بِسْمِ اللَّهِ الرَّحْمَٰنِ الرَّحِيمِ

HISTOLOGY

MID | Lecture 11

وَلَقَدْ خَلَقْنَا الْإِنسَانَ وَنَعْلَمُ مَا تُوَسْوِسُ بِهِ نَفْسُهُ ۖ وَنَحْنُ أَقْرَبُ إِلَيْهِ مِنْ حَبْلِ الْوَرِيدِ

Connective Tissue Pt.2 and Bone Tissue Pt.1

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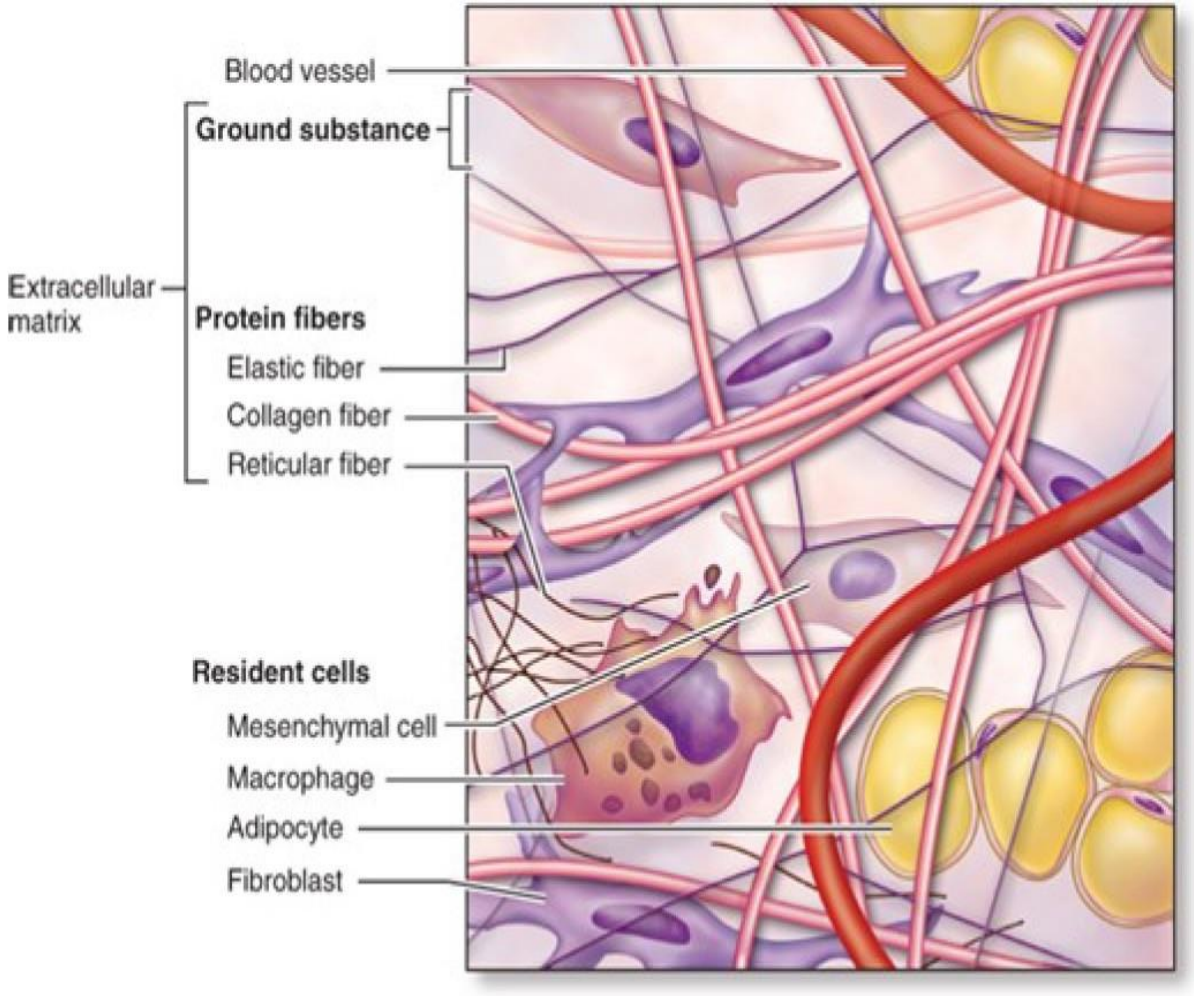
Color coding used in the modified:

- *Black: the original slides*
- *Maroon: the doctor's explanation/words*
- *Gray: additional information and explanation*
- *Red: important information*

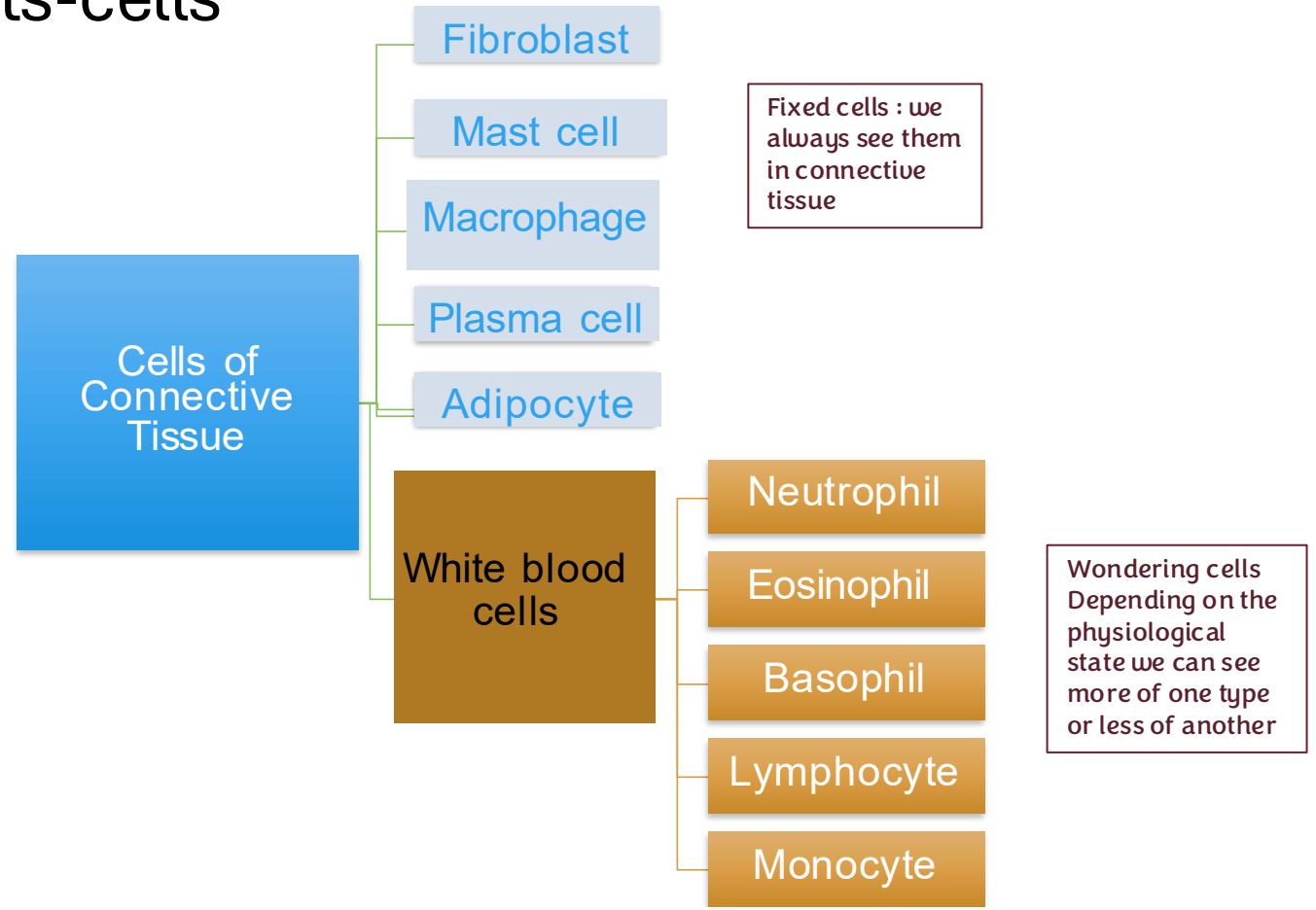
In the previous lecture we discussed the general overview about connective tissue and we said that it is a cells are surrounded by extracellular matrix , ECM divided to fibers and ground substances and the difference in it give different types of connective tissue.

Components

- Cells
- Fibers
- Ground substance



Components-cells



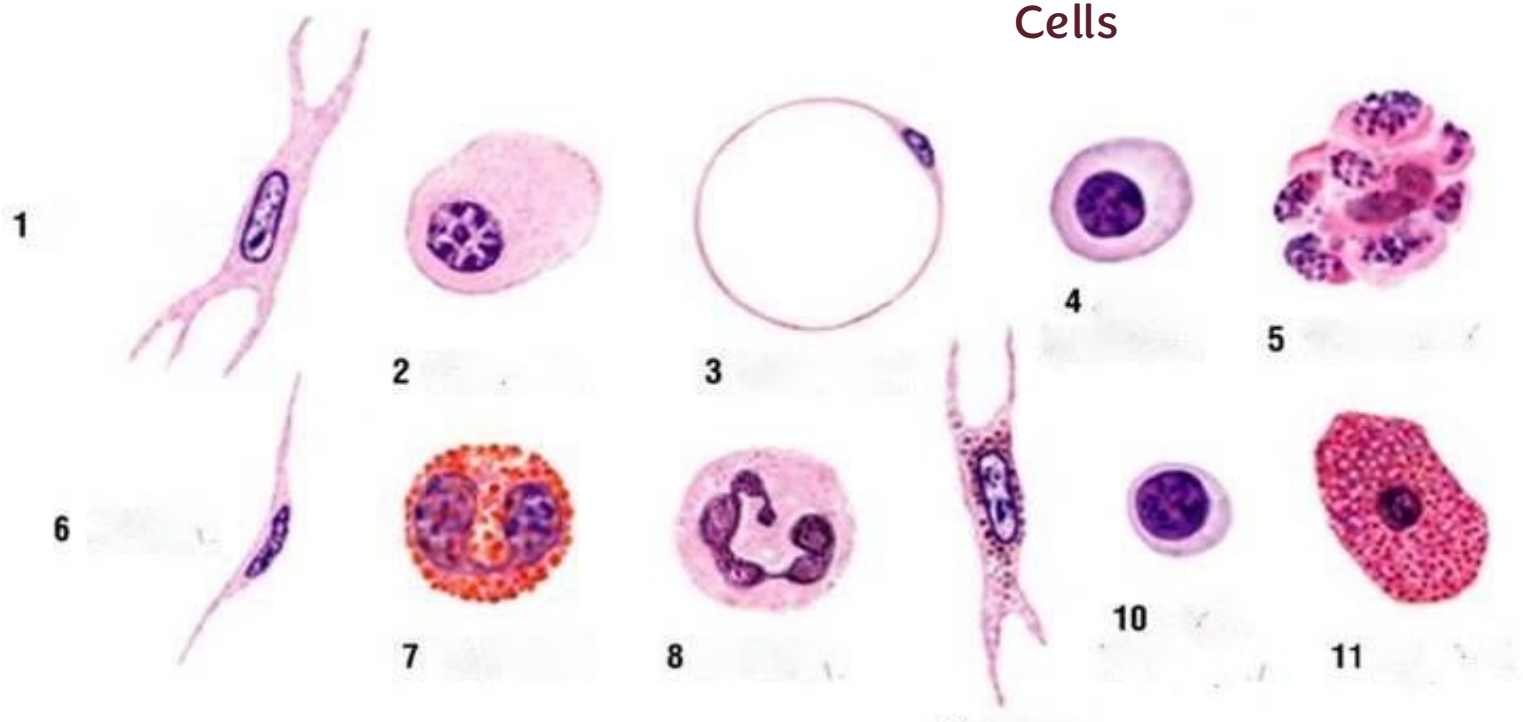
اللهم إني وكلتك أمري فكن لي خير وكيل ، ودبر لي أمري فإني لا أُحسن التدبير.

Cells

2-Plasma cells : WBCs that synthesize antibodies (very effective and sophisticated method of immune response)

3-Adipocyte (fat cells) : the hole in the center isn't lumen, but there was a fat vacuole in the center and during tissue processing the fat will be dissolved so it looks empty , and the cytoplasm is pushed to the periphery next to the nucleus

4-large lymphocyte + 10- small lymphocyte : WBCs found in B cells (antibody production), T cells (killing infected cells), and Natural Killer cell



1. **Fibroblast** 2. Plasma cell 3. Adipocyte 4. large lymphocyte
5. Macrophage 6. Fibrocyte 7. Eosinophil 8. Neutrophil
9. Cell with pigment granules 10. Small lymphocyte
11. Mast cell

7-Eosinophils are one type of white blood cell. They are not usually seen regularly in connective tissue, but they may be present.

Mast cells, eosinophils, and neutrophils and basophils all share the same origin, which is the bone marrow. Each of them has a specific function.

5-Macrophage : phagocytosis of microorganisms, when it has contact with the microorganism it surrounded the microorganism and enter in a vacuole then the lysosome fusion with the vacuole and break it down Macrophages are important immune cells that help clean up tissue after injury or an inflammatory reaction. After any new inflammatory response, tissue destruction occur, and the body needs to remove the damaged cells and debris. This is one of the main functions of macrophages.

Macrophages also remove foreign substances. When they come into contact with non-biological materials or microorganisms, they engulf them through a process called phagocytosis, where the material is enclosed in a phagocytic vacuole and then digested inside the cell.

Therefore, macrophages are responsible for cleaning up unwanted substances and eliminating microorganisms.

Macrophages originate from monocytes in the blood. When monocytes leave the bloodstream and enter connective tissue, they differentiate into macrophages. During this process, they increase in size and undergo changes in their cytoplasmic organelles to become highly active phagocytic cells.

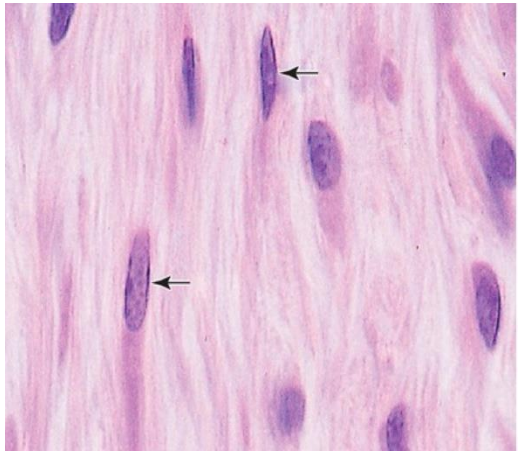
Connective tissue cells

Cell Type	Major Product or Activity
Fibroblasts (fibrocytes)	Extracellular fibers and ground substance
Plasma cells	Antibodies
Lymphocytes (several types)	Various immune/defense functions
Eosinophilic leukocytes	Modulate allergic/vasoactive reactions and defense against parasites
Neutrophilic leukocytes	Phagocytosis of bacteria
Macrophages	Phagocytosis of ECM components and debris; antigen processing and presentation to immune cells; secretion of growth factors, cytokines, and other agents
Mast cells and basophilic leukocytes	Pharmacologically active molecules (eg, histamine)
Adipocytes	Storage of neutral fats

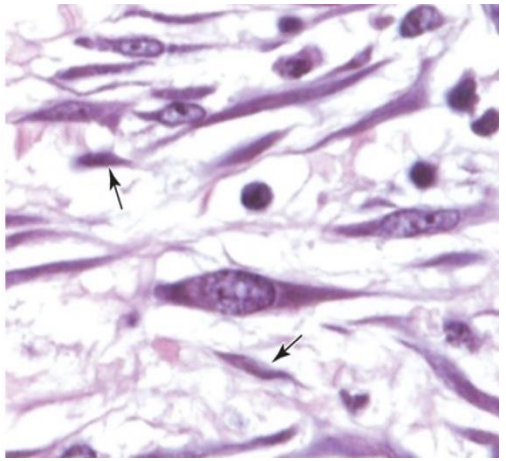
Fibroblast

- The most common cells in connective tissue proper
- Produce and maintain most of the tissue's extracellular components.
- Most of the secreted ECM components undergo further modification outside the cell before assembling as a matrix.

Fibroblast



Fibrocyte



Fibroblast is responsible for synthesis and release of ECM's components (fibers and ground substances) and they had extracellular modifications.
Fibroblast is the young and active form so it is large ,its nucleus is large and euchromatic ,its cytoplasm is large and it rich in organelles vs Fibrocyte is the inactive form ,These cells are in a dormant (inactive) state, meaning they are alive but not actively synthesizing connective tissue components so cell is smaller , the nucleus smaller and condensed = heterochromatic , its cytoplasm is less and the number of organelles is less (just enough to maintain cell survival -means that it is alive cell- not to be engage in synthesis and release) .However, when we needed them (such as during wound healing or tissue repair = connective tissue injury):
Fibrocytes become activated, they transform back into fibroblasts ,the nucleus becomes larger and less condensed=euchromatic and number of organelles increase so the cell starts synthesize and release ECM components.

Connective tissue proper is a type of connective tissue that is widely distributed in the body. It is found beneath epithelial tissue, between organs, and it surrounds muscles and nerves. It has different types, but it does not have a single specific name; it is generally grouped under the term connective tissue proper.
In contrast, specialized connective tissues include bone, cartilage, blood, and adipose tissue.
In bone tissue, the main cells responsible for bone formation are osteoblasts, not fibroblasts.
In cartilage tissue, the cells responsible for cartilage formation are chondroblasts (and chondrocytes in mature cartilage). Fibrous connective tissue may be present in the surrounding layer (perichondrium), but it is not the main cartilage-forming tissue.

The origin of these connective tissues is the mesoderm, which differentiates into mesenchymal cells that later give rise to different types of connective tissues.

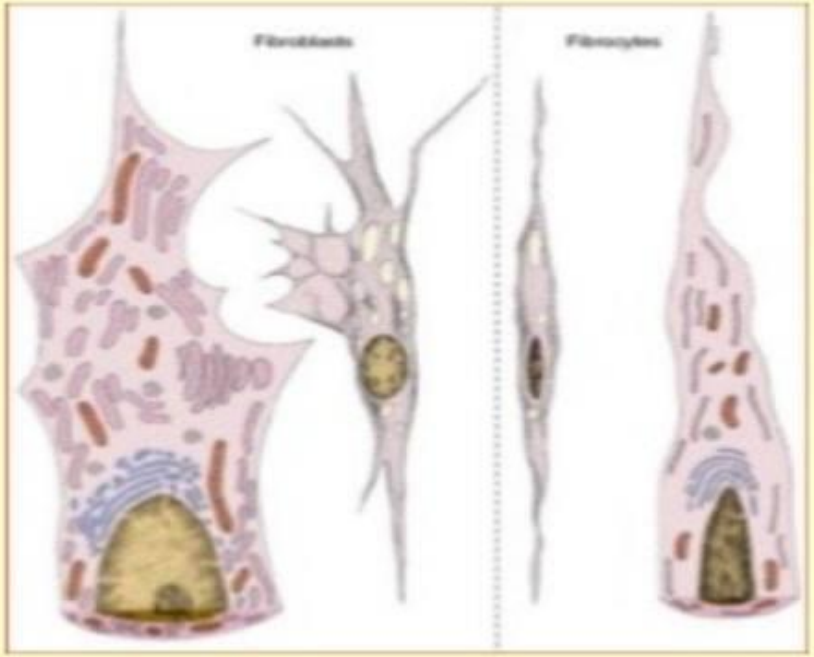
Side by side, fibroblasts have a large, active cell with a euchromatic nucleus. In contrast, fibrocytes are smaller cells with a dark, condensed (heterochromatic) nucleus.
In general, whenever you see the suffix "-cyte", it usually refers to cells that are relatively inactive or less secretory, meaning they are not highly involved in synthesis or production.
On the other hand, cells such as fibroblasts, osteoblasts, and chondroblasts are active cells that are involved in synthesis and tissue formation.

because they are needed for the cell to synthesize the molecules required for secretion and for creating the surrounding extracellular matrix.

Fibroblasts _ Fibrocytes

✓ Fibroblasts

- the most common cells in connective tissue
- cells responsible for the synthesis of extracelullar matrix components
- an abundant and irregularly branched cytoplasm
- ovoid, large and pale staining nucleus with nucleolus
- rich in RER and well developed Golgi complex and mitochondria
- produce the growth factors → influence growth and cells differentiation
- proliferate when the additional fibroblasts are required



✓ Fibrocytes

- smaller than fibroblasts
- fewer processes
- smaller, darker, elongated nucleus
- small amount of RER

Two stages of activity

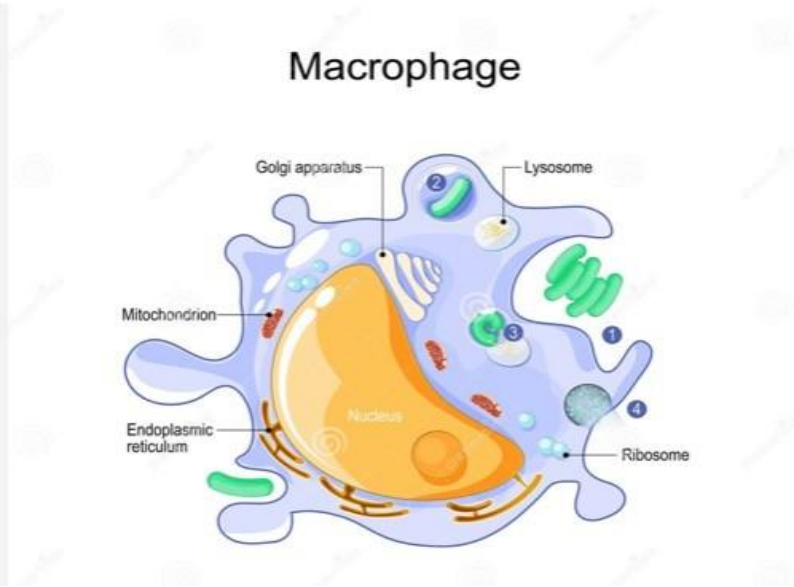
The active cells → Fibroblasts

The quiescent cells → Fibrocytes

Dormant / relatively inactive

Connective Tissue Cells-Macrophage

- Macrophages have highly developed phagocytic ability and specialize in turnover of protein fibers and removal of apoptotic cells, tissue debris, or other particulate material
- Being especially abundant at sites of inflammation.
- Size and shape vary considerably, corresponding to their state of functional activity.
- A typical macrophage measures between 10 and 30 µm in diameter and has an eccentrically located, oval or kidney-shaped nucleus.
- They generally have well-developed Golgi complexes and many lysosomes.



Connective tissue – macrophages:
this is a very important cell. It plays a major role in the mononuclear phagocyte system, which is based on a single precursor cell in the blood called the monocyte.
Monocytes are produced in the bone marrow and circulate in the blood. They do not remain circulating all the time; there is a limited number in the blood, and if they decrease, they are replenished by the bone marrow.
From the blood, monocytes leave the circulation and migrate into different tissues. They first pass through small blood vessels (capillaries) and enter peripheral tissues. Once they enter the tissue, they differentiate into macrophages.
While circulating in the blood, they are called monocytes. They are round cells with a kidney-shaped nucleus. When they migrate into peripheral tissues, they become macrophages, and their morphology changes: the nucleus becomes larger and the cytoplasm increases. These cells are motile and can move from one place to another, which is important for their function in capturing microorganisms and cleaning up debris.
This transition is also important for fibroblasts, which can also move within tissues.

Monocytes can migrate to almost all tissues, including connective tissue, liver, CNS, skin, lymph nodes (lymphoid tissue), and bone, among other locations.
Because these cells are found in different locations and have different appearances and functions, they were given different names, which were originally based on the scientists who discovered or described them.

In all these locations, their function is immune-related, meaning they are involved in recognizing foreign substances and getting rid of them. However, macrophages are somewhat unique compared to basophils, eosinophils, and neutrophils.
The specific function of macrophages is antigen presentation. This means they take antigens (foreign substances) and present them to other immune cells (lymphocytes).
Basically, macrophages have a limited role: they perform engulfing (phagocytosis) and breaking down of foreign material, then they “present” the antigen to other immune cells to continue the immune response.
This process is called antigen presentation. The role of the macrophage mainly stops at this stage, while other white blood cells complete the reaction. One example is the plasma cells, which are derived from B lymphocytes.

There is an exception in bone. When monocytes migrate into bone tissue, they can fuse together and form cells called osteoclasts. The function of osteoclasts is the digestion (breakdown) of bone matrix.
This is important because bone contains a large amount of inorganic calcium. The body needs to maintain calcium levels, as calcium is essential for many functions such as muscle contraction and nerve signaling. If needed, calcium can be released from bone.
The cells responsible for this are osteoclasts. This function is not directly related to the immune response. In this case, macrophage-lineage cells undergo a kind of “functional shift” when they enter bone and fuse (it becomes multinucleated)to form osteoclasts.

Mononuclear Phagocyte System

Cell Type	Major Location	Main Function
Monocyte	Blood	Precursor of macrophages
Macrophage	Connective tissue, lymphoid organs, lungs, bone marrow, pleural and peritoneal cavities	Production of cytokines, chemotactic factors, and several other molecules that participate in inflammation (defense), antigen processing, and presentation
Kupffer cell	Liver (perisinusoidal)	Same as macrophages
Microglial cell	Central nervous system	Same as macrophages
Langerhans cell	Epidermis of skin	Antigen processing and presentation
Dendritic cell	Lymph nodes, spleen	Antigen processing and presentation
Osteoclast (from fusion of several macrophages)	Bone	Localized digestion of bone matrix
Multinuclear giant cell (several fused macrophages)	In connective tissue under various pathological conditions	Segregation and digestion of foreign bodies

Macrophage (immune cell) in the skin

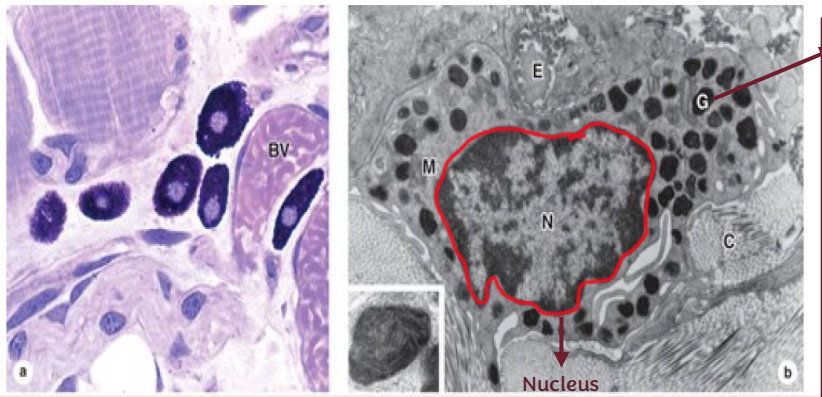
Connective Tissue Cells- Mast

- Oval or irregularly shaped cells.
- Filled with basophilic secretory granules that often obscure the central nucleus
- Mast cells function in the localized release of many bioactive substances, includes the following:

1. Heparin: an anticoagulant.
2. Histamine: increases vascular permeability and smooth muscle contraction
3. Serine proteases: activate various mediators of inflammation
4. Chemotactic factors: attract those leukocytes
5. Many others.

Highly active cells that are versatile (have many functions) and responsible for allergy symptoms

Acquired by TEM, 2D image with too much details

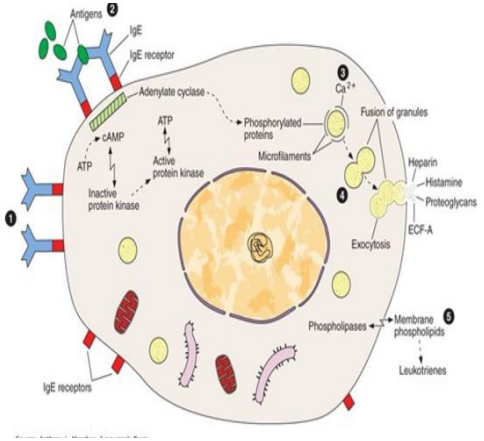


Granules are dark distinguished which make ,store bioactive substances and release them such as histamine

Mast cells are components of loose connective tissues, often located near small blood vessels (**BV**).

(**a**) They are typically oval shaped, with cytoplasm filled with strongly basophilic granules. (X400; PT)

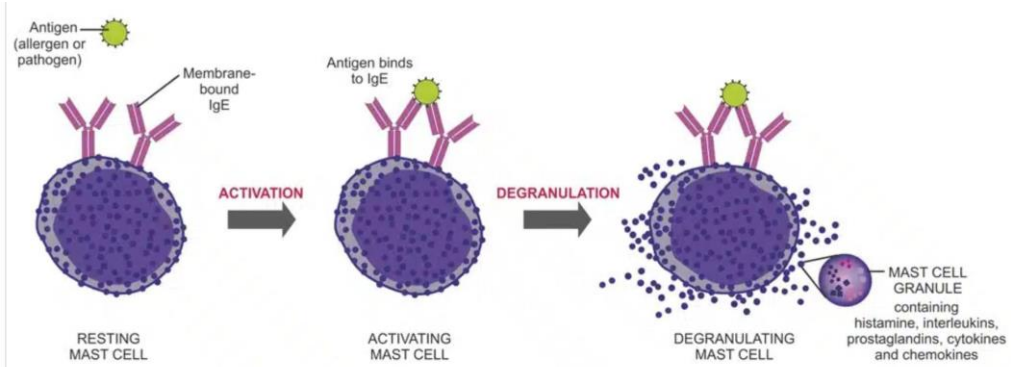
(**b**) Ultrastructurally mast cells show little else around the nucleus (**N**) besides these cytoplasmic granules (**G**), except for occasional mitochondria (**M**). The granule staining in the TEM is heterogeneous and variable in mast cells from different tissues; at higher magnifications some granules may show a characteristic scroll-like substructure (inset) that contains preformed mediators such as histamine and proteoglycans. The ECM near this mast cell includes elastic fibers (**E**) and bundles of collagen fibers (**C**).



Connective Tissue Cells- Mast

Antihistamines block histamine receptors so they prevent histamine from exerting its effects in allergic reactions and deactivate its function.
Histamine is associated with seasonal allergies, antigens will bind to IgE (Immunoglobulin E) lead to activation ,intercellular events and diffusion of granules with membrane and release of bioactive substances like histamine .
In trachea (Microscopic ones) which its wall is supported by smooth muscles ,histamine causes contraction of the smooth muscle in it, leading to narrow of the airway lumen and the air doesn't enter the alveolai(site of gas exchange) . This reduces airflow to the lungs, making breathing more difficult.
The first exposure to an antigen (allergen), such as bee venom, causes antibody-producing cells to produce an immunoglobulin of the IgE class that binds avidly to receptors on the surface of mast cells. Upon a second exposure to the antigen, it reacts with the IgE on the mast cells, triggering rapid release of histamine, leukotrienes, chemokines, and heparin from the mast cell granules that can produce the sudden onset of the allergic reaction. Degranulation of mast cells also occurs as a result of the action of the complement molecules that participate in the immunologic reactions

Same as in skin allergies, antigens will bind to IgE (Immunoglobulin E) lead to activation ,intercellular events and diffusion of granules with membrane and release of bioactive substances like histamine .
The skin become warmer with red color and increasing its size (redness, heat, and swelling) , that due to the increasing of the amount of blood (vasodilation), diffusion of solutions and activation of blood circulation.



Additional image

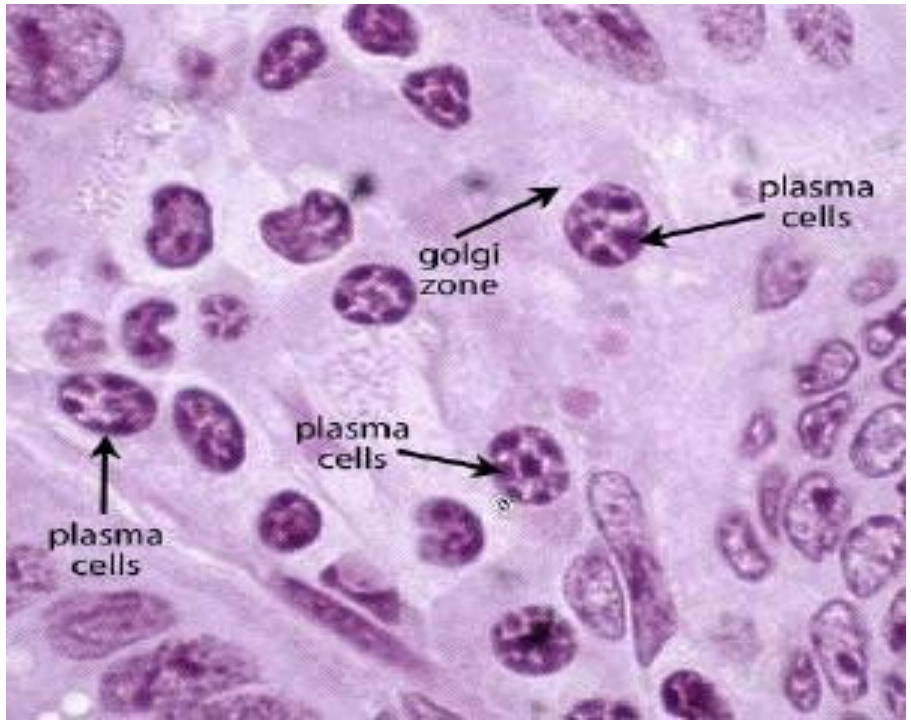
Mast cells also release heparin with the releasing of histamine because of the increasing amount of blood (Vasodilation) it will stay longer so to prevent that and avoid blood clots they release heparin

Connective Tissue Cells- Plasma Cell

Its function is antibodies production and gives immunity (antibody-antigen is important in immune reactions) so when cell produces antibody , it binds to an antigen which is on cell or soluble in solution.
Cell Mediated is when cell interact with and destroy another cell.

- Plasma cells are B lymphocyte-derived, antibody-producing cells.
- Unique-looking nucleus: cartwheel; regions of condensed chromatin alternating with regions of euchromatin.

  Plasma cells are cartwheel-shaped by the appearance of nucleus.
  They are actually arised from precursor which is B lymphocyte
- Relatively large, ovoid cells have basophilic cytoplasm rich in RER.
- Large Golgi apparatus near the nucleus that may appear pale in routine histologic preparations

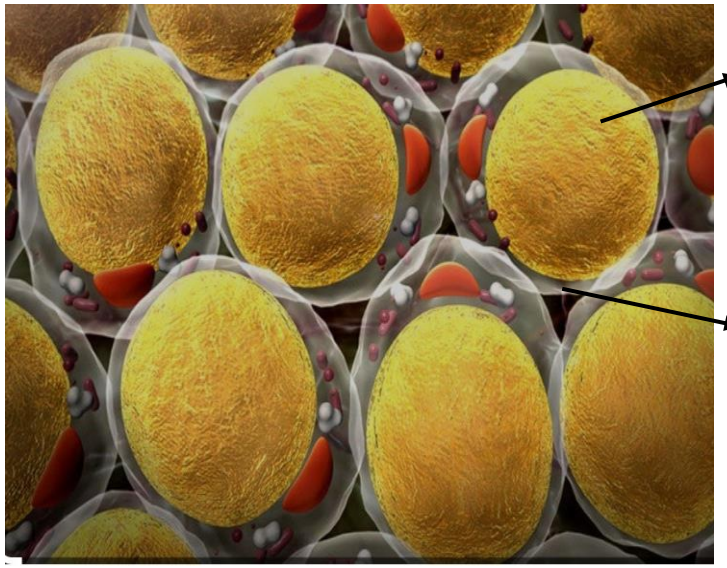


Most prominent organelles :
Because plasma cell produce an antibodies, it rich in rough endoplasmic reticulum and has Golgi apparatus and mitochondria because it an active cell
A large amount of RER appears basophilic (bluish color)

Connective Tissue Cells- Adipose Cells

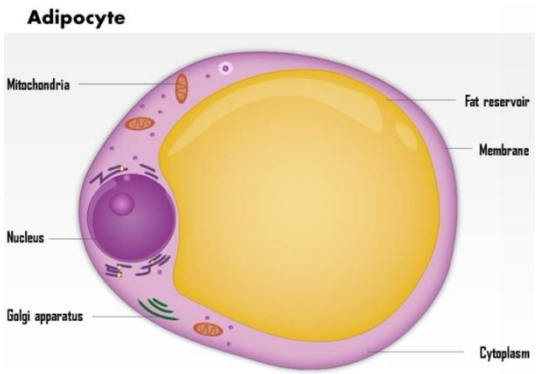
- Fat cells
- Found in the connective tissue of many organs.
- Large, mesenchymal-derived cells are specialized for cytoplasmic storage of lipid as neutral fats, or less commonly for the production of heat.
- Tissue with a large population of adipocytes, called adipose connective tissue: cushion and insulate the skin and other organs.

They found in connective tissue in everywhere, when the amount of adipocytes in tissue is large it is called adipose connective tissue so usually these are large cells (depends on the type), but we still see them in loose connective tissue .



It has one large vacuole of fats, the bigger the cell the bigger the fats vacuole .

They have cytoplasm cushions to the periphery and surrounds the fat vacuoles creating what is called Signet Ring.



There is nucleus , little amount of cytoplasm and the rest is occupied by fat vacuole

Additional image

Now , test yourself by this quiz:

press

فائدة قرآنية

وَقُل رَّبِّ أَدْخِلْنِي مُدْخَلَ صِدْقٍ وَأَخْرِجْنِي مُخْرَجَ صِدْقٍ وَاجْعَل لِّي مِن لَّدُنكَ سُلْطَانًا نَّصِيرًا ﴿٨٠﴾

[الإسراء]

وهذه الدعوة من أنفع الدعاء للعبد؛ فإنه لا يزال داخلًا في أمر وخارجًا من أمر. فمتى كان دخوله لله وبالله وخروجه كذلك، كان قد أدخل مدخل صدق وأخرج مخرج صدق.

ابن القيم

رسالة من الفريق العلمي:

Additional Resources:

أيّام الامتحاناتِ أقبَلت والدّراسة اشتدّت واستَحكمت..

استعينوا بالله..

وتذكروا قول الشيخ ابن عثيمين-رحمه الله- :

"إنّ اللهَ تعالى قد ينزلُ البركةَ للإنسانِ في وقتِه، بحيثُ يفعلُ في الوقتِ القصيرِ ما لا يفعلُ في الوقت الكثيرِ.

ومن أعظمِ ما يعينُك هو أن تستعينَ باللهِ عزَّ وجلَّ في جميعِ أفعالك، بأن تجعلَ أفعالَك مقرونةً بالاستعانةِ بالله، حتَّى لا توكَلَ إلى نفسِك؛ لأنَّك إن وُكِّلتَ إلى نفسِك فقد وُكِّلتَ إلى ضعفٍ وعجزٍ.

وإن أعانَك اللهُ، فلا تسألْ عمَّا يحصلُ لك من العملِ والبركةِ".

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			