



Blood Cells

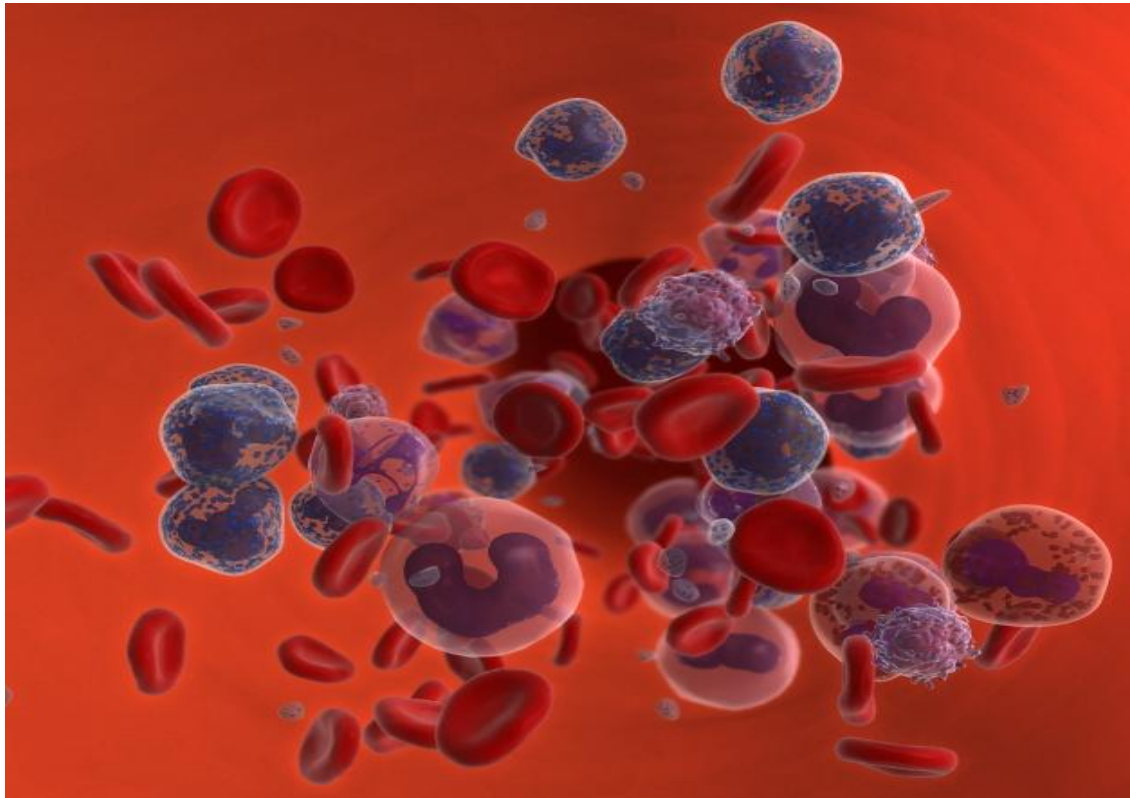
Dr. Heba Kalbouneh

DDS, MSc, DMD/PhD

Professor of Anatomy, Histology and Embryology

Blood

- Specialized form of **connective tissue**
- Components:
 - Blood cells (several types)
 - Plasma (extracellular matrix)



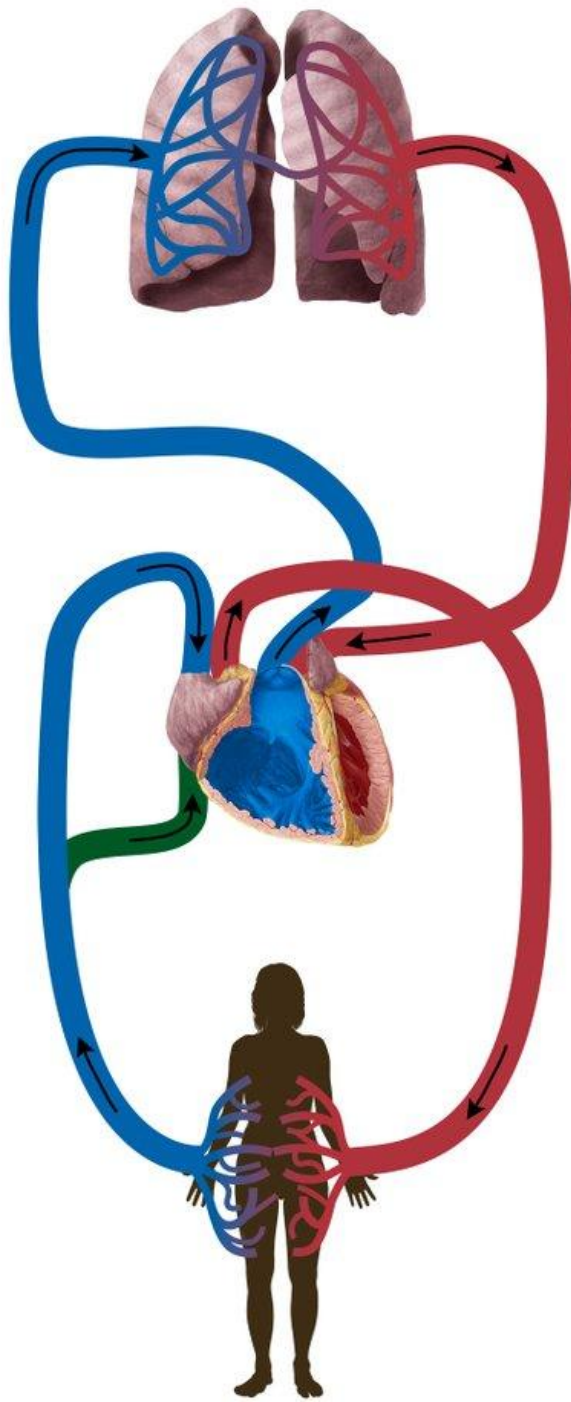
Functions of Blood

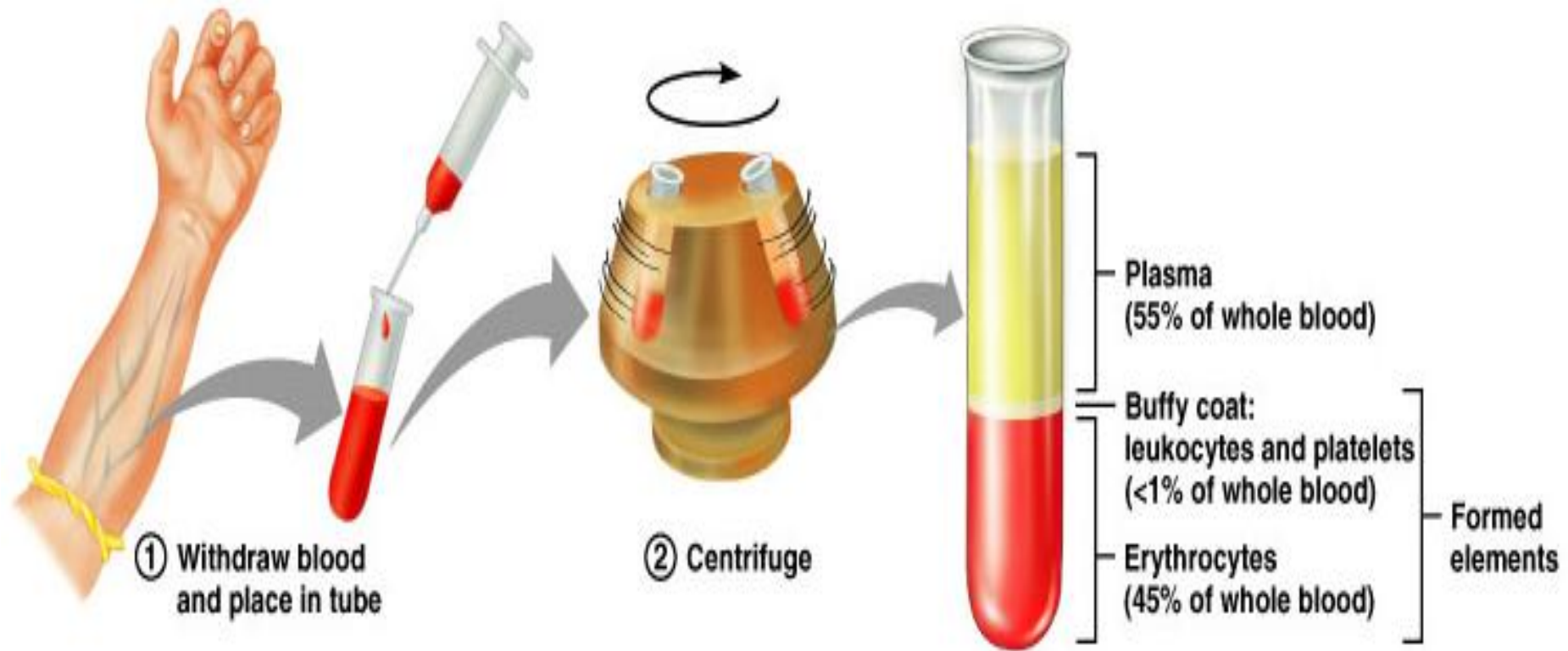
- Transports nutrients and respiratory gases
- Transports waste products to organs and tissues where they can be recycled or released
- Transports hormones
- Transports immune cells throughout the body
- Helps regulate body temperature
- Maintains acid-base and osmotic balance

✓ pH of 7.4
✓ Color is dependent on amount of Oxygen
More oxygen = brighter the red
Less oxygen = duller the red

Blood is propelled mainly by rhythmic contractions of the heart

About **5-6 Liters** of blood in an average adult moves unidirectionally within the closed circulatory system





Collected blood in which clotting is prevented by the addition of anticoagulants (eg, heparin , citrate or EDTA) can be separated by centrifugation into layers that reflect its heterogeneity

Physical Characteristics

Fluid

- **Living 45%**

 - Cells (**formed elements**)

 - RBC **Erythrocytes** (carry oxygen)

BUFFY
COAT

 - WBC **Leukocytes** (immune)
 - Platelets **Thrombocytes** (clotting)

- **Non living (Matrix) 55%**

 - Plasma (pale yellow fluid)

 - 90% water
 - 10 % (electrolytes, nutrients, proteins (albumin), waste (CO₂, ammonia, urea), gases, hormones)

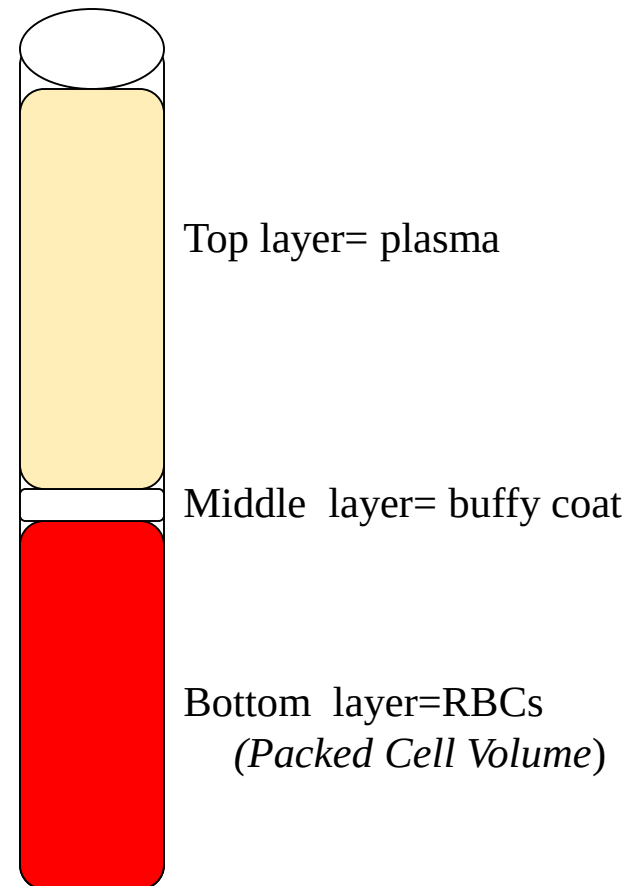
HEMATOCRIT: Ratio of the volume of RBCs to the volume of whole blood

Example: a hematocrit value of 40% means that there are 40 ml of RBCs in 100 ml of whole blood

Normal hematocrit:

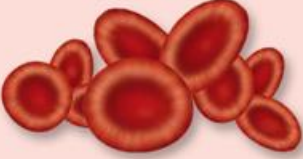
Males=40-53%

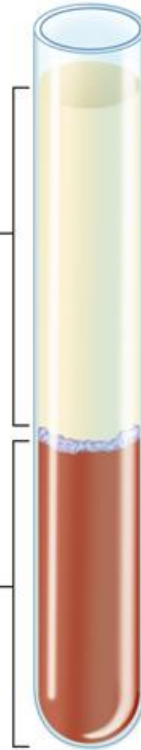
Females= 36-48%

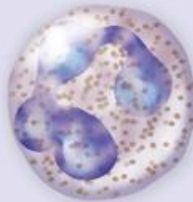
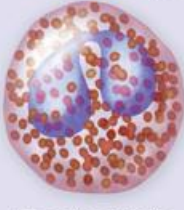


Values are those used by the US National Board of Medical
Examiners

Plasma		
Water 92% by weight	Proteins 7% by weight	Other solutes 1% by weight
	Albumins 58%	Electrolytes
	Globulins 37%	Nutrients
	Fibrinogen 4%	Respiratory gases
	Regulatory proteins 1%	Waste products

Erythrocytes
Erythrocytes 3.5-5.5 million/mm ³




Buffy Coat	
Platelets 150,000-400,000/mm ³	Leukocytes 4500-11,000/mm ³
	
	Lymphocytes 25%-33%
	
	Neutrophils 54%-62%
	
	Monocytes 3%-7%
	
	Eosinophils 1%-3%
	
	Basophils 0%-0.75%

Serum = everything in plasma, minus
the clotting factors

Albumin:

- ✓ The most abundant plasma protein
- ✓ Is made in the liver
- ✓ Helps maintain the osmotic pressure in capillaries
- ✓ Transports steroid hormones and fatty acids

Fibrinogen:

- ✓ The largest plasma protein
- ✓ Is made in the liver
- ✓ Important for clot formation

Fresh plasma



The importance of proteins inside the plasma is to prevent fluid loss and to create osmotic pressure (to keep the blood inside the blood vessels)

Globulins (α , β and or γ globulins):

α and β globulins

- ✓ Are made mainly by liver
- ✓ Transport fat soluble vitamins, lipids and iron

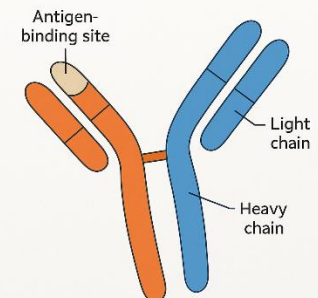
γ -globulins (Immunoglobulins (antibodies):

secreted by plasma cells

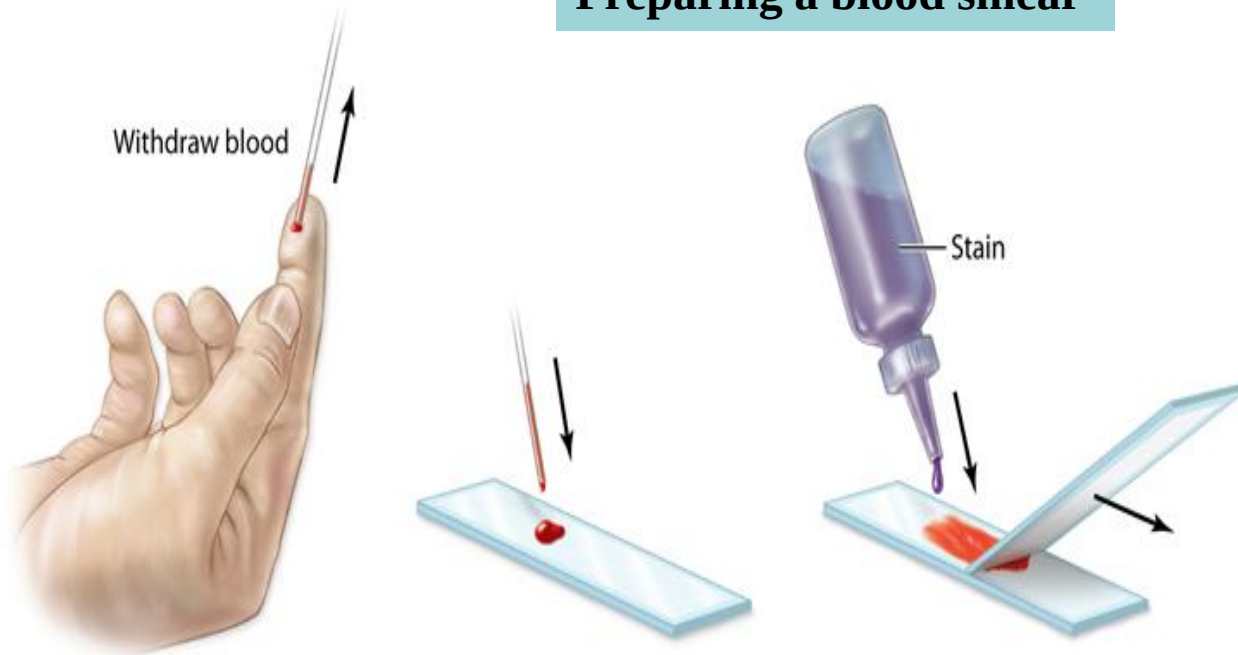
Plasma cell



ANTIBODY



Preparing a blood smear

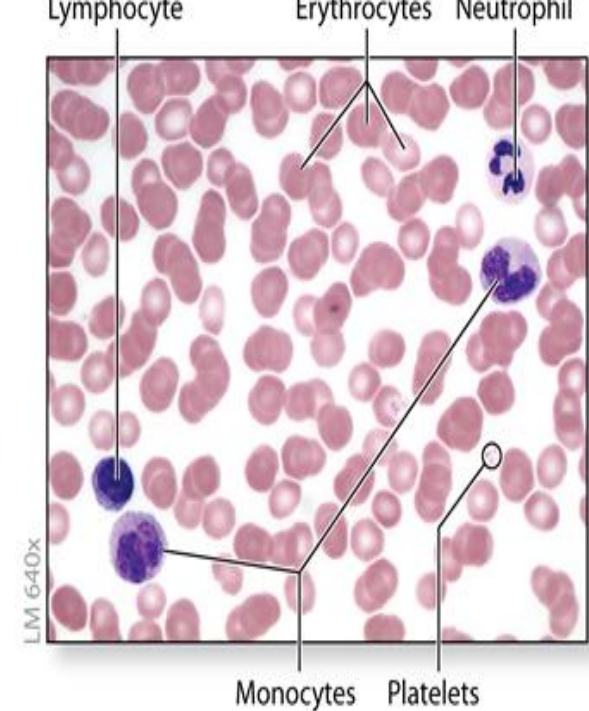


① Prick finger and collect a small amount of blood using a micropipette.

② Place a drop of blood on a slide.

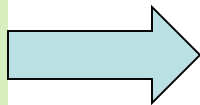
③a Using a second slide, pull the drop of blood across the first slide's surface, leaving a thin layer of blood on the slide.

③b After the blood dries, apply a stain briefly and rinse. Place a coverslip on top.



④ When viewed under the microscope, blood smear reveals the components of the formed elements.

Polychromatic stains:
Giemsa
Wright
Leishman



Blood cells can be studied histologically in smears prepared by spreading a drop of blood in a thin layer on a microscope slide

The Staining of Blood Cells

Blood film/ smear: a drop of blood is spread on a glass slide and left dry in air

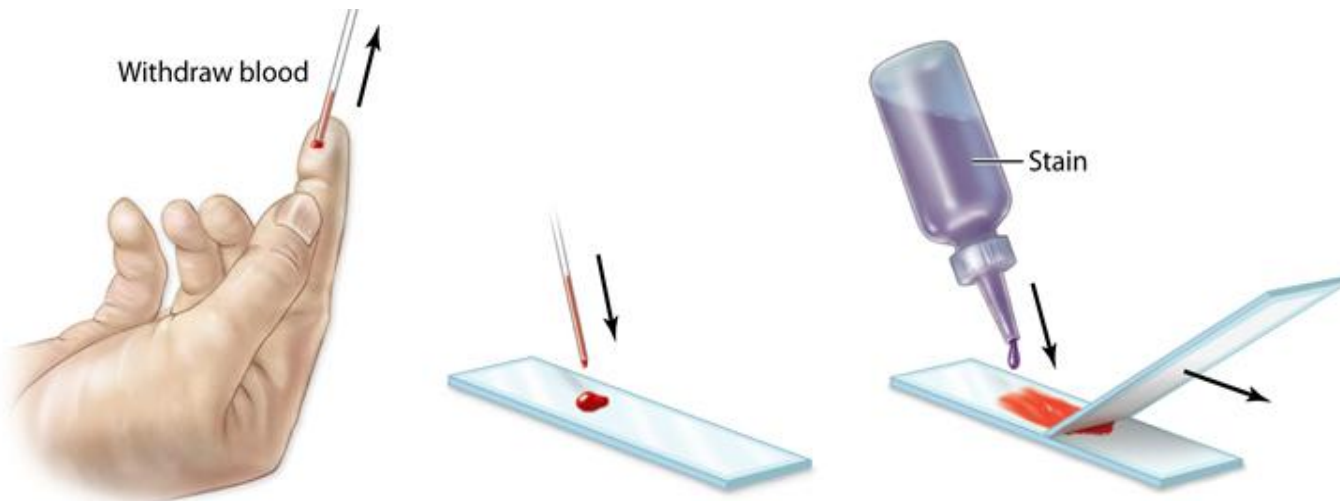
Staining: with neutral stain e.g **Leishman's stain**

Leishman's stain: formed of a mixture of:

- **Eosin**, an acidic dye that stains pink to red
- **Methylene blue**, a basic dye that stains blue to purple

Dissolved in methyl alcohol (fixative)

Azure dye!!



Blood film/smear

Erythrocytes (RBCs)

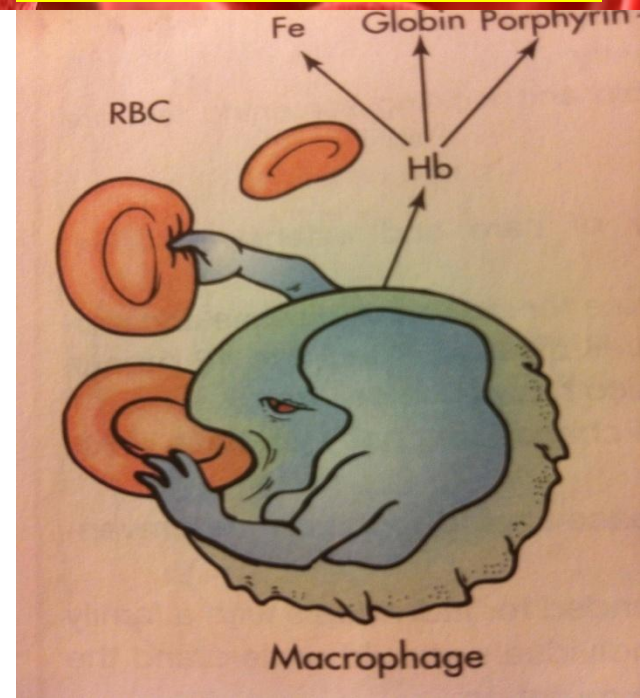
- Small, biconcave discs
- Transport oxygen and CO₂, cytoplasm is full of hemoglobin molecules
- Have no nuclei or organelles
- Pick up O₂ at lung capillaries and release it at body tissue capillaries

During their maturation process, the erythrocytes extrude their nuclei, and the mature RBCs enter the bloodstream, without their nuclei

- **Fate:** Survive for ~100-120 days in the circulation. Worn out RBCs are removed by macrophages of the spleen, bone marrow and liver.



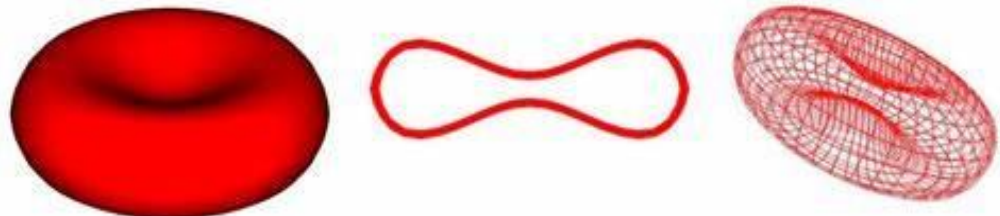
Male: 4.5-5.5 million/mm³
Female: 4-5 million/mm³



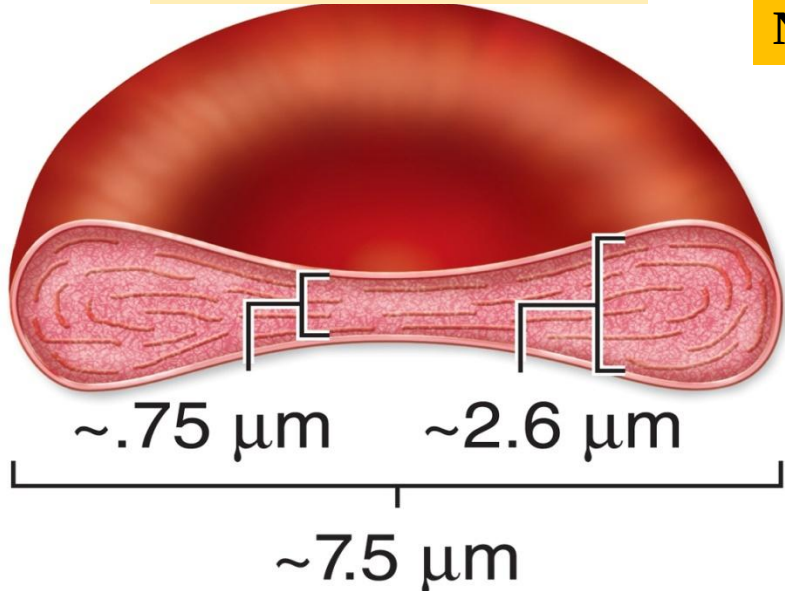
Immediately beneath the plasma membrane is a **meshwork of proteins** (Spectrin and Ankyrin) forming a cytoskeleton



This submembranous meshwork stabilizes the membrane, maintains the cell shape, and provides the cell elasticity required for passage through capillaries



Sectional view



Normocytic RBCs

Top view



The cell membrane is highly selective and flexible

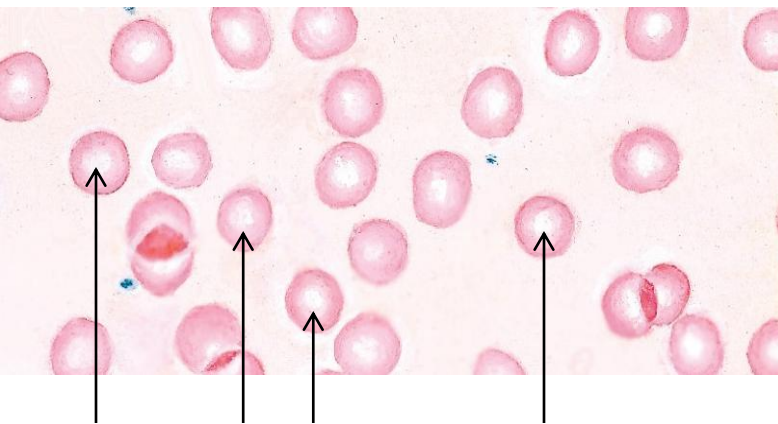
- Size**
6-9 μm in diameter (7.5 μm)
- Thickness**
2.6- μm thick at the rim, but only 0.75- μm thick in the center

!!!! Erythrocytes can be used as a size reference for other cell types

Biconcave shape provides 20-30% greater surface area than a sphere relative to cell volume, facilitating gas exchange

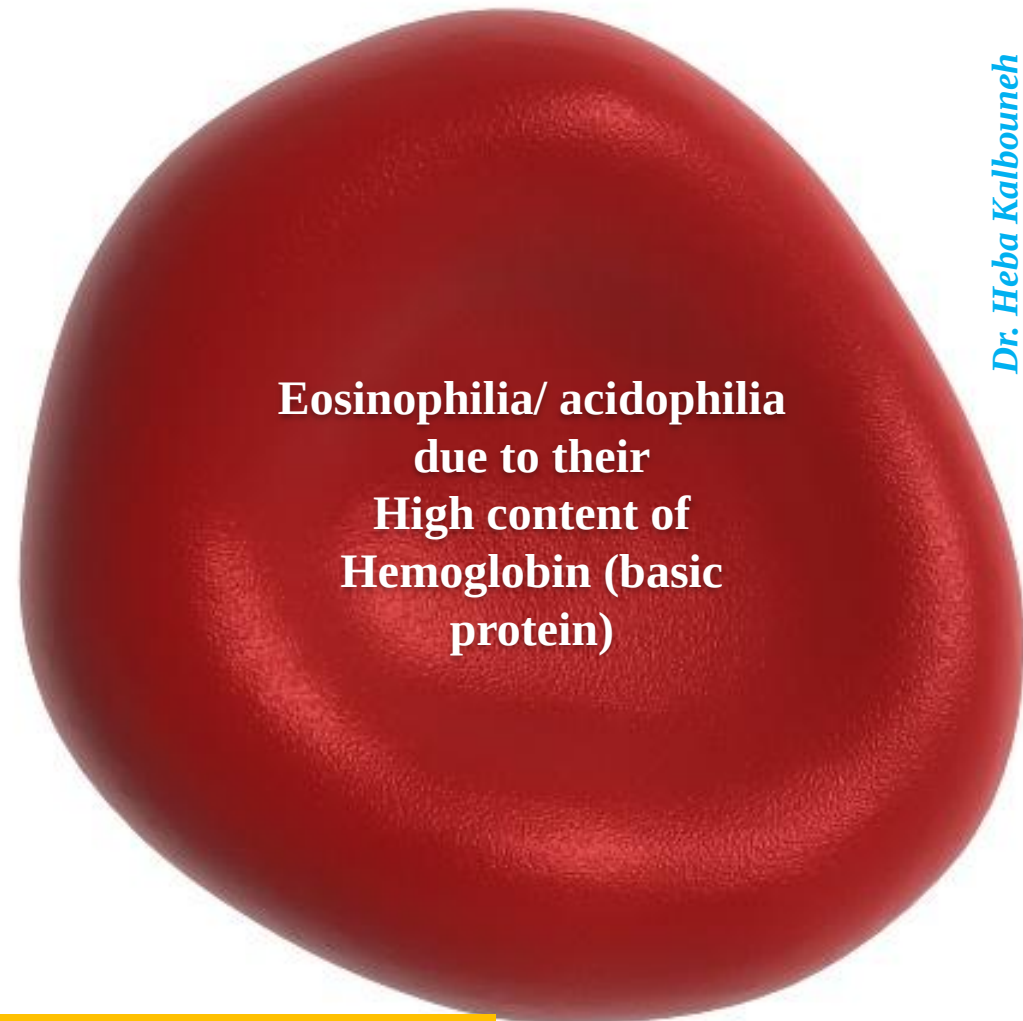
The biconcave shape along with the fluidity of the plasma membrane (50% proteins) permits erythrocytes to bend and adapt to the small diameters and irregular turns of capillaries

Erythrocyte consists of an **outer plasma membrane** enclosing hemoglobin and a **limited number of enzymes** necessary for maintenance of plasma membrane integrity and gas transport functions



The pale staining of the central region is a result of its biconcave disc shape $\Rightarrow$

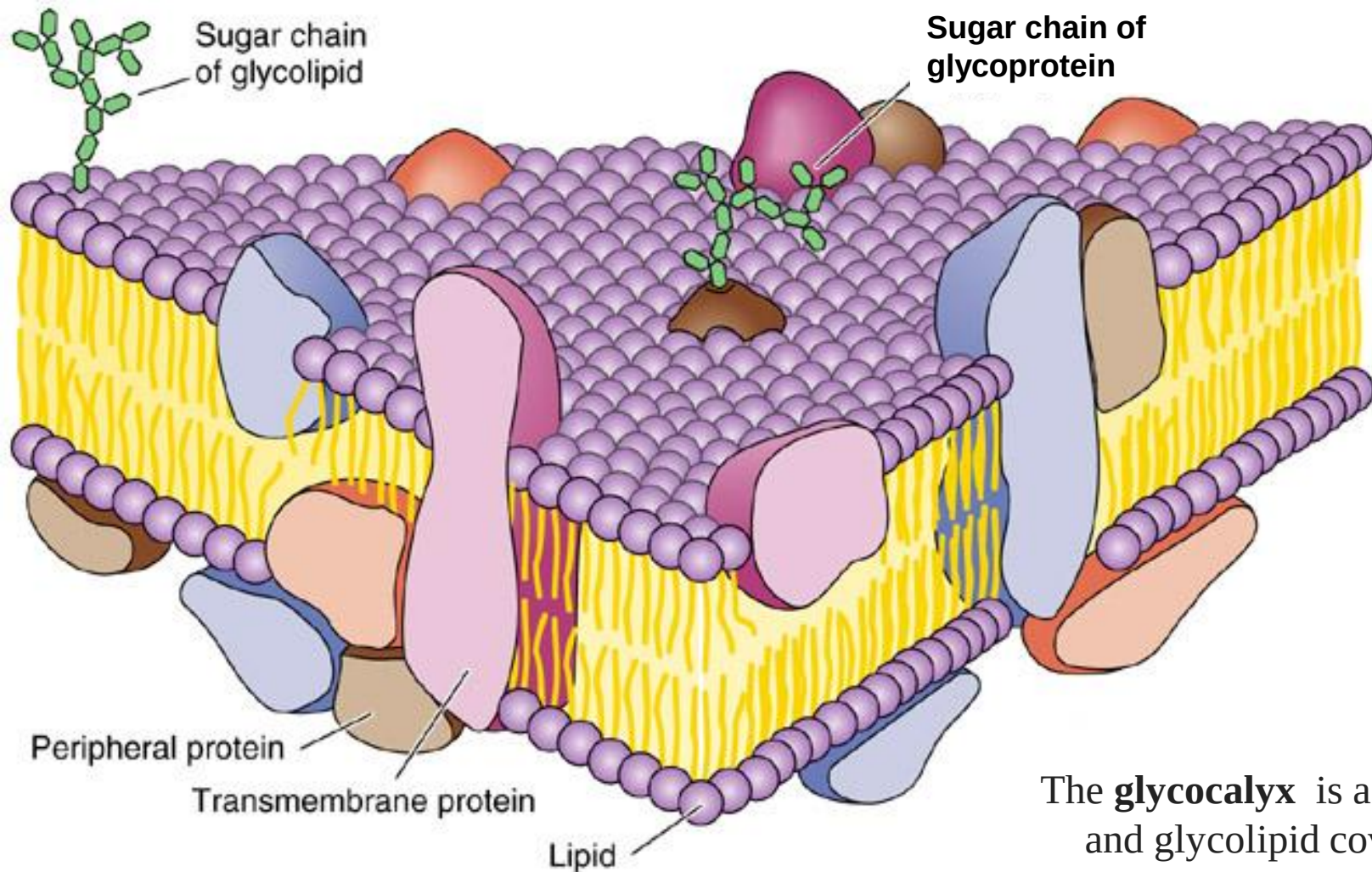
Normochromic RBCs



**Eosinophilia/ acidophilia
due to their
High content of
Hemoglobin (basic
protein)**

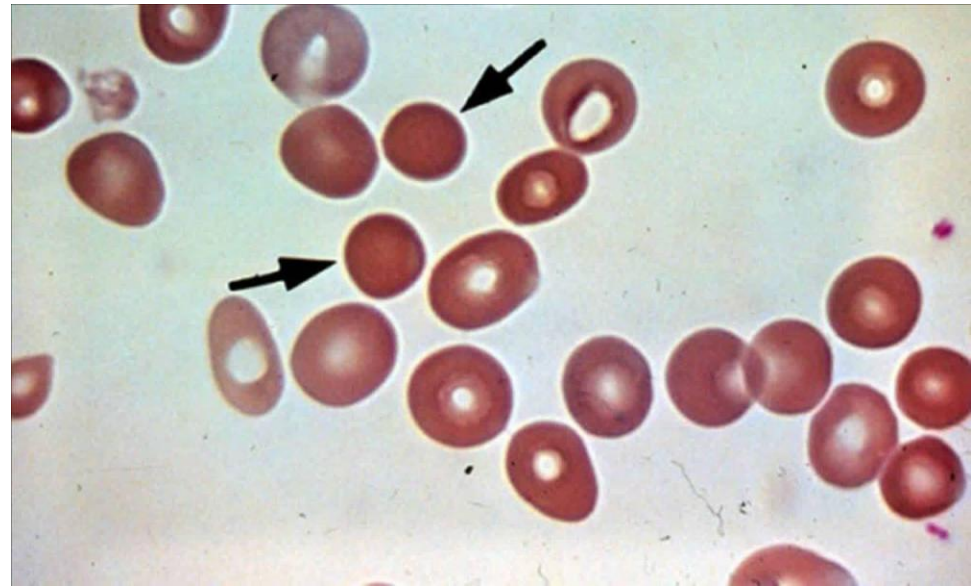
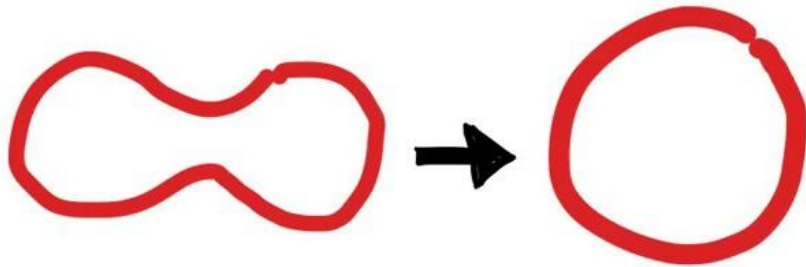
Cell Membrane

A Carbohydrate chains bound to lipids and proteins



The **glycocalyx** is a glycoprotein and glycolipid covering that surrounds the cell membranes

Hereditary Spherocytosis



BICONCAVE RBCs

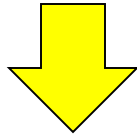


SPHEROCYTES



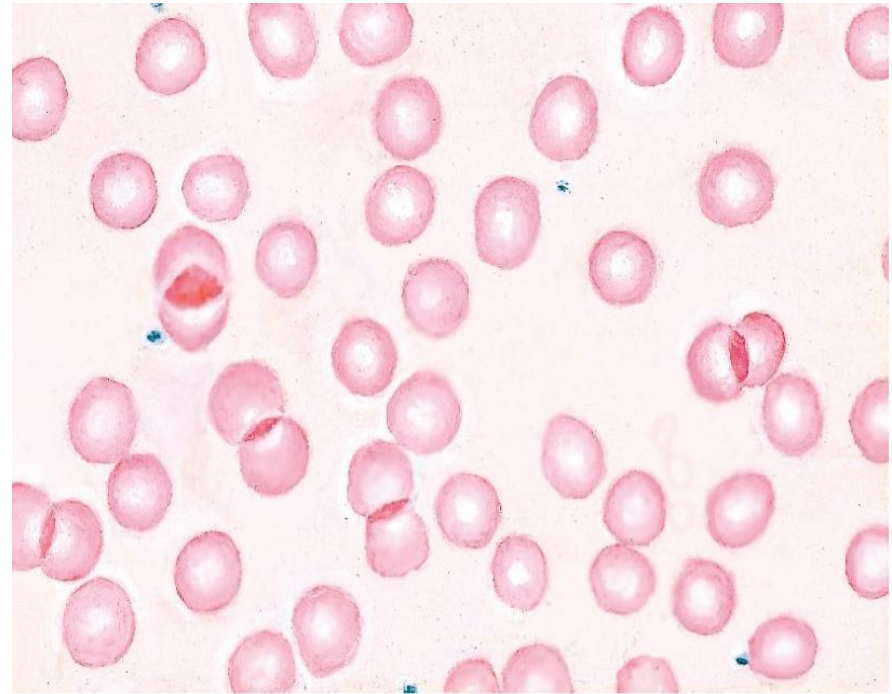
Caused by **mutations** in genes relating to membrane proteins (mostly Spectrin and Ankyrin) that allow for the erythrocytes to maintain their biconcave shape

LM:
Blood film stained with Leishman:
Rounded
Non nucleated
Acidophilic (with pale central area)



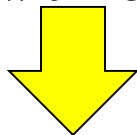
A zone of **central pallor** is about 1/3
the size of the RBC

LM



Dr. Heba Kalbouneh

EM:
✓ Have no nucleus or organelles
✓ Filled with hemoglobin

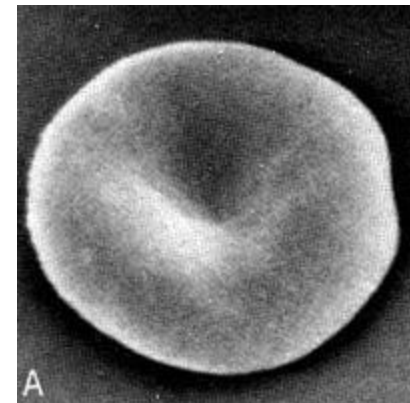


Electron dense and homogenous

TEM



SEM



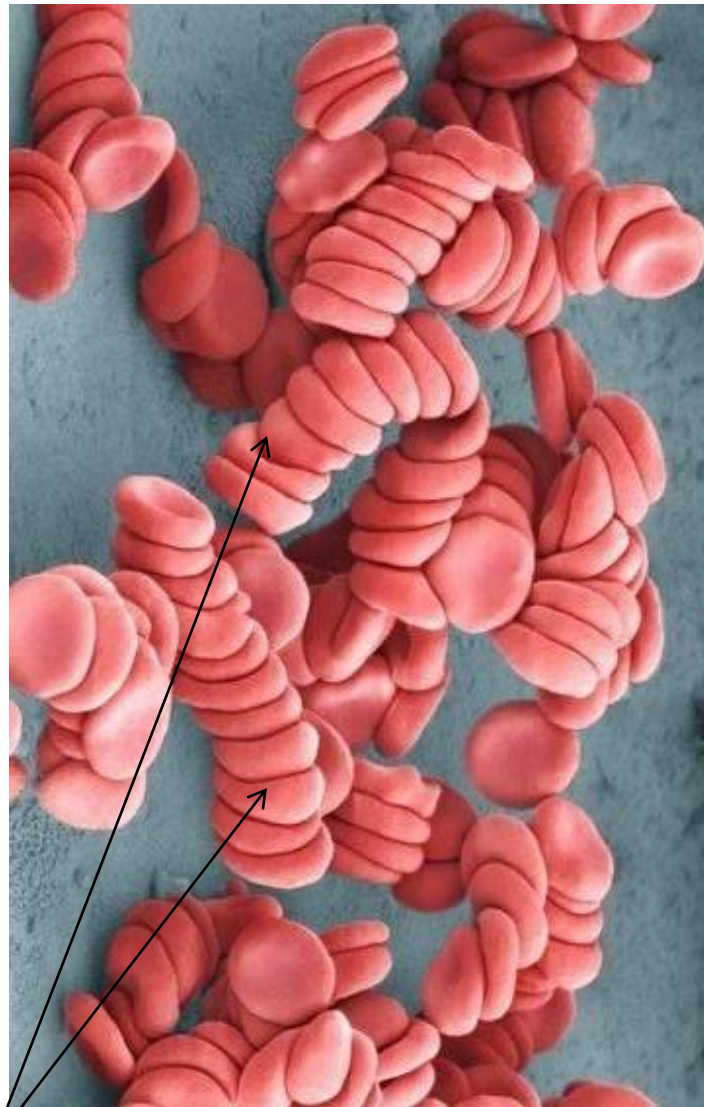
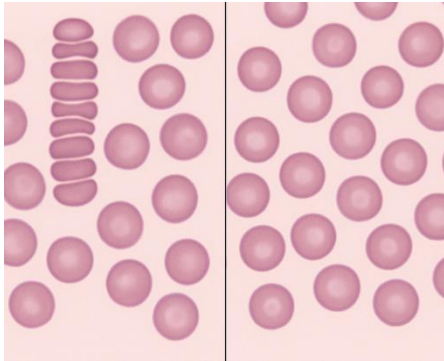
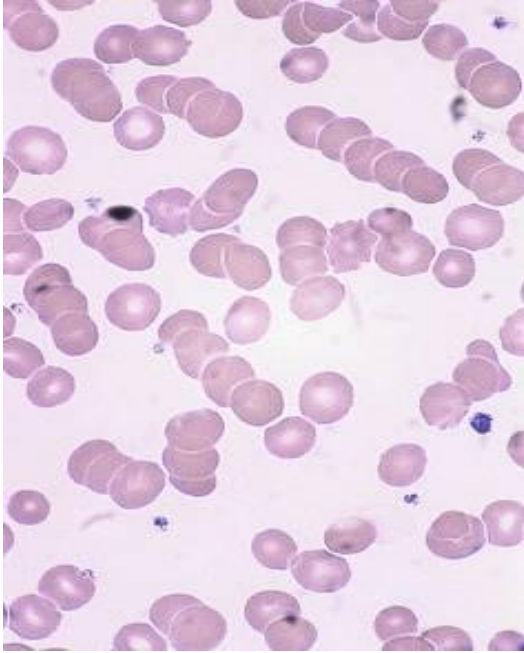
**Single Erythrocyte squeezing
through capillary**



**TEM Of Erythrocytes Passing Through
Capillary Wall**



Rouleaux appearance occurs to some extent in all films



Rouleaux formation:

- ✓ RBCs may adhere to one another loosely in stacks called Rouleaux (pile of coins)
- ✓ In slow (not in normal) circulation

Due to surface tension caused by their biconcave surface (reversible)

Abnormalities of Erythrocytes

Change from the normal **size**, **shape** or **staining properties** of erythrocytes are **important indicator of disease**. However, some of these abnormalities may be found in healthy individuals

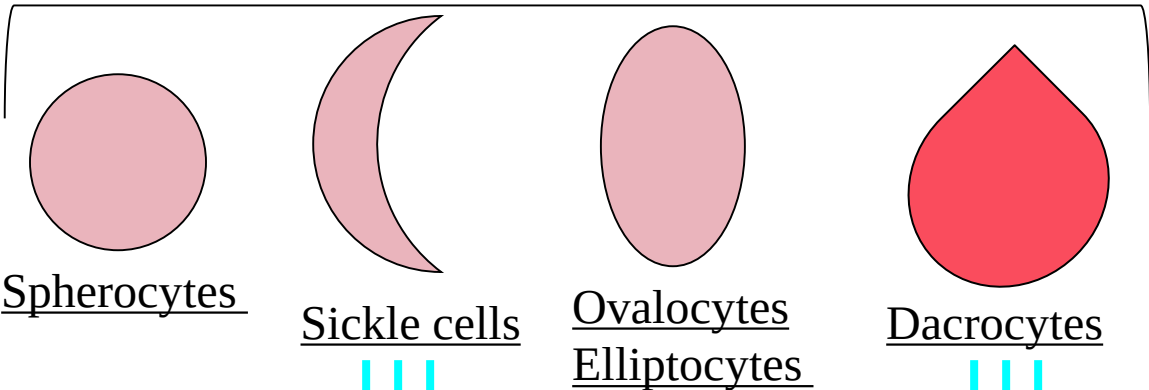
Abnormal sizes:

- Microcytes (<6um)
- Macrocytes (>9um)
- Anisocytosis (different sizes)

Abnormal shapes:

Due to changes either in the cell membrane or Hb content

Poikilocytes (Poikilocytosis)



One of the most sever changes in shape occurs during SICKLING of RBCs in sickle cell anemia where erythrocytes take on the form of crescents

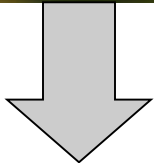
Teardrop shaped cells

Abnormal staining:

Hypochromia: Denotes a decrease in the intensity of staining
Indicates a decreased amount of hemoglobin
Frequently accompanies microcytosis



Hypochromic microcytic anemia



Sickle cell anaemia results from abnormal hemoglobin

Based on Hemoglobin Content (color /chromasia):

Normochromic: RBCs have a normal hemoglobin concentration → normal color, normal central pallor (about one-third of the cell).

Hypochromic: RBCs have less hemoglobin than normal → appear paler with an abnormally large central pallor (Common in iron deficiency anemia).

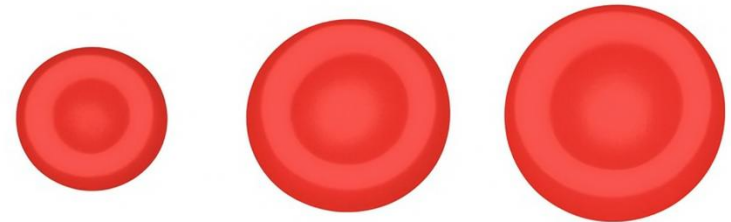
Hyperchromic: RBCs have more hemoglobin concentration than normal → cells look denser and darker with absent central pallor (seen in spherocytosis).



MICROCYTIC

NORMOCYTIC

MACROCYTIC



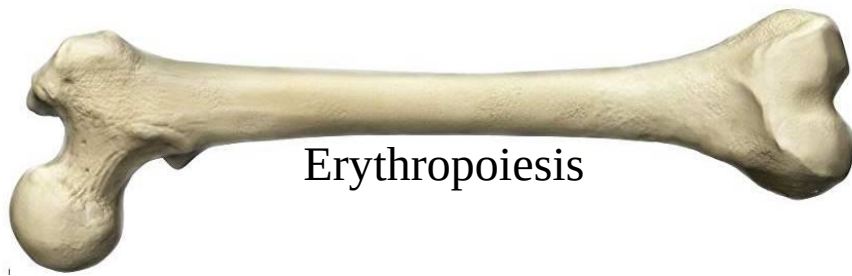
Together, these terms are used to describe and classify anemias (e.g., microcytic hypochromic anemia in iron deficiency, or macrocytic normochromic anemia in B12 deficiency).

Based on Cell Size (cytometry):

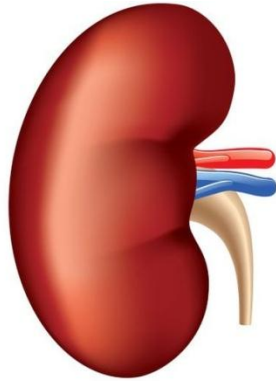
Normocytic: RBCs are of normal size, about 7–8 μm in diameter.

Microcytic: RBCs are smaller than normal (seen in iron deficiency anemia).

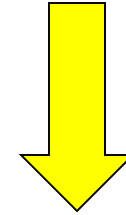
Macrocytic: RBCs are larger than normal (seen in vitamin B12 or folate deficiency anemia).



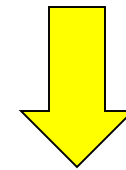
Erythropoiesis



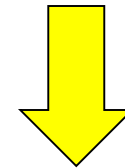
Production of erythrocytes in the bone marrow, is stimulated by erythropoietin



Erythropoietin is produced by the kidneys



When RBC count drops, such as during blood loss, the resulting oxygen-deficiency state, **hypoxemia**, is detected by the kidneys.



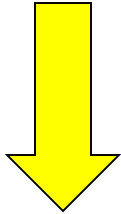
The kidneys respond by increasing their erythropoietin secretion, which leads to increased red blood cell production

Anemia: a decrease in the total number of RBCs (and/or hemoglobin)

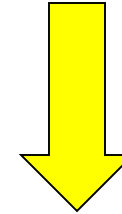
Polycythemia: an increase in the total number of RBCs (and/or hemoglobin)

Consequently

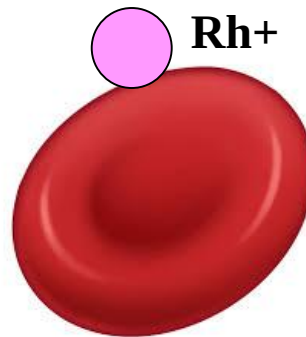
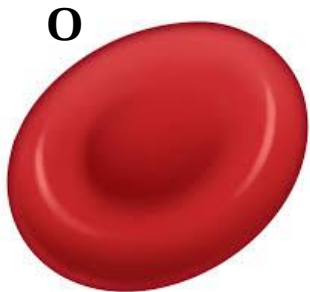
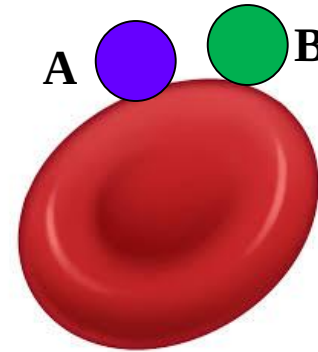
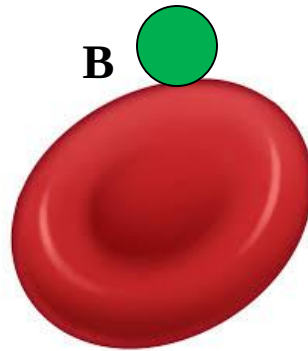
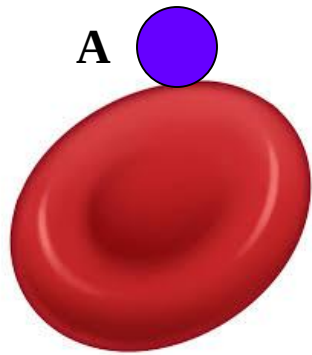
People living at high altitudes usually have higher RBC count as a response to lower oxygen levels.



Athletes whose demand for oxygen is more elevated, also have higher RBC counts.



RBC plasma membranes have glycoprotein antigens on their external surfaces



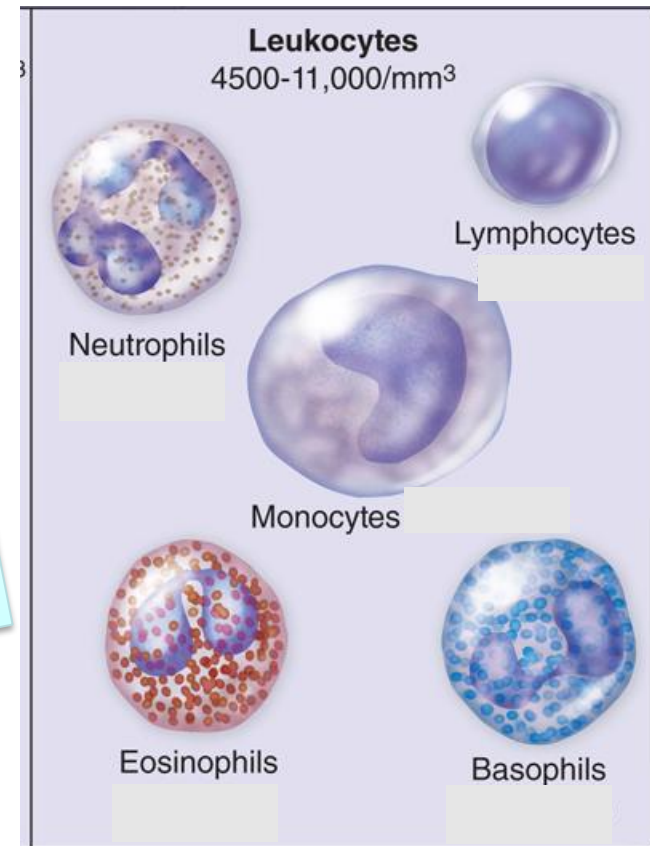
There are four common blood groups in the ABO system: O, A, B, and AB. The blood groups are defined by the presence of specific carbohydrate sugars on the surface of red blood cells

	RBCs (Erythrocytes)	WBCs (Leukocytes)
Types	1 type	5 types
	Not true cells	True cells
Number	Male: 4.5-5.5 million/mm3 female:4-5 million/mm3	4500-11000/mm3
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
Function	Gas exchange	Defense
Motility	Non motile	Motile
	Function exclusively within vascular system	Function mainly OUTSIDE blood vessels in the tissues

Leukocytes

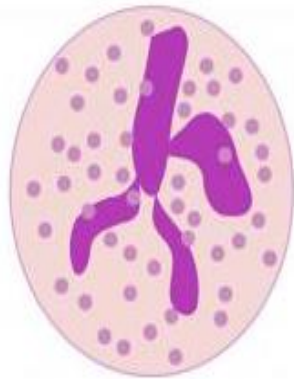
- Originate in the bone marrow and released continuously into the blood
- Travel in bloodstream but function mainly **outside** blood vessels (in loose CT)
- Leukocytes form a mobile army that helps protect the body from damage by bacteria, viruses, parasites, toxins and tumor cells
- 5 types organized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

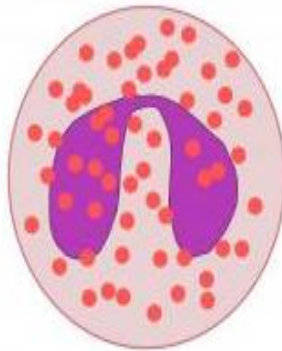


Leukocytes (White Blood Cells)

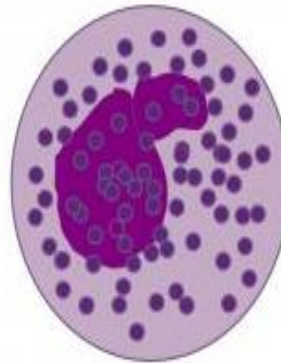
Granulocytes



Neutrophil



Eosinophil



Basophil

Agranulocytes



Monocyte



Lymphocyte

Cytoplasmic granules

Specific granules
Secondary granules

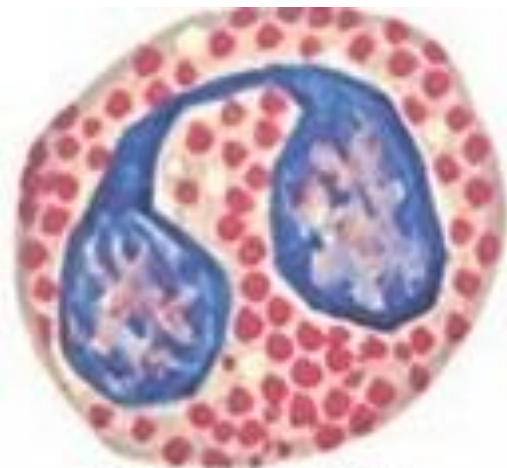
Non-specific granules
Azurophilic granules
Lysosomes
Primary granules

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:

Dr. Heba Kalbouneh

Large granules, Red



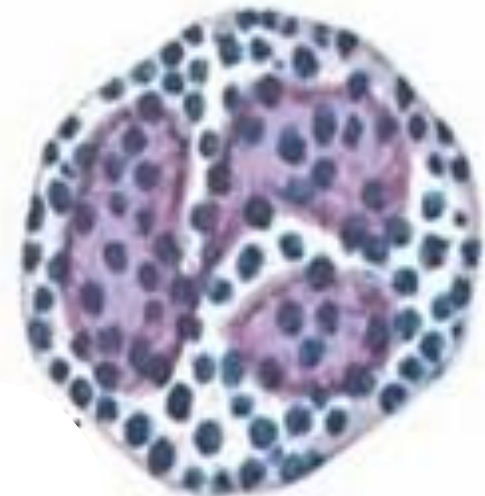
Eosinophil

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



Neutrophil

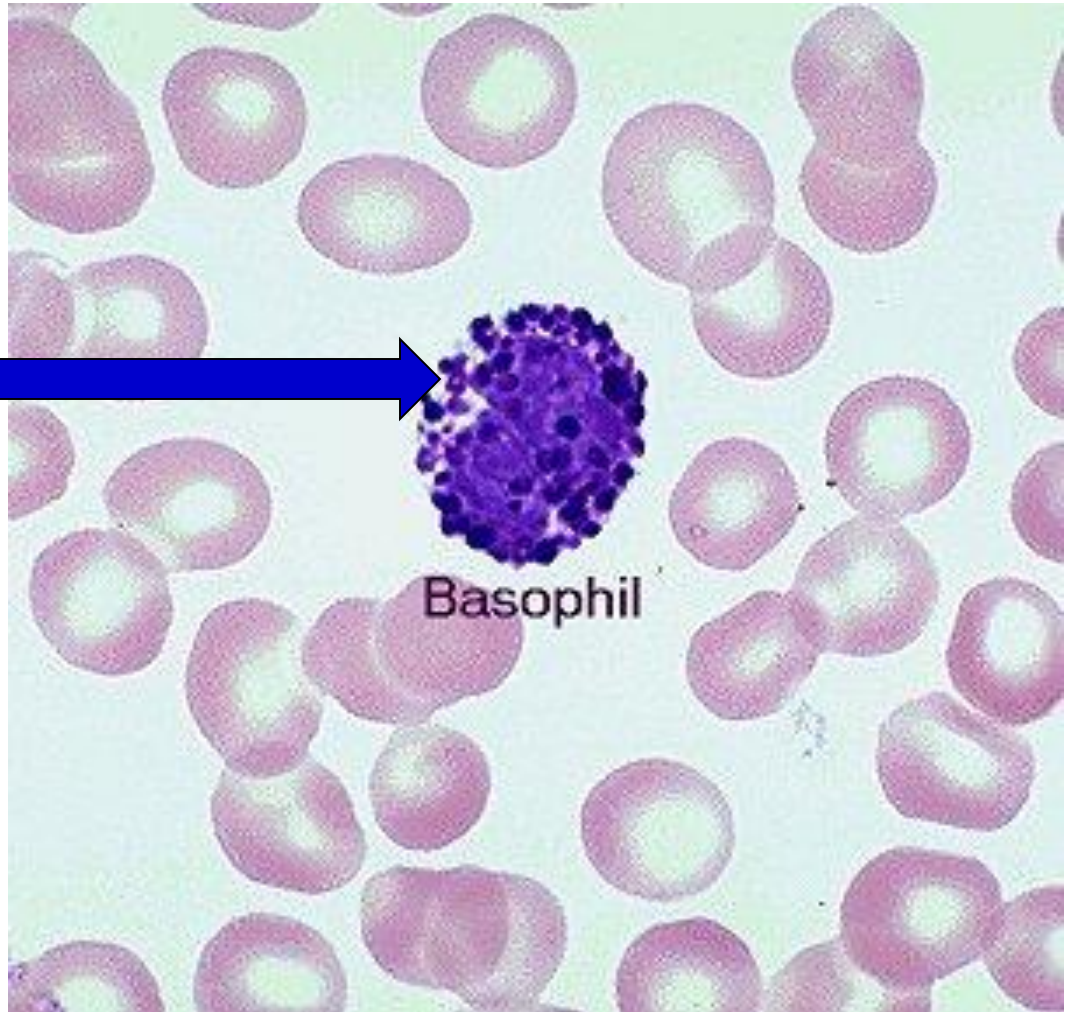
Large granules, blue



Basophil

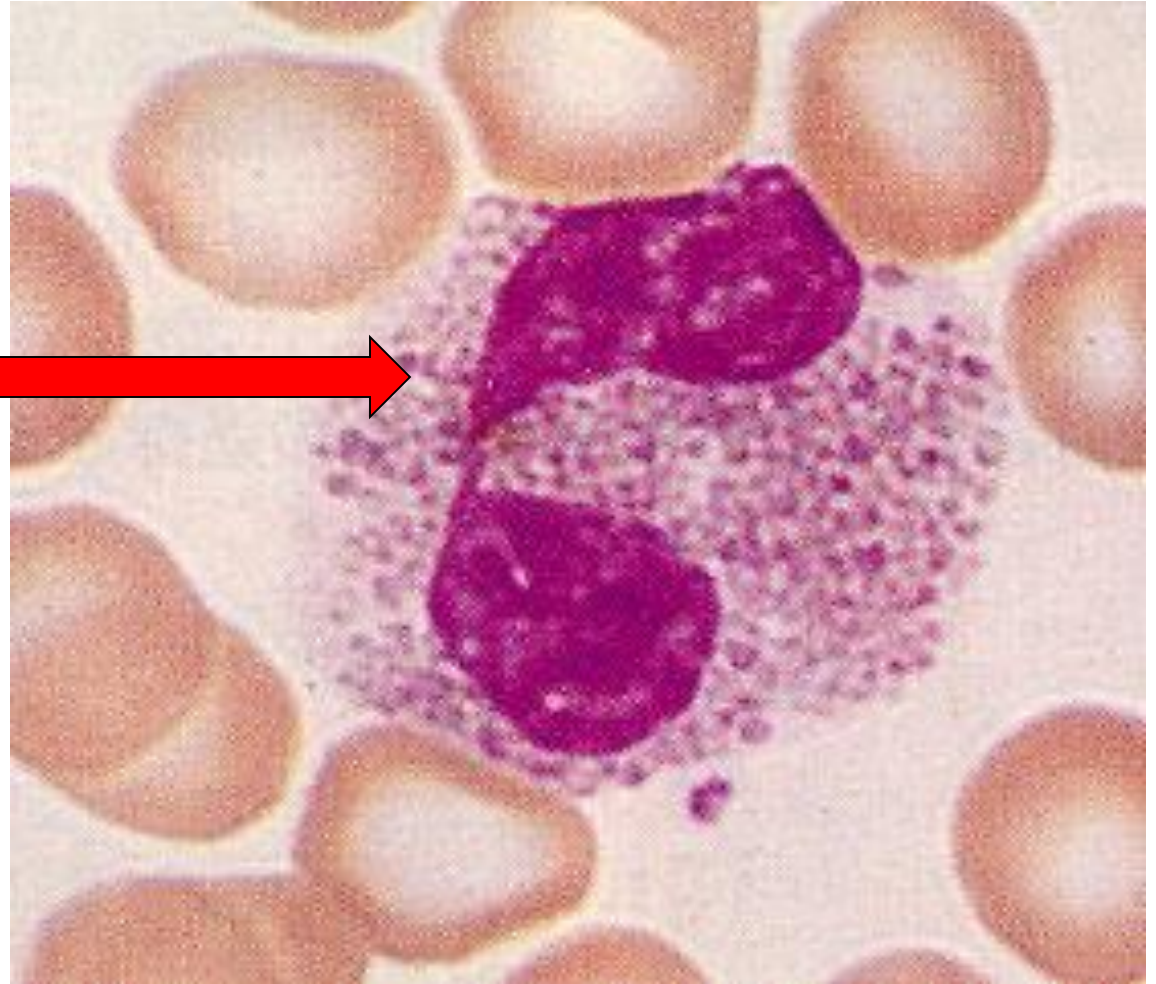
Basophil

*These specific granules
stain with basic stains*



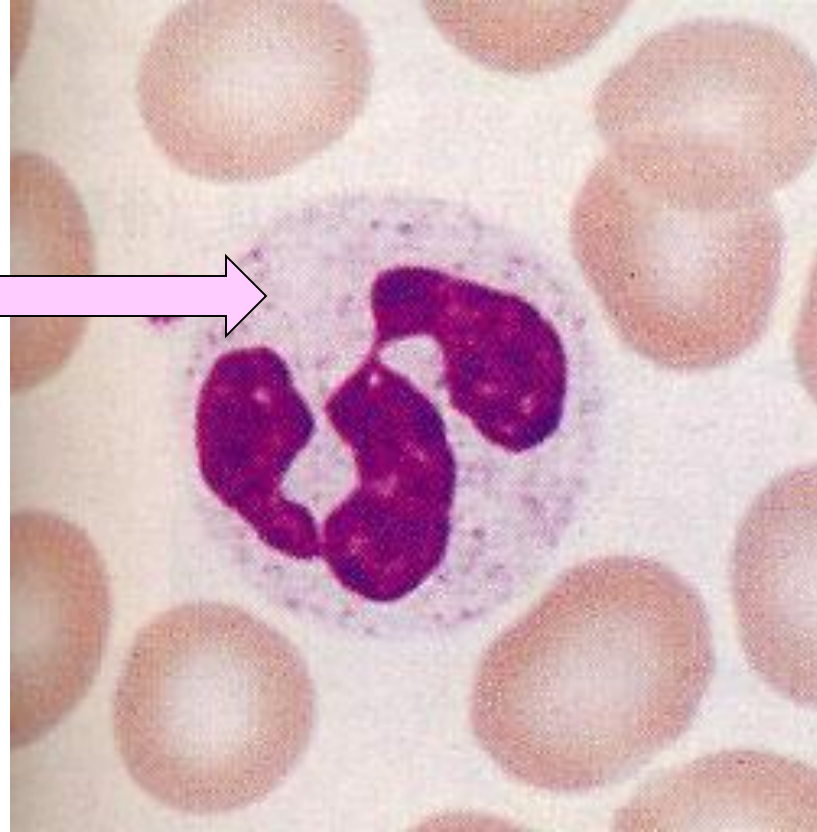
EOSINOPHIL

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



Neutrophil

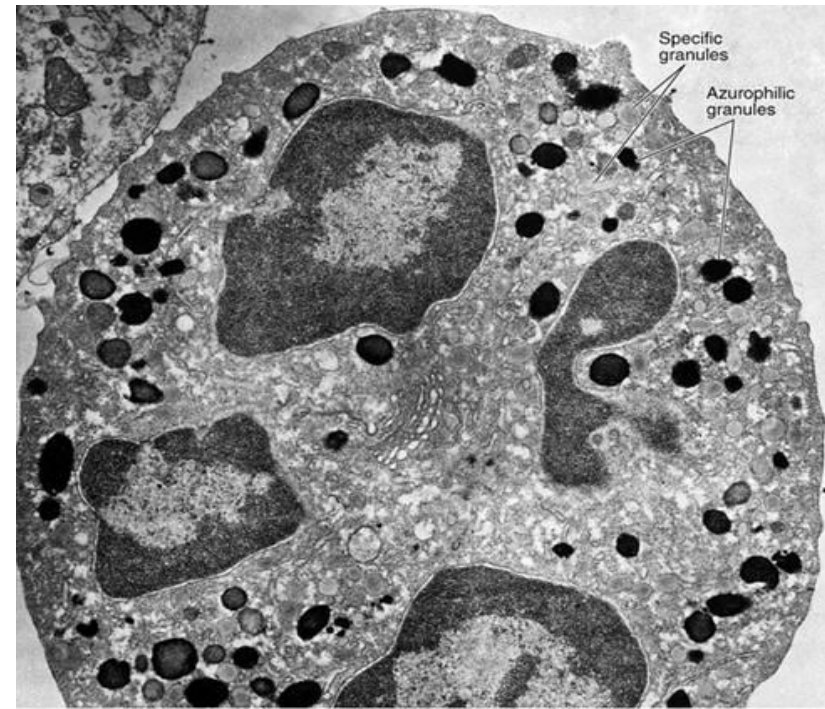
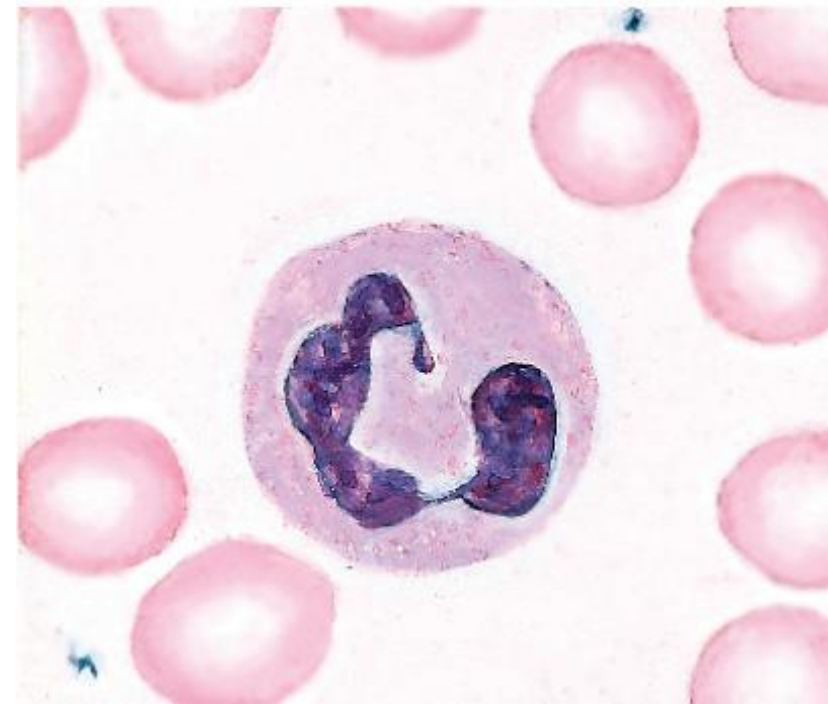
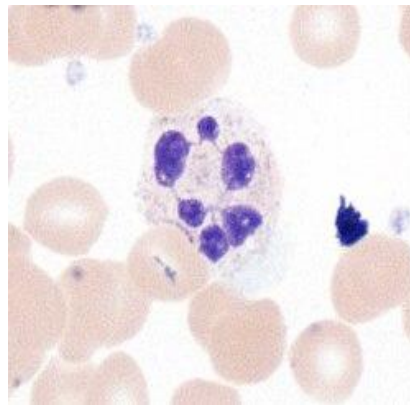
These granules are neutrophilic, meaning they show no special affinity for either acidic or basic stains but are stained mildly by both



Neutrophils

- The most common leukocyte
- 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.

Note: Neutrophils will show increasing segmentation (many segments of the nucleus) as they mature. A normal neutrophil should have 3–5 segments. Hypersegmentation is not normal but occurs in some disorders, most notably vitamin B₁₂ deficiency.



Specific granules (secondary)

Smaller, more numerous, formed later in development.

- **Lysozyme**
- **Lactoferrin**
(bacteriostatic)
- **Collagenase**
- **NADPH oxidase**

Azurophilic granules (primary)

Larger, formed early in neutrophil development.

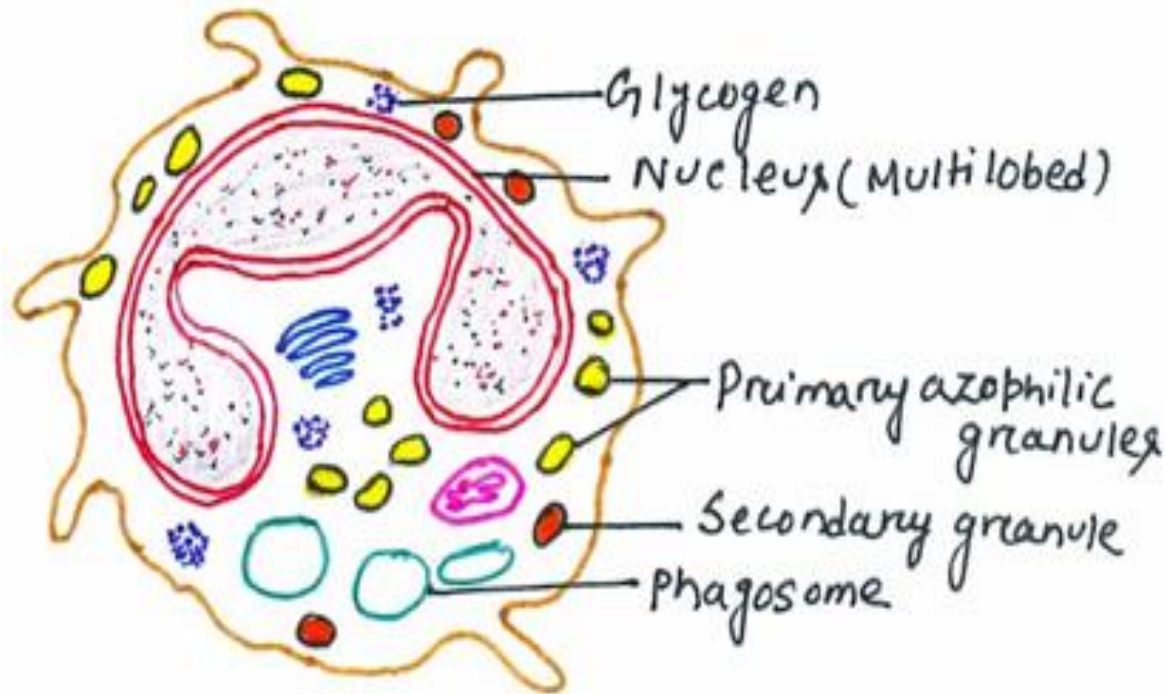
- **Myeloperoxidase**
- **Acid hydrolase**
- **Defensins**
- **Protease (eg. Elastase)**

Form H_2O_2 ,
HOCL: powerful
cytotoxin

Different names for neutrophils:

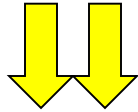
Polymorphs
Pus cells
Myelocytes
Microphages
Cells of acute inflammation

Pus is pyrogenic

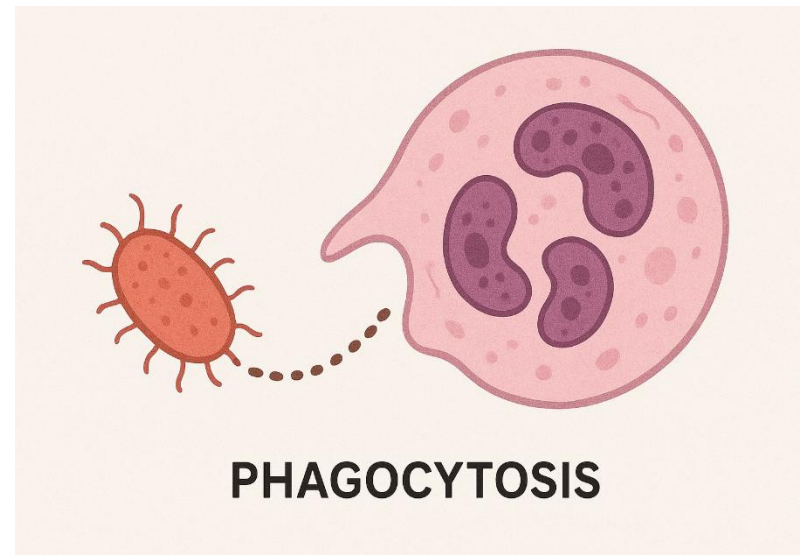


Oxygen-dependent killing:

The neutrophil undergoes a ‘respiratory burst’—activating NADPH oxidase to produce reactive oxygen species. Hydrogen peroxide is formed, and with the help of myeloperoxidase, it generates hypochlorous acid.

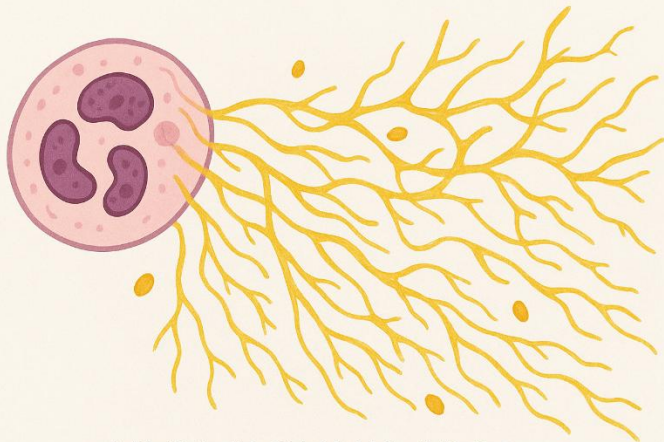


This is extremely toxic to microbes.



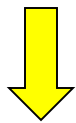
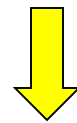
Oxygen-independent killing:

Granules inside the neutrophil release enzymes like defensins, lysozyme, and proteases. These proteins break down microbial walls and deprive bacteria of nutrients.



NEUTROPHIL NETs

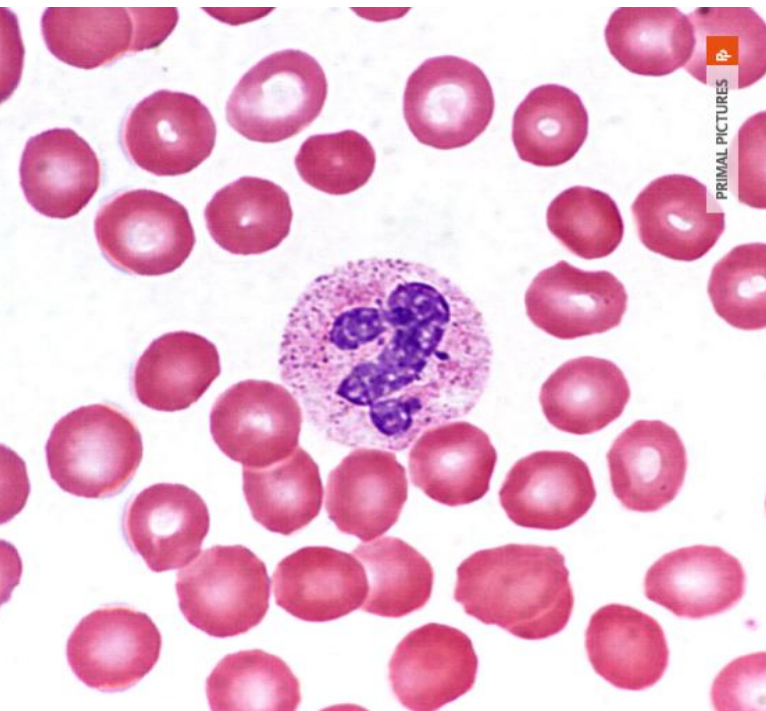
the **Neutrophil Extracellular Trap**, or **NET**. When overwhelmed, a neutrophil can undergo NETosis—a unique cell death where it releases its DNA coated with antimicrobial proteins.



This sticky web traps and kills microbes outside the cell, preventing them from spreading.”



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*)



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

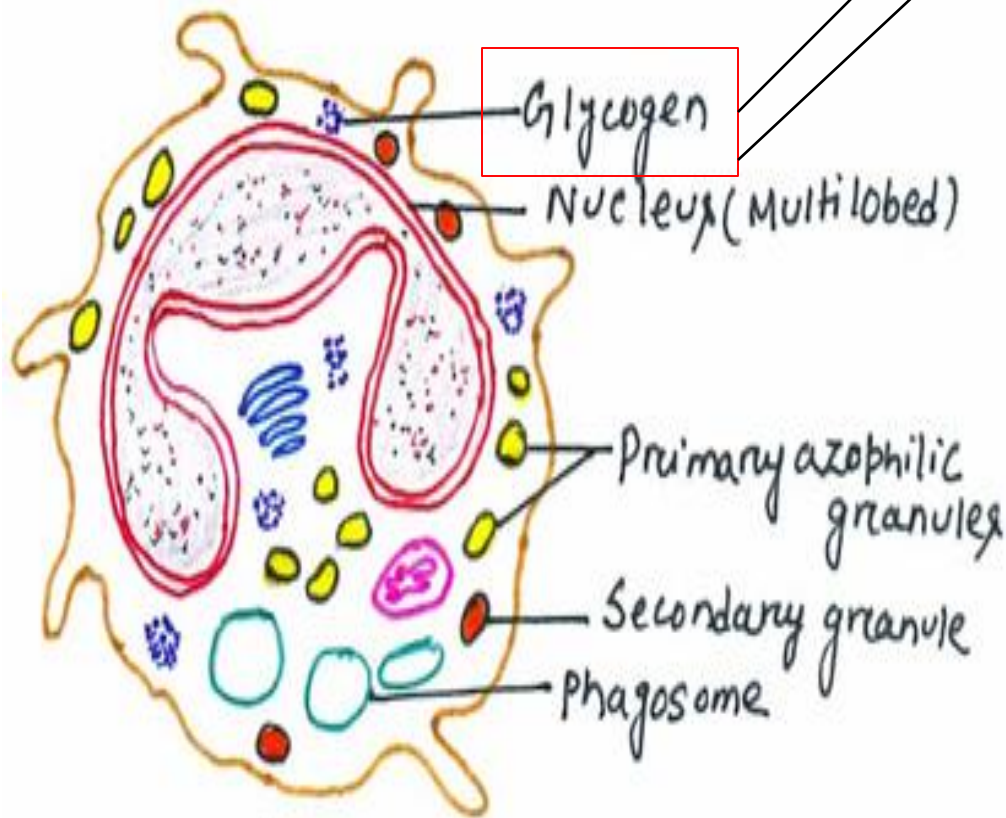
Why???

Cells of acute infection

- 1- The most abundant
- 2- The most motile
- 3- Neutrophil chemotactic factors are the first released

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

Few organelles



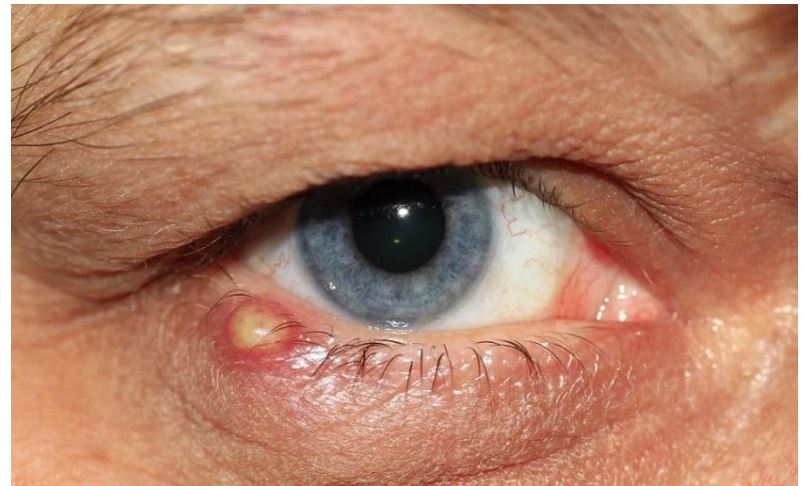
The ability of neutrophils to survive in an anaerobic environment is highly advantageous, because they can kill bacteria and help clean up debris in poorly oxygenated regions, for example, damaged or necrotic tissue lacking normal microvasculature.

Neutrophilia
Neutropenia



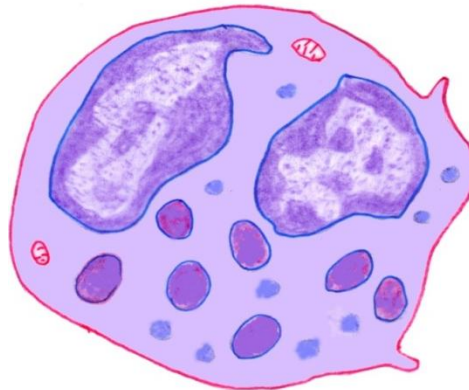
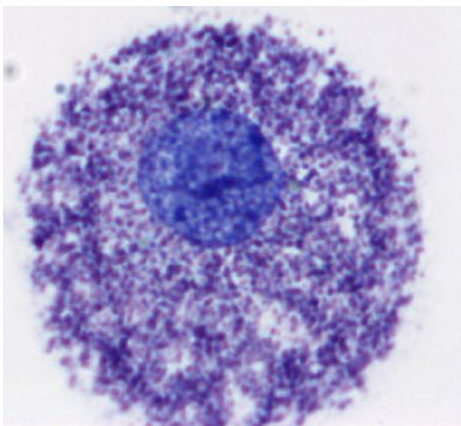
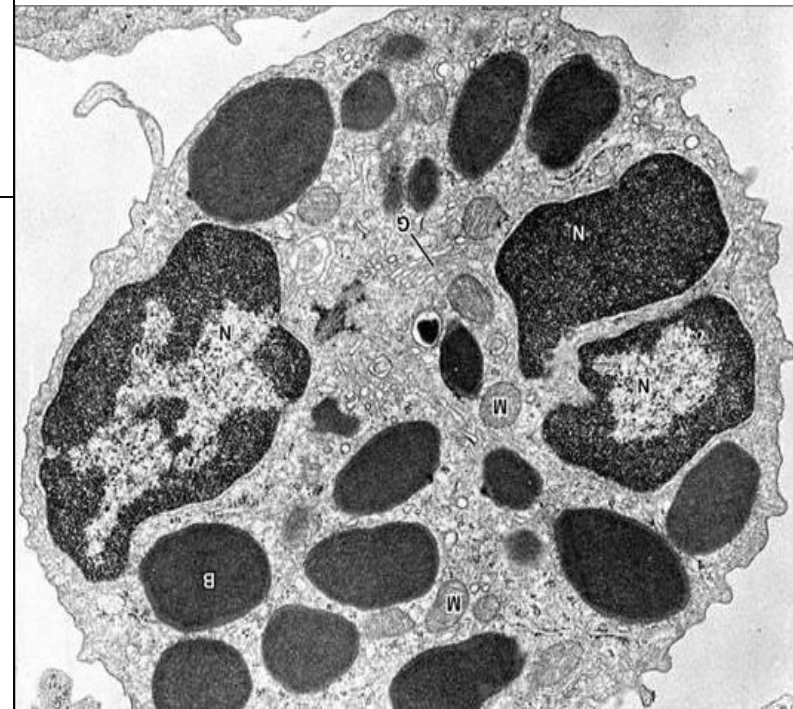
Pus is a viscous, usually yellow collection of fluid.

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



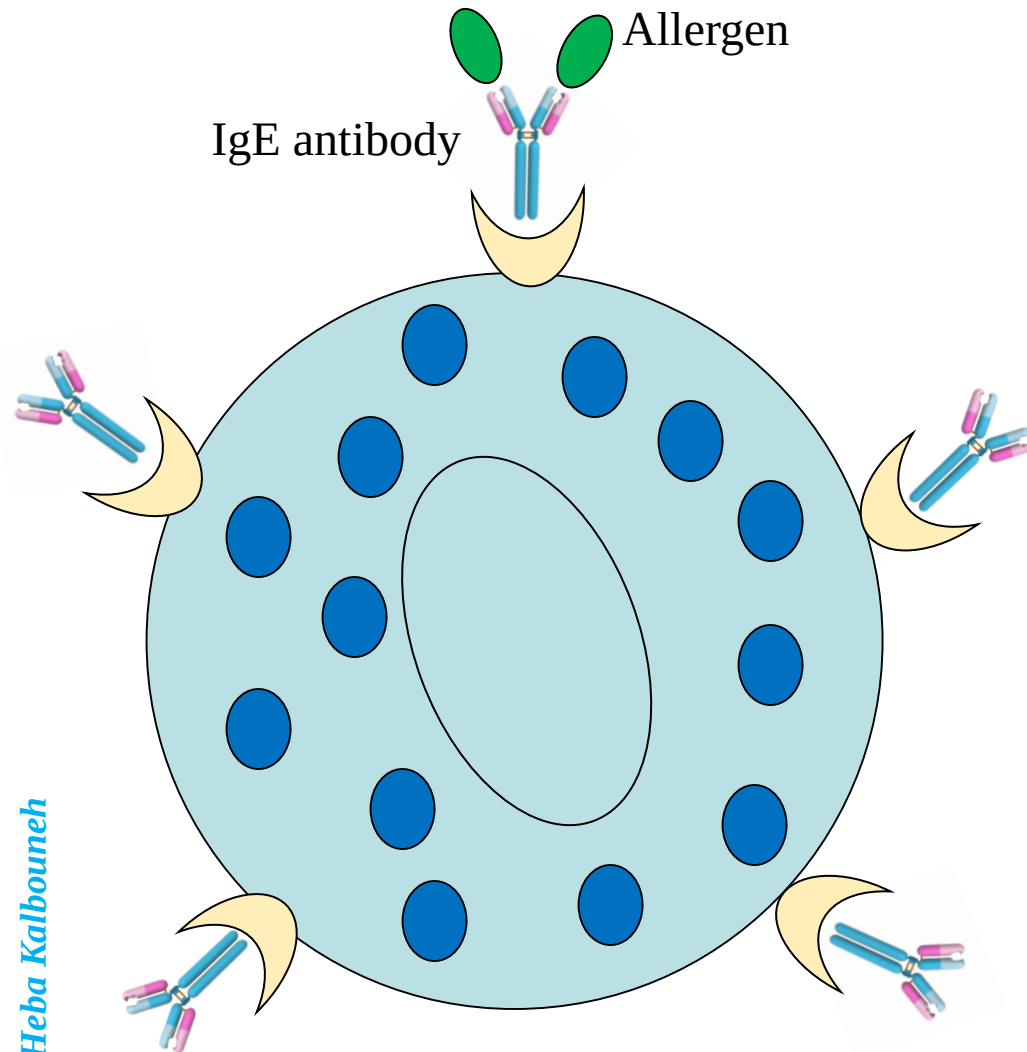
Basophils

- Rarest leukocyte – might not see these under the microscopes
- Usually have bi-lobed, S-shaped nuclei obscured by the large basophilic granules
- 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

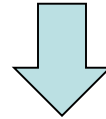
Both basophils and mast cells have surface receptors for immunoglobulin E (IgE), and secrete their granular components in response to certain antigens and allergens.



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

First
exposure

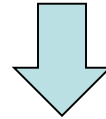
In some individuals substances such as certain pollen proteins or specific proteins in food are allergenic, that is, elicit production of specific IgE antibodies, which then bind to receptors on mast cells and immigrating basophils.



Second
exposure

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.



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

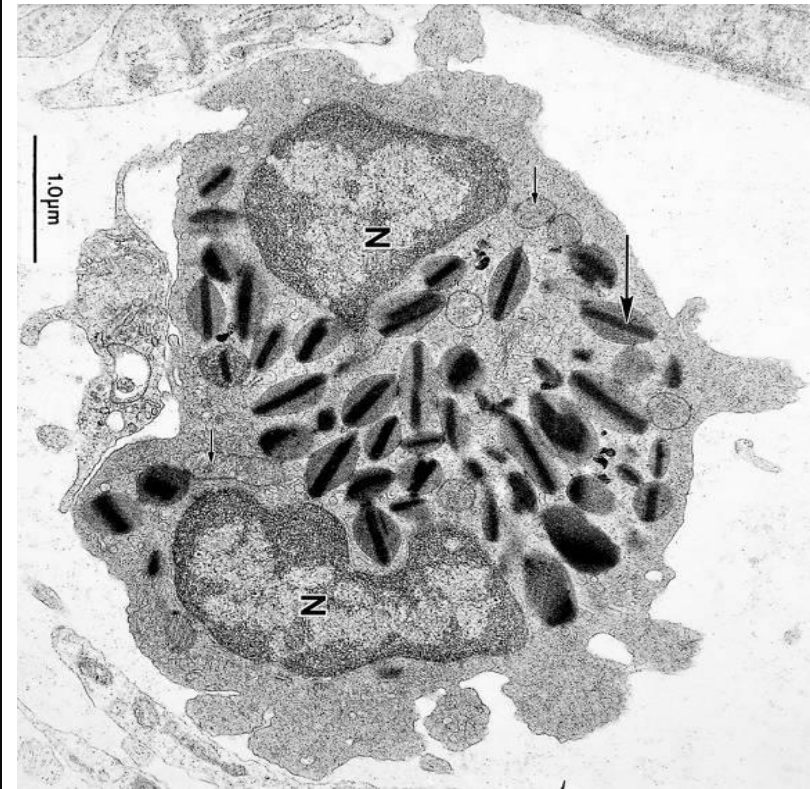
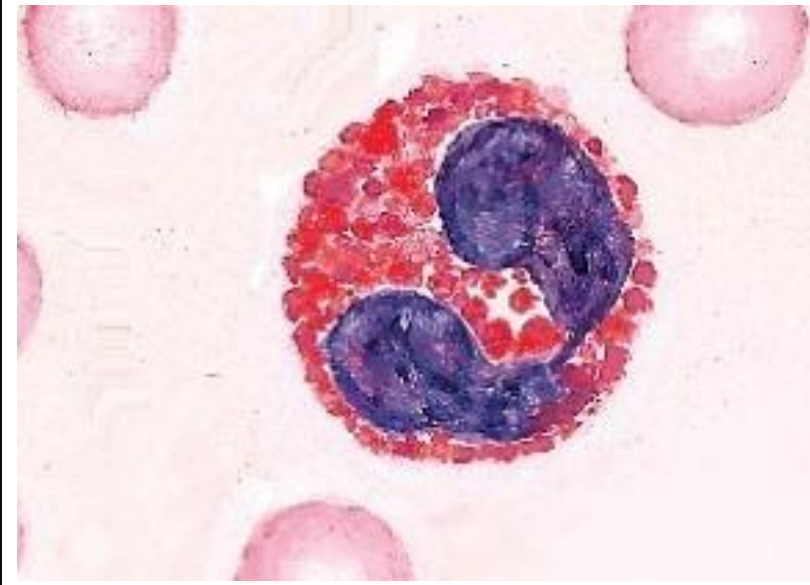


Allergic dermatitis (eczema) is an itchy skin rash that develops when you come into contact with an **allergen**



Eosinophils

- 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



Crystalloid granule

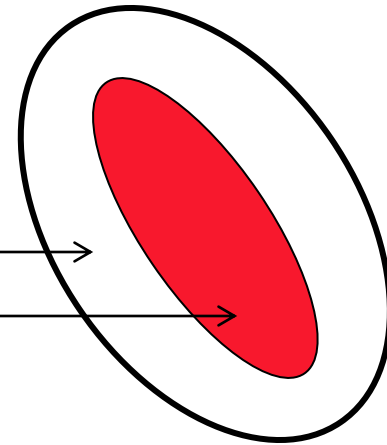
Specific granules (Crystalloid granules):

- Oval in shape, with flattened crystalloid cores

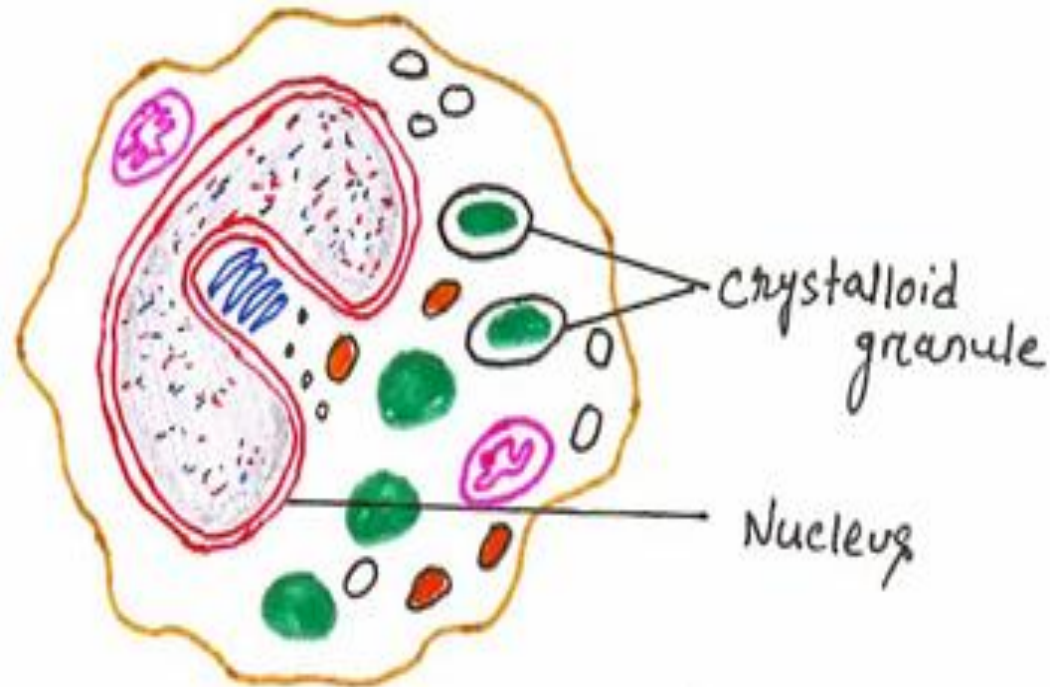
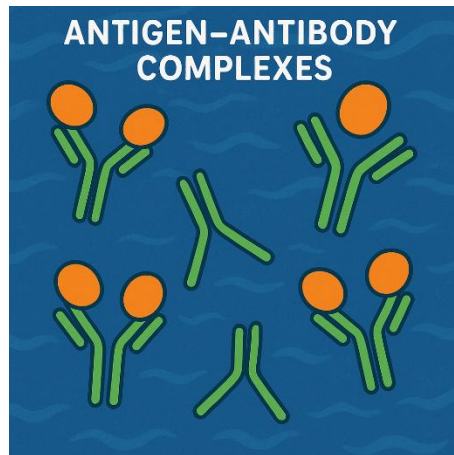
- Two parts:

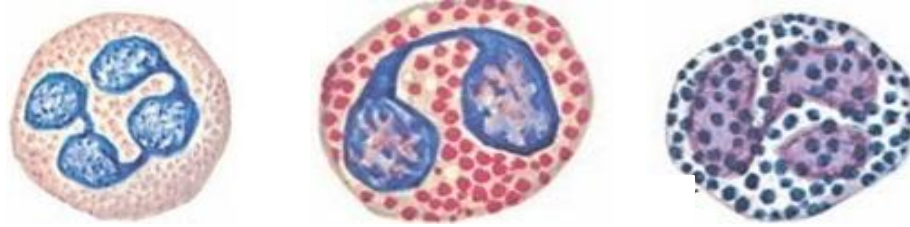
Externum (pale): contains histaminase and sulfatase

Internum (dark): contains basic protein to kill parasites



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





	Neutrophil	Eosinophil	Basophil
Percentage (WBCs)	Most	—————>	Least
Size	12-15um	12-15um	12-15um
Life span	Few days	Few days	Few days
Nucleus	2-5 lobes	2 lobes	Irregular (S-shaped)
Phagocytic activity	Most	—————>	Least
Motility	Most	—————>	Least

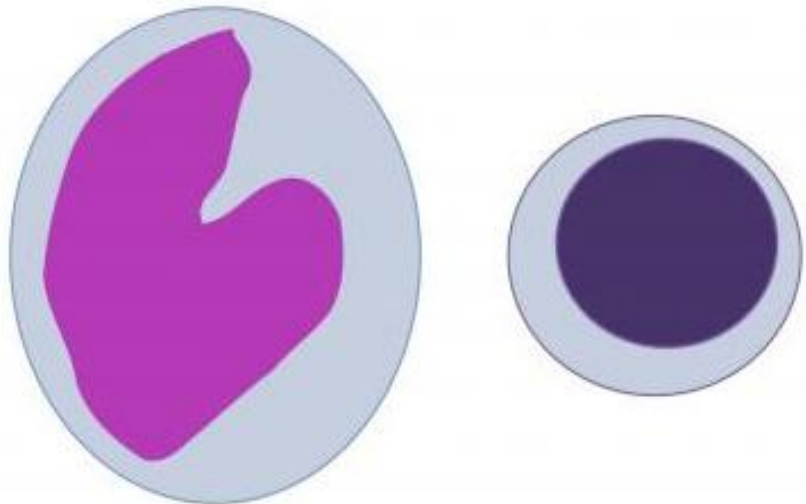
General features of granulocytes

- Spherical in blood stream, irregular in connective tissue
- Highly motile with different shapes due to their amoeboid movement
- Leave blood stream by migrating between the endothelial cells by a process called **diapedesis**

Diapedesis
(Gr. dia, through + pedesis, to leap)

Agranulocytes

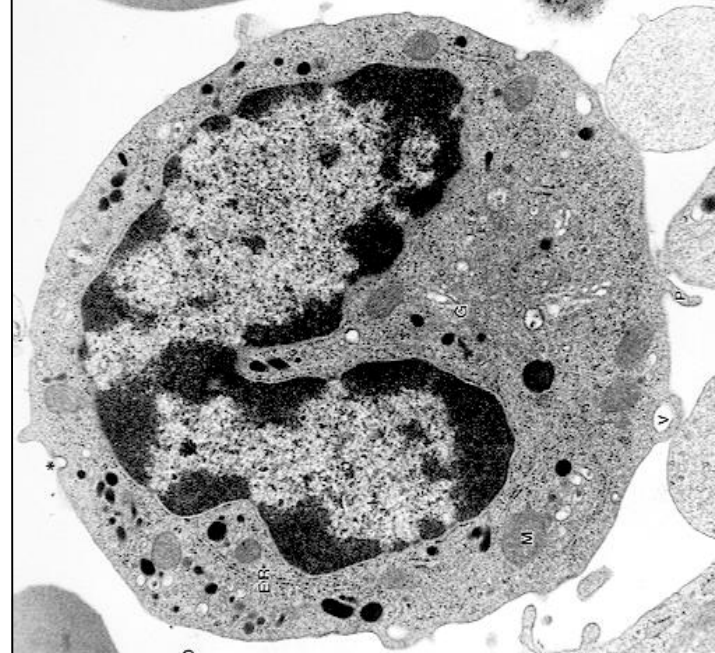
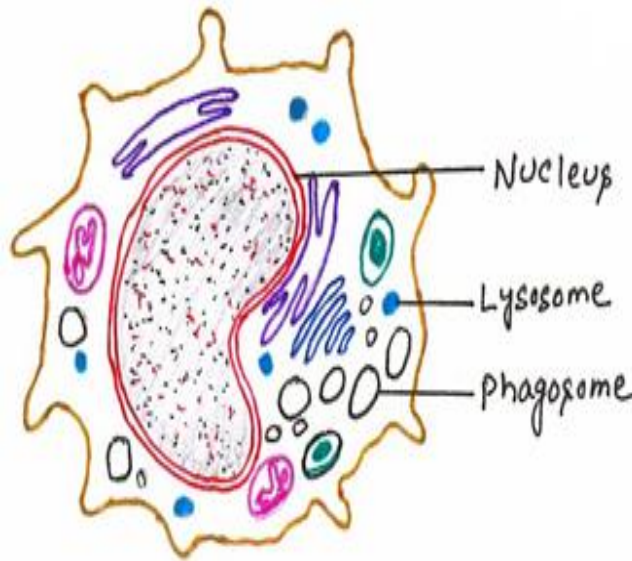
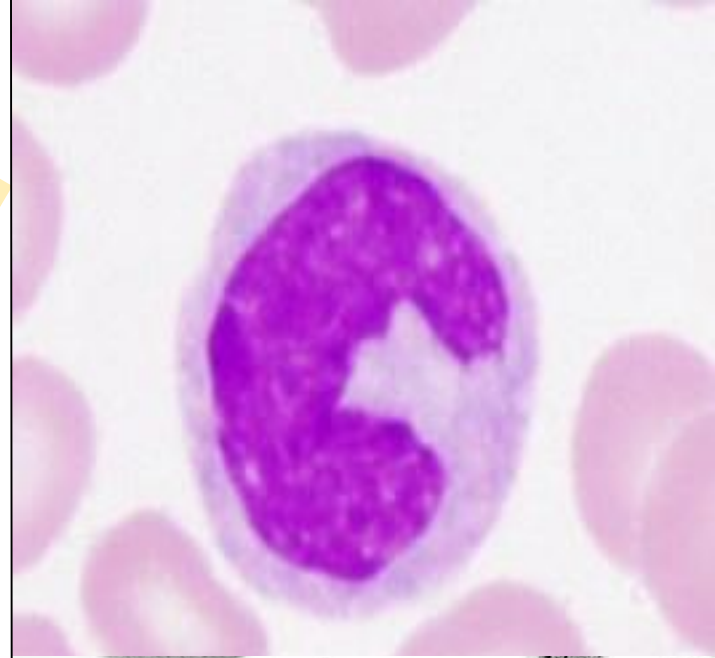
- Single non-lobulated nucleus
- Granules in cytoplasm are too small to see (nonspecific granules, azurophilic granules, primary granules, lysosomes)
- 2 types based on structure (not cell lineage):
 - **Lymphocytes**
 - **Monocytes**



Monocytes

- Largest leukocytes
- Bluish cytoplasm (*frosted glass appearance*) & a large C-shaped nucleus
- Highly motile and phagocytic
- Travel through bloodstream to reach connective tissues, where they transform into **macrophages** (large phagocytic cells)

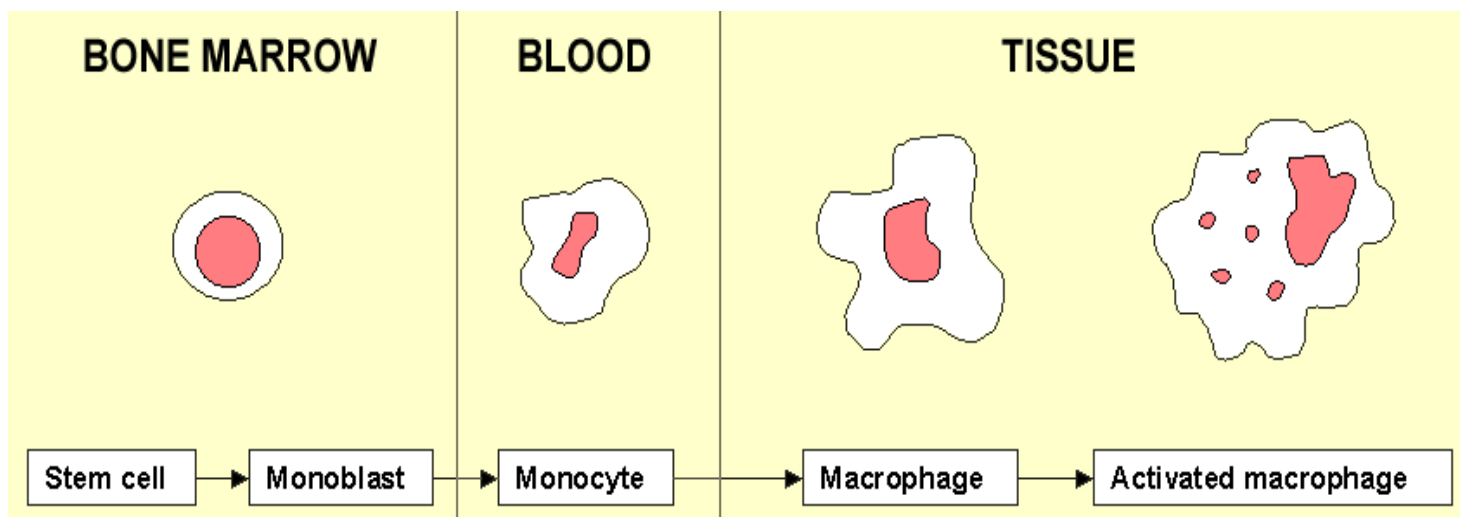
Azurophilic granules
(lysosomes)



Are precursor cells of macrophages, osteoclasts, microglia, and other cells of the **mononuclear phagocyte system** in connective tissue

All monocyte-derived cells are **antigen-presenting cells**

Monocytes and macrophages are the same cells at different stages of maturation



Kupffer Cells

Liver



Macrophages

Bone marrow
Connective tissue



Osteoclasts

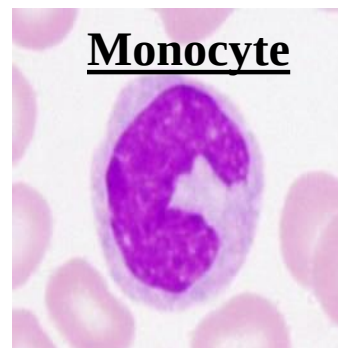
Bone
resorption

MONONUCLEAR PHAGOCYtic SYSTEM



Dust cells

Lung



Monocyte

(all characterized by phagocytic activity)



Microglia

CNS



Dendritic cells

Lymph node
Spleen

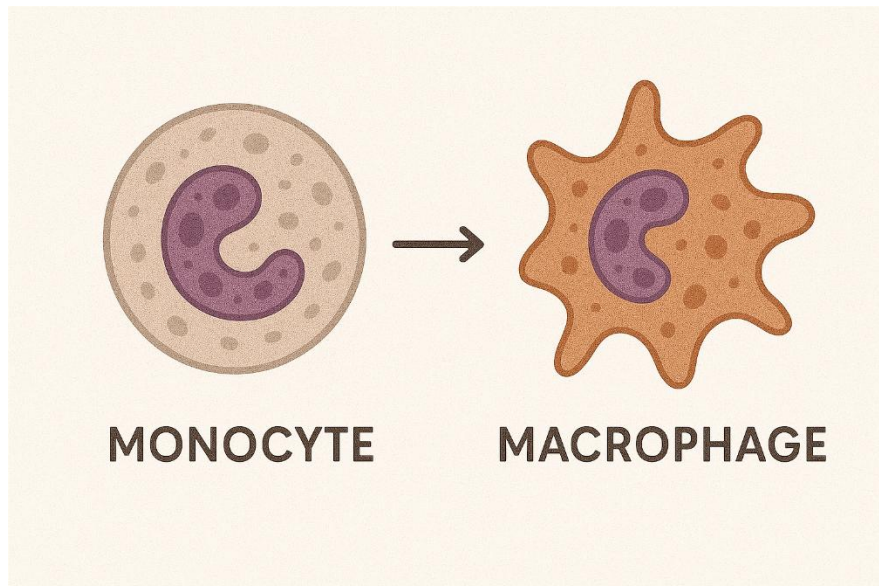


Langerhans cell

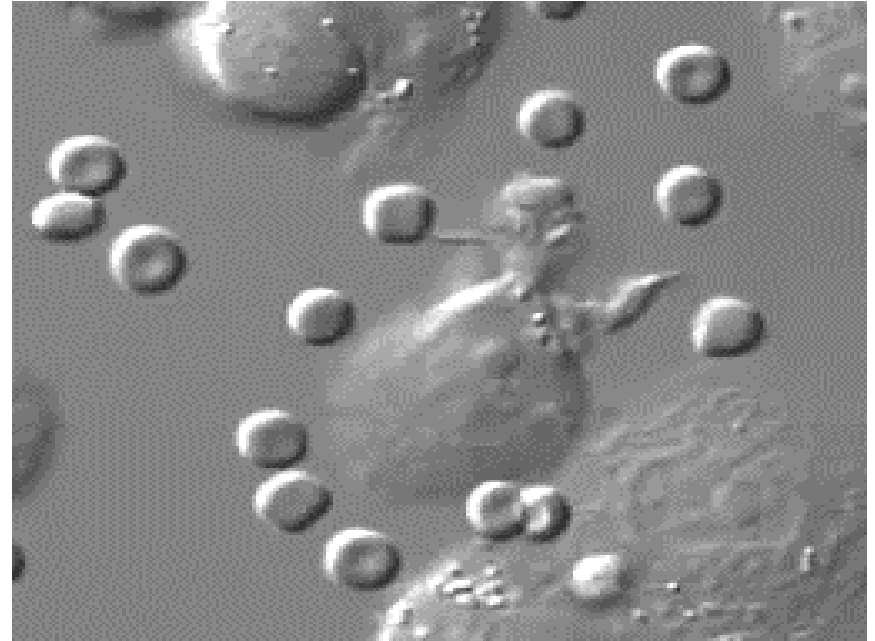
Epidermis

Morphologic changes occur upon differentiation of monocytes into macrophages:

- The cell increases in diameter more than threefold
- The cell acquires more cytoplasmic granules and vacuoles
- Cell surface receptors increase in number
- The phagocytic activity improves



A macrophage eating bacteria



Lymphocytes

- Smallest leukocytes
- Round nucleus occupies most of cell volume
- Cytoplasm is light clear blue
- Increased numbers are commonly seen in **viral infections**
- Lymphocytes vary in life span according to their specific function, some live for a few days and some live for many years

Cell mediated immunity

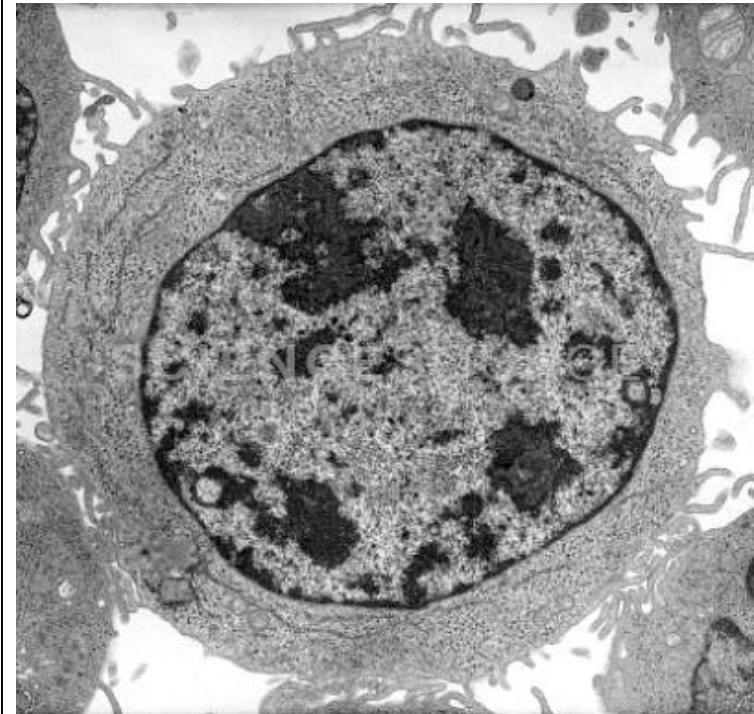
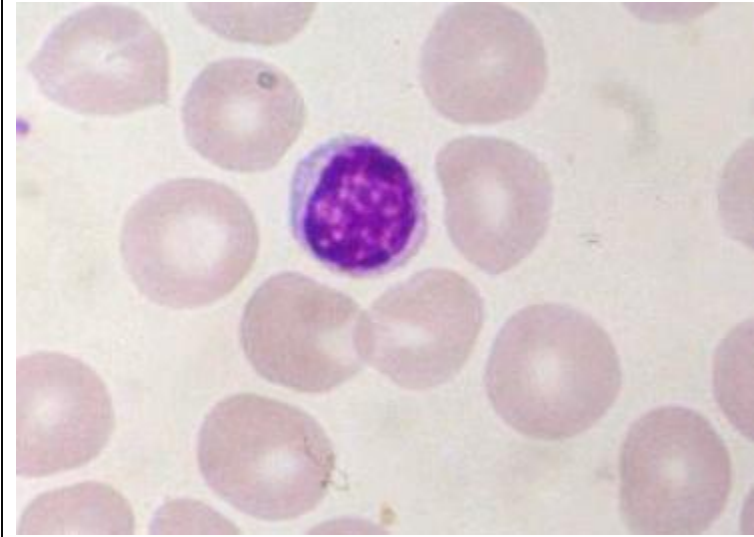
- **T cells**
 - Has different types, some directly kill foreign or infected cells; others activate phagocytes to destroy microbes

Humoral immunity

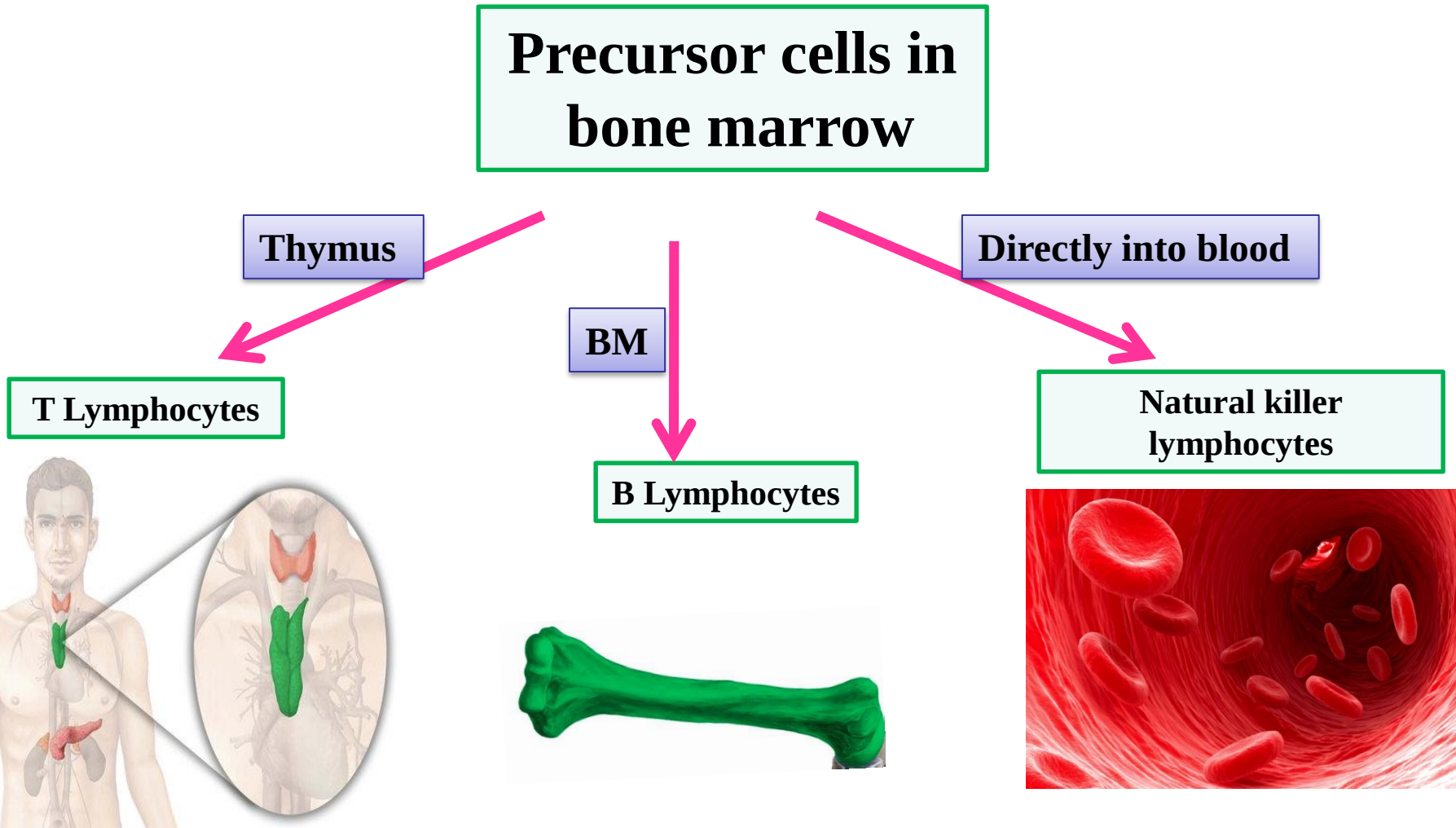
- **B cells**
 - Differentiate into plasma cells
 - Secrete antibodies that bind to specific antigens and mark them for destruction by phagocytic cells

Long term immunity

Humoral means
body fluids



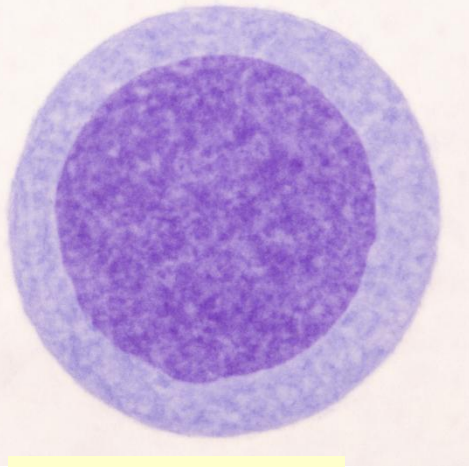
Lymphopoiesis: the process by which lymphocytes are formed



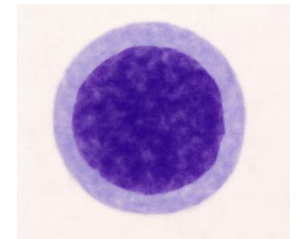
Morphologically lymphocytes can be classified into:

The amount of cytoplasm depends upon **state of activity** of the lymphocyte

In circulation blood there is **predominance of small inactive lymphocytes**

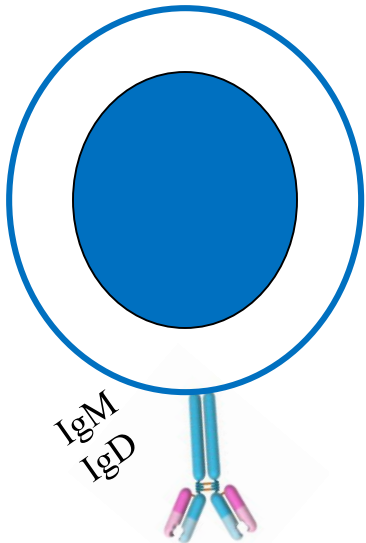


Large
(9-18 μm)
Active lymphocyte

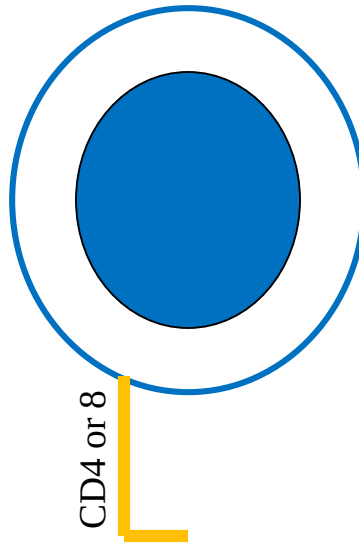


Small
(6-9 μm)
Inactive lymphocyte

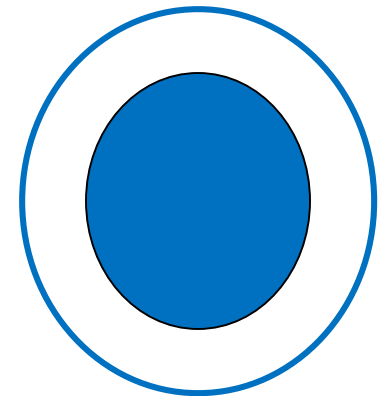
Different types express specific cell surface proteins



B lymphocyte



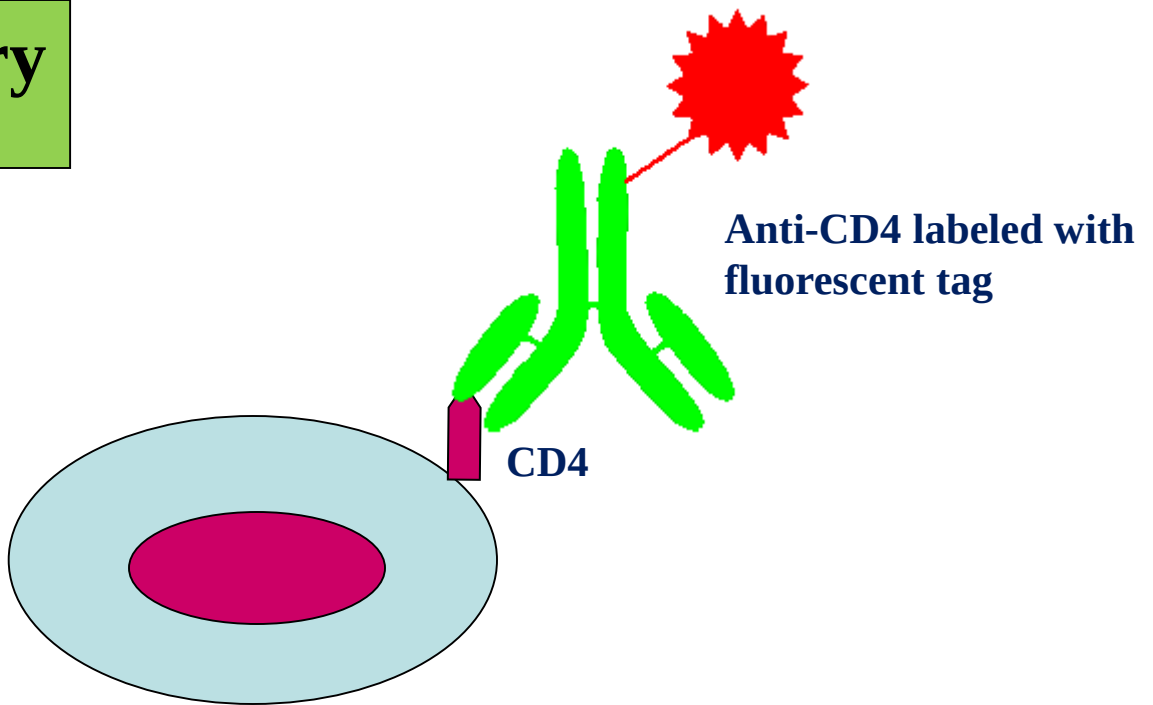
T lymphocyte



Natural killer lymphocyte

Immunohistochemistry

Direct method

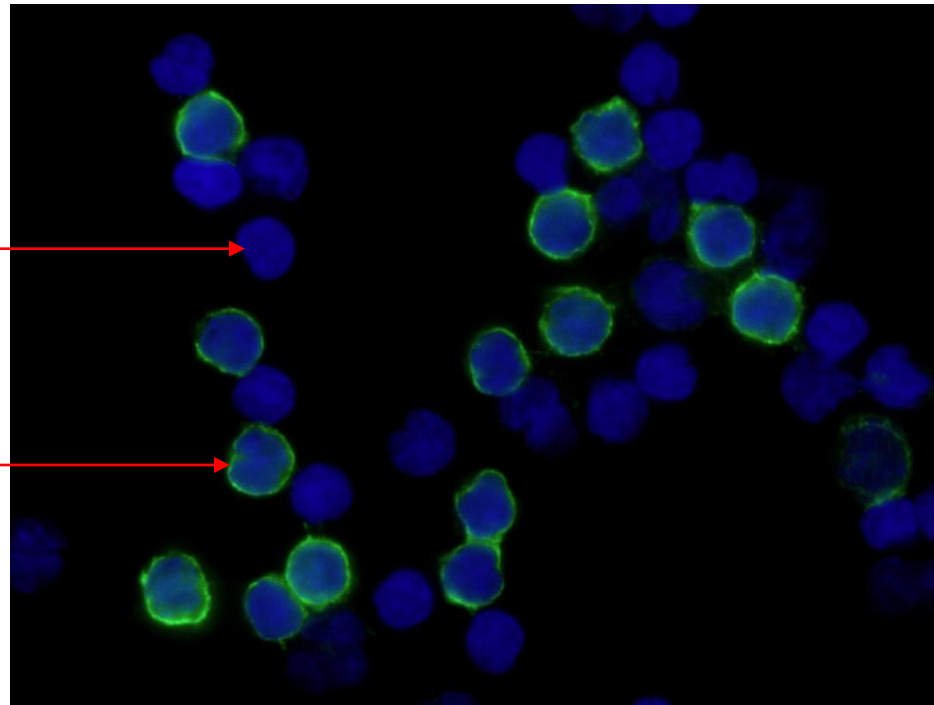


Immunohistochemistry

Using CD 4 Antibody

???????

CD 4 +
T Helper lymphocyte



Neutrophils and monocytes are highly phagocytic and engulf microorganisms and cell debris in a **NON-SPECIFIC** manner (**Innate immunity**)

While

The activity of lymphocytes is always directed against **SPECIFIC** foreign agents (**Adaptive immunity**)

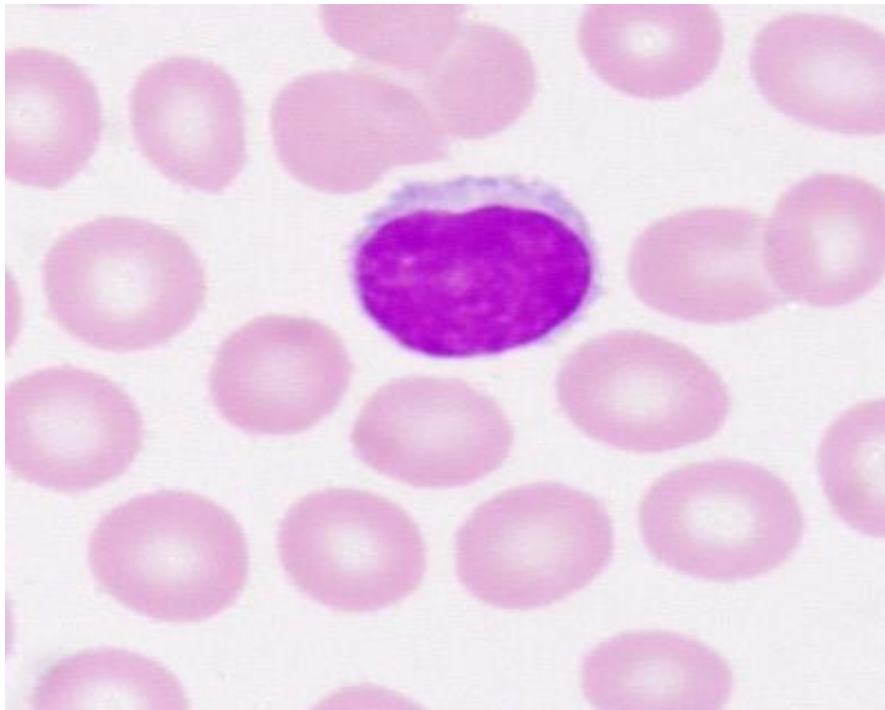
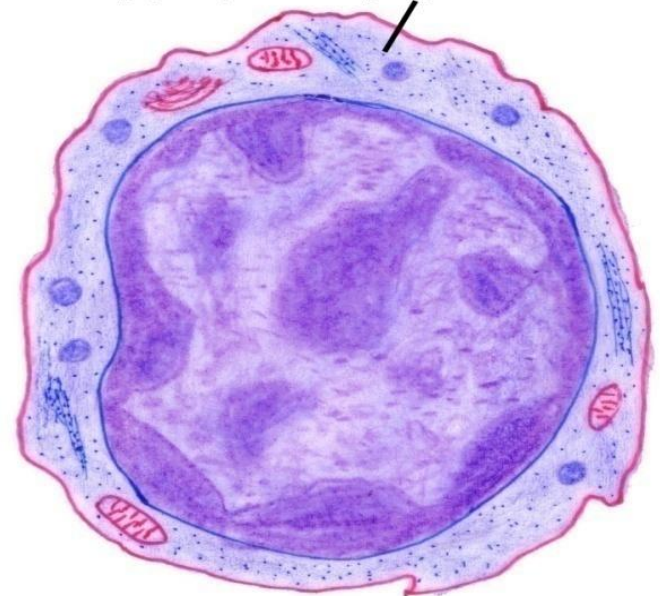
The small lymphocyte has scanty cytoplasm (contain few organelles but large number of ribosomes)



Account for basophilic cytoplasm



Scanty peripheral cytoplasm

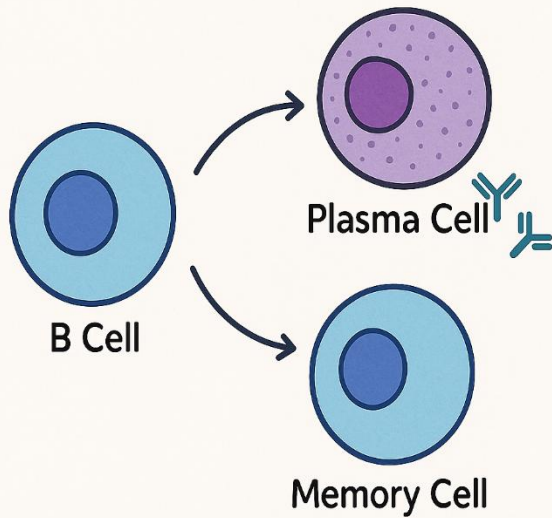


B Lymphocyte

Memory cell

Plasma cell

Produces
antibodies



T Lymphocyte

Cytotoxic

Kill virus-infected, transplanted
and neoplastic cells
(adaptive immunity)

Helper

Help cytotoxic T cells and
B cells in their immune
functions

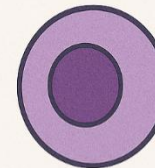
Suppressor

Suppresses immune response to
self Ag
Suppresses immune response of T
and B lymphocytes

T helper
(CD4+)

T cytotoxic
(CD8+)

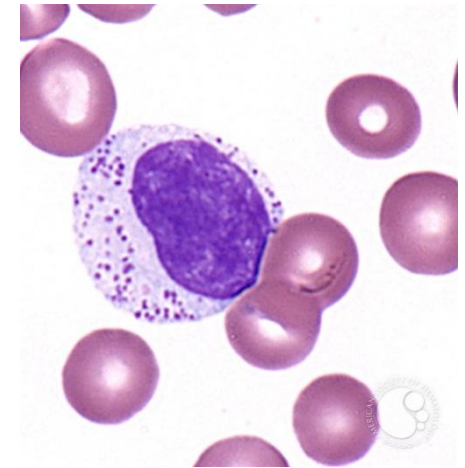
Suppressor
T cell
(CD8+ or CD4+)



Natural killer cells (NULL Lymphocyte)

Kill virus-infected, transplanted
and neoplastic cells
(innate immunity)

Large granular lymphocytes Activated lymphocytes



Innate immunity: We are born with innate immunity. It is non-specific, which means that the innate cells are not able to distinguish one type of pathogen from another.

Cells of innate immunity: Neutrophils, Basophils, Eosinophils, Mast cells, Monocytes (macrophages and dendritic cells), Natural killer cells

Adaptive (acquired) immunity is the body's ability to recognize and respond to specific foreign substances (antigens: microbes, parts of microbes, or non-microbial substances, such as pollen)

Cells of adaptive immunity: B and T lymphocytes

Suppressor T cells switch off the immune response when the stimulus is removed



Damage to suppressor cells can result in **autoimmune disease**

Memory cells allow a more rapid response if the antigen appears again later



which allows a very rapid response upon subsequent exposure to the same antigen.

Basis of immunity/vaccination

Natural killer cells and T cells play a major role in **graft rejection**

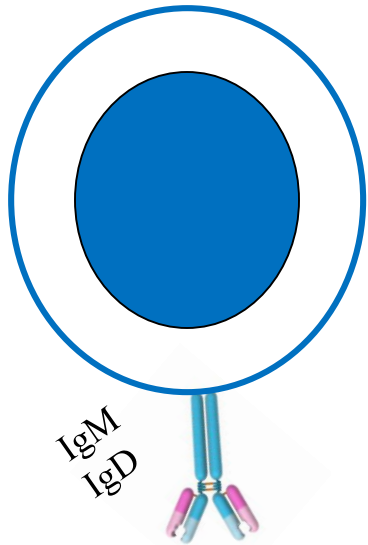
HIV affects Helper T cells

The retrovirus that produces acquired immunodeficiency syndrome (AIDS) infects and rapidly kills helper T cells.

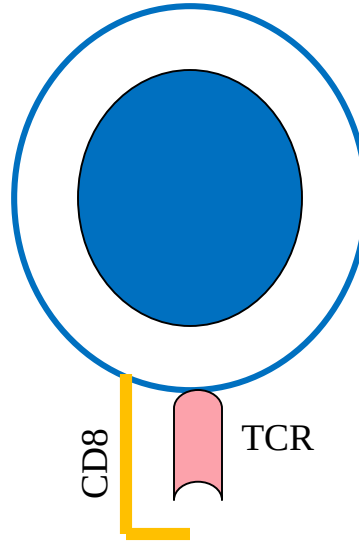


Reduction of this key lymphocyte group cripples the patient's immune system rendering them susceptible to opportunistic bacterial, fungal, protozoan, and other infections that usually dealt with easily in immunocompetent individuals.

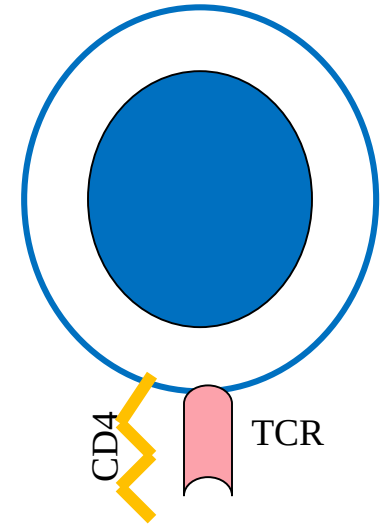
Different types express specific cell surface proteins



B cell



Cytotoxic T cell



Helper T cell

Note: Receptors of B cells are immunoglobulins that bind antigens directly; those on T cells react only with antigen on MHC molecules and this requires the additional cell surface proteins CD4 or CD8.

T lymphocytes are said to be **MHC restricted**

"CD" stands for "cluster of differentiation": are surface molecules that help differentiate one cell type from another

Major histocompatibility complex

MHC

Glycoprotein on cell membrane

Two classes:

MHC-I

On surface of **all nucleated cells**

Coupled to peptide formed within the cell

MHC –II

On surface of **APCs**

Coupled to peptide product of proteins the cells had ingested (peptide product of Ag digestion)

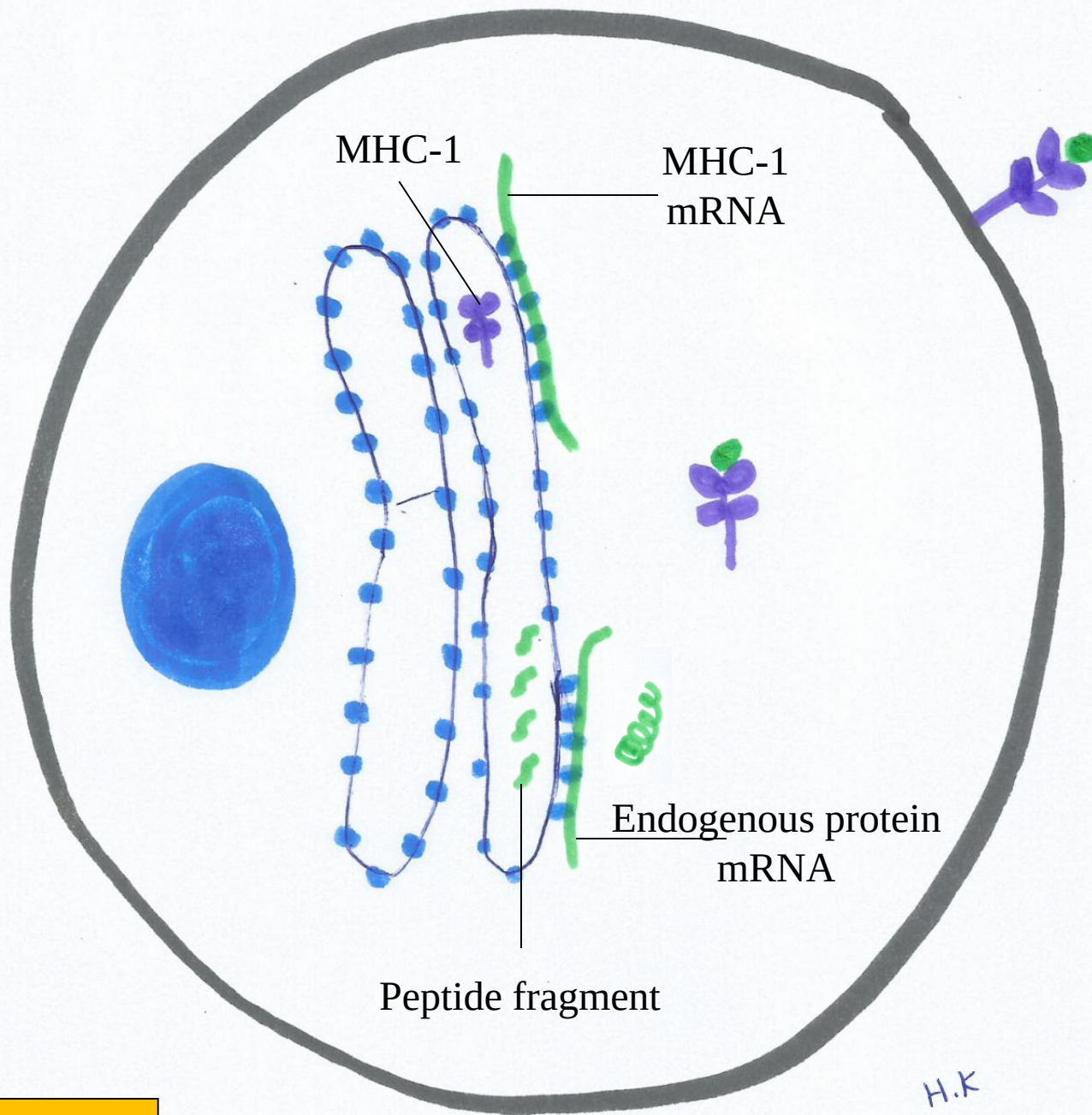
Also called human
leukocyte antigens
(HLAs)

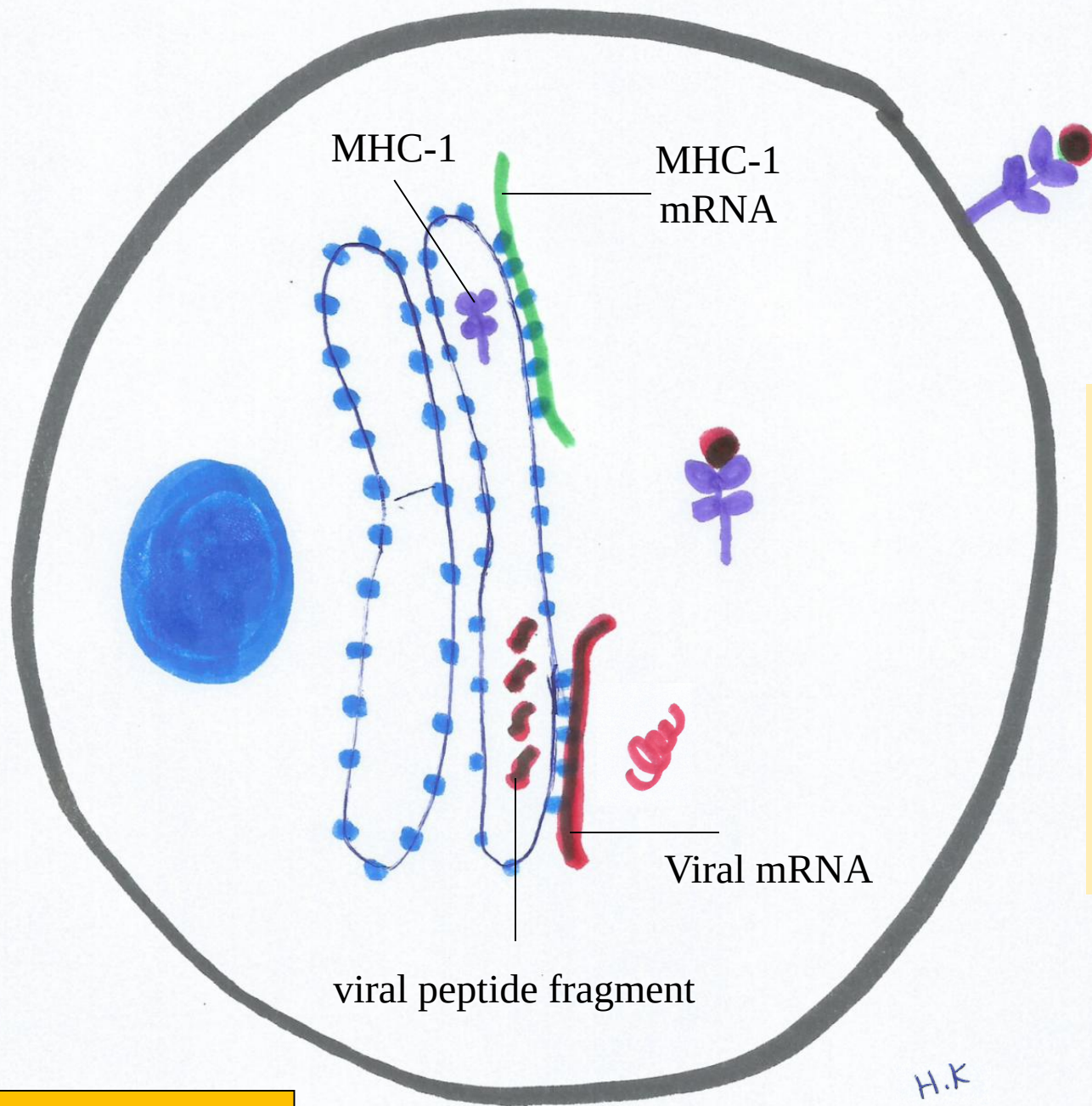
T lymphocytes are specialized to recognize both classes of MHC proteins and the antigens they present



If the MHCs on cells of a tissue graft are not similar to those that T lymphocytes encountered during their development, the grafted cells will induce a strong immune reaction by T cells of the recipient.

To these lymphocytes, the unfamiliar MHC epitopes on the graft's cells are recognized as markers of “non-self ” cells that they must eliminate.

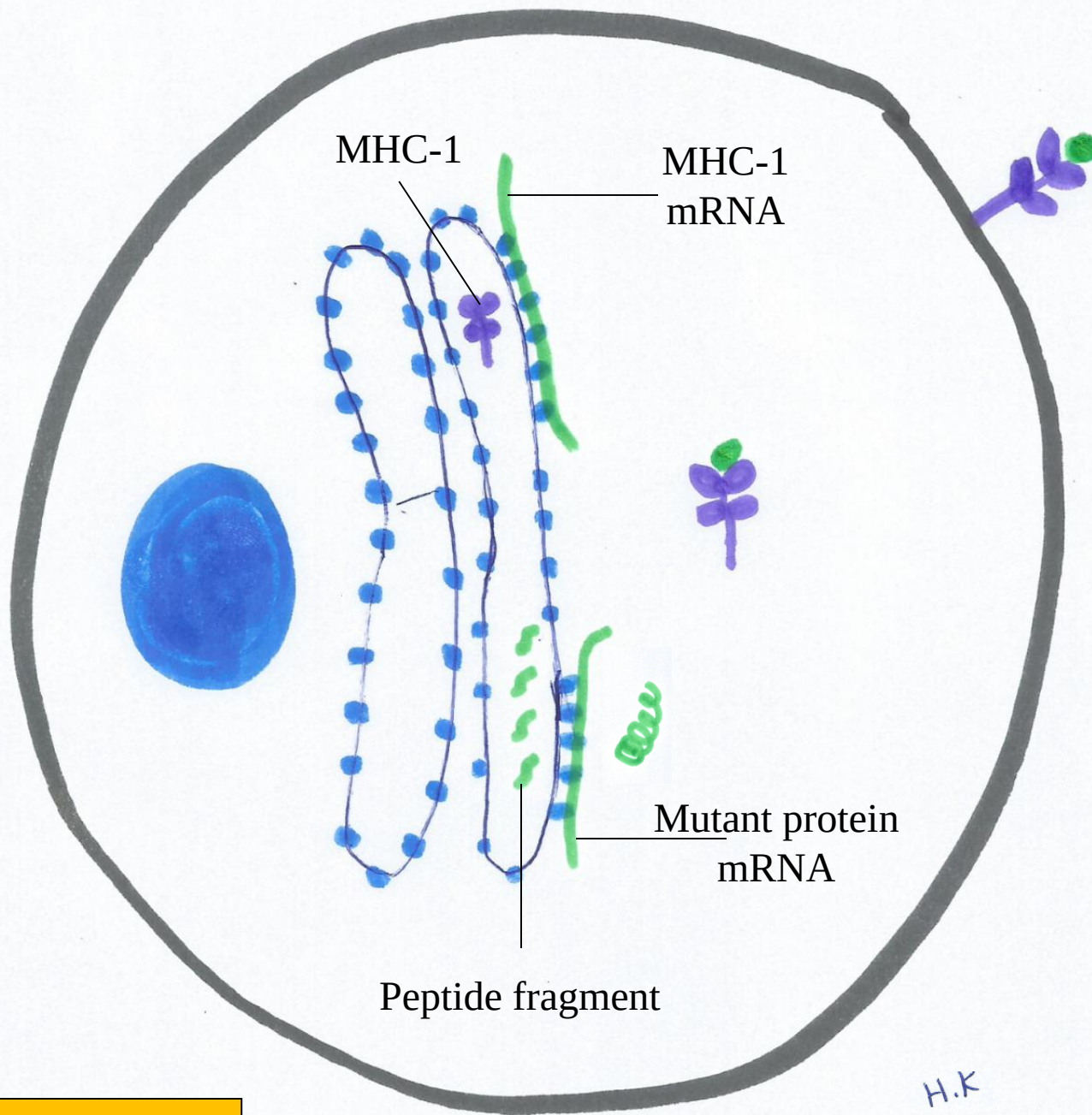




Viral- peptide
bound to
MHC-1

Viral peptide
is derived
from the viral
proteins that
are
synthesized
by the viral
infected cell
(non-self
Antigen)

Viral infected cell



Mutant peptide
bound to
MHC-1

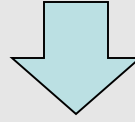
Mutant
peptide is
derived from
the mutant
proteins that
are
synthesized
by the
cancerous cell
(non-self
Antigen)

Cancerous cell

H.K

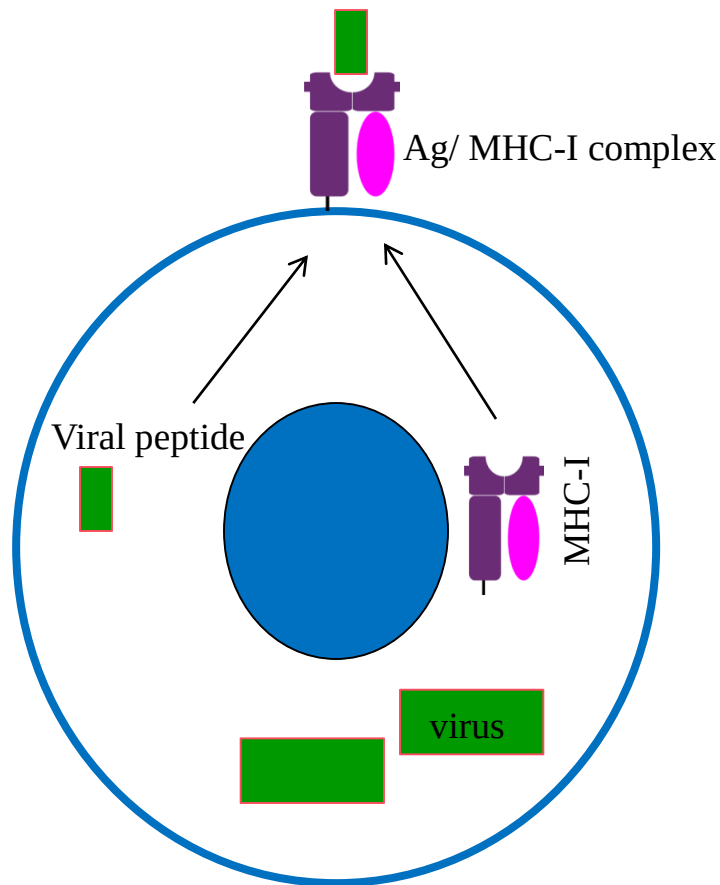
Cytotoxic CD8 T cells:

Antigen in virus infected, transplanted or neoplastic cells bind to MHC-I molecules

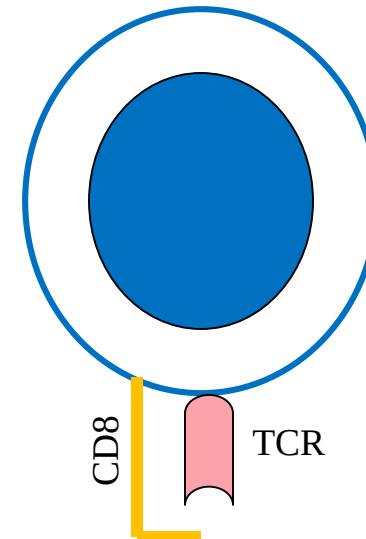


Ag-MHCI complex

Cell-mediated immunity

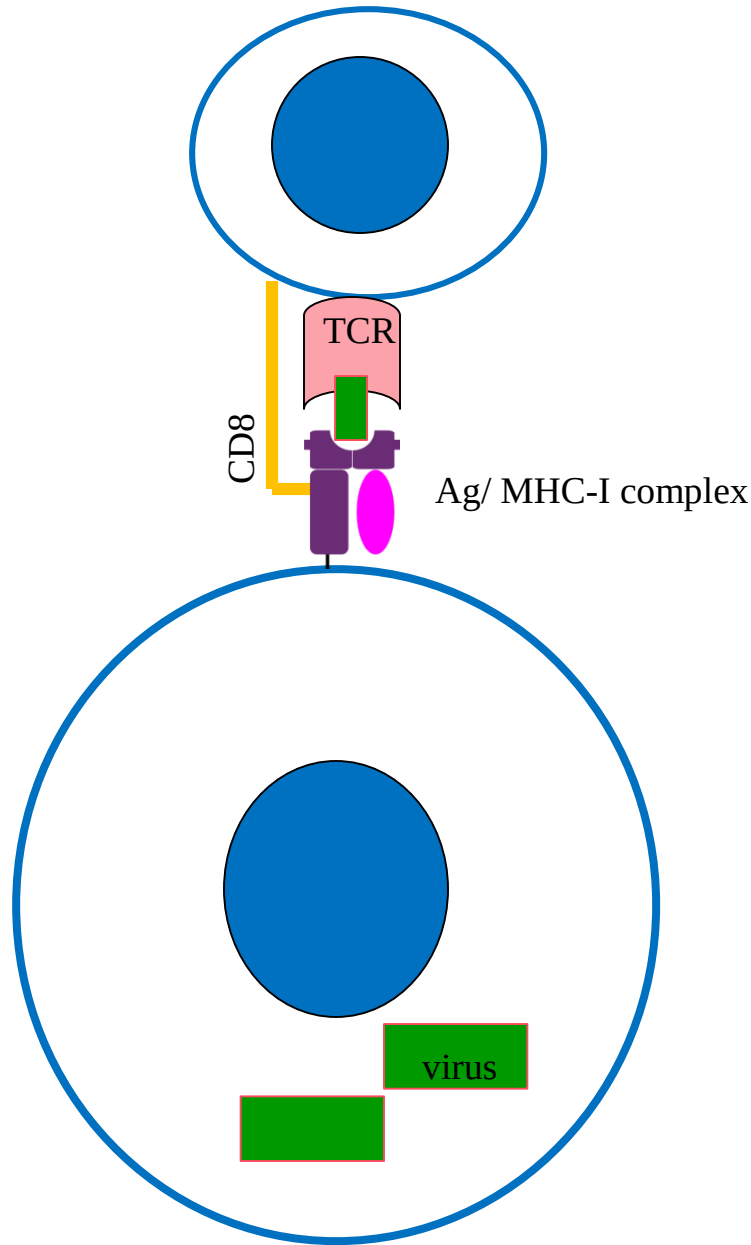


Viral infected cell



Cytotoxic T cell

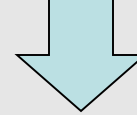
Cytotoxic T cell



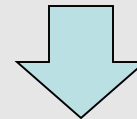
Viral infected cell

When the Ag- MHC-I complex binds to receptors on cytotoxic CD8 T cells

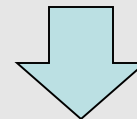
They



Proliferate
Activate



Release
Perforins and granzymes
(proteases)



Perforins form pores in the cell membrane through which granzymes can enter, inducing apoptosis

Ag/ MHC-II complex

Antigen presenting cell
(macrophage, dendritic cell,
B lymphocyte)

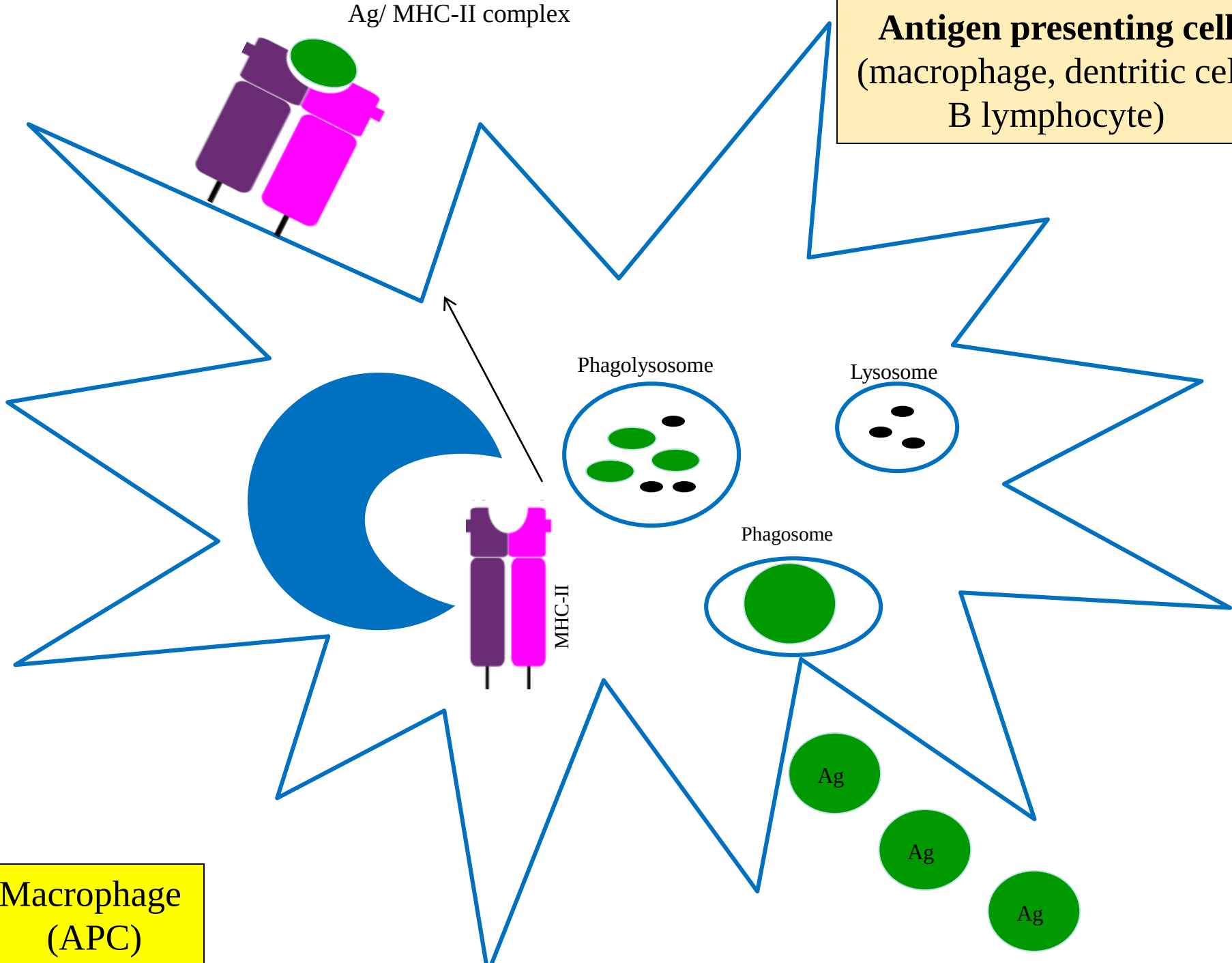
Phagolysosome

Lysosome

Phagosome

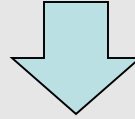
MHC-II

Macrophage
(APC)



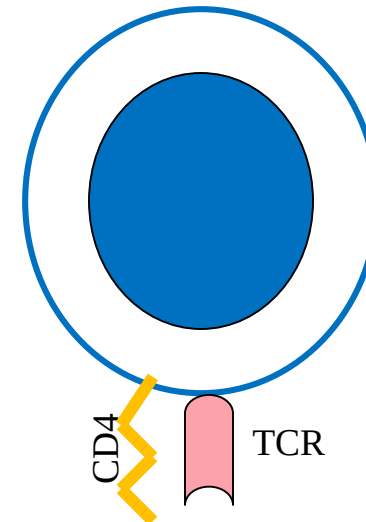
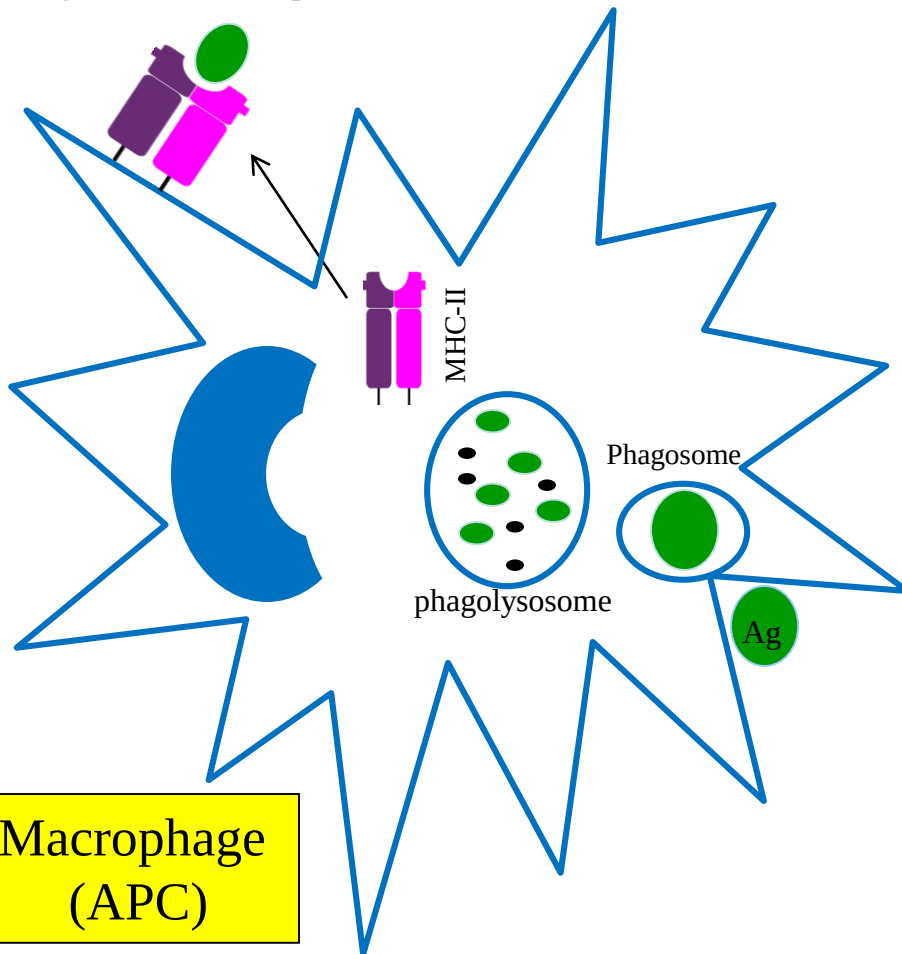
Helper CD4 T cells:

When Ag is phagocytosed by antigen presenting cells (APCs)
e.g macrophages, dentritic cell and B lymphocytes
It binds to MHC-II molecules



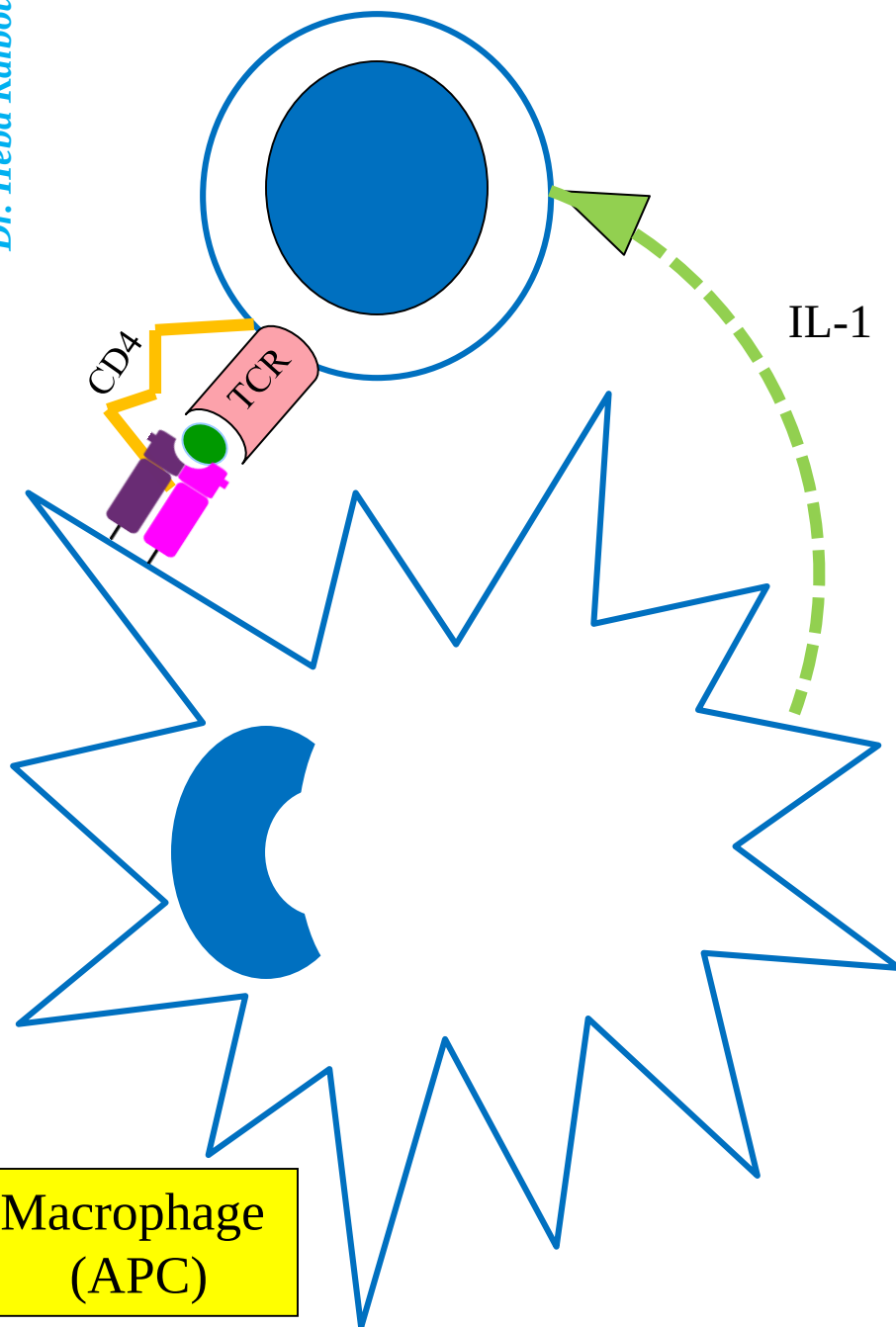
Ag-MHCII complex

Ag/ MHC-II complex



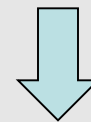
T Helper cell

T Helper cell

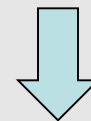


When the Ag- MHCII complex binds to receptors on Helper CD4 T cells

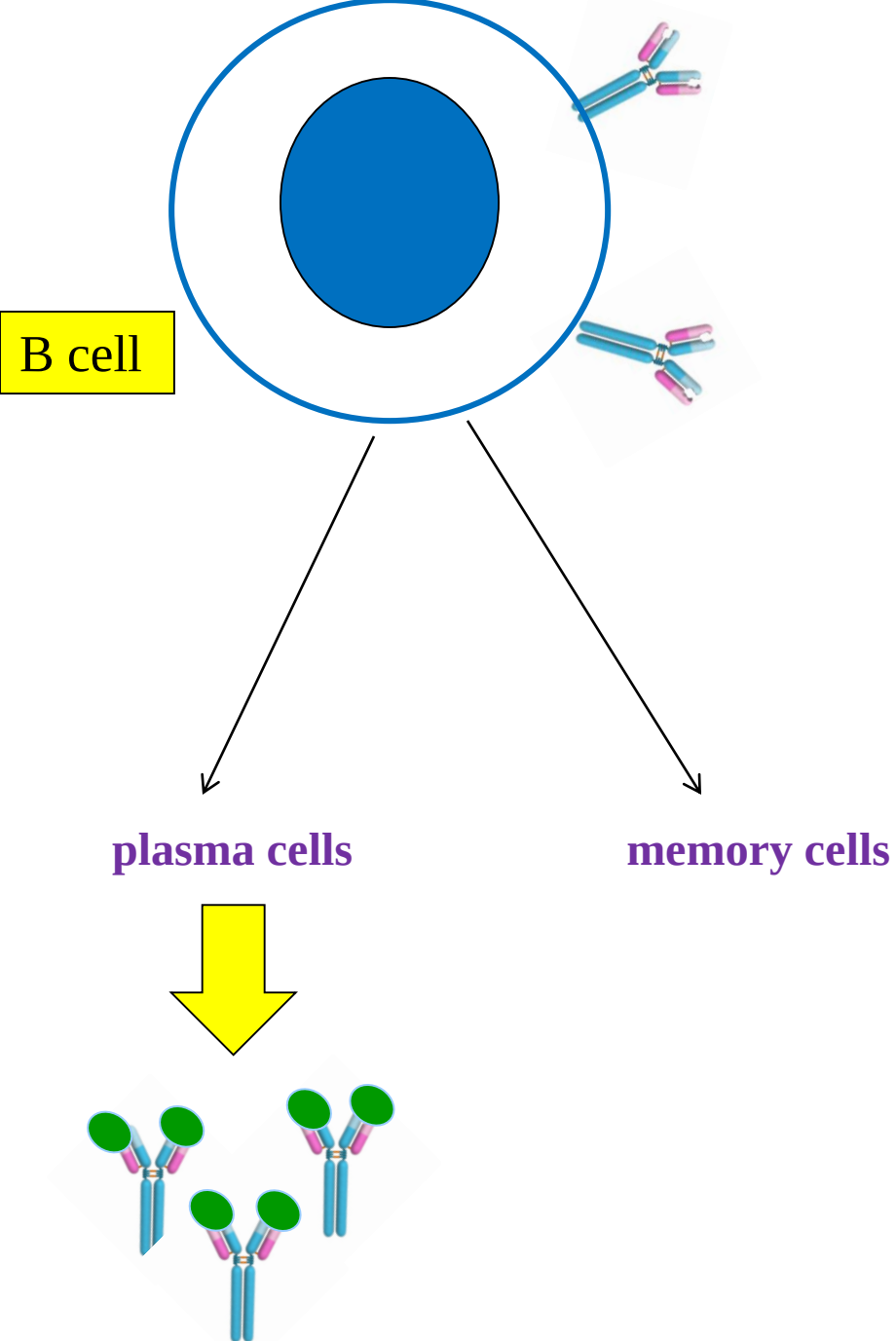
They



Proliferate
Activate



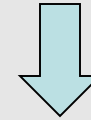
Secrete Lymphokines (cytokines) to Stimulate
T and B cells



When a B lymphocyte is stimulated by T helper cells



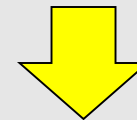
Proliferate
Activate



Activated B lymphocytes:

1- differentiate into **plasma cells** (secrete antibodies)

2- differentiate into **memory cells**
(Rapid response on the 2nd exposure to the same Ag)



Life long immunity (vaccination)

Humoral immunity

B cells:

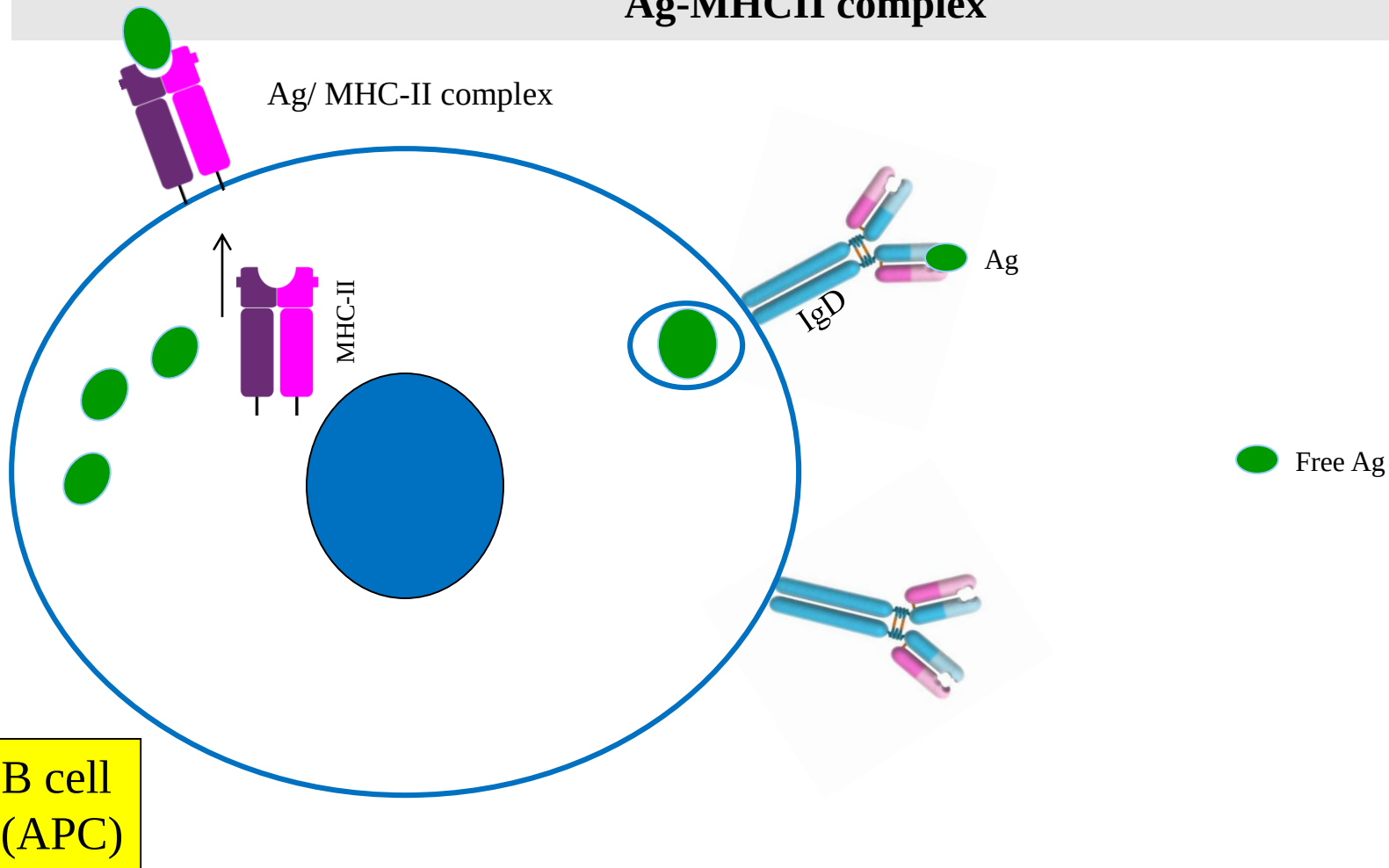
When the specific Ag binds to receptors on B cells

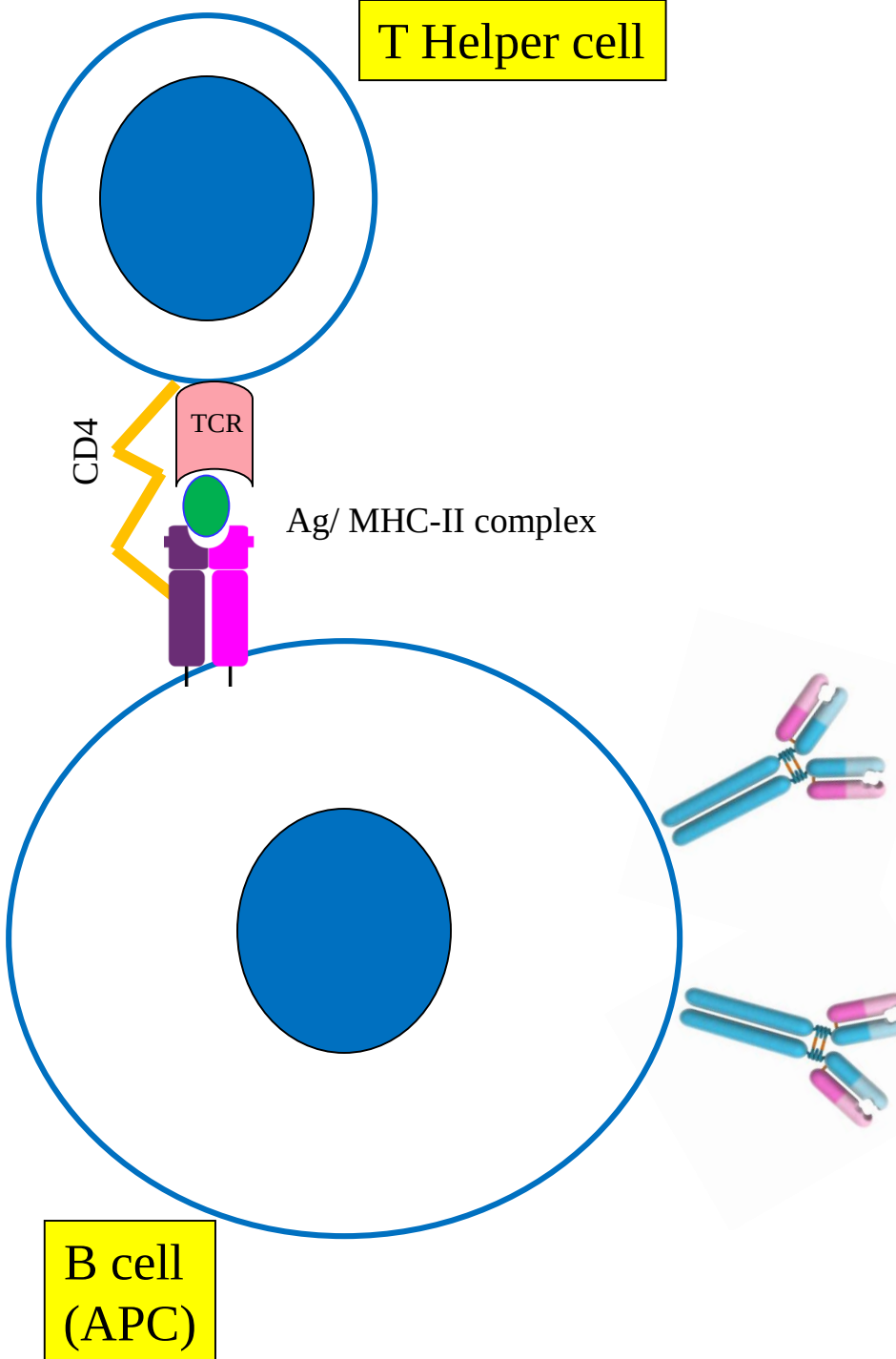


receptor-mediated endocytosis and fragments of the Ag bind to MHC-II molecules

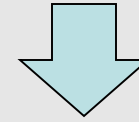


Ag-MHCII complex

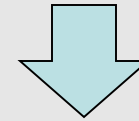




T Helper cells bind to Ag-MHCII complex on the B cells



Stimulates proliferation and differentiation (activation) of B cells



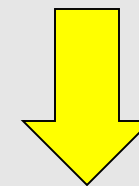
B cells

Proliferate
Activate

Activated B lymphocytes:

1- differentiate into **plasma cells**
(secrete antibodies)

2- differentiate into **memory cells**
(Rapid response on the 2nd exposure to the same Ag)



Life long immunity (vaccination)

Never Let Monkeys Eat Bananas

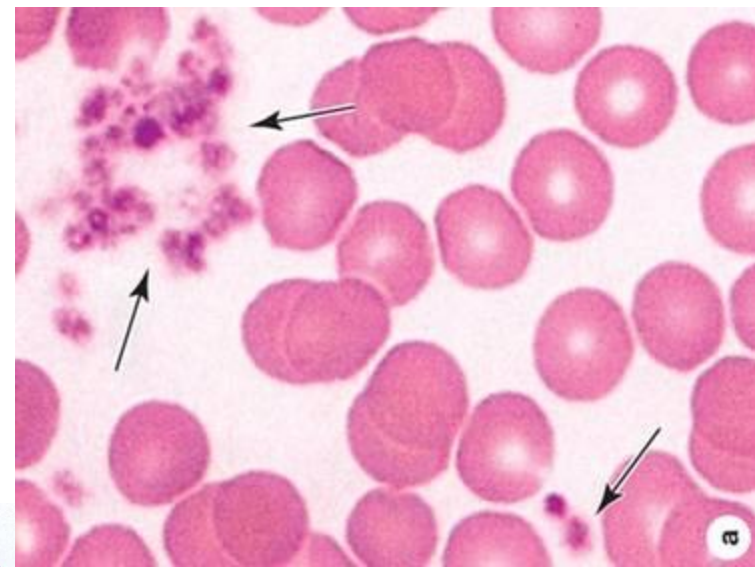
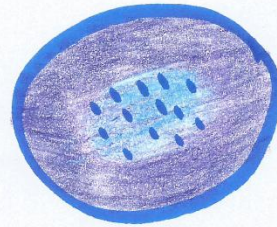


Most common to least

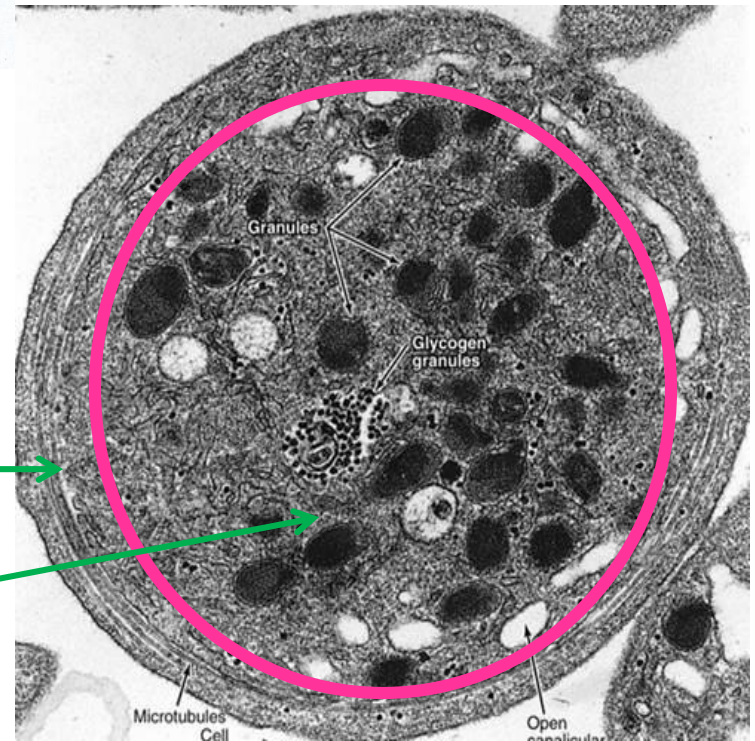
***Which type of lymphocyte is
most abundant in peripheral
blood?***

Thrombocytes (Platelets)

- Small non-nucleated cytoplasmic fragments
- Formed by fragmentation of the cytoplasm of **megakaryocytes** in the bone marrow
- **Number: 200,000-400,000/mm³**
- **Shape: biconvex discs**
- **Cytoplasm: purple, granular**
- **Diameter: 2-4 um**
- **Lifespan about 10 days**
- Control the bleeding by plugging the defects in blood vessels and activating blood clotting cascades

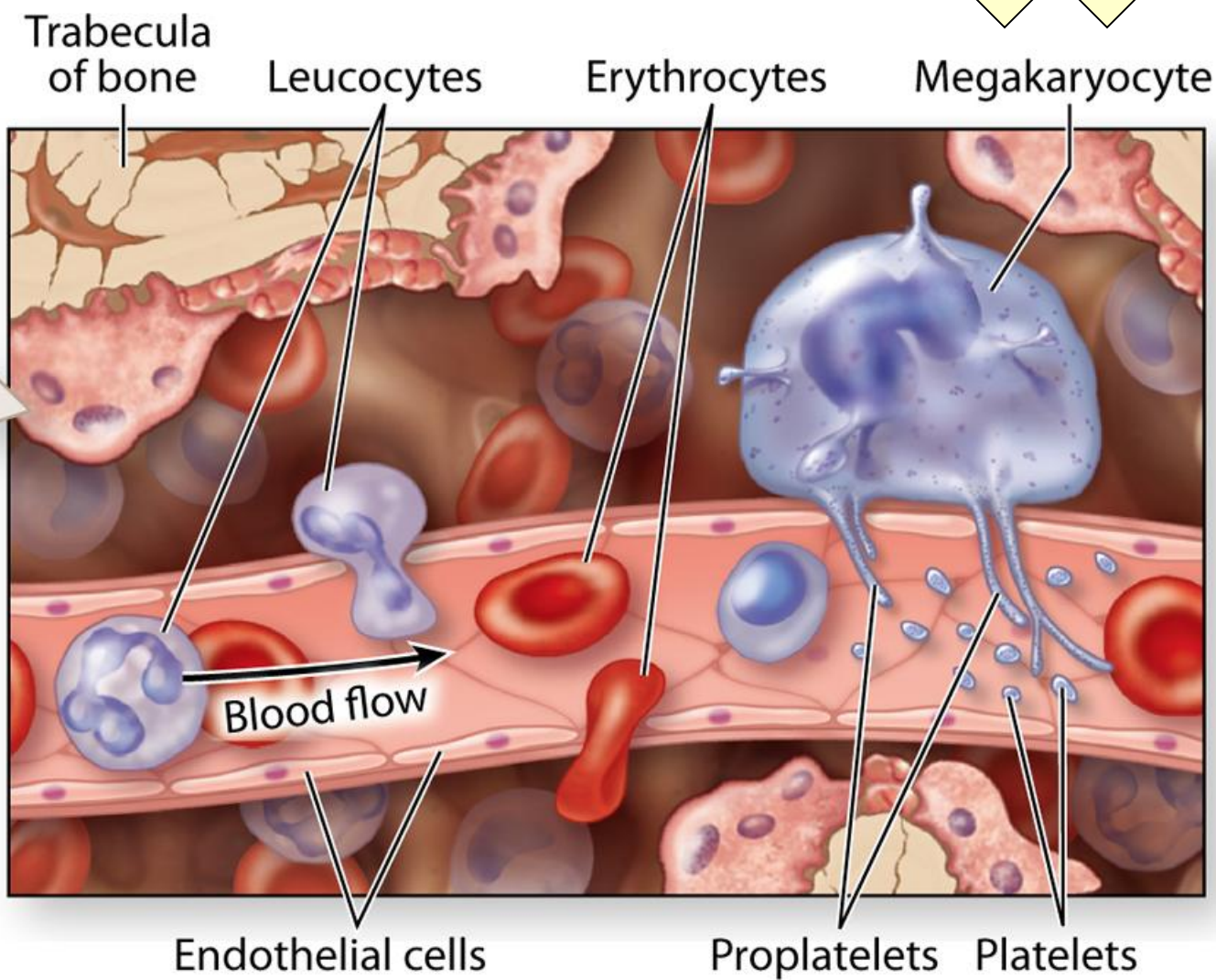
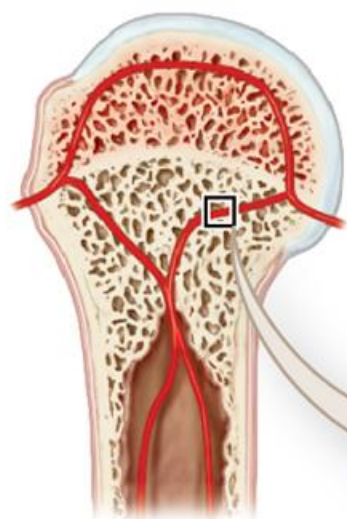


In stained blood smears, platelets often appear in clumps



Platelet has 2 zones

- Outer pale basophilic (clear) peripheral zone: **hyalomere**
- Central dark granular zone: **granulomere**



Hyalomere: contains cytoskeleton and membranous channels

Cytoskeletal elements

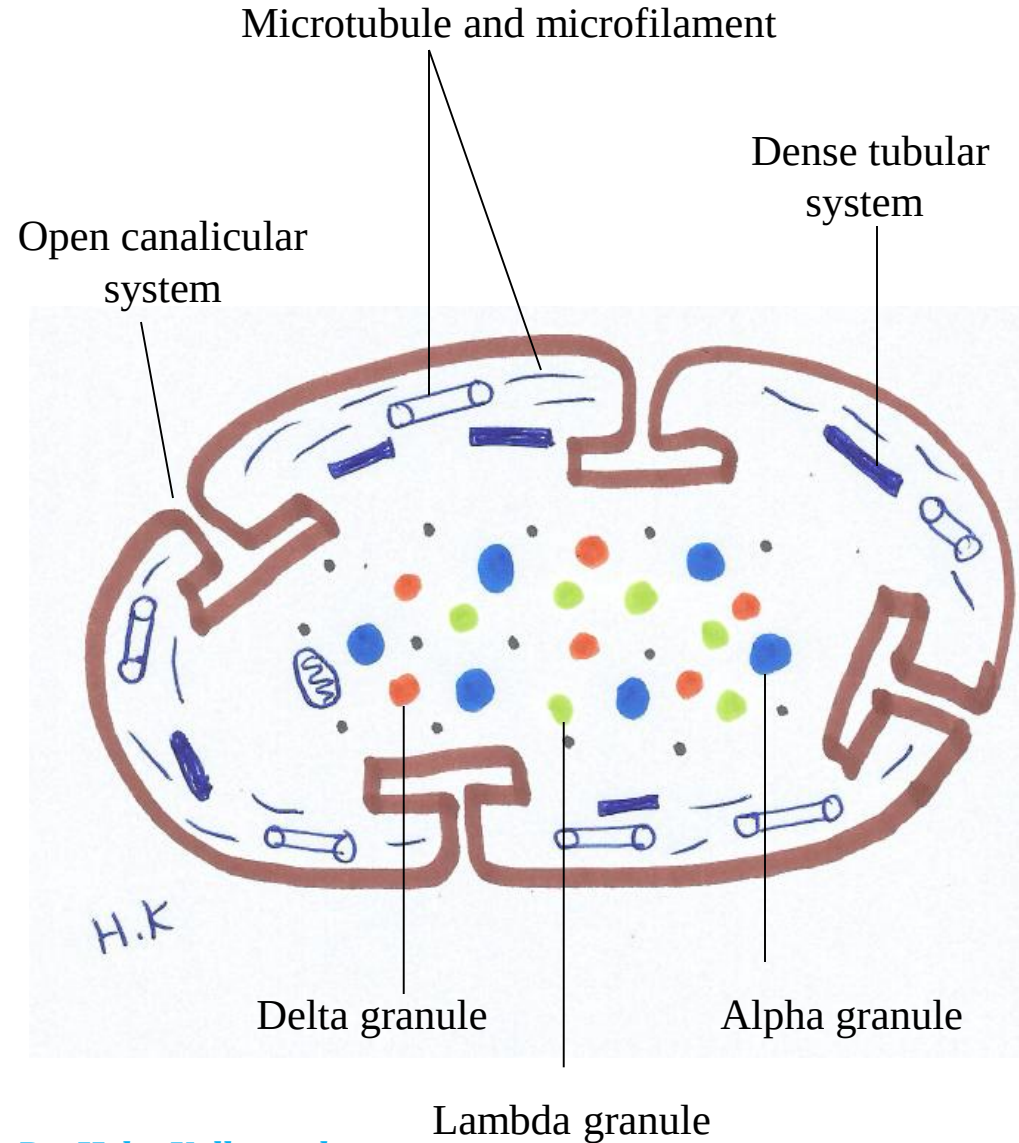
- Microtubule
- Actin filaments

Maintain shape and help contractions of platelets and squeezing, clot retraction

Membrane channels

- Open canalicular system
- Dense tubular system

Have thick glycocalyx



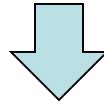
Granulomere: contains granules and organelles

Alpha granules: clotting factors, growth factors

Dense (delta) granules: serotonin (absorbed from plasma), ATP, ADP

Lambda granules: lysosomes (aid in clot resorption)

Their main function is to continually monitor the vascular system and detect any damage to the endothelial lining of the vessels. If the endothelial lining breaks, the platelets adhere to the damaged site and initiate a highly complex chemical process that produces a **blood clot**



Thus preventing blood loss

