

Blood cells / lec 2

*Edited by: Rua'a Nader

	RBCs (Erythrocytes)	WBCs (Leukocytes)
Types	1 type	5 types
	Not true cells	True cells { Nucleated & have few organelles within cytoplasm }
Number	Male: 4.5-5.5 million/mm ³ female:4-5 million/mm ³	4500-11000/mm ³
Diameter	6-9um (7.5um)	6-20um
Life span	120 days	Few days-years
Origin and maturation	Bone marrow	Bone marrow and lymphoid tissue
Shape	Biconcave discs	Spherical (when passing inside the blood & irregular in shape when enter connective tissue)
Function	Gas exchange	Defense
Motility	Non motile (They flowing with blood flow)	Motile
when it leaves the blood, Function exclusively within hemorrhage or bleeding vascular system		Function mainly OUTSIDE blood vessels in the tissues ECM of C.T

* WBCs —> motile, in order to perform their function, they have to leave the blood stream and enter the interstitial fluid of connective tissue in order to fight infection.

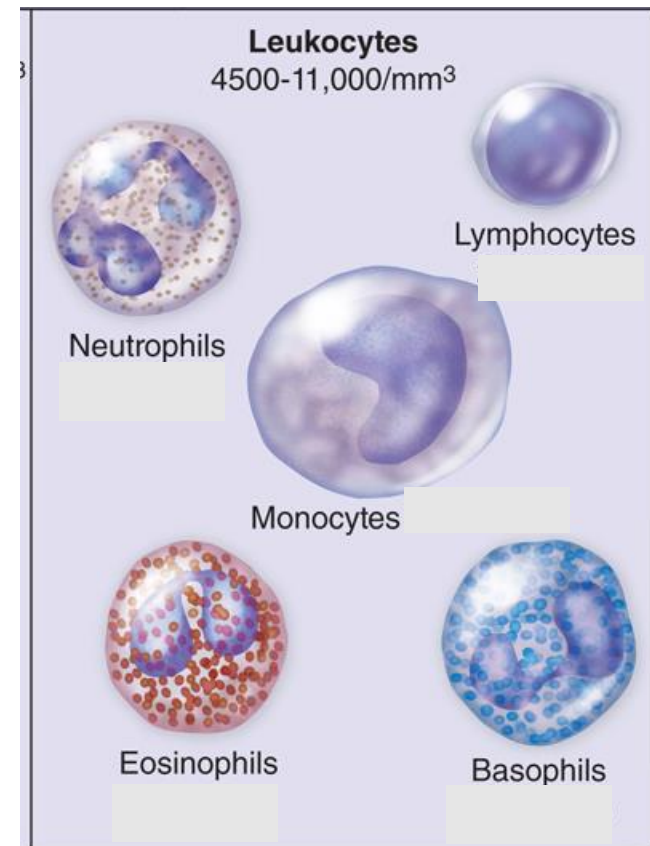
*Clarification of the animation:

If we have an infection (microbes) inside the spaces of C.T and in order to attract WBCs to the site of infection by chemotactic agents , it happens some processes inside blood vessel ,firstly, margination then Rolling and WBCs will squeeze between endothelial cells reaching site of infection, we called this whole process {Diapedesis} —> migration of WBCs from blood into surrounding tissue.

Leukocytes

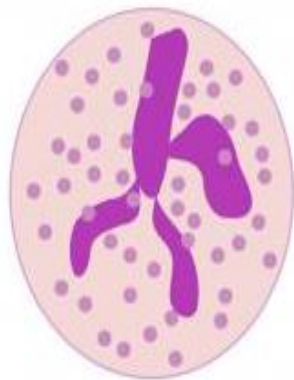
- Originate in the bone marrow and released continuously into the blood
- Travel in bloodstream but function mainly **outside** blood vessels (in loose CT)
- Leukocytes form a mobile army that helps protect the body from damage by bacteria, viruses, parasites, toxins and tumor cells
- 5 types organized into 2 groups
 - **Granulocytes**
 - Neutrophils
 - Eosinophils
 - Basophils
 - **Agranulocytes**
 - Lymphocytes
 - Monocytes

Leukocytes, or WBCs, are nucleated and subdivided into granulocytes and agranulocytes, depending on the presence or absence of **specific** granules in their cytoplasm.

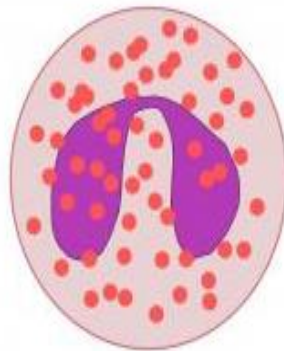


Leukocytes (White Blood Cells)

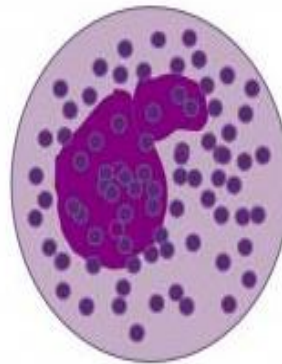
Granulocytes



Neutrophil



Eosinophil



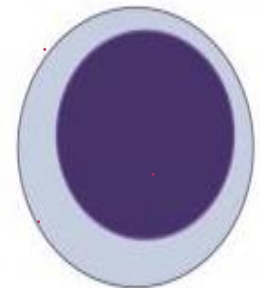
Basophil

Agranulocytes



Monocyte

The largest cell
of WBCs



Lymphocyte

Cytoplasmic granules

Specific granules

Secondary granules

Non-specific granules

Azurophilic granules

Lysosomes

Primary granules

they are stained with Azure dye (blue color) and this dye stains only lysosomes within cytoplasm.

Granulocytes

- Cytoplasmic granules (containing enzymes or chemicals) → makes cytoplasm look grainy
- Single multi-lobed nucleus (segmented)
- All are phagocytic; they engulf and consume foreign cells and material
- 3 main types:

2 lobes

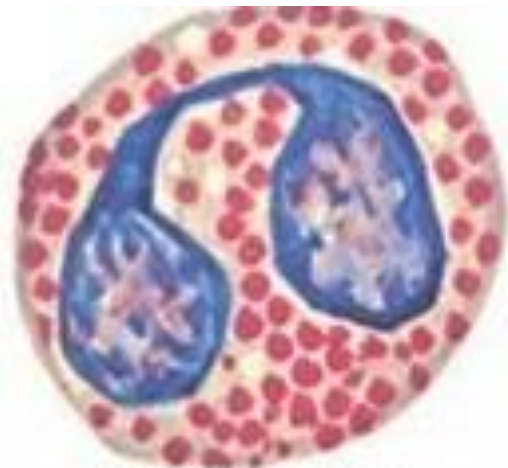
Large granules, **Red**

4 lobes

Small granules, **pale pink/ salmon pink**

irregular (S - shaped)

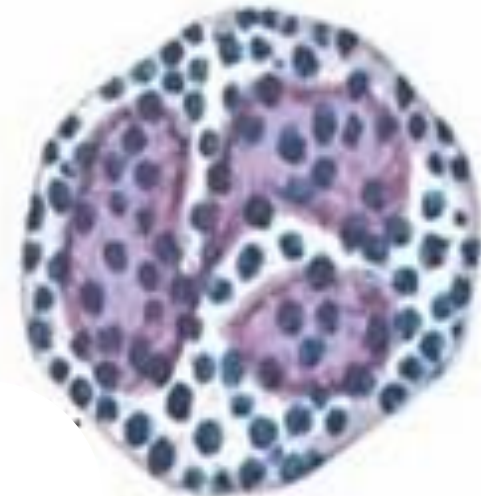
Large granules, **blue**



Eosinophil



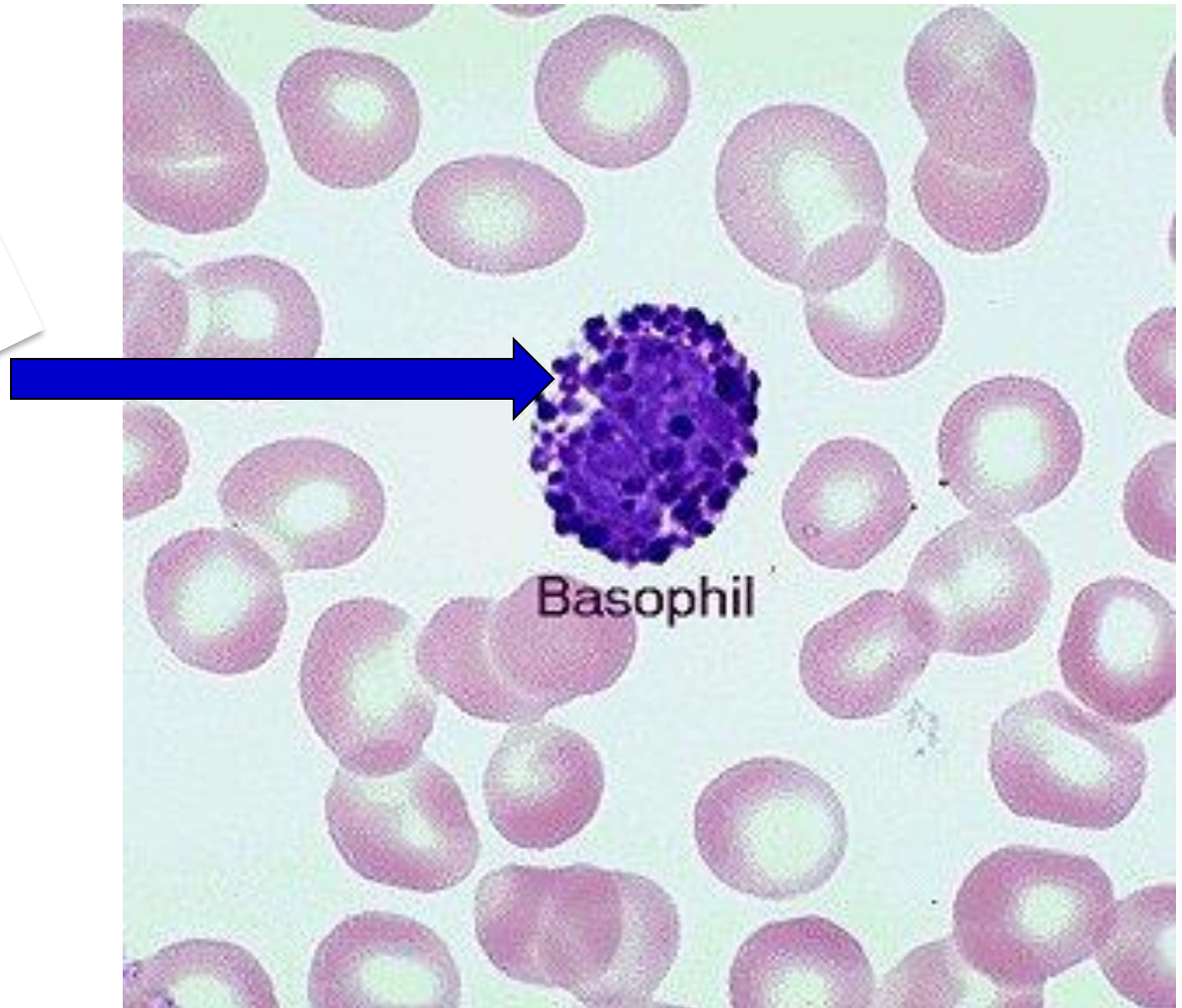
Neutrophil



Basophil

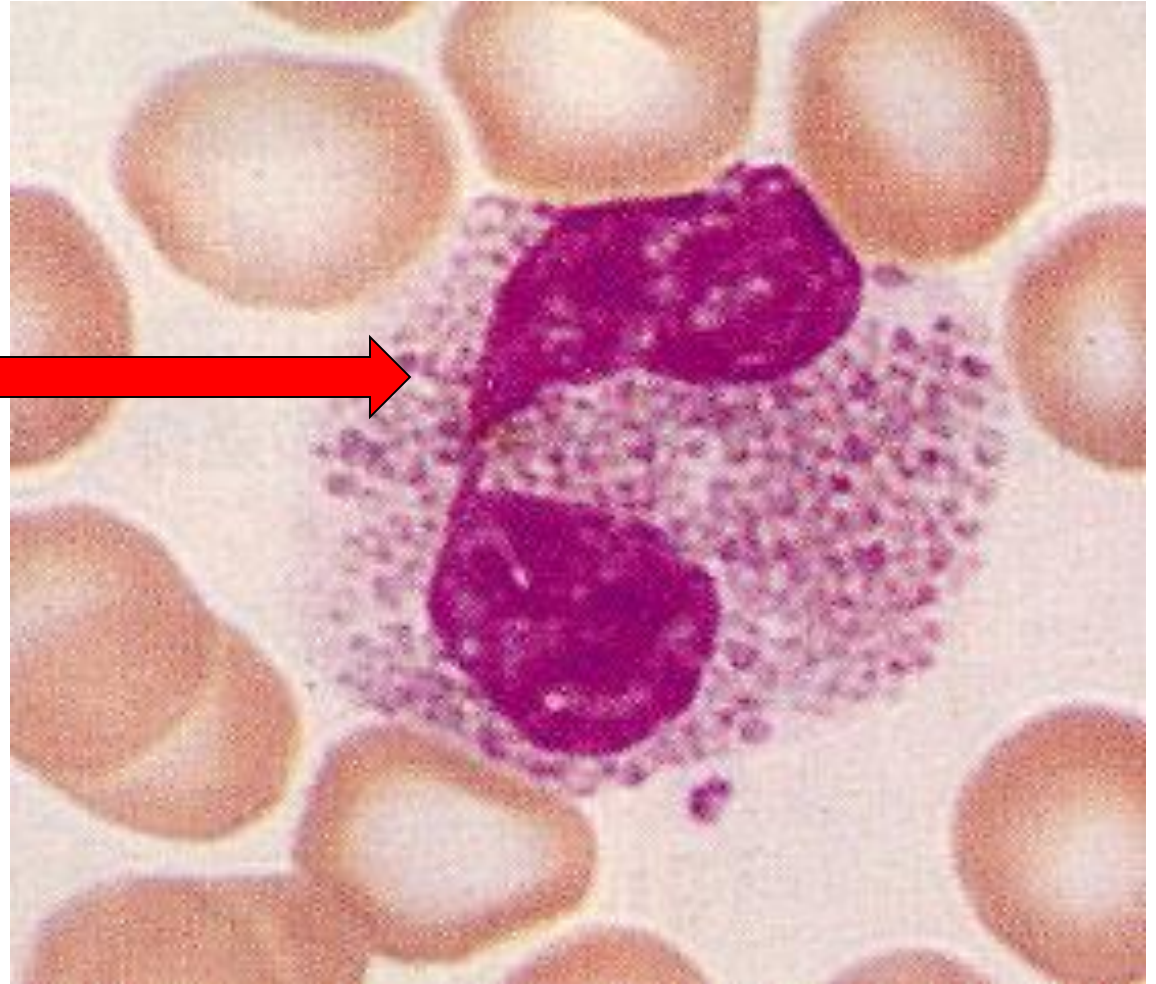
Basophil

*These specific granules
stain with basic stains*



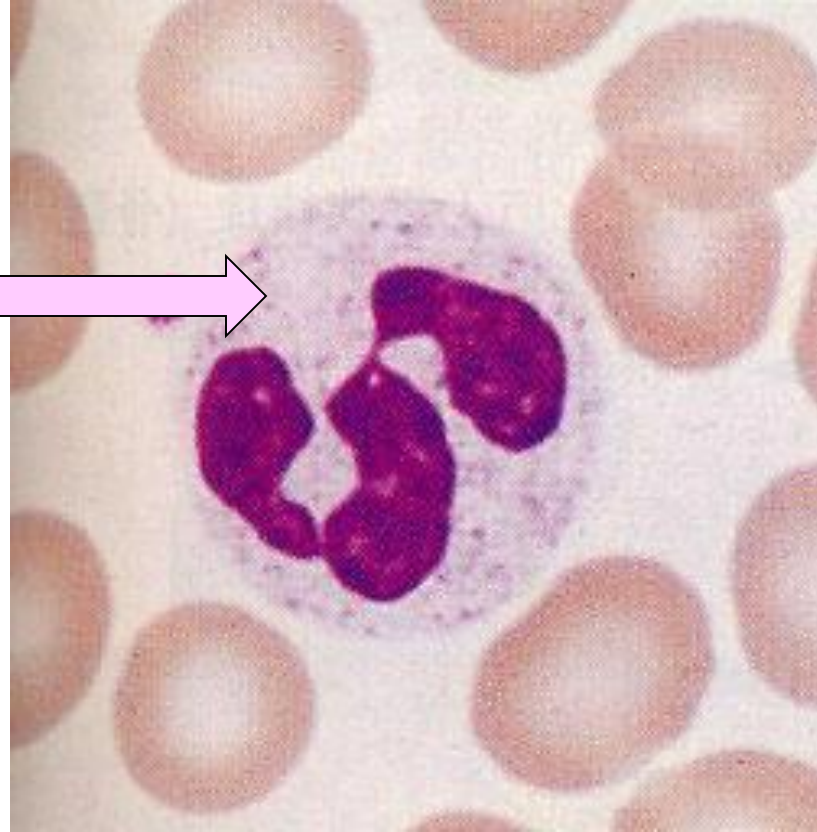
EOSINOPHIL

**These specific granules
stain red with acidic
stains such as eosin**



Neutrophil

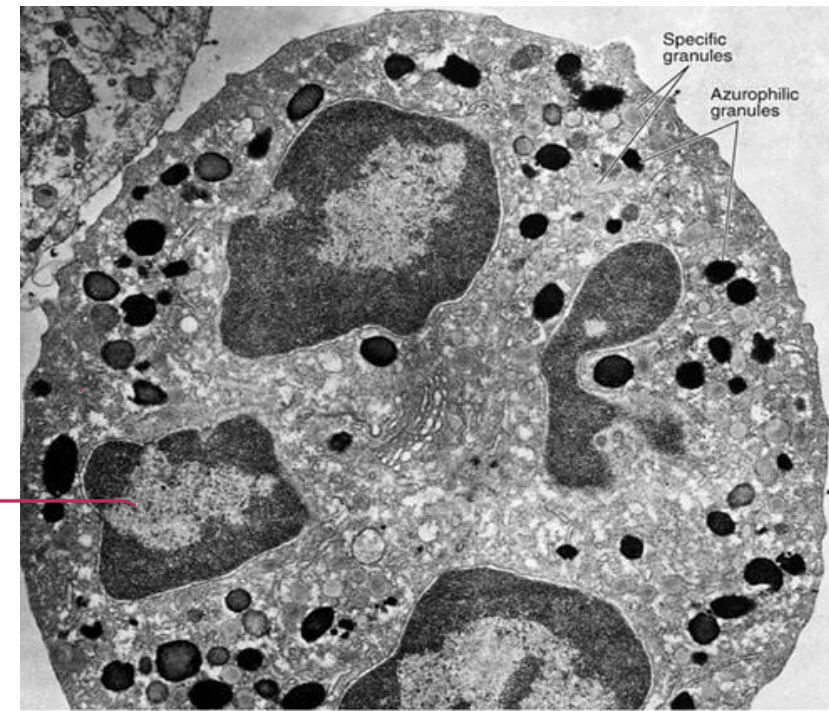
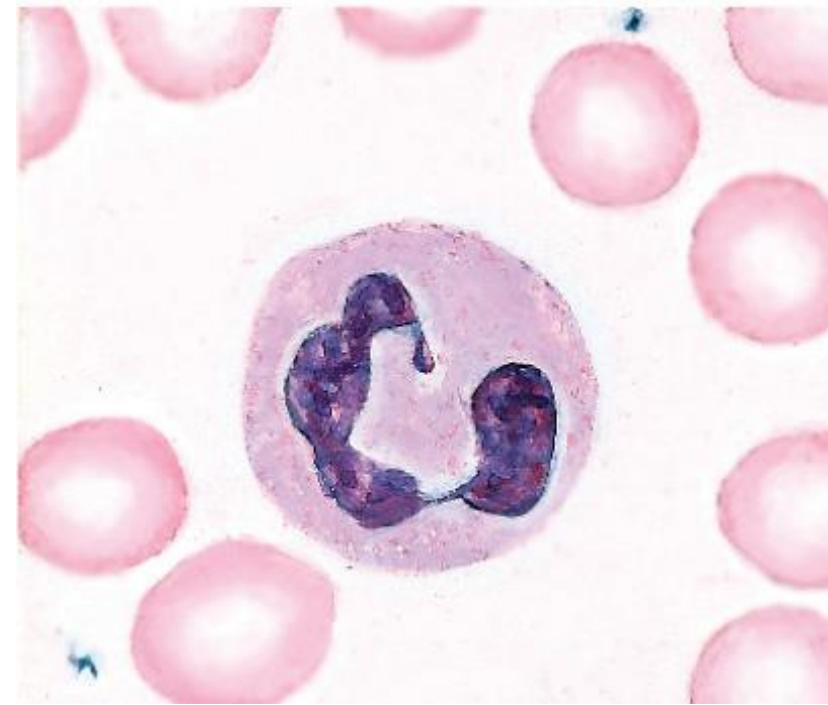
These granules are neutrophilic, meaning they show no special affinity for either acidic or basic stains but are stained mildly by both



Neutrophils

- The most common leukocyte and the most abundant WBCs in peripheral blood.
- 2-5 lobes in nucleus connected by “threads” of nuclear material (**polymorphs**)
- Light pink cytoplasm
- Called neutrophils because cytoplasm takes up red (acidic) and blue (basic) stains equally
- Specialized for responding to bacterial invasions- Acute infections- acute pyrogenic infections
- Neutrophils are short-lived cells with a half-life of 6-8 hours in blood and a life span of 1-4 days in connective tissues before dying by apoptosis.

* The lobes of nucleus appear separated in EM because of the plane of section.



Neutrophils are formed in bone marrow (Hematopoiesis), once the cell is ready to be released in blood, it has 2 lobes , it circulates for a few hours in blood, then it has 3 lobes , about to leave the blood to enter the C.T , it has 4 lobes and inside the connective tissue and it's about to die , it has 5 lobes. So, it is called {Polymorphs}.

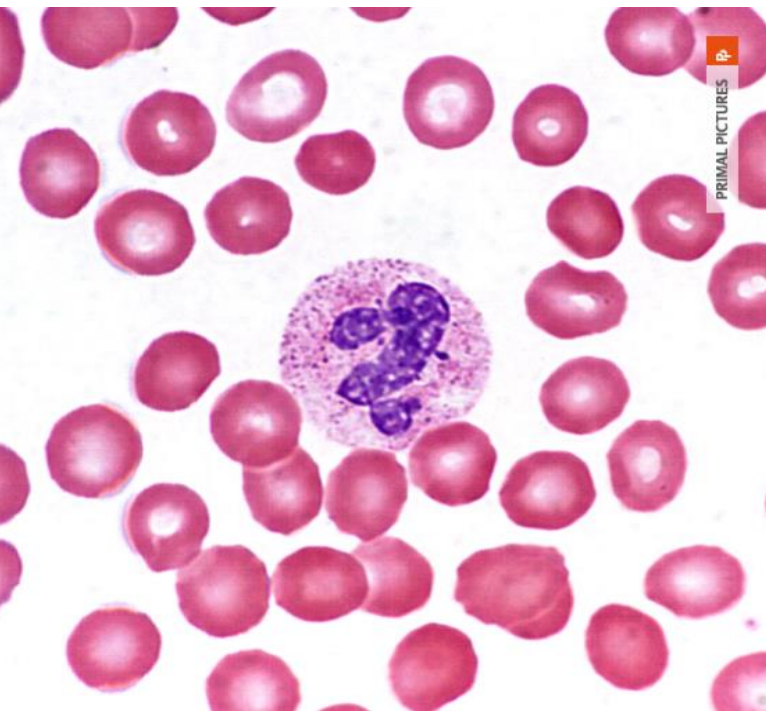
* The number of lobes indicates the maturity state of the cell.



Only!

In females, the inactive X chromosome (**Barr body**) may appear as a drumstick-like appendage on one of the lobes of the nucleus (*about 3% of neutrophils in peripheral blood*)

* In females, inside nucleus we have XX chromosome (one is for survival of the cell) and the other X chromosome is usually clumped and condensed at inner aspect of the nuclear membrane (that's Barr body!)



Neutrophils are the first WBCs that leave the blood in large numbers to reach the site of inflammation

Why???

Cells of acute infection

1- The most abundant

2- The most motile

3- Neutrophil chemotactic factors are the first released

- **Specific granules (secondary)**

- **Lysozyme** (diff. than lysosome): destroys the cell wall of bacteria so killing them.
- **Phagocytin** (bactericidal) → It kills bacteria directly.
- **Lactoferrin** (bacteriostatic)
- **Collagenase** Destroys collagen fibers in ECM of C.T
*Also, we have elastase & protease

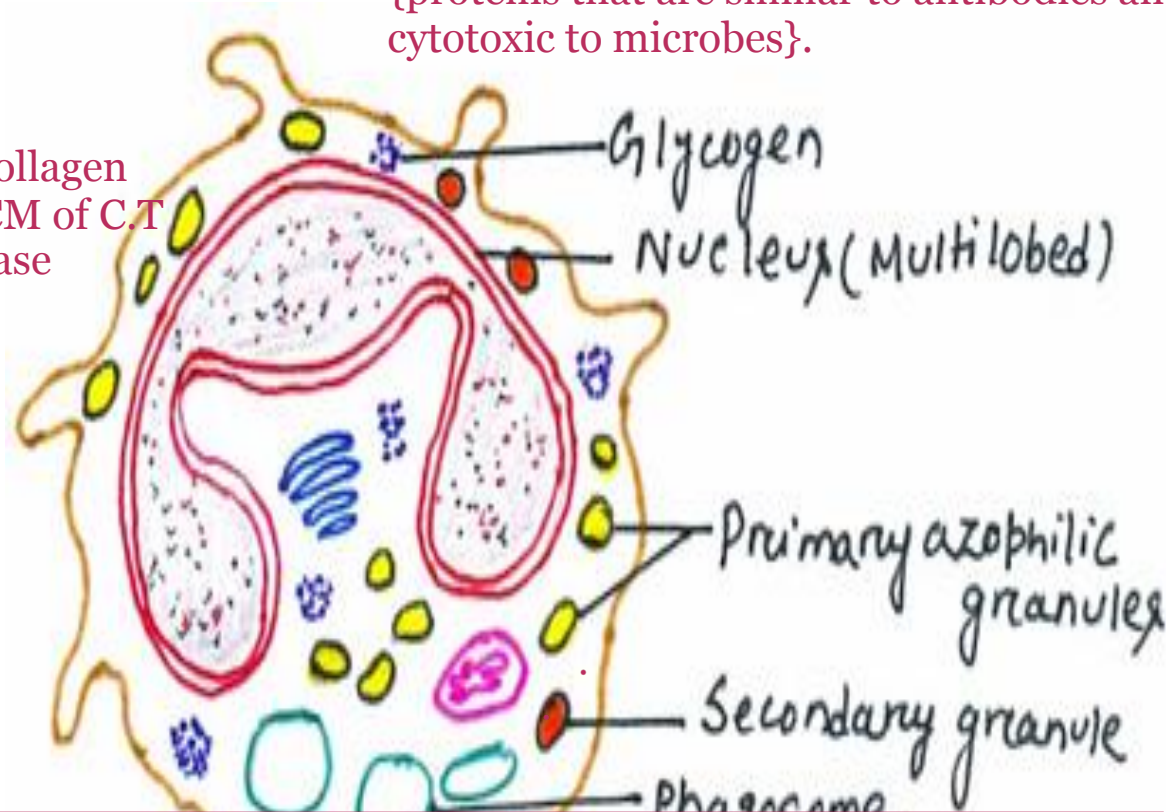
Different names for neutrophils:

Polymorphs
Pus cells
Myelocytes
Microphages
Cells of acute inflammation

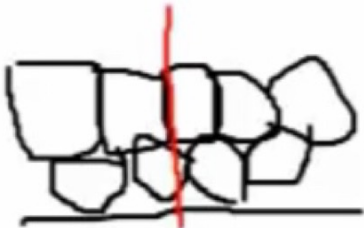
Pus is pyrogenic

- **Azurophilic granules (primary)**

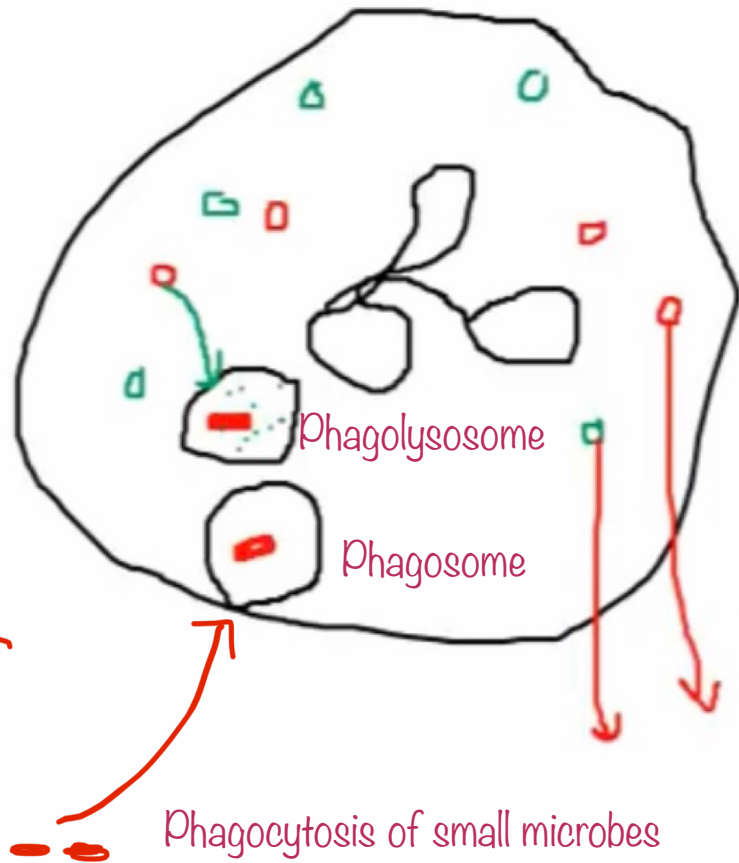
- **Myeloperoxidase** Form H_2O_2 , HOCL: powerful cytotoxin
- **Acid hydrolase**
- **Defensins** {proteins that are similar to antibodies and cytotoxic to microbes}.



*Lactoferrin: stops the proliferation of bacteria without killing. { bcz iron is necessary to bacteria to multiply, so once withdraw iron from site of infection, this will stop the proliferation of bacteria }.



p45



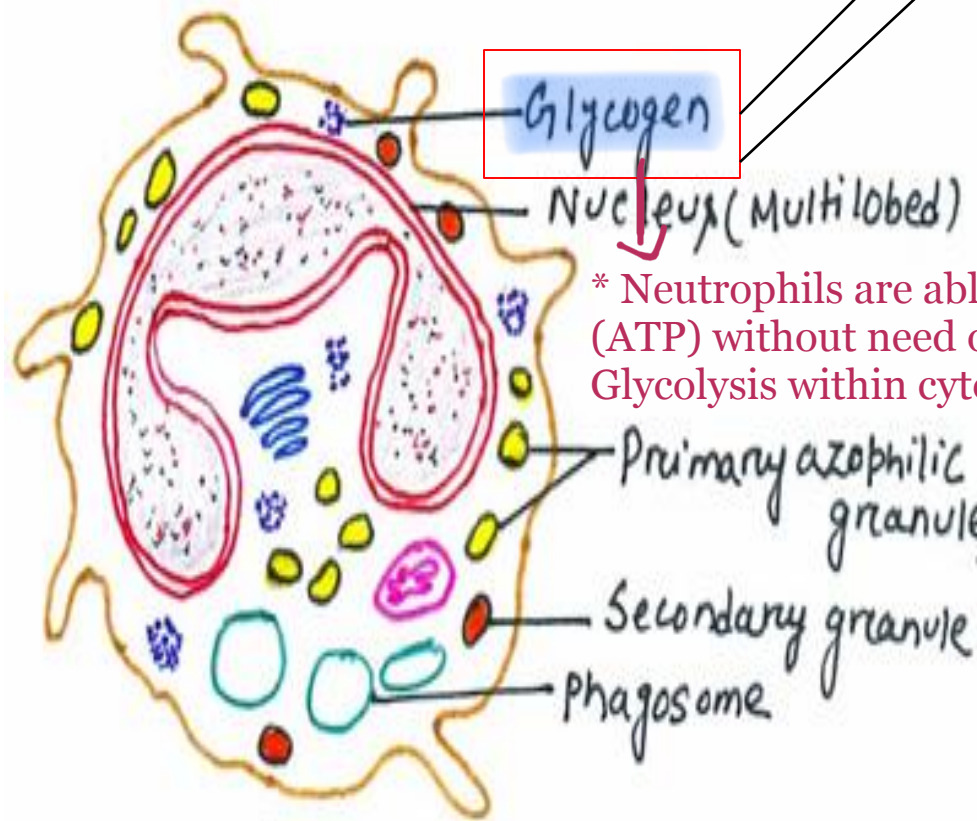
* Clarification & Function of Neutrophils:

- We all know that the first barrier in our body is epithelium that rests on basement membrane and under it we have C.T (that contains: fixed cells like Fibroblasts, resident cells(Macrophages) and scattered Mast cells that have many granules containing histamine & heparin also other inflammatory mediators). ECM contains collagen fibers & other fibers , and ground substance (proteoglycans & glycoproteins) , and C.T is a Vascularized tissue .
- If we have break in skin and bacteria get access to underlying C.T , it starts to proliferate and produce toxins that damage the host cells , these toxins also gonna stimulate mast cells to secrete their granular contents and inflammatory mediators released by Macrophages , damaged host tissue & toxins—> all of these act as chemotactic agents to attract Neutrophils to the site of infection.
- The 1st mechanism of neutrophils to kill bacteria is Phagocytosis & digestion by hydrolytic enzymes by lysosomes or chemicals of specific granules, we call these cells (Microphages) ?? because it's a phagocytic cell that kills up small-sized microbes.

- If there's large microbes, so the other option is by secreting the contents of their lysosomal enzymes & contents of specific granules into ECM of C.T by exocytosis .
- Neutrophils also secrete Collagenase, elastase to destruct the ECM of C.T , and that's important to facilitate the movement of these cells in infected tissue. After performing their function, they die within C.T .
- At the infection site, we have: lysed ECM of C.T , dead neutrophils, dead bacteria, damaged host cells and fluid: (that comes from plasma of blood by the action of histamine which + the blood flow to area of infection & + permeability of B.Vs , so we have redness and swelling) —> all of these make PUS .
- After eliminating bacteria from the site of infection, the last WBCs to be recruited from blood to enter the infection site is Monocyte (large cell, when it leaves the blood and enter C.T , it differentiate to Macrophage starting to eat up the dead cells and everything in that site , it's Transient Macrophage).

Dead neutrophils, bacteria, lysed ECM, and tissue-fluid form a viscous, usually yellow collection of fluid called **pus**.

Few organelles



* Neutrophils are able to produce their energy (ATP) without need of O₂ or mitochondria by Glycolysis within cytoplasm.

The ability of neutrophils to survive in an anaerobic environment is highly advantageous, because they can kill bacteria and help clean up debris in poorly oxygenated regions, for example, damaged or necrotic tissue lacking normal microvasculature.

* Neutrophilia: + in number of neutrophils (in case of bacterial acute infections, pyogenic infections and pyrogenic infections), we expect high number of neutrophils.

* Neutropenia : — number of neutrophils in peripheral blood.



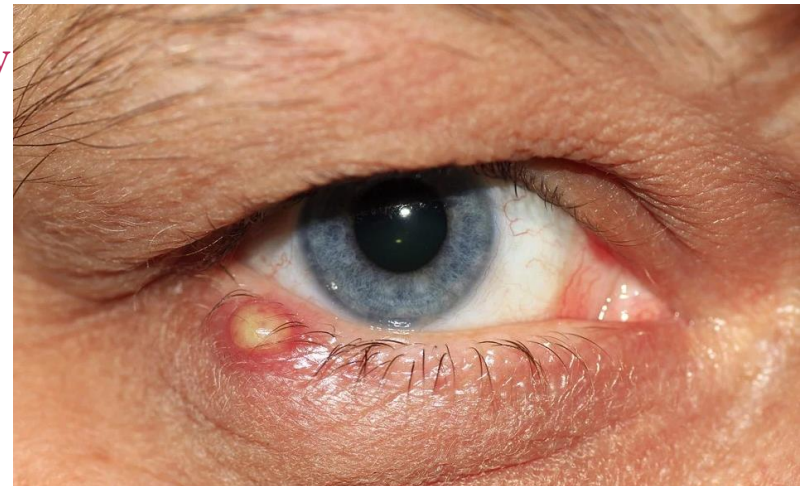
Pus is a viscous, usually yellow collection of fluid.

Pyogenic is referring to bacterial infections that make pus while **pyrogenic** is producing heat

* Fever is important to kill bacteria.

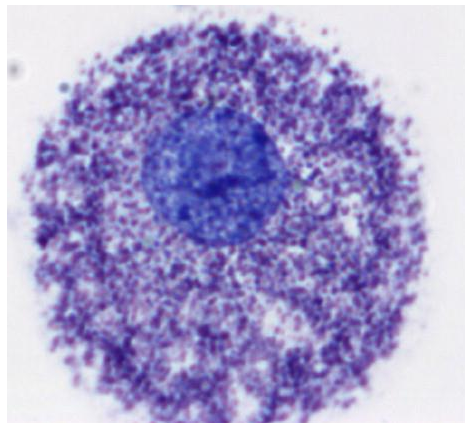


*PUS appears slightly yellowish or greenish —> (from bacteria containing green pigment, also myeloperoxidase enzyme inside lysosome of neutrophils has a greenish color.

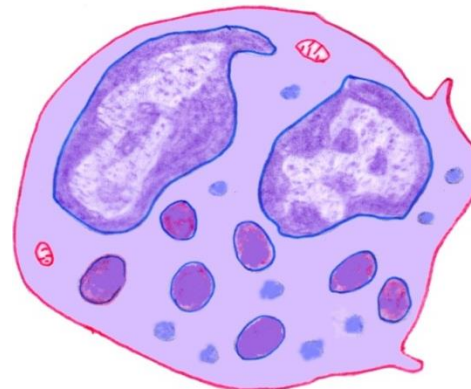


Basophils

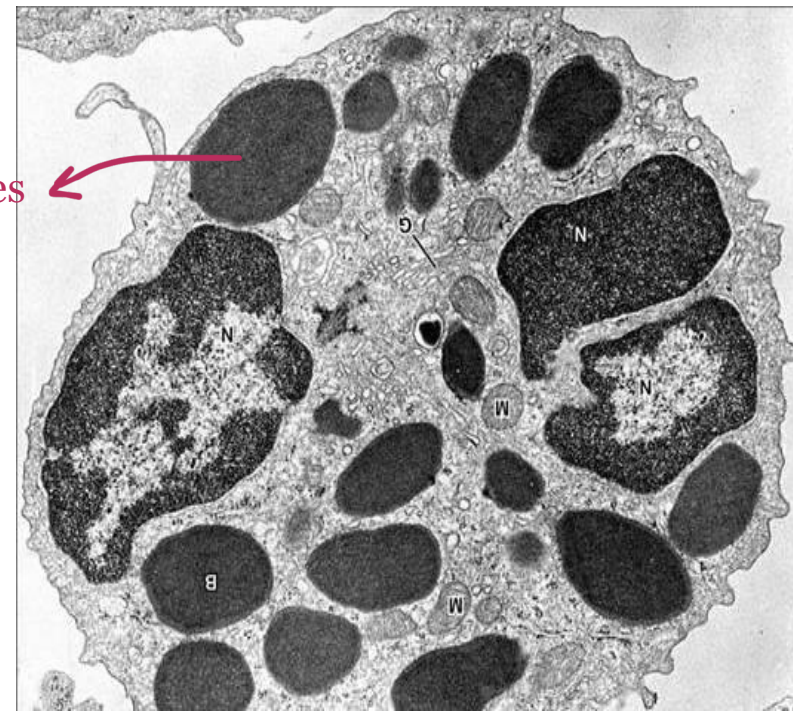
- Rarest leukocyte – might not see these under the microscopes (it ranges 0-1%)
- Usually have bi-lobed, S-shaped nuclei obscured by the large basophilic granules /We can't see the nucleus under the LM, bcz of density of large basophilic granules, so they mask the nucleus of basophils.
- Has large granules that stain dark purple/ blue in basic dyes (*basophil* = basic loving)
- Granules contain histamine, heparin and eosinophilic chemotactic factor that mediate inflammation in allergic reactions and parasitic infections



Mast cell



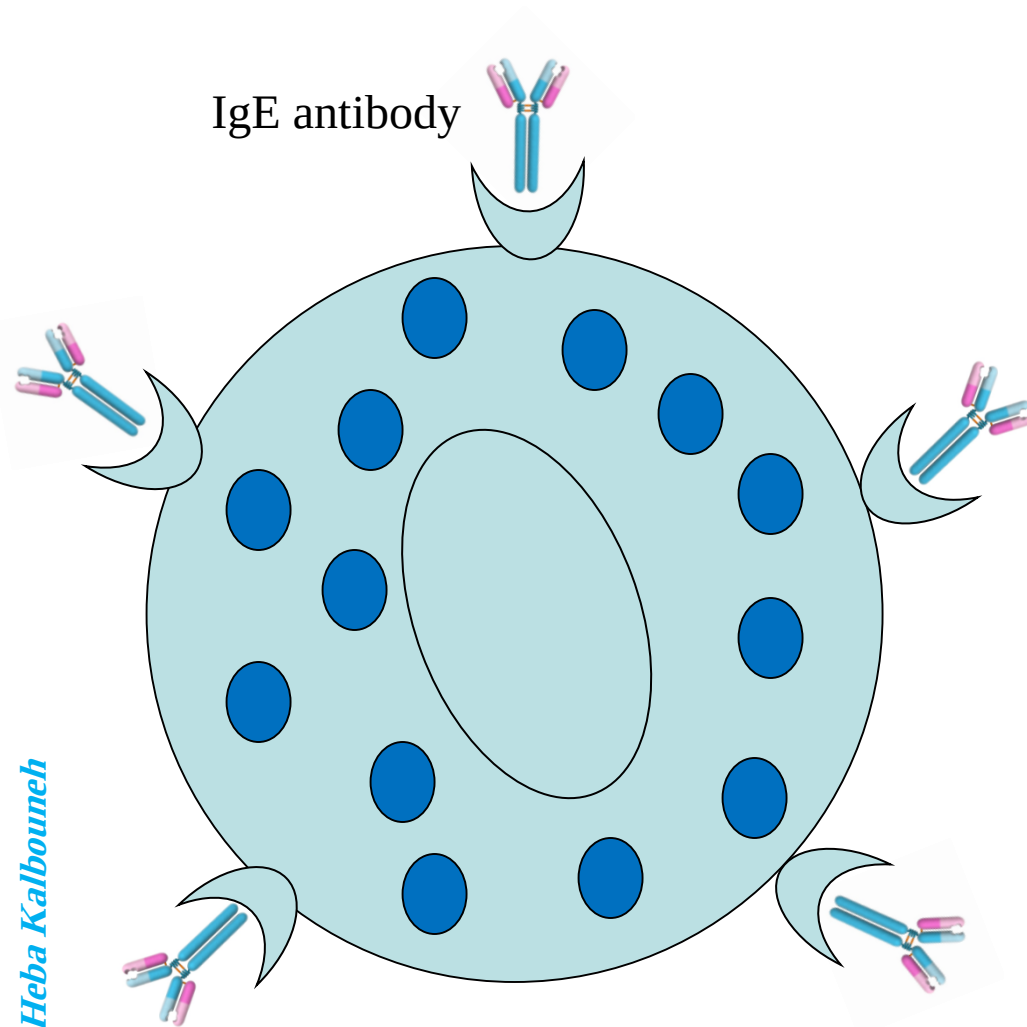
electron dense granules



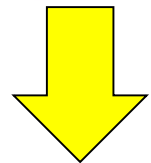
* Mast cells:

- It has round nucleus & cytoplasm filled with basophilic granules (containing histamine & heparin).
- This cell is found inside C.T fixed in it especially: mucosa of GI tract , mucosa of respiratory tract , and cutaneous membrane (skin) —> areas expected to have allergic reaction. Once these cells are stimulated by a certain allergen, they will degranulate releasing the contents into interstitial fluid of C.T and the allergic symptoms appear.
- We have 3 main symptoms of allergy (Swollen , redness in color, itchy) why??
 - * Histamine cause vasodilation of B.V so + blood flow to area of allergy & + permeability of B.V , so more fluid leaving the plasma. —> that's why swollen .
 - * Itchy : because inflammatory mediators are gonna irritate nerve endings of the area resulting in itchy sensation .
 - * We treat the symptoms of allergy by using antihistamine to stop the action of histamine.

Both basophils and mast cells have surface receptors for immunoglobulin E (IgE), and secrete their granular components in response to certain antigens and allergens.



Plasma cell

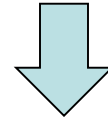


First exposure

Exposure may be by ingestion, inhalation, injection, or direct contact

In some individuals substances such as certain pollen proteins or specific proteins in food are allergenic, that is, elicit production of specific IgE antibodies, which then bind to receptors on mast cells and immigrating basophils.

Second exposure



During 1st exposure, there's no symptoms

Upon subsequent exposure, the allergen combines with the receptor-bound IgE molecules, triggering rapid exocytosis of the cytoplasmic granules.



Release of the inflammatory mediators in this manner can result in bronchial asthma, cutaneous hives, rhinitis, conjunctivitis, or allergic gastroenteritis.

Some of inflammatory mediators are leukotrienes that cause spasm in smooth muscles of bronchi.

Skin rashes, red & itchy

Runny, swollen & red nose.

Redness & swollen of the eye.

Immediate or type 1 hypersensitivity

In some individuals a second exposure to a strong allergen, such as that delivered in a bee sting, may produce an intense, adverse systemic response. Basophils and mast cells may rapidly degranulate, producing vasodilation in many organs, a sudden drop in blood pressure, and other effects comprising a potentially lethal condition called

Anaphylaxis or anaphylactic shock.

Basophils account for up to 15% of infiltrating cells in allergic dermatitis and skin allograft rejection



Allergic dermatitis (eczema) is an itchy skin rash that develops when you come into contact with an **allergen**

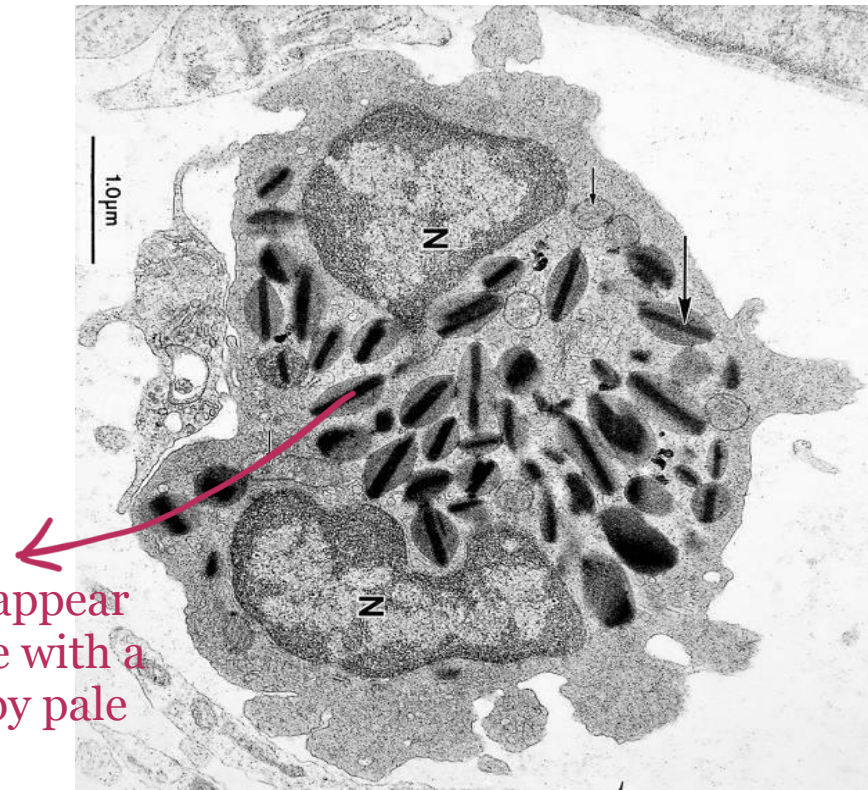
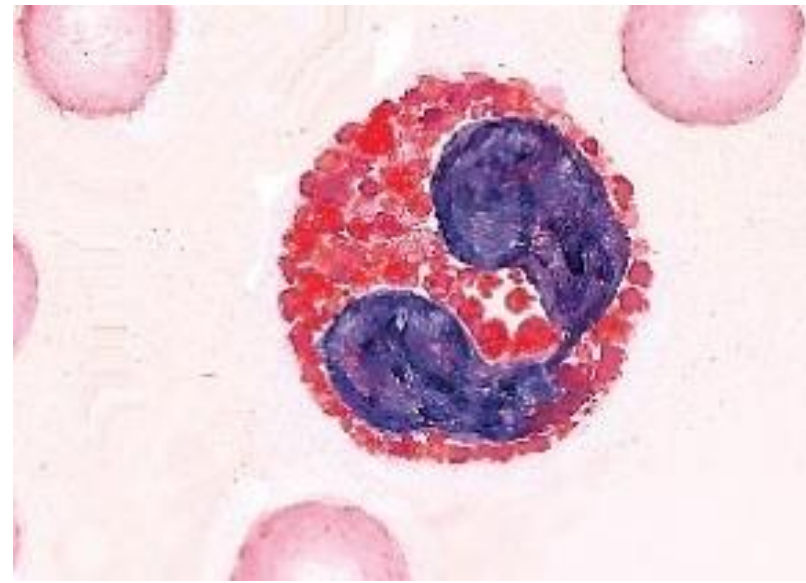


Eosinophils

Eyeglasses in appearance

- Usually have bi-lobed nuclei connected by a short “thread” of nuclear material
- Large cytoplasmic granules, which stain red with the acidic eosin dye (*eosinophil* = eosin loving)
- Help in ending allergic reactions and in fighting parasitic infections

* Under EM: granules appear like crystalloid in shape with a dark core surrounded by pale area .



Crystalloid granule

Specific granules (Crystalloid granules):

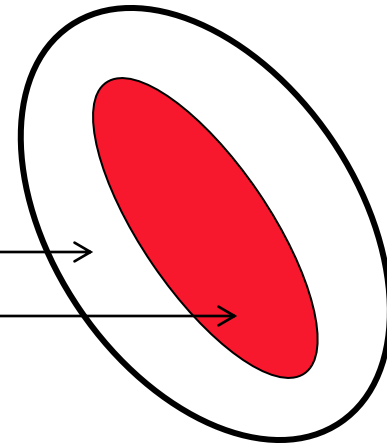
- Oval in shape, with flattened crystalloid cores

- Two parts:

Externum (pale): contains histaminase and sulfatase

Internum (dark): contains basic protein to kill parasites

so, it stained
with acidic dye



- * Histaminase : stops the action of histamine.
- * Sulfatase : stops the action of heparin (sulfating proteoglycans) .

Eosinophils have a particular phagocytic affinity for **antigen-antibody complex**

* Eosinophilia : + number of eosinophils and it indicates parasitic infection.

