

Doctor 022



The hypothalamus and pituitary gland

Histology

Sheet no.5



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In the previous sheet we talked about the cells of connective tissue and their types (highly found in blood vessels so it can nutrify the epithelial tissue).

What are the types of connective tissue?



Permanent (resident cells)

1. Fibroblast
2. Adipocytes
3. Macrophages



Transient cells (live for short periods as needed and then die by apoptosis)

1. Mast cells
2. Leukocytes (white blood cells)
3. Plasma cells

✓ The last one of permanent connective tissue is **macrophages**

- **Macrophages**

A typical macrophage measures **between 10 and 30 μm in diameter.**

The origin of macrophage is monocytes that is found in the blood.

(Doctor said that monocytes are resident in the blood but if it leaves the blood it will have a new name) the main function of monocyte is precursor of macrophages, the monocyte is a large and has a nucleus and it combines with more monocytes to form a multi nuclear macrophage.

Monocytes(macrophages) leave the blood and become a member in other tissues, it may go to the:

☐ liver: (and is called a **kupffer cell** because the first person who identify the macrophage in the liver is kupffer).

☐ CNS(central nervous system) and is called **microglial cell**.

☐(epidermis of skin)and is called **langerhans cell**.

☐(lymph nodes, spleen)and is called **dendritic cell**.

☐Bone and is called **osteoclast**.

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	Localiz
Multinuclear giant cell (several fused macrophages)	In connective tissue under various pathological conditions	Segreg

All are from monocytes but in different organs with a major function: phagocytosis, antigen presenting, secretion of cytokines

❖ (Osteoclast) we'll talk about it in details.

There are two types of macrophages but doctor mentioned one is a resident species, which has formed during embryonic life and has a lifespan for several years.

➤ Functions:

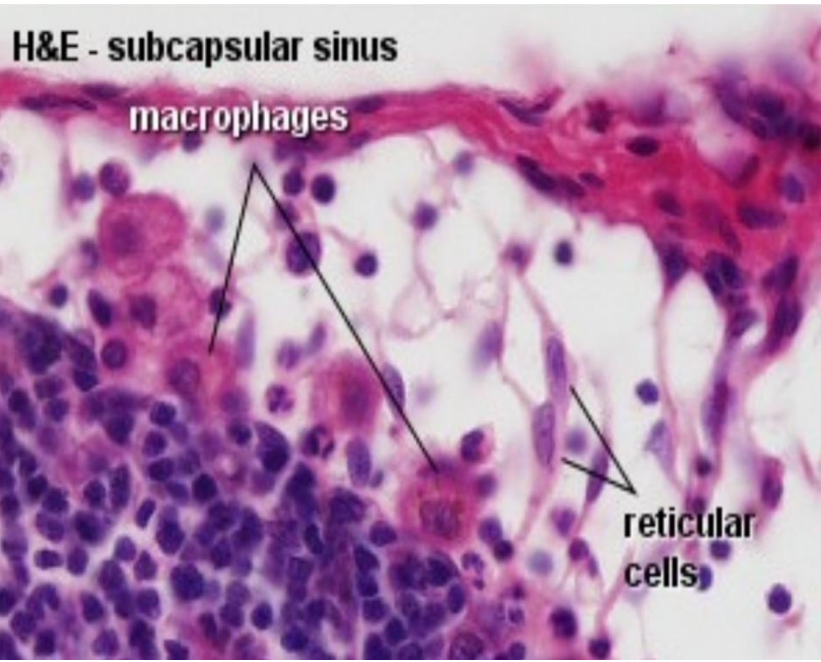
All immune functions:

- Phagocytosis
- Inflammation
- Antigen processing and presentation
- The osteoclast (comes from fusion of several macrophages)
 - **degrades bones** to initiate normal bone remodeling (constant state) and mediate bone loss in pathologic conditions by increasing its resorptive activity.
 - **Calcium is extremely important molecule in our body in almost all the biological activities that happen inside our body.**

In case we couldn't get calcium from kidney

(الجسم بمتص الكالسيوم من البول ويرجعه للدم بدل ما ينطرح برا الجسم)

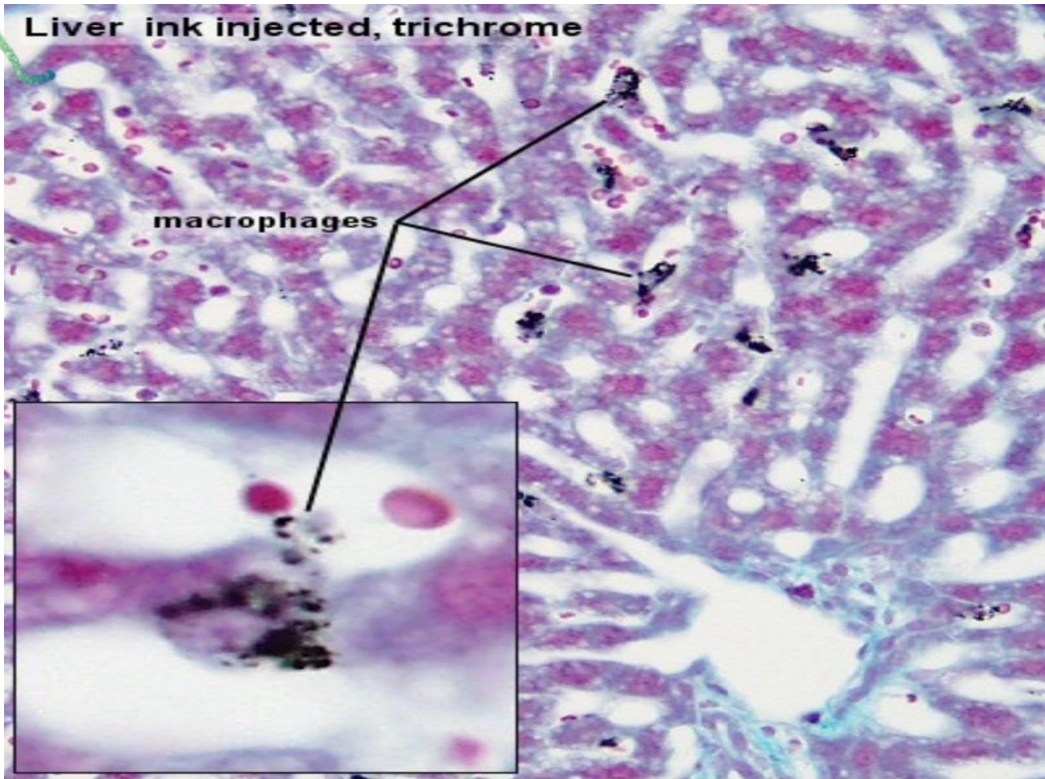
our body through specific hormones signals in bone(which contain calcium) indirectly through osteoclast corrects the level of calcium and preserves biological activities and contraction of muscles. (The most important muscle to contractile is heart).



- H&E: because it is stained pink and blue, bright field microscope.
- Macrophages: Large cells with large nucleus and cytoplasm.

Blood in liver comes from the GI tract and after the absorption of it, it returns to the blood circulation.

Kupffer in liver



Spaces field in the blood with endothelium

The stain: NOT H&E (ثلاثية الألوان), because the cytoplasm is blue and nuclei are pink! It is Masson's trichrome, is a three colour staining protocol used in histology.

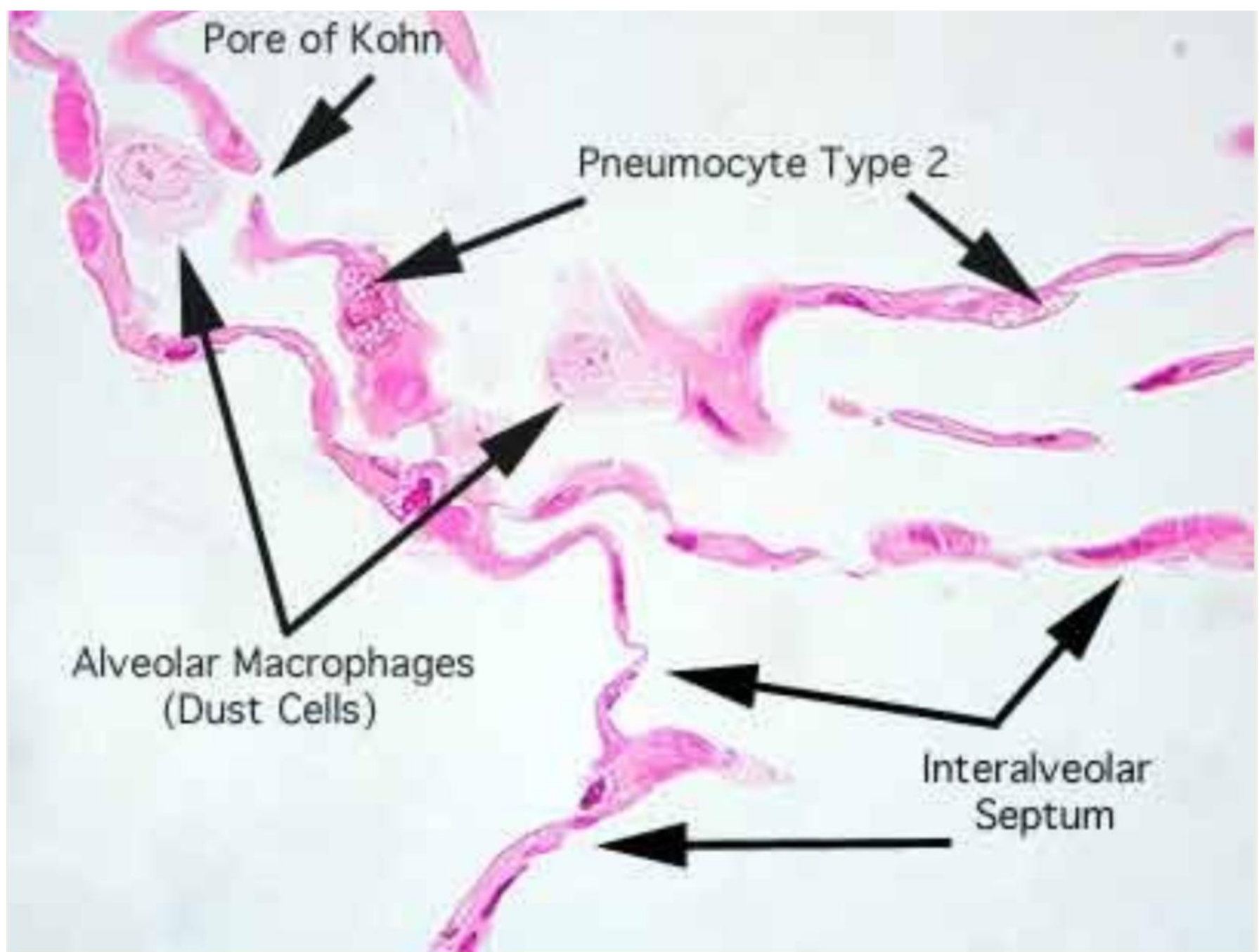
How I can identify the macrophages in the section above?

- The macrophage has a black color, but why? Because of the ink.

Injection of ink in the circulation of animal (mouse) (doctor said you can't inject the human by ink) **when the blood arrives to the liver the macrophage contacts with ink, picks it up and store it inside.**

- The other way is: (**immunostaining**), macrophage has its own specific antigen so we stain it with antibody and visualize the antibodies by **immunofluorescence or immunohistochemistry.**

بعدين بتبين الخلية اما بالازرق او بالأخضر او بالأحمر



- Another type of macrophages (doctor said the dust is more clear in presentation and she will add the dust

histo soon)(Not included in the previous table) but you should know it: Alveolar macrophages (Dust Cells).

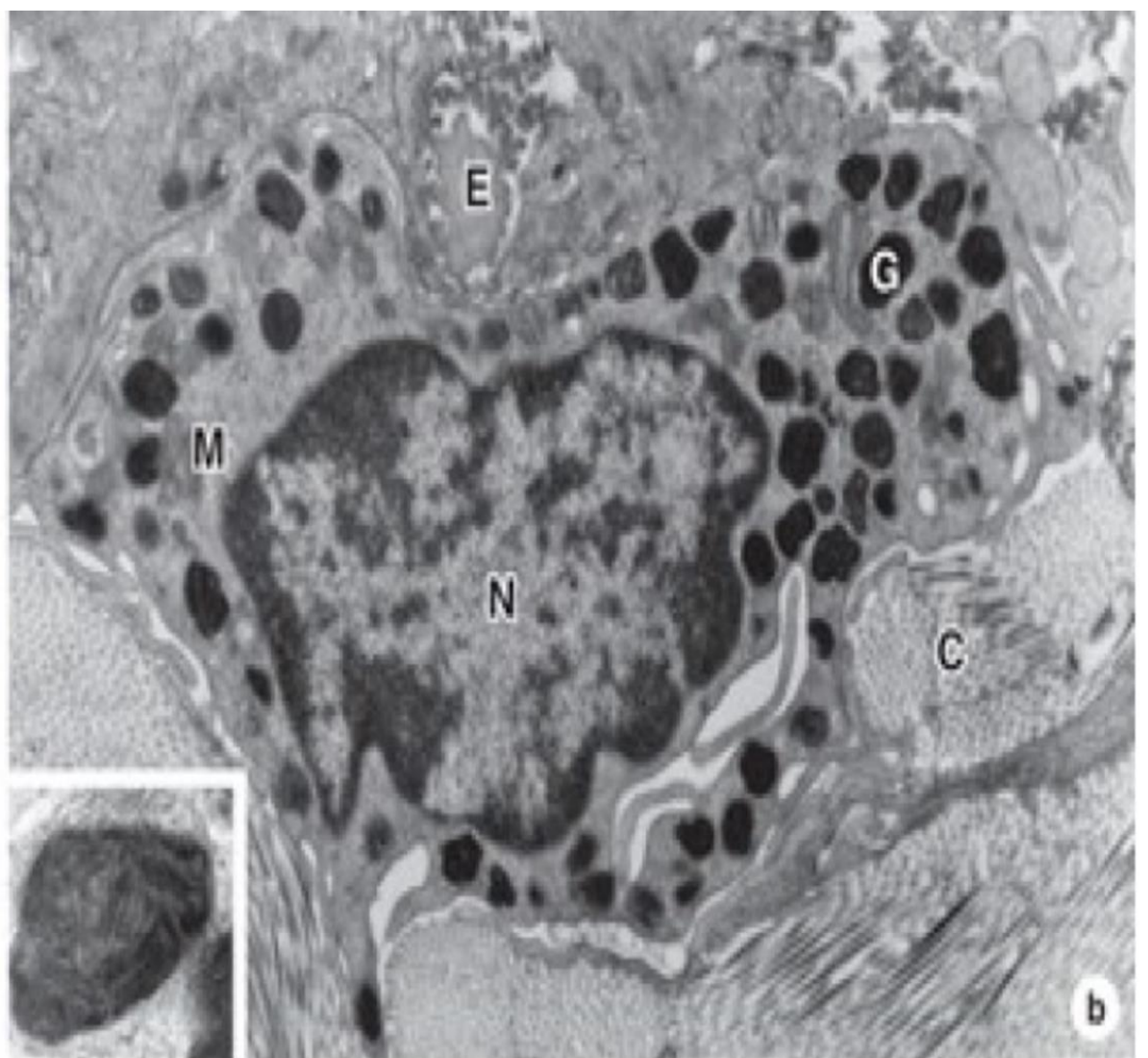
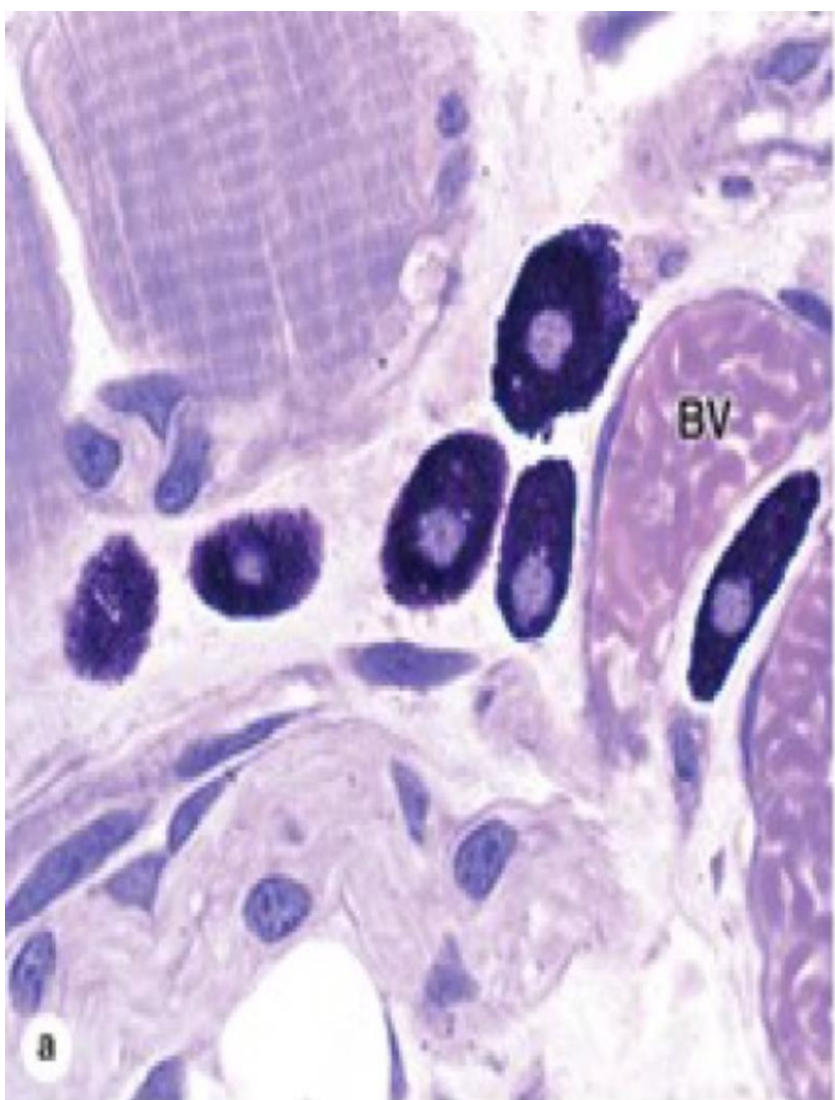
هل الهواء يلي بنستنشقه نظيف ؟ لا ولكن في الأجزاء العلوية من

Respiratory tract the mucus and cilia can clean up to certain limit but eventually something will escape in, so the macrophage will clean it up. usually dust cells are darker than the surrounding especially if the patient is old and living in unclean region.

Dust cells (alveolar macrophage) are **mononuclear phagocytes** found in the alveoli of the lungs. They ingest small inhaled particles resulting in the **degradation, clearance and presentation of the antigen.**

■ Mast cells

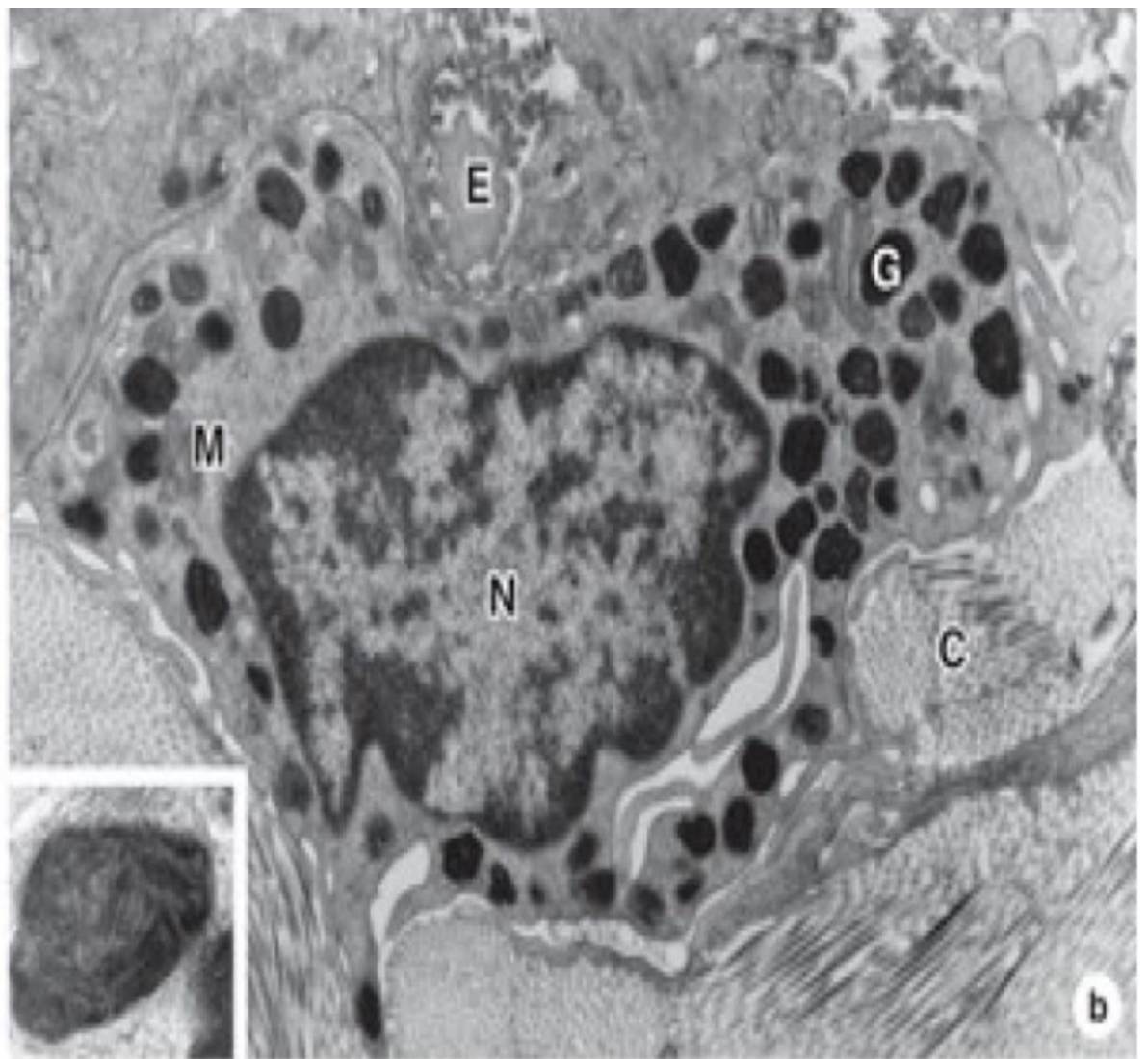
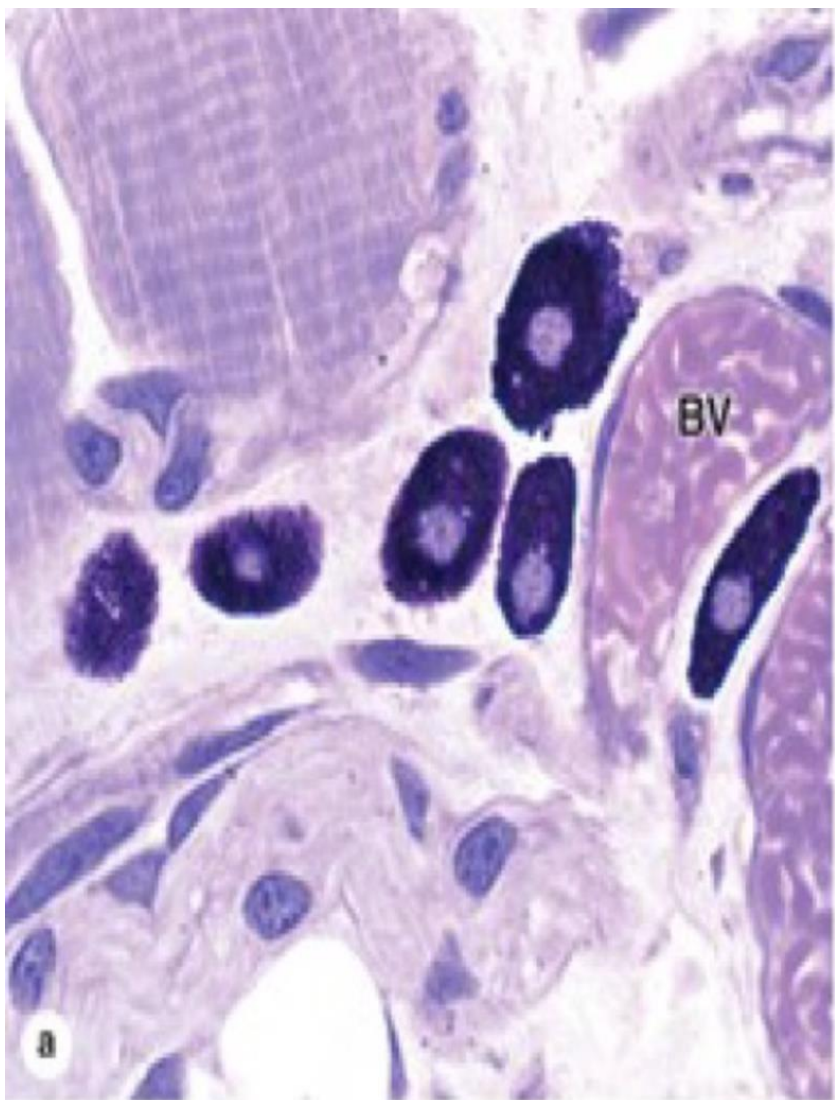
(نفسها خلايا صارية يلي اخذناها بالتوجيهي)



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).



Mast cells are oval or irregularly shaped cells of connective tissue between 7 and 20 micrometer in diameter, they are filled with basophilic secretory granules. (أوضح دليل لتمييزها)

Look how detailed the cytoplasm is in the left image, it is extremely detailed because of the high resolution power of EM , G states for granules that I can distinguish.

- All granules are something cytoplasmic but I can't distinguish in the left image, Because the resolution power of LM is weak.

- TEM

- Black, white and gray
- Actual interaction of the nuclei with electrons
- The electrons May pass in the space or reflect
 - And remember the scanning image also appears in black, white and gray but it has a 3D shape.

Additional note on the section above just for knowledge(not required)

Because of the high content of acidic radicals in their sulfated GAGs, mast cell granules display metachromasia (the ability to change its color), which means that they can change the color of some basic dyes (eg, toluidine blue) from blue (as It should) to purple or red. The granules are poorly preserved by common fixatives, so that mast cells may be difficult to identify in routinely prepared slides.

- Mast cells are important in allergies and immune reactions in general,

Generally some events will happen to the cell and cause a compound to bind to an antigen on the cell which will lead for second messenger formation inside and release of granules content to the ECM.

- **The major product of mast cell** is pharmacologically active molecules (**histamine**), Mast cells function in the localized release of many bioactive substances important in the local inflammatory response
- The main molecules they release inside granules **are heparin (an anticoagulant)** and **histamine (causes vasodilation)**
 - (بسبب الهستامين الذي يسبب افرازه مضاعفة كمية الدم عشرة اضعاف بسبب توسيع الاوعية الدموية).
- More blood means more fluid in the tissue and high temperature
Histamine causes the temperature of the tissue to increase and cause swelling and redness.
- Mast cells locate in the connective tissue in the airways, histamine in the airways works in other job, the histamine promotes contractions of smooth muscles. There are tiny airways surrounded by smooth muscle cells and if the antigen enters this region, histamine will promote smooth muscles contraction which will lead to airways constriction.

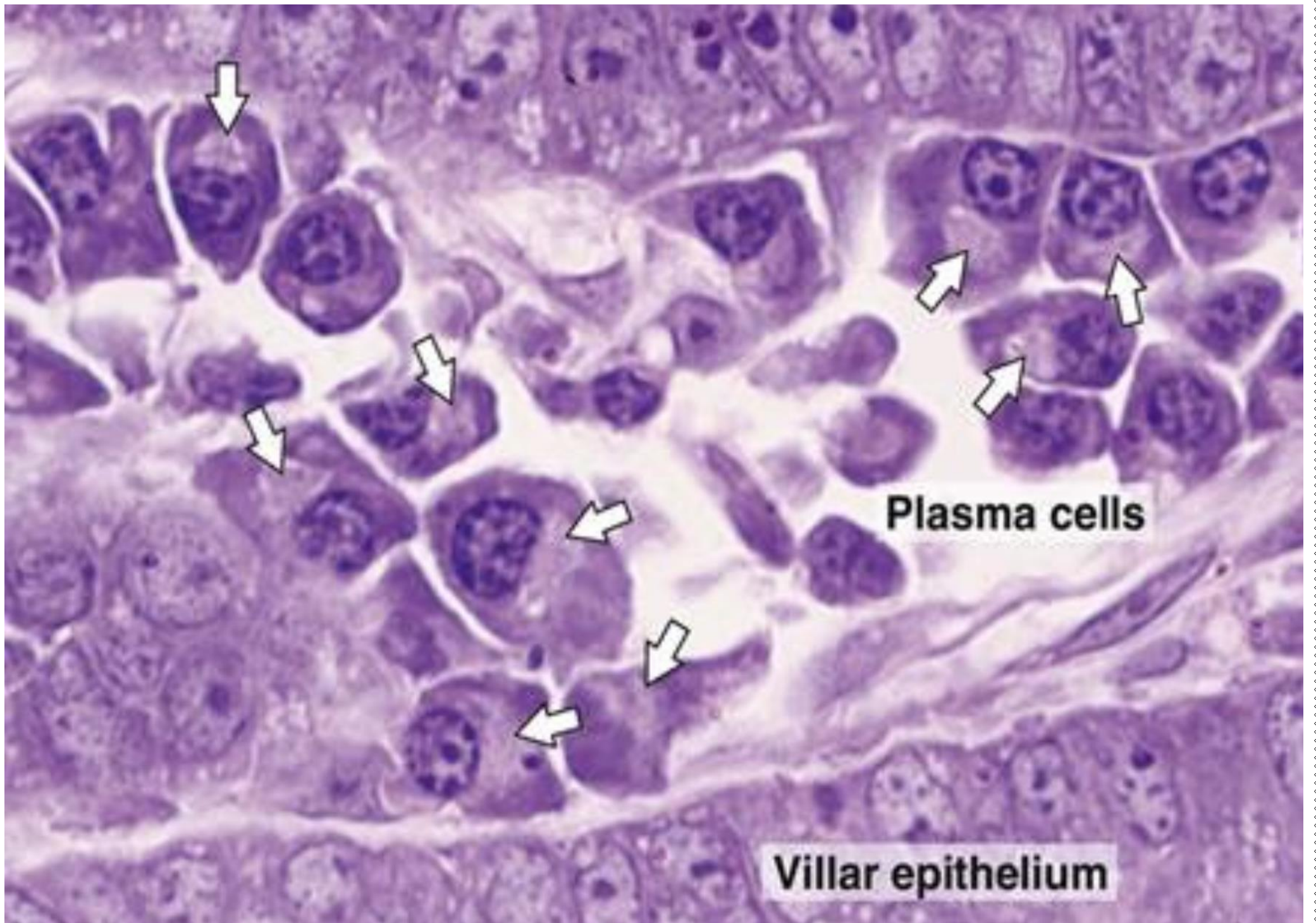
يعني الهواء يدخل عادي بالقناة الهوائية الكبيرة لكن لما يبش بالصغيرة ما بقدر يدخلها منيح فبنعالجها بال antihistamine وبمواد بتعمللنا ارخاء للعضلات الي بتحيط بال airway.

(They are involved in allergic reactions known as immediate hypersensitivity reactions)

يعني مثلاً الدكتور حكت انه وقت تعمل اختصاص برّا وتحط ابنك بمدارس هناك ممنوع تحط معه مكسرات لانه حساسية المكسرات مشهورة هناك ، يعني المشكلة بانه الواحد يتحسس من اشي مش لازم يتحسس منه.

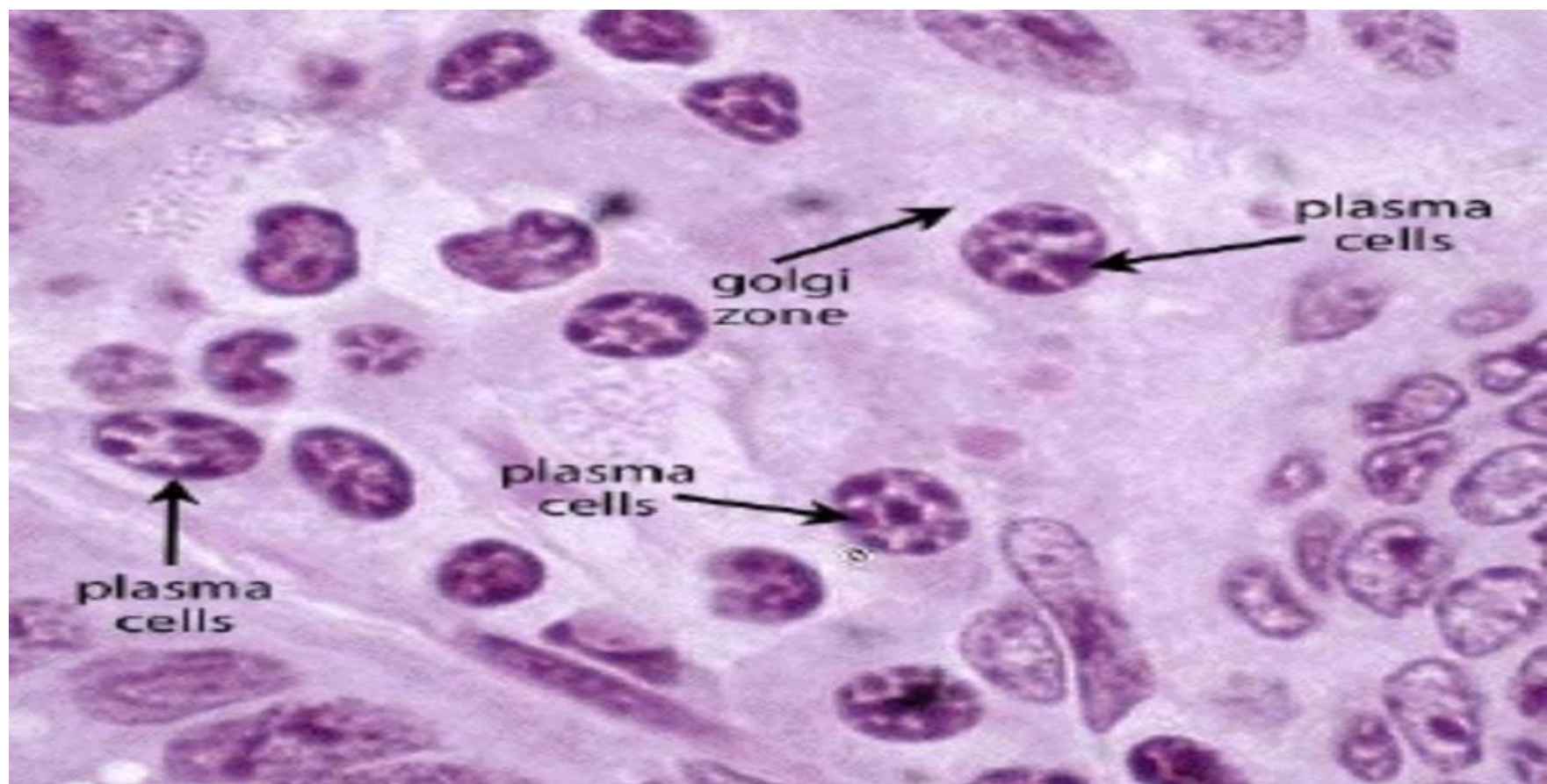
Plasma cells

Plasma cells are **lymphocyte-derived, antibody-producing cells**. They are relatively large ovoid cells with basophilic cytoplasm rich in RER and a large Golgi apparatus near the nucleus that may appear pale in routine histologic preparations (negative Golgi staining). The nucleus of the plasma cell is generally spherical eccentrically placed. Many of these nuclei contain



compact, peripheral regions of heterochromatin alternating with lighter areas of euchromatin (clock-face or cart-wheel appearance). Their average lifespan is only 10-20 days.

- You could see them or not, but you will see a lot of them in inflammation, because its function is antibodies production and secretion.
- **Precursor: B lymphocytes.**
- Relatively big in size, as well as its nucleus; you can easily distinguish it.



Doctor doesn't mention all the types of connective tissue because we'll take it in blood.

☐ connective tissue fibers

- **Collagen: undulating course of longitudinally striated bundles** (حُزْمَة حَبِل) the biggest form of the collagen but the collagen is formed from small subunits (later on), **stained with H&E and appears pinkish.** in the connective tissue **other type forms meshwork of variable texture (3D structure), Non extensible** (can't be stretched يُقاوم الشدّ). It is extremely important, **it is the**

protein that gives the bone it's strength.(bone contains calcium phosphate, bone without collagen عبارة عن كوكيز

The one that catches calcium and phosphate crystals is collagen يعني الكولاجين يشتغل شغل الحديد بالمباني،المباني لولا الحديد على اقل اهتزاز رح تقع)

- Elastic: (delicate) fibers that may form what is called lamina (صفائح) when 10 fibers together side by side make sheets we call them lamina-**they are usually faint-** , unstained with H&E (this is not totally correct because they are poorly stained , but if they are side by side with collagen you will not distinguish them because of the intensity eosinophilic of collagen, elastic is very faint but if the fibers make lamina you might see them with H&E so generally we call it unstained) that is why we require more special stains in order to visualize elastic fibrous, such as: **orcein, Resorcin fuchsin, and Verhoeff van-giesons** stain and they give us a grade of(brown to black). and **elastic is extensible.**
- Reticular: network and they are delicate (مثل ليفة الجلبي فتحات صغيرة) and interconnected same team with the reticular fibrous , **unstained in H&E**, we need Ag it is (argyrophilic) silver loving accept stain with silver , stains black in Ag(No)3(Argyrophilic), PAS +ve.

This is a nice summary for fibers:

Connective Tissue Fibers

Collagen	Undulating course of longitudinally striated bundles, form meshwork of variable texture, stain pink-red in H&E. Nonextensible.
Elastic	Forms sheets or lamina, Unstained in H & E. Reversibly extensible. Stains brown-black in Orcein, Resorcin Fuchsin, and <u>Verhoeff-van Gieson's</u>
Reticular	Delicate network, Unstained in H & E. Reversibly extensible. PAS +ve, stains black in AgNO ₃ (Argyrophilic).

● Collagen

Collagen is a big family, it's the most type of fibers we usually see in the connective tissue, it's the toughest and the strongest type especially the fibrillar one, it's non-extensible (we can't stretch it), it's usually stained with H&E and other stains.

this family is composed of subfamilies which they are:

- **Fibrillar collagens**, which we distinguish them as fibers or bundles, notably collagen types I, II, and III. Form structures such as tendons, organ capsules, and dermis. (wherever there's strength applied to that structure) You can see a lot of type I in the connective tissue proper, You'll find type II in cartilage and type I as well.

Usually fibrillar assembly (type I) is long strands or long fibers much involved in structures where we need or require strength

- Fibrillar collagens are the most widely spread type

-Type I collagen is the most abundant and widely distributed collagen

- **Network or sheet-forming** collagens such as type IV collagen have subunits produced by epithelial cells and are major structural of external laminae and all epithelial basal laminae (basement membrane) .

It forms a network-like structures and it connects different structures It's much more complicated than the fibrillar.

- **Linking/anchoring** collagens are short and small proteins (type VII). As their name shows they link or connect different other proteins together

-Most of the specialties or properties that gives the strength are found in type I.

* وَأَنْ لَيْسَ لِلْإِنْسَانِ إِلَّا مَا سَعَى * وَأَنْ سَعْيُهُ سَوْفَ يُرَى * ثُمَّ يُجْزَاهُ الْجَزَاءَ الْأَوْفَى *