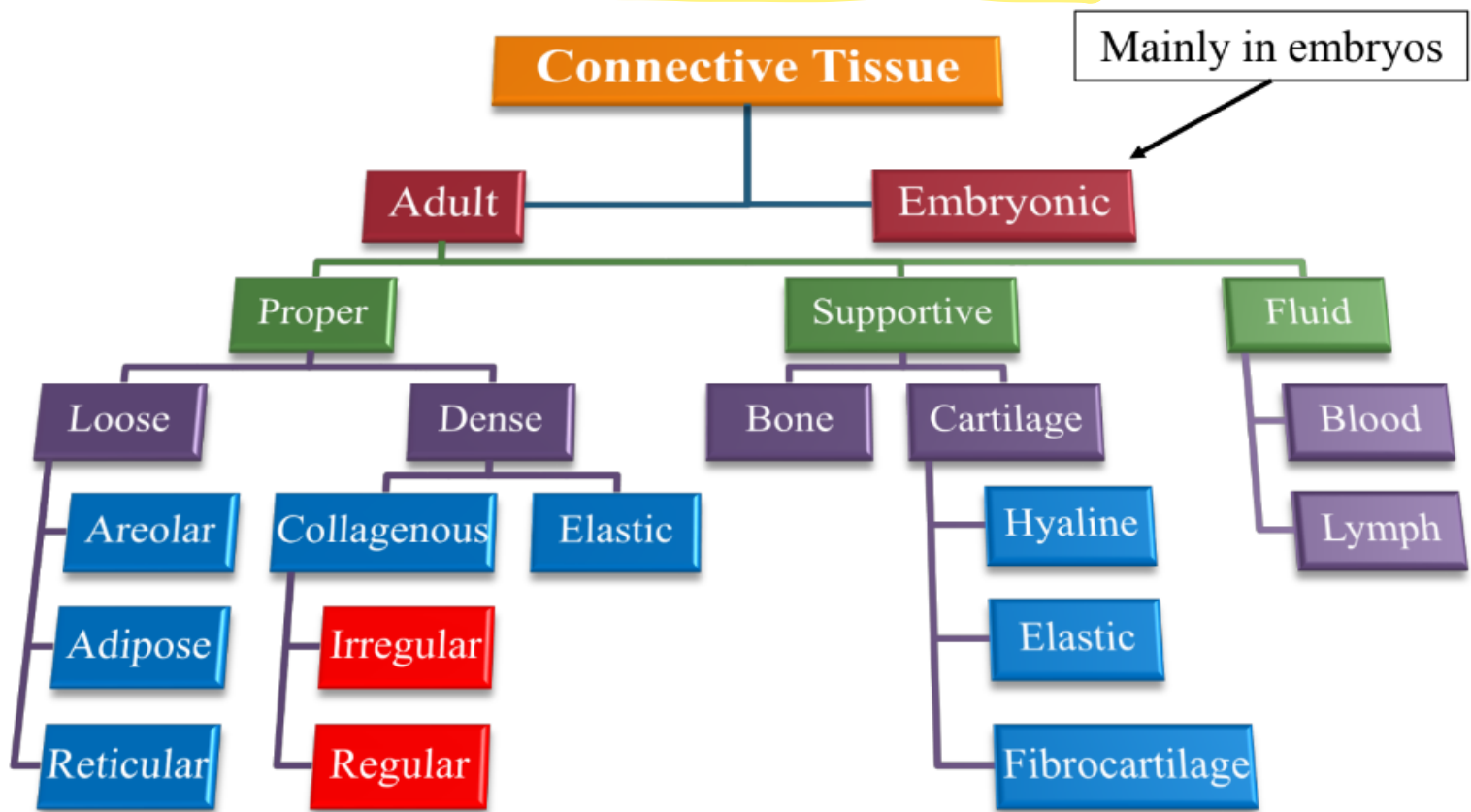
[?] Laminin of the basal lamina can bind to integrin protein of the epithelial cells and the other components of the basal lamina.

[?] Laminin, therefore, plays an important role in adhering the epithelium to the underlying connective tissue.



Laminin in the basal lamina under the epithelium (immunohistochemical study)

Classification of Connective Tissue



Mainly in embryos

- ☐ Proper connective tissue is the connective tissue in which the main type of cell that forms the ECM is the fibroblast.
- ☐ Loose connective tissue: the fibers are loosely arranged forming a network.
- ☐ Dense connective tissue: the fibers are densely packed.

1. Areolar Connective Tissue :

Features:

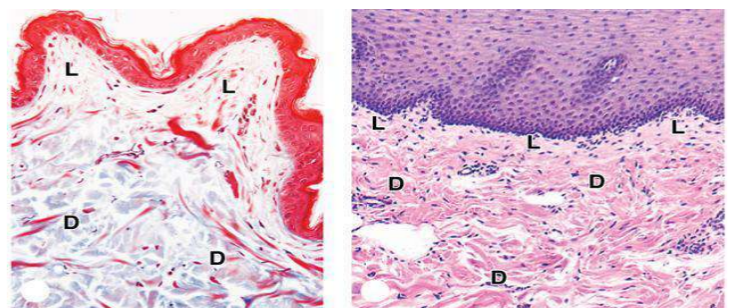
- ☐ Contain all three types of fibers arranged loosely.) collagen/reticular/elastic)
- ☐ All types of connective tissue cells (especially fibroblasts and macrophages) are present here.
- ☐ All these components are embedded in an abundant semi-fluid ground substance.
- ☐ It's highly vascular.

Functions:

- It gives organs their shape.
- It is a medium for the diffusion of gases, nutrients, and waste product.
- It is usually the first tissue where microorganisms and foreign particles enter the body; therefore, it's an important site for immune and inflammatory responses

Found:

- Under epithelia
- Around glands.
- In the spaces between muscle and nerve fibers.
- Around blood and lymphatic vessels.
- It fills many small spaces making it the 'packing material' of our body.



Left: Skin. Right: Esophagus. In both images, the loose connective tissue is indicated by L. Note its position under the epithelium. (The Ds in both images indicate dense collagenous irregular connective tissue).

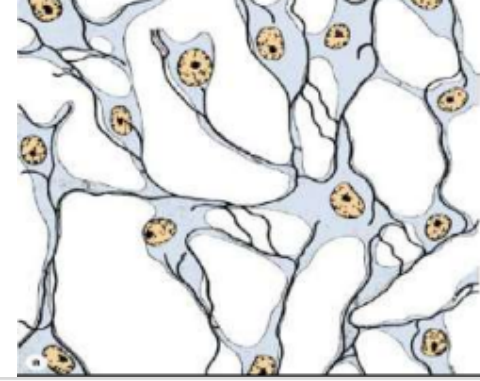
? Reticular Tissue: شبكي

? Composed mainly of loosely arranged reticular fibers

forming a network within haematopoietic organs (bone marrow., spleen) and lymph organs.

? Fibers formed by Reticular cells (modified fibroblasts) whose cytoplasmic processes extend on the reticular network forming a cell-lined sponge-like structure

Macrophages are also present in this tissue



Reticular tissue. Note how there are several spaces in this tissue giving it a sponge-like appearance.

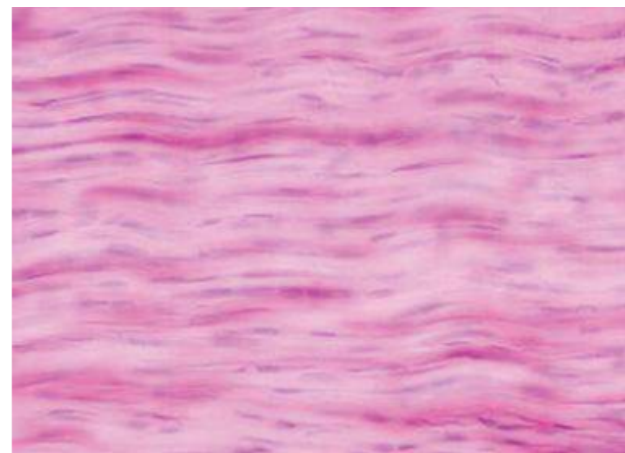
? Dense Collagenous Connective Tissue:

? A type of connective tissue that has numerous densely packed collagen fibers (between fibroblast) with few cells and ground substance. Highly resistant to stress

? Could be irregular or regular:-

1. Irregular: fibers arranged in no specific orientation forming a 3-dimensional network that resist stress from all directions. It is found in organ subject to great stresses

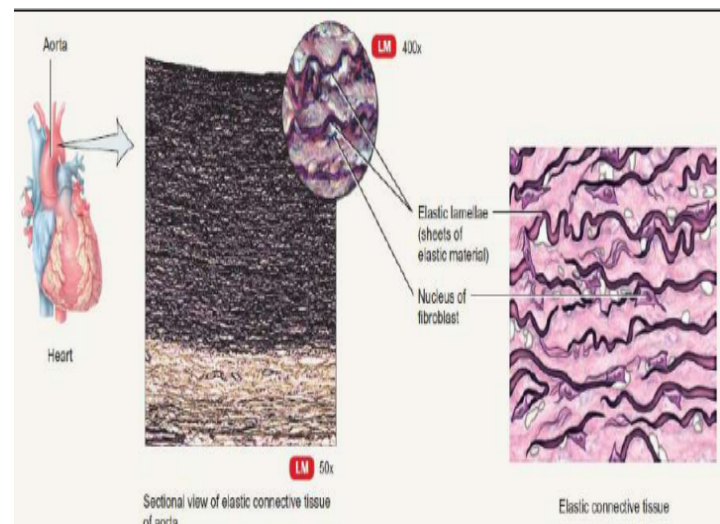
2. Regular: fibers arranged parallel to each other in a specific orientation with flattened fibroblasts dispersed between them. Provides great resistance to forces traction. Found in tendons and some ligaments giving the living tissue a white color



Dense collagenous regular connective tissue of a tendon (longitudinal section). مقطع طولی

? Dense Elastic Tissue:

? Composed mainly of elastic fibers. Found in aorta, some ligaments, and true vocal cords. Gives the organ elasticity



Adipose Tissue:-

- ❓ Is a type of connective tissue in which adipocytes predominate.
- ❓ It's present throughout the body.
- ❓ It constitutes about 15-20% of the body weight of males with normal weight, and 20-25% of females body weight.
- ❓ It could be White (WAT) or Brown (BAT)

Functions of Adipose Tissue

- 1) Storage of energy in the form of Triglycerides.
- 2) Endocrine role by the release of certain hormones and cytokines.
- 3) Insulator, because it's a poor conductor of heat.
- 4) Fills the large spaces between tissues and keeps some organs in place
- 5) Subcutaneous fat helps shape the surface of the body.
- 6) Fat pads act as shock absorbers (palms and soles).
- 7) Warming of the blood (brown fat).

White Adipose Tissue

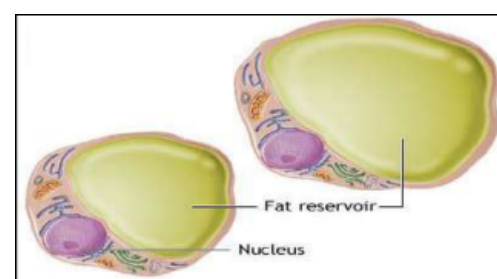
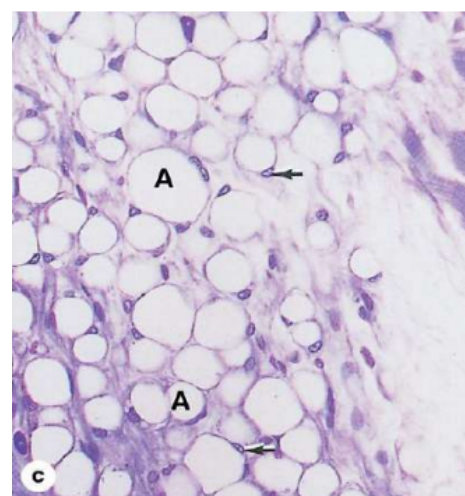
- o Specialized in energy storage in white adipose cells.
- o Depending on diet, its color varies from white to bright-yellow.

Features of white adipose tissue:

- 1) Fibroblasts and macrophages are present in the tissue.
- 2) Reticular fibers form a network that supports individual adipose cells and bind them together.
- 3) Divided by connective tissue partitions into incomplete lobules.
- 4) Highly vascularized.

Histological features of White Adipocytes

1. Large spherical cells with a single large fat droplet (unilocular).
2. Flattened nucleus on one side (pushed by the droplet).
3. A thin film of cytoplasm around the droplet with thicker cytoplasm around the nucleus.
4. Around the nucleus are several mitochondria, Golgi apparatus, polyribosomes, and poorly developed RER.
5. In the thin film of cytoplasm, there are well developed SER (smooth endoplasmic reticulum) and pinocytotic vesicles.
6. The droplets are surrounded by Vimentin intermediate filament.
7. The cell is surrounded by a thin basal lamina.



The image above shows the features of white adipocyte. On the right, the image shows the typical appearance of fatty tissue in a routine preparation. Fat droplets **dissolve** **بنتوب** during tissue preparation and the cell appears as a **thin ring** with the nucleus projecting on one side (the **signet-ring appearance**). **شكلها زي الخاتم**.

? Clinical aspects of White adipose tissue

- 1) WAT secretes the hormone Leptin which is a 'Satiety Factor' ? Could obesity be treated by hormonal therapy?
- 2) Adiponectin is released by adipocytes. The larger the adipocyte, the less adiponectin it releases. This hormone protects against diabetes and other diseases.
- 3) Obesity is characterized by a state of chronic mild inflammation because WAT secretes several inflammatory factors ? Could these be related to the cardiovascular or diabetic complications of obesity?
- 4) Although histologically similar, Visceral and Subcutaneous WAT have different gene
- 5) At birth, fat stores are already formed and distribution and density varies with age and gender

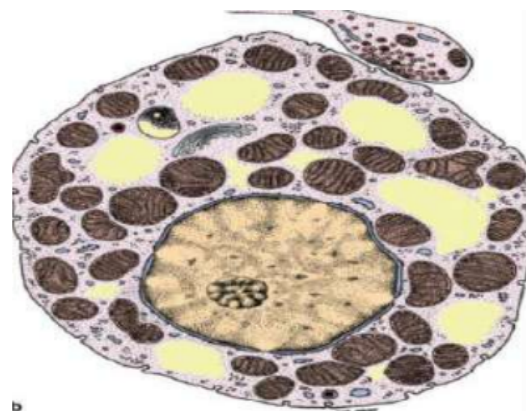
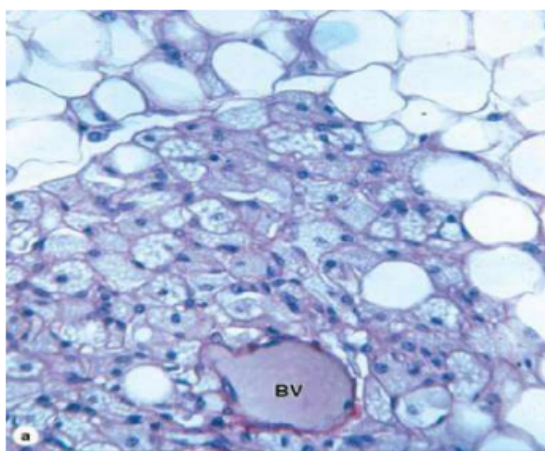
Obesity in adults is hypertrophic results from increase in size of the already present adipocytes .

In Children, the obesity could be hyperplastic increase in the number of cells) because new adipocytes can be formed from precursor cells that are still present at this age. Such obese children are more liable to develop a more severe hypertrophic obesity because they have more adipocytes.

? Treat/prevent obesity at an early age.

Brown Adipose Tissue

- o Specialized in heat production.
- o Brown adipocytes are smaller than white adipocytes, polygonal, with multiple fat droplets (multilocular). They have numerous mitochondria and a central spherical nucleus.
- o Cells arranged in an almost epithelial arrangement around a blood capillary. The tissue is divided into lobules by connective tissue partitions
- o The brown color is due to the mitochondria and the blood vessels
- o At birth, brown adipose tissue is maximal for body weight. It then decreases with age .
- o In adults, it's found in scattered areas especially around the kidneys, the adrenals , the aorta, and in the mediastinum .
- o It increase during cold adaptation.



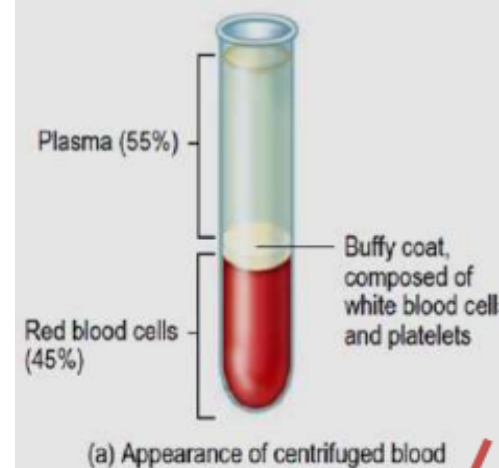
Above, a brown adipocyte, note the **several small fat droplets**. Right, brown adipose tissue, note how the cells surround a blood vessel (BV).

Blood

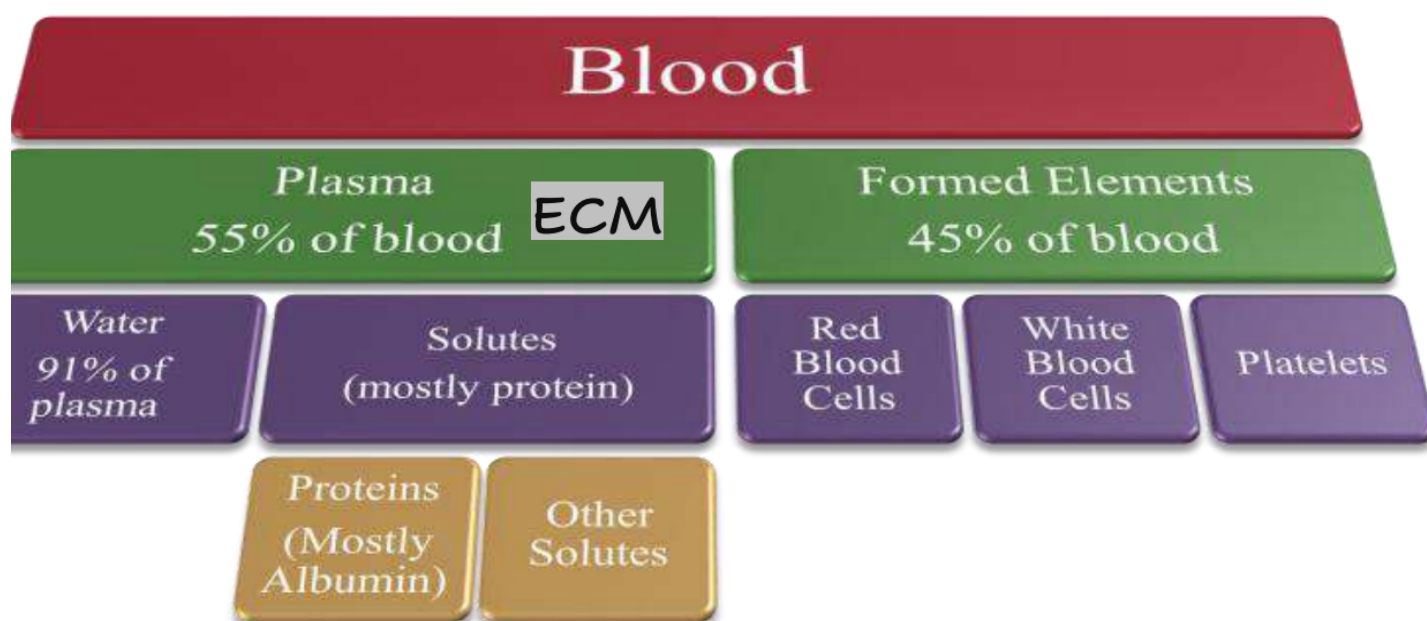
- Blood Is a fluid type of connective tissue characterized by having a liquid extracellular matrix (plasma) in which are dispersed the formed elements of blood: (1) Red blood cells (Erythrocytes), (2) White blood cells (Leukocytes) and (3) Platelets (Thrombocytes).

Functions of blood:

- 1) Transportation: Gases, nutrients, waste products, hormones.
- 2) Regulation: pH, body temperature.
- 3) Protection: Clotting, white blood cells, proteins (antibodies).



Components of Blood



Formed Elements of Blood

[?] Erythrocytes (Red Blood Cells)

- [?] The most abundant type of cell in blood
- [?] This cell is normally only present in blood inside the blood vessels
- [?] Biconcave disc in shape. This increases surface area.
- [?] Lack nucleus and other organelles.
- [?] Cytoplasm is filled with the oxygen-carrying protein hemoglobin. Because it has no mitochondria, it doesn't use oxygen
- [?] Strong, flexible plasma membrane. This allows the cell to change its shape without rupturing as it passes through narrow
- [?] Life span about 120 days



8 μ m



Functions of the red blood cells

1. The hemoglobin in the RBCs functions in the transportation of:

Oxygen – this is the main function of RBCs

CO₂

Nitric Oxide (NO) – this gas is a vasodilator that helps in increasing blood flow

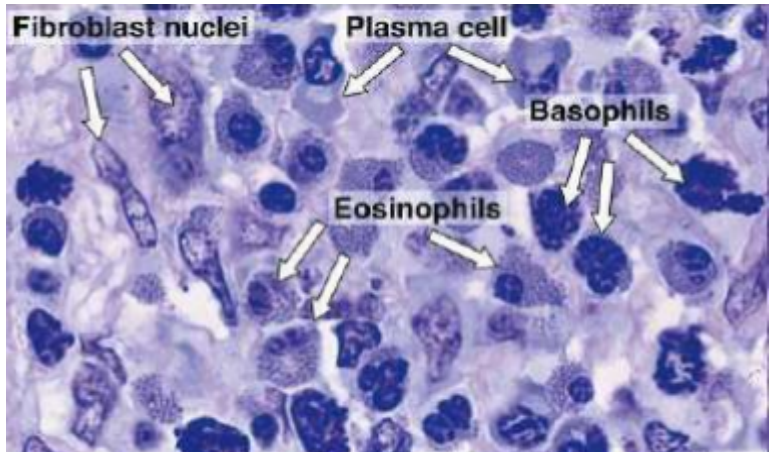
2. Glycolipids in plasma membrane are responsible for ABO and Rh blood groups.

3. When RBCs are destroyed by some microorganism, they release substances that can kill the microorganism.

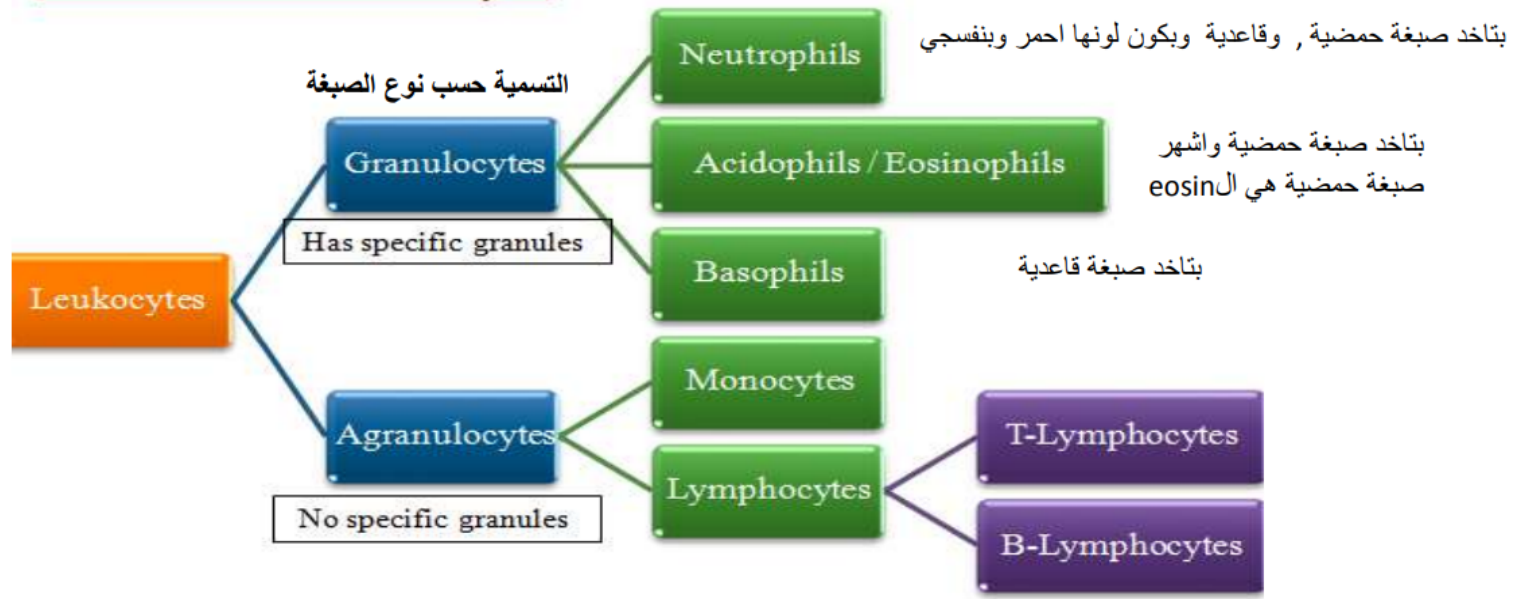
Leukocytes (White Blood Cells)

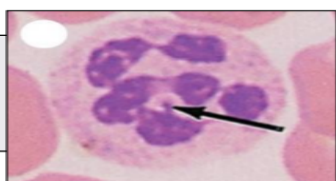

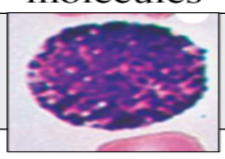
Wandering cells: formed in bone marrow, circulate in blood and enter tissues.

Respond to local factors in inflammation.



Classification of Leukocytes

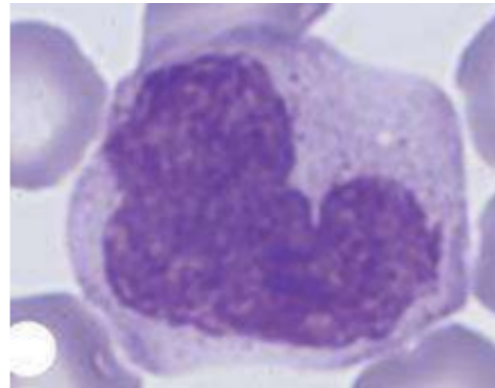


Granulocytes	Neutrophils	Eosinophils	Basophils
Abundance (% of leukocytes)	60-70%	2-4%	0.5%
Nucleus	Multilobed (with inactive X-chromosome of females appearing as a drumstick appendage)	Bilobed	S shaped (obscured by granules)
Granules	Sparse and stain variably	Large eosinophilic	Large basophilic
Function	Phagocytosis	<ul style="list-style-type: none"> Defense against parasitic infection Allergic reactions 	Release of inflammatory molecules
			

Agranulocytes:

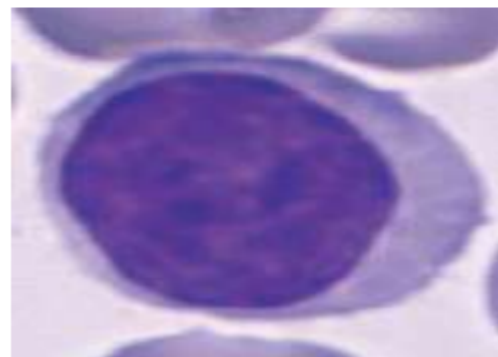
Monocytes (5%):

- ☐ Kidney or U-shaped nucleus.
- ☐ Cytoplasm basophilic.
- ☐ **Function:** formation of macrophages.



Lymphocytes (28%):

- ☐ Variable in size.
- ☐ Nucleus very dark and occupies most of the cell.
- ☐ **Functions:**
 - ☐ T-cells : Cell mediated immunity
 - ☐ B-cells :Antibody-mediated immunity



Platelets/ Thrombocytes

- ☐ Large cells in the bone marrow called Megakaryocytes send processes into blood vessels. These processes will splinter into small fragments called Platelets.
- ☐ This process continues until each megakaryocyte gives rise to about 2000 platelets.
- ☐ Each platelet is a disc-shaped structure surrounded by cell membrane and containing no nucleus but numerous vesicles containing blood-clotting promoting factor.
- ☐ Short life span: 5-9 days

Function: Stops bleeding by the formation of (1) platelet plug and (2) blood clot

ABO Blood Groups

- ☐ Blood group is type of blood designated to a person based on the presence/absence of an antigen on the surface of RBCs.
- ☐ The ABO blood groups are based on the A and B antigens.
- ☐ Reason for antibodies presence not clear.

Blood Type	Antigen on RBCs	Antibody in Plasma
A	A	Anti-B
B	B	Anti-A
AB	A & B	None
O	None	Anti-A & Anti-B

