BLOCK HEM-210

Heamatology - lymphatic System

Lecture (I)

Haematology

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Learning objectives

- **After this lecture, students should be able to:**

- **Describe the cytological characteristics of Blood Elements (RBCs, WBCs, Platelets)**
- **Differentiate between the different types of WBCs**
- **Differentiate between RBCs & WBCs**
- **Describe the constituents of bone marrow.**
- **Differentiate between 2 types of bone marrow, red and yellow.**

- **Blood is a specialized type of CT formed of blood cells in a fluid matrix (plasma).**
  - **Blood cells (45%) are of three types:**
  -
    - **Erythrocytes (RBCs): 4-6 million per cubic millimeter.**
    - **Leucocytes (WBCs): 4-11 thousand per cubic millimeter.**
    - **Thrombocytes (platelets): 150-400 thousand per cubic millimeter.**
  -
  - **Plasma (55%) is formed of water, gases, inorganic substances, organic substances, hormones and enzymes. The volume of blood is about 5 liters.**

- **Functions of the blood:**
  - Transport of oxygen, nutrients and hormones to tissues.
  - Removal of carbon dioxide and waste product from tissues.
  - Regulation of body temperature.
  - Regulation of acid-base balance.
  - Protection against infections.

Red blood corpuscles (RBCs) or erythrocytes

- **LM: they are rounded biconcave discs (with pale thin center and dark thick periphery).**
- **EM: they are corpuscles and not true cells (as they have neither nuclei nor organelles) so cannot divide.**
- **Adaptation of red blood corpuscles for their function:**

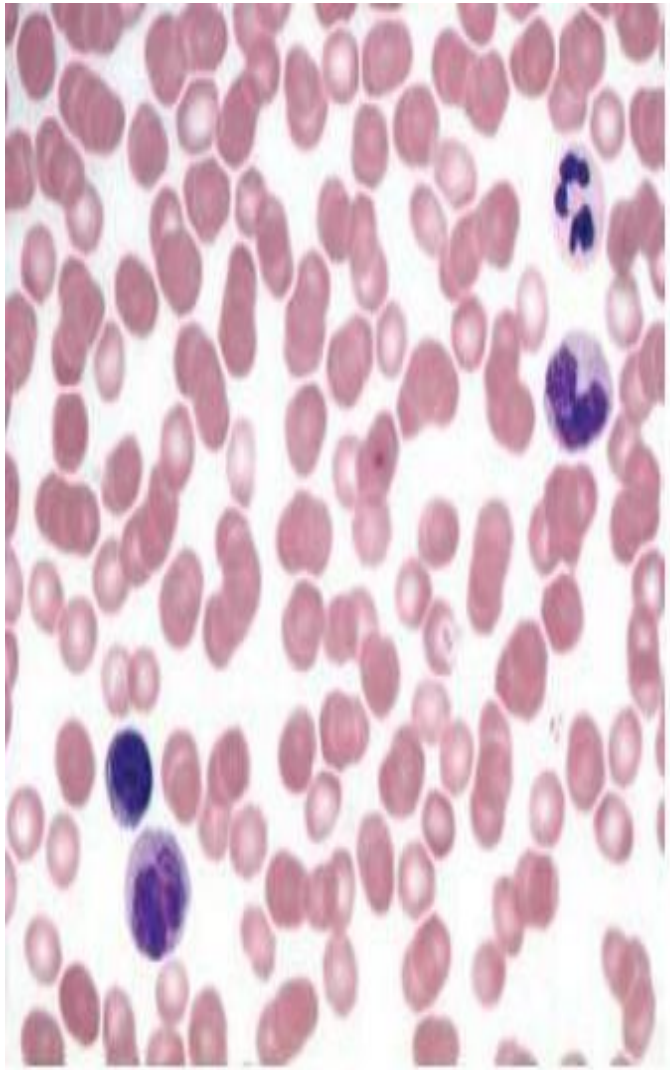
✓ They contain free spaces for:

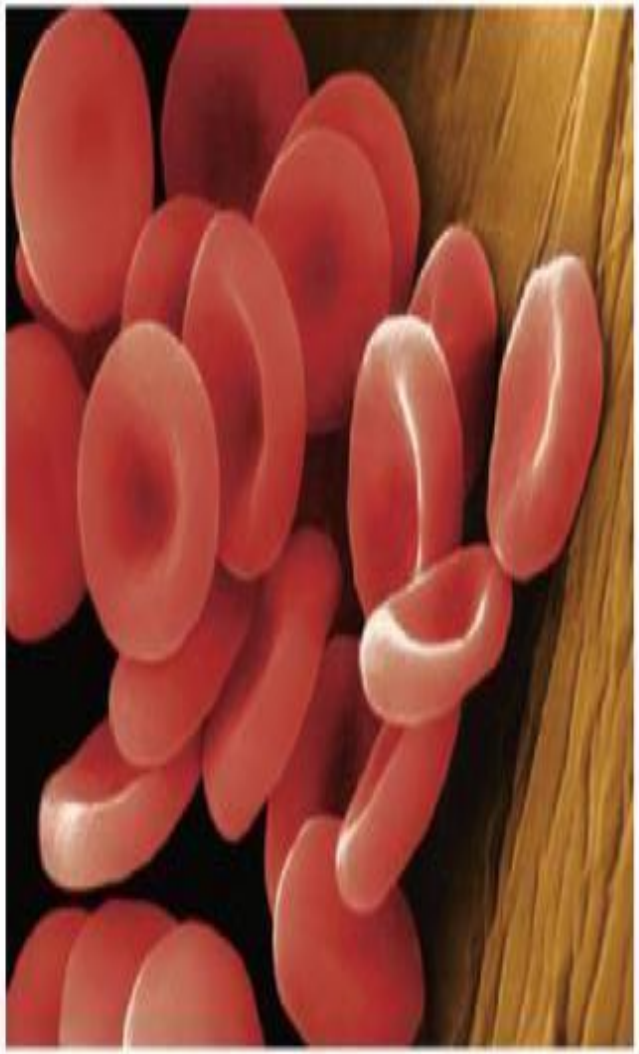
- **Hemoglobin (33%): to combine easily with O_2 and CO_2.**
- **Enzymes (1%): Hb reductase (for O_2) and carbonic anhydrase (for CO_2).**

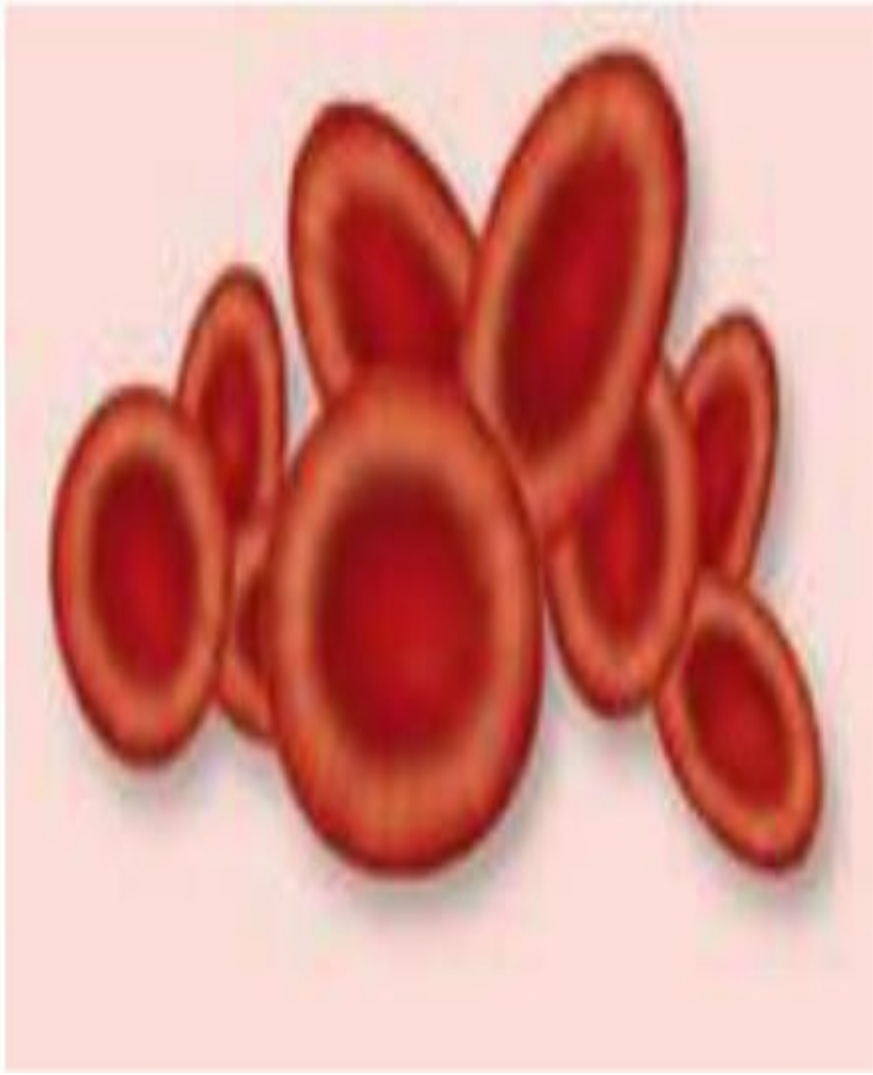
✓ The cell membrane is:

- **Biconcave (to increase their surface area for gas exchange).**
- **Formed of lipoprotein (to be highly selective for O_2 and CO_2 exchange).**
- **Elastic and flexible (to allow their squeeze inside narrow capillaries).**

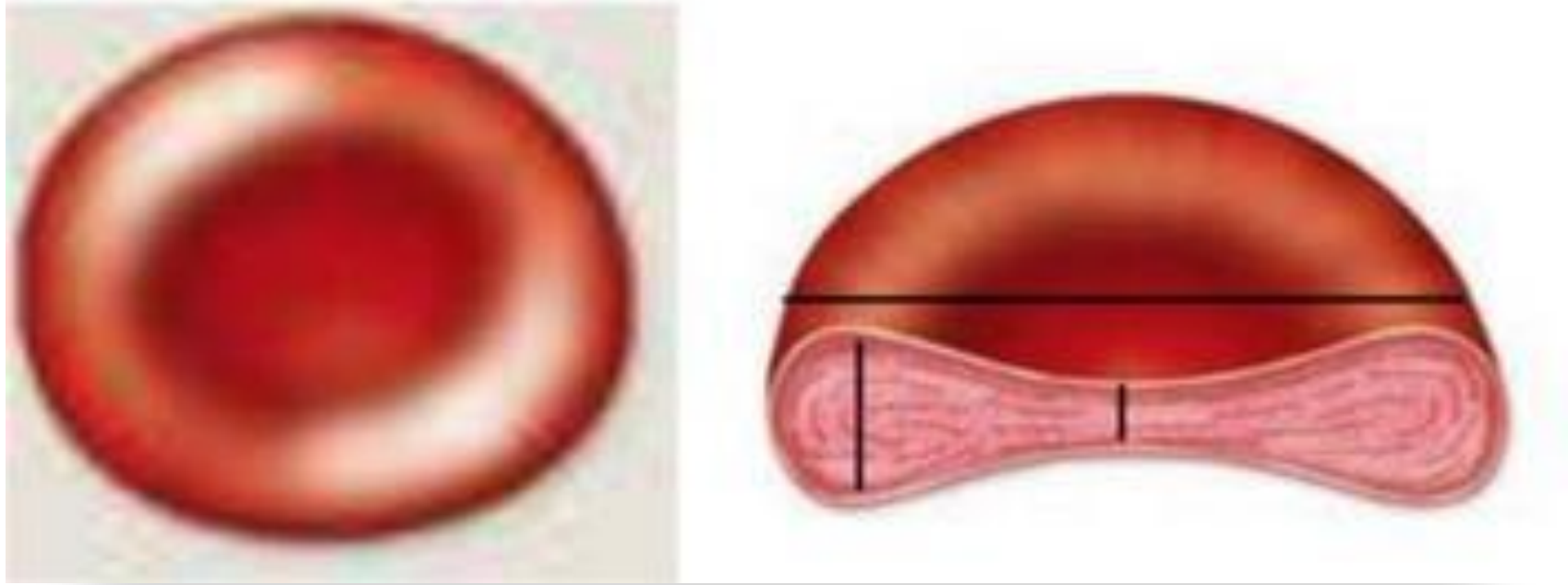
- **Osmotic pressure of RBCs and plasma is isotonic (0.9% saline) and their life span is about 4 months.**
- **Old RBCs are phagocytosed in liver and spleen (after that iron is reused while pigments are excreted).**



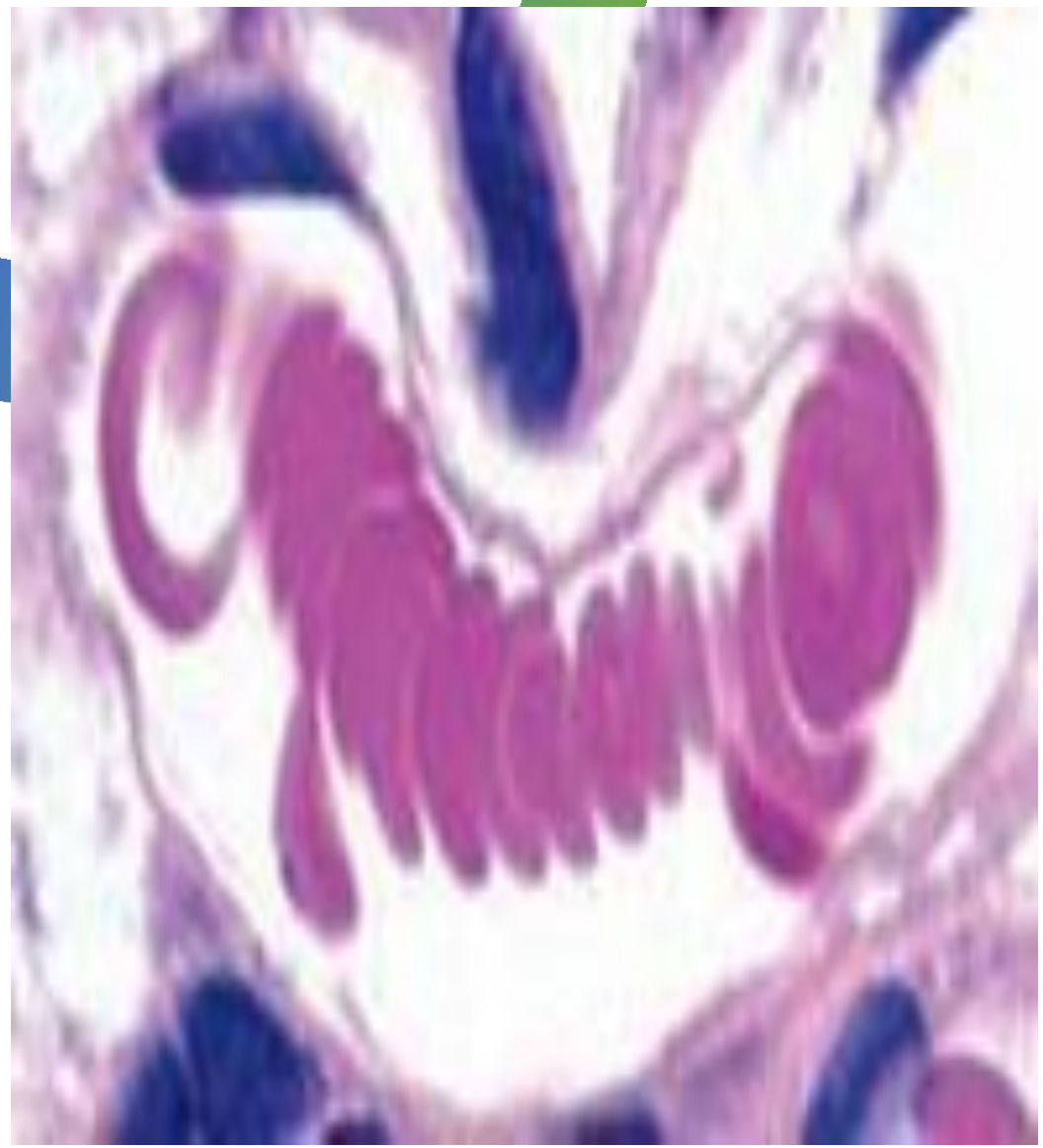




- **Normal number of RBCs:**
- -In ♀ 4.5-5 million/3mm (due to menstruation and ♀ hormones). o In ♂ 5-5.5 million/3mm.
- o Anemia (RBCs less than 4 million/3mm): it has many types:
- Deficiency anemia: due to deficiency of iron, vitamin B12, copper, proteins ...
- Hemolytic anemia: due to destruction of RBCs which may be:
- Congenital: ▯ Abnormal cell membrane (spherocytosis).
- Decrease of G6PD enzymes (favism).
- Abnormal Hb F (thalassemia).
- Abnormal Hb S (sickle cell anemia).
- Acquired: incompatible blood transfusion, malaria, toxins ...
- Hemorrhagic anemia: due to hemorrhage from wound, nose, menses, piles ...
- Aplastic anemia: due to bone marrow depression by radiation, drugs ...
- o Polycythemia (RBCs more than 6 million/3mm): occurs with hypoxia (▯ O2) whether physiological (high attitude and exercise) or pathological (lung disease or heart disease).



- **Size of RBCs:**
- **Normal size of RBCs: diameter 6-9 (7.5) µm**
- **- central thickness 0.75 µm .**
- **Peripheral thickness 2.6 µm.**
- **Abnormal size of RBCs:**
- **o Increase diameter (macrocytic anemia).**
- **o Decrease diameter (microcytic anemia).**
- **o Different diameters (aniso-cytosis).**



- **Shape of RBCs:**
- **Normal shape of RBCs**: rounded biconcave non-nucleated discs showing rouleaux appearance (as rows of coins).
- **Abnormal shape of RBCs:**
  - Rounded biconvex (sphero-cytosis).
  - Oval (ovalo-cytosis).
  - Pear-shaped (poikilo-cytosi

- Color of RBCs:
- Normal color of RBCs: hemoglobin is greenish yellow (if unstained) and acidophilic (if stained by Leishman stain).
- Abnormal color of RBCs:
- o Increase hemoglobin (hyper-chromic RBCs).
- o Decrease hemoglobin (hypo-chromic anemia). o Central hemoglobin (target cell anemia).

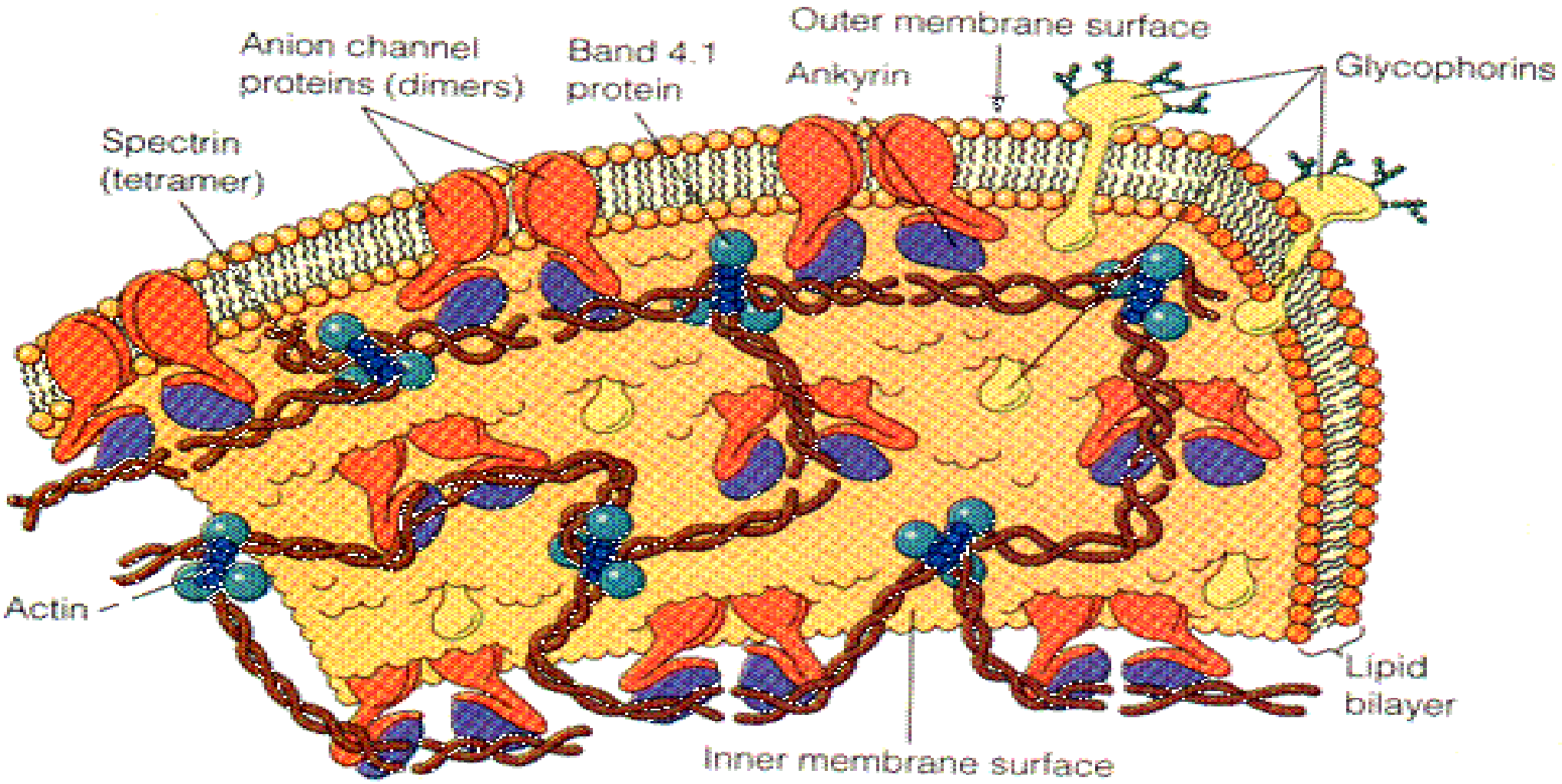
- **How the structure of the R.B. Cs is adapted to their function?**

1-The biconcave disc appearance increases the surface area by about 25% that increase the respiratory efficiency.

2-Erythrocytes are normally quite flexible, which permits them to bend and adapt to the small diameters and irregular turns of capillaries.

- **Several cytoskeletal proteins (ankyrin, spectrin, and actin) stabilizes the membrane, maintains the RBC's shape, and provides its elasticity**

3. The glycosylated extracellular domains of integral proteins in the Erythrocyte cell membrane (glycophorins) include antigenic sites for the ABO blood typing system. Another type of antigen is present in 85% of individuals which is the Rh antigen (D antigen)and is called Rh positive, while the remaining 15% have no antigen and called Rh negative


Outer membrane surface
Anion channel proteins (dimers)
Band 4.1 protein
Ankyrin
Glycophorins
Spectrin (tetramer)
Actin
Lipid bilayer
Inner membrane surface

- Blood groups

- **Blood groups are important for blood transfusion and for medico -legal applications.**
- **There are 4 types of blood groups:**
- **1. Group A:**
- **– Genotype: A1A1, A2A2, A1O or A2O.**
- **– Phenotype: antigen A on RBCs and anti-B antibody in plasma.**
- **2. Group B:**
- **– Genotype: BB or BO.**
- **– Phenotype: antigen B on RBCs and anti-A antibody in plasma.**
- **3. Group AB:**
- **– Genotype: A1B or A2B.**
- **– Phenotype: antigens A and B on RBCs without antibodies in plasma (universal recipient).**
- **4. Group O:**
- **– Genotype: OO.**
- **– Phenotype: no antigens on RBCs (universal donor) with anti-A and anti-B antibodies in plasma.**

- There are other less important blood subgroups as MNSs, P, Duffy Lewis, Kell and Rh.

- Rhesus (RH) factor is an antigen present on RBCs of 85% of individuals (Rh +ve persons)
- it is important for females because positive fetus may die by hemolysis (erythroblastosis fetalis) if his negative mother was sensitized by previous exposure to positive RBCs.

Blood Type	Donate Blood To	Receive Blood From
A+	A+ AB+	A+ A- O+ O-
O+	O+ A+ B+ AB+	O+ O-
B+	B+ AB+	B+ B- O+ O-
AB+	AB+	Everyone
A-	A+ A- AB+ AB-	A- O-
O-	Everyone	O-
B-	B+ B- AB+ AB-	B- O-
AB-	AB+ AB-	AB- A- B- O-

- **White blood cells (WBCs) or leucocytes**
- **WBCs are true cells (as they have nuclei, organelles and inclusions).**
- **They are colorless (devoid of hemoglobin) but appear white when packed together.**
- **They have amoeboid movement to penetrate capillaries and perform their phagocytic function in CT.**

- **Number of WBCs:**

- **Normal number of WBCs:**
- **WBCs count 4-11 thousand/3mm and around 16 thousand/3mm at birth.**
- **Abnormal number of WBCs:**
- **o Leucopenia (WBCs less than 4 thousand/3mm): occurs with typhoid fever,influenza viral infection, some drugs and radiation.**
- **o Leukocytosis (WBCs more than 11 thousand/3mm): which may be physiological (pregnancy, newborn, cold bath ...) or pathological (acute and chronic infections).**

• **Types of WBCs: according to types of granules leucocytes are classified to:**

• **1. Granular leucocytes (with specific and non-specific granules):**

• **basophils, eosinophils and neutrophils.**

• **2. Non-granular leucocytes (with only non-specific granules): monocytes and lymphocytes (T and B).**

	count (/ ^{3}mm)	diameter (µm)	life span	nucleus	specific granules
RBCs	4-6 million	7.5 µ	4 months	absent	absent
platelets	150-400 th.	2-4 µ	5-10 days	absent	present
WBCs	4-11 th.	6-18 µ	day-years	present	may be

Differential leucocytic count (percentage of each type of leucocytes relative to total leucocytic count):

	basophils	00 -0.75 %	12-15 µ	months	S-shape	histamine
	eosinophils	01-03 %	12-16 µ	1-2 weeks	bi-lobed	histaminase
	neutrophils	57-67 %	12-15 µ	1-4 days	2-5 segments	collagenase
	monocytes	3-7 %	14-18 µ	days-years	kidney-shape	non
	lymphocytes	25-33 %	06-18 µ	hours-ys	1 segmnt	non
	▪ small	▪ 15-20 %	▪ 06-09 µ		▪ dark	
	■ large	■ 05-10 %	■ 09-18 µ		■ pale	

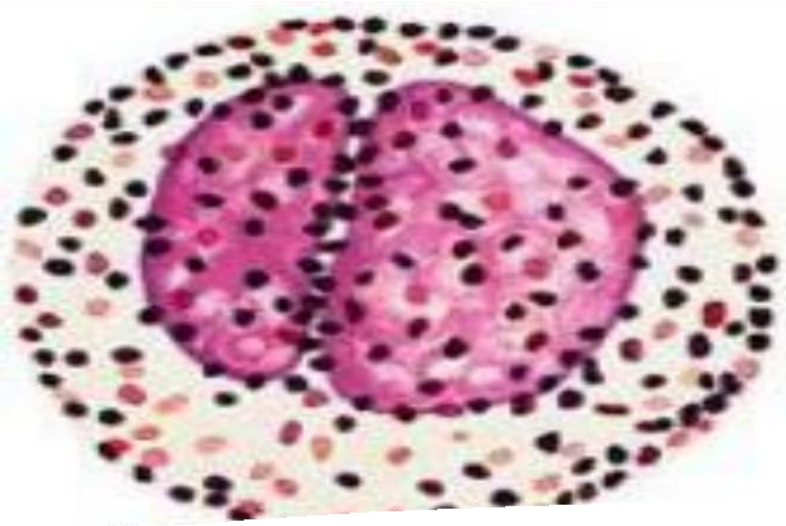
T-lymphocytes count 60-80 % of all lymphocytes and can life 2 years while ○ B-lymphocytes count 25-30 % of all lymphocytes and can life 3 months

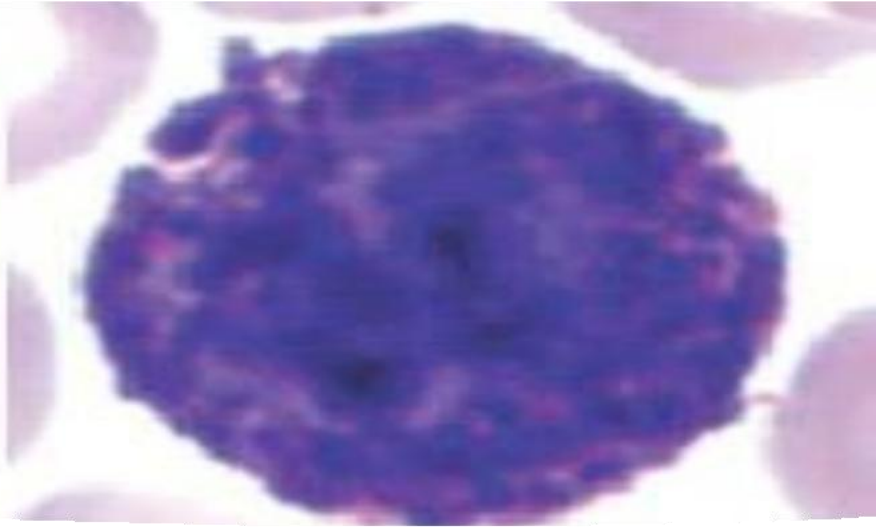
- Counting of blood cells:
- Counting of RBCs, WBCs and platelets are made by:

- Haemo-cyto-meter that is formed of: diluting pipette of RBCs, diluting pipette of WBCs and counting slide.

- Differential leucocytic count is made by:

Examination of blood film (stained by neutral Leishman stain).





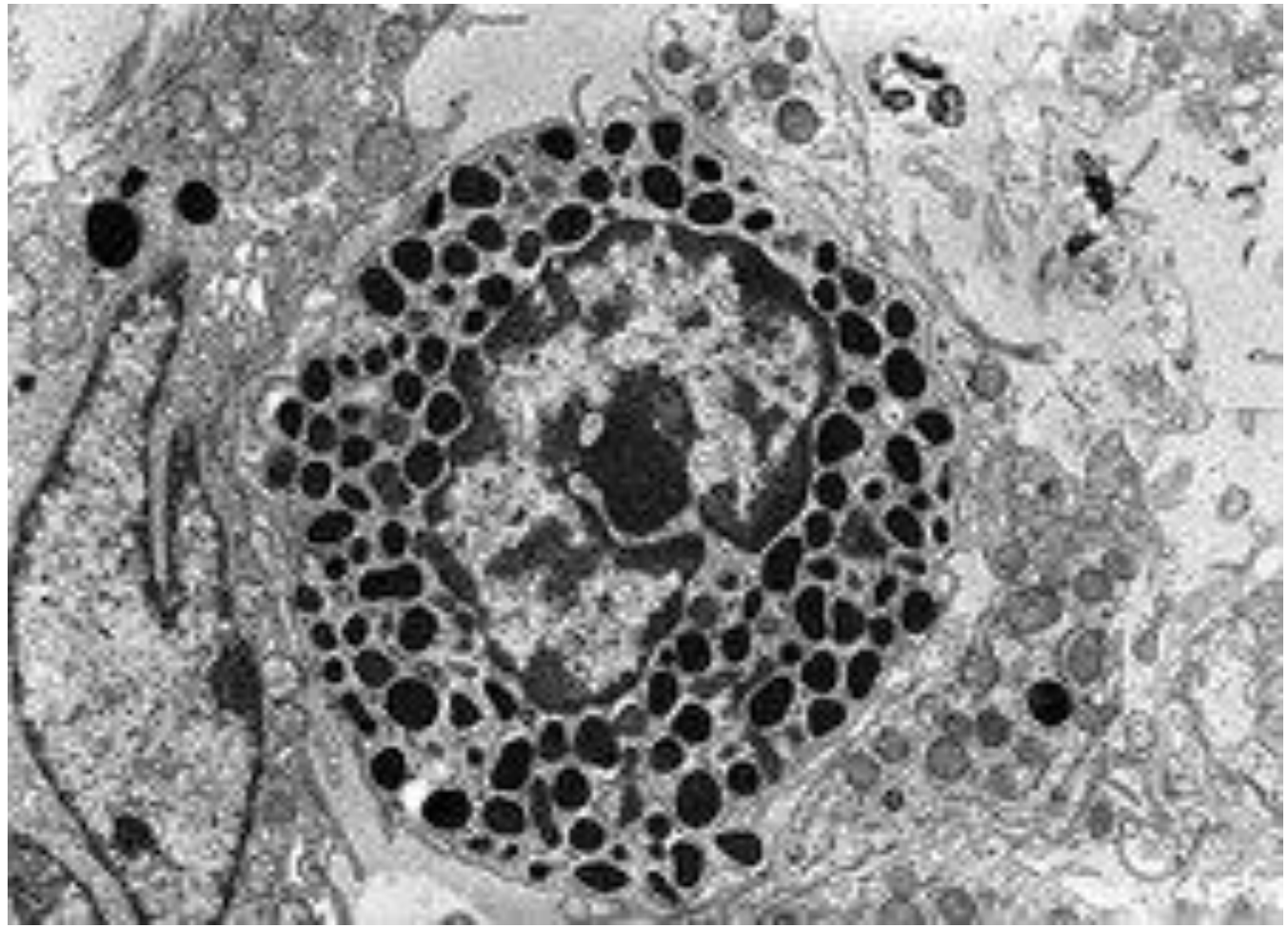
Basophils (0-0.75 % of leucocytes):

1.

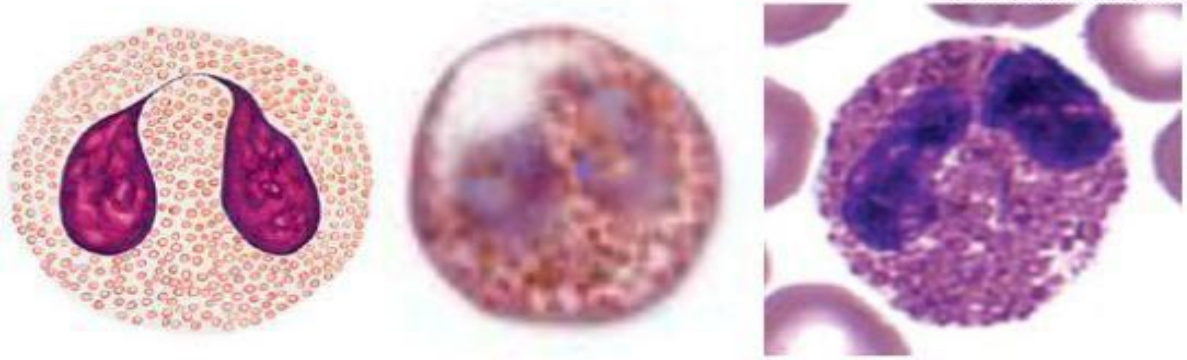
Concerned with allergy production.

- **The diameter of basophils is 12-15 µm and their life span is months.**
- **LM: Nucleus of basophil is single, irregular and S-shaped.**
- **EM: Granules:**

1. **1ry non-specific azurophillic granules (primary lysosomes).**
2. **2ry specific basophilic large granules as that of mast cells (histamine, heparin and eosinophil chemotactic factor "ECF") - these granules mask nucleus and can stained by Gimsa.**



- **Functions**: production, storage and secretion of histamine (capillary vasodilator released during allergy), heparin (anticoagulant) and eosinophil
- chemotactic factor "ECF" (that attract eosinophils to terminate allergy).
- **Basophilia** (increase number of basophils): It occurs in allergic diseases, parasitic infestations, liver cirrhosis ...

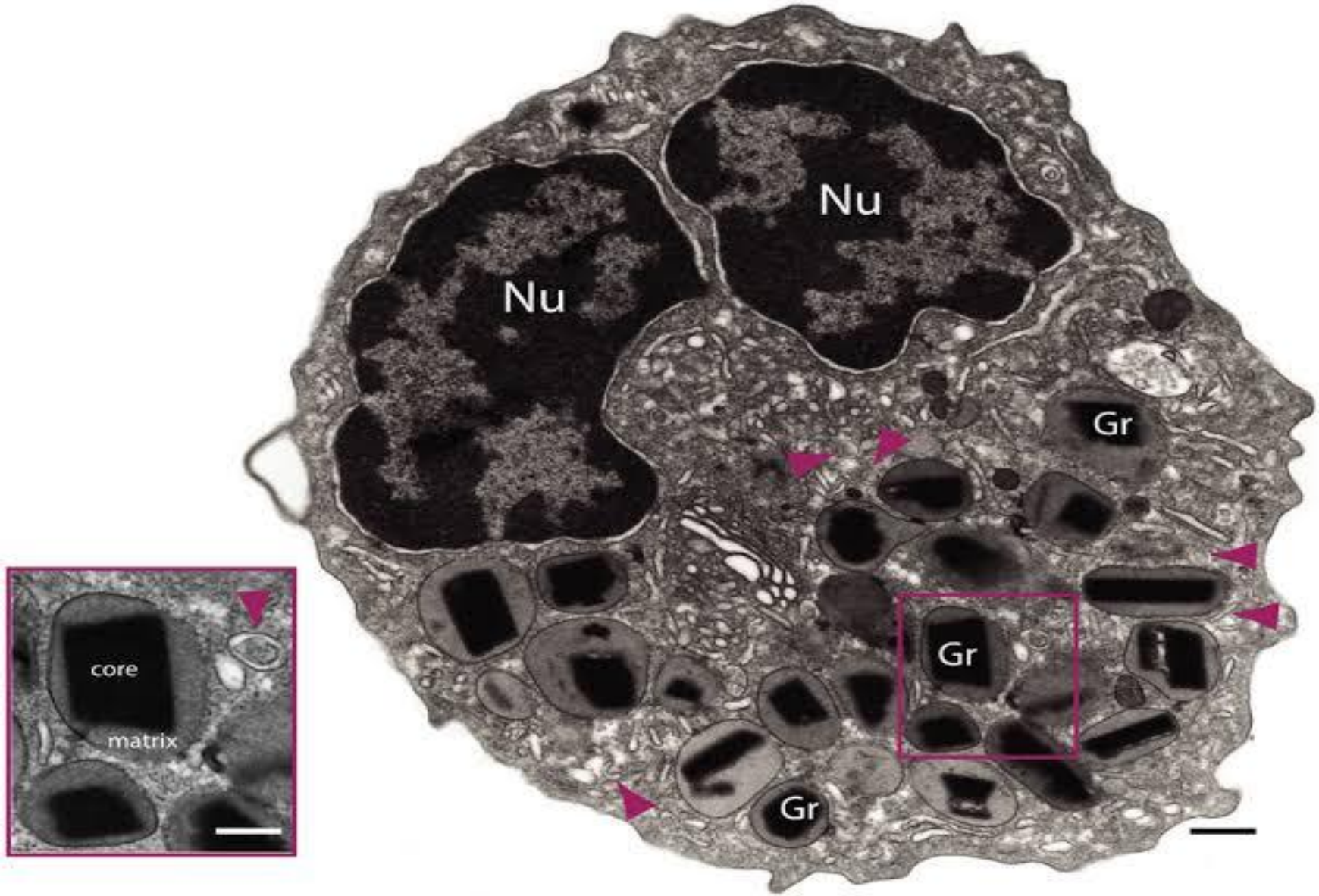


2. **Eosinophils (1-3 % of leucocytes): concerned with allergy termination.**

- **The diameter is 12-16 µm and their life span is 1-2 weeks.**
- **LM: Nucleus of eosinophil is single, horseshoe and bilobed.**
- **EM: Granules:**

1-1ry non-specific azurophillic granules (primary lysosomes).

2-2ry specific acidophilic large granules (histaminase and sulphatase).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- **Functions: Attracted to allergic sites (by ECF of basophils or mast cells) to terminate allergy by destruction of histamine and phagocytosis of allergic antigen-antibody complexes.**

o **Inactivate and kill parasitic larvae.**

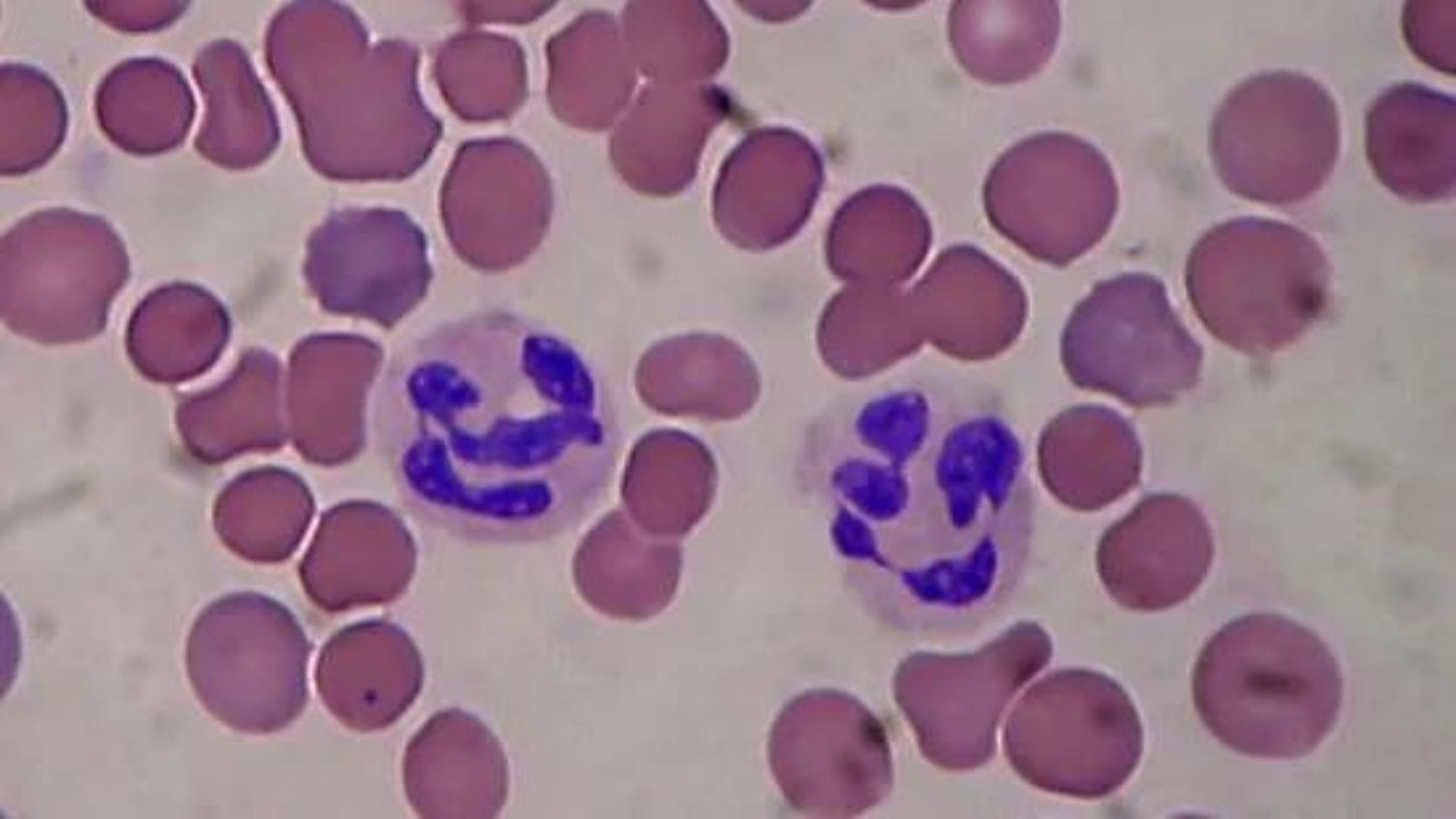
- **Eosinophilia (increase number of eosinophils):It occurs in allergic diseases and parasitic infestations.**
- **Eosinopenia (decrease number of eosinophils): It occurs with cortisone therapy that inhibits bone marrow.**

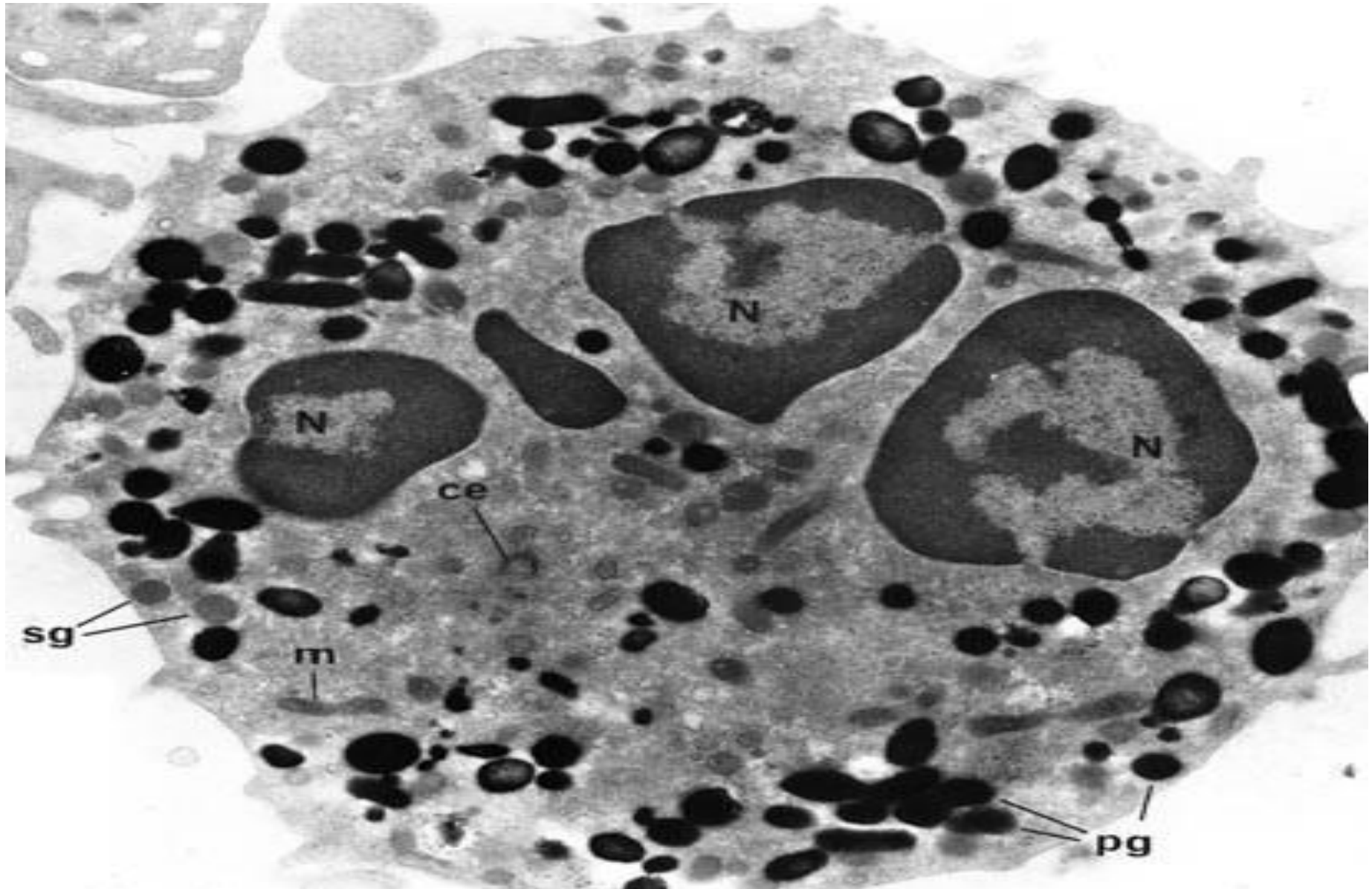
NB: Eosinophils are present under skin and mucosa of respiratory, intestinal and ♀ genital tracts.

Neutrophils (57-67 % of leucocytes):

Concerned with non-specific immunity.

- **The diameter of neutrophils** is 12-15 µm and their life span is 1-4 days.
- **LM:** Nucleus of neutrophil is single and formed of connected 2-5 segments (so neutrophils are called "polymorph-nuclear leucocytes").

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- **Neutrophils are classified according to number of their nuclear segments into:**
  - **Two classes by Schilling count: immature with non-segmented nuclei (4%) and mature with segmented nuclei (96%).**
  - **Five classes by Arneth count: class I, II, III, IV and V with 1, 2, 3, 4 and 5 segments in their nuclei respectively.**

Class I	1 segment	5%
Class II	2 segments	35%
Class III	3 segments	41%
Class IV	4 segments	17%
Class V	5 segments	2%

Arneth classification of neutrophils

- **EM: Granules:**

- **1. 1ry non-specific azurophillic granules (1ry lysosomes).**

- **2. 2ry specific pale large granules (bactericidal phagocytin, bacteriostatic lactoferrin, collagenase and alkaline phosphatase).**
- **Functions: non-specific immunity (which is the first line of defense mechanism) through the following:**

- **1. They leave blood vessels and enter CT (through their amoeboid movement) to phagocytose bacteria by their pseudopodia.**

- **2. Thy destruct bacteria by proteolytic enzymes present in their granules (that dissolve bacterial proteins).**

- **3. They attract monocytes to inflamed areas to remove pus (dead neutrophils, dead bacteria and tissue debris).**

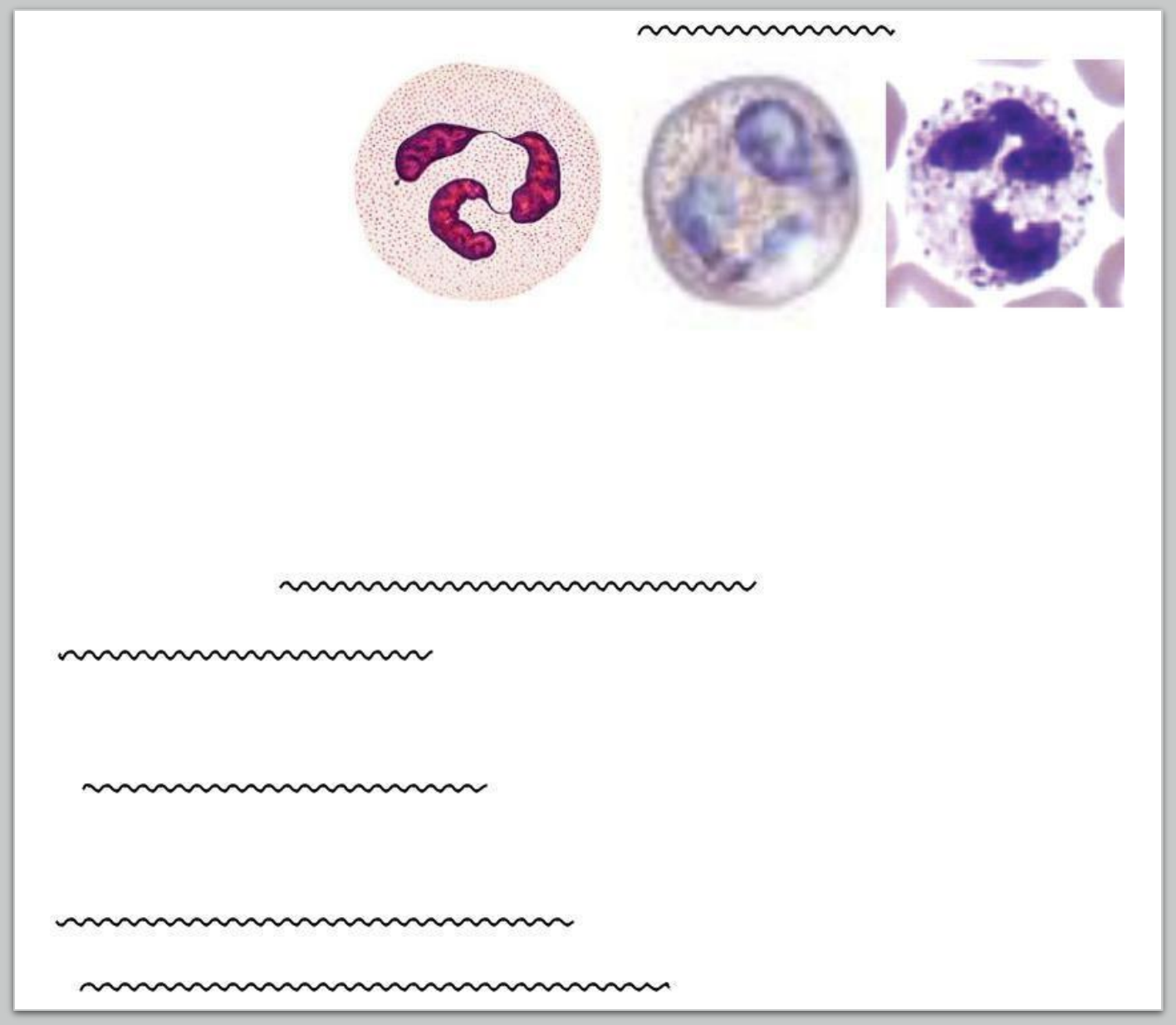
- **4. Thy stimulate bone marrow (to form neutrophils).**
- **5. They secrete trephine substance (that perform healing).**

- **Neutrophilia**

(increase number of neutrophils): It occurs in appendicitis, tonsillitis, abscess ...

- **Neutropenia**

(decrease number of neutrophils): It occurs in typhoid fever, drugs, radiation ...

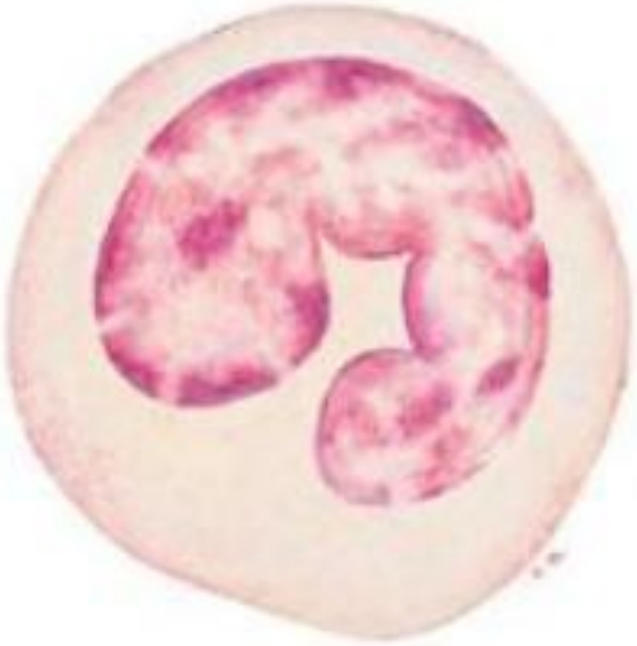


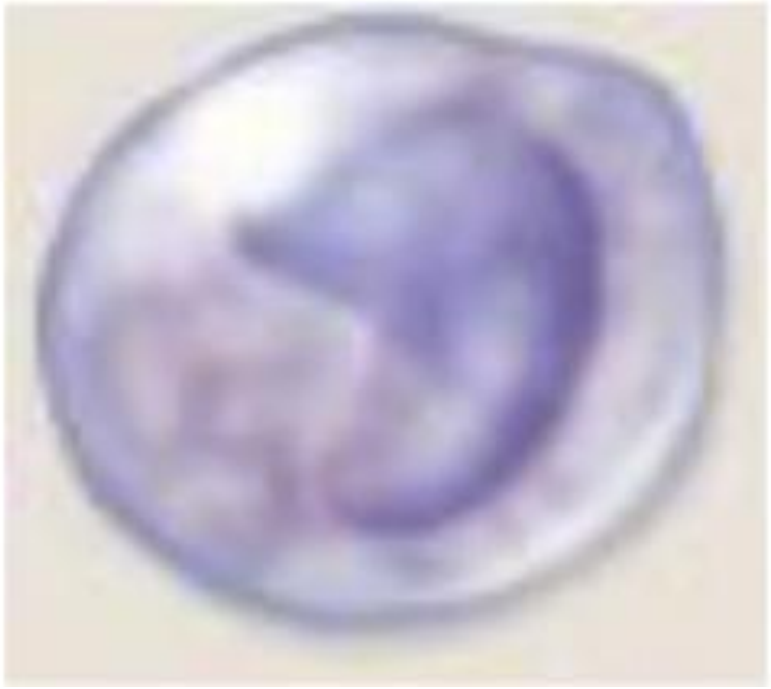
4. **Monocytes (3-7 % of leucocytes): concerned with non-specific immunity.**

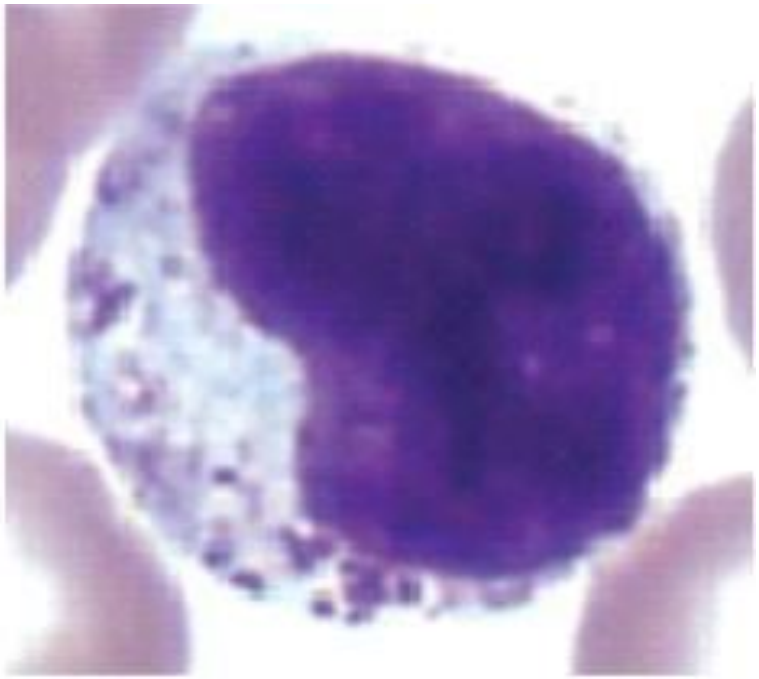
- **The diameter of monocytes is 14-18 µm and their life span is 3 days in blood, 3 months in CT proper and years outside them.**
- **LM: they have large pale kidney-shaped nuclei with pseudopodia.**
- **EM: few organelles with well-developed Golgi apparatus and many azurophilic granules (lysosomes).**
- **Functions: o Change to macrophage (and other mononuclear phagocytic cells) to phagocytose small foreign bodies.**

o Fuse together to form giant cells (as osteoclasts) to phagocytose large foreign bodies.

- **Monocytosis (increase number of monocytes): It occurs in chronic infections as syphilis, malaria, TB ...**







• 5. **Lymphocytes (25-33 % of leucocytes):** concerned with specific immunity. According to size lymphocytes are classified into small & large lymphocytes:

• o **Small inactive lymphocytes (15-20 % of leucocytes):**

• The diameter of small lymphocytes is 6-9 µm (like RBCs).

• **LM:** they have dark rounded nuclei with pale scanty cytoplasm (forming a thin rim around nucleus).

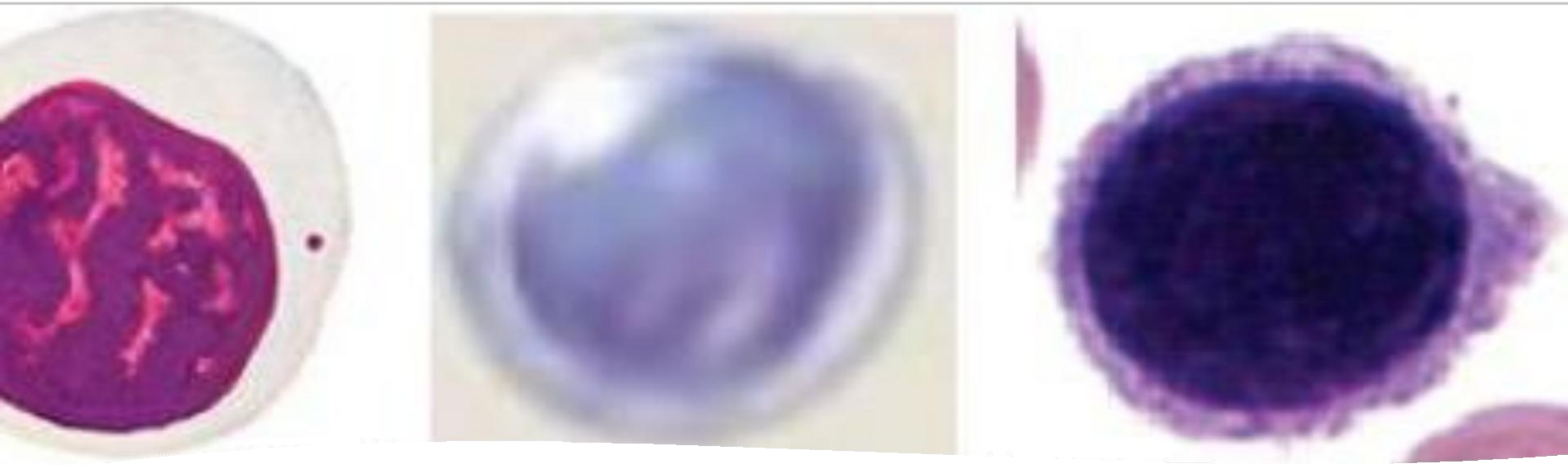
• **EM:** few organelles with many free ribosomes and microvilli.

• o **Large active lymphocytes (5-10 % of leucocytes):**

• The diameter of large lymphocytes is 09-18 µm.

• **LM:** they have pale rounded nuclei with clear nucleolus and dark abundant cytoplasm.

• **EM:** many mitochondria, many rER and well developed Golgi apparatus.



- **Function of lymphocytes**: specific immunity (which is the second line of defense mechanism).

- **NB:** Lymphocytes can pass through oral epithelium and appear in oral cavity as "salivary corpuscles".

- According to function lymphocytes are classified into B, T & NK lymphocytes:

- (1) **B-lymphocytes (25-30% of circulating small lymphocytes):**
- They can life for 3 months.
- They are bursa dependent as they develop in bursa of fabricius (of birds) and in bone marrow (of human).
- They originate from B-type colony forming cells of bone marrow that differentiate (to B-lymphoblasts then B-lymphocytes) and acquire surface receptors then migrate from bone marrow to peripheral lymphoid organs (lymph nodes, spleen, tonsils ...) as small inactive B-lymphocytes.
- Antigens are picked by T-helper lymphocytes then delivered to small B-lymphocytes their activation to:
- o Plasma blasts plasma cells antibodies (gamma globulins "IgG, IgM, IgA, IgE and IgD") primary humoral immunity.
- o B-memory cells rapid response after further exposure to the same antigen secondary humoral immunity.

- (2) **T-lymphocytes (60-80% of circulating small lymphocytes):**

- **They can life for 2 years.**
- **They are thymus dependent (as they require thymus gland for their development and maturation).**
- **They originate from T-type colony forming cells of bone marrow that differentiate (to T-lymphoblasts) then migrate from bone marrow to the cortex of thymus gland.**
- **In the cortex of thymus gland they proliferate, differentiate (to T-lymphocytes) and acquire surface receptors (T-cell receptors "TCRs").**
- **o In early life: small inactive T-lymphocytes migrate from the cortex of thymus gland to its medulla to post-capillary venules and enter circulation to reach thymus depended zones of lymph nodes (in para-cortex) and spleen (in peri-arteriolar lymphatic sheath "PALS" of white pulps).**
- **o In adult life: thymus depended zones of lymph nodes and spleen give small inactive T-lymphocytes throughout life.**

- Antigens or foreign cells (viruses, fungi or tumor cells) activation of small T-lymphocytes to:

• 1. **T-cytotoxic cells (T-killer cells):** that performs primary cellular immunity (by secretion of perforins which produce pores in the cell membrane of foreign cells leading to their lyses).

• 2. **T-memory cells:** that performs secondary cellular immunity which defends body against secondary infection (further exposure to the same antigen).

• 3. **T-helper cells:** that helps in humoral immunity of B-lymphocytes.

• 4. **T-suppressor cells**: that suppresses both humoral and cellular immunity.

- **5-T-lymphokines producing cells: that secrete the following hormone-like factors:**
- **– Interferon (anti-viral) and cytotoxic factor (anti-bacterial).**
- **– Chemotactic factor (that attract macrophages to the site of infection).**

- **– Colony stimulating factor and mitogenic factor (that stimulate proliferation of bone marrow cells).**

- (3) **Natural killer lymphocytes (5% of circulating lymphocytes):**

- **They can life for 3 months.**

- **They have non-B non-T receptors and can kill some tumor cells and infected cells.**

- **Lymphocytosis (increase number of lymphocytes):**

It occurs in chronic diseases (as pertussis, TB, syphilis ...) and in leukemias.

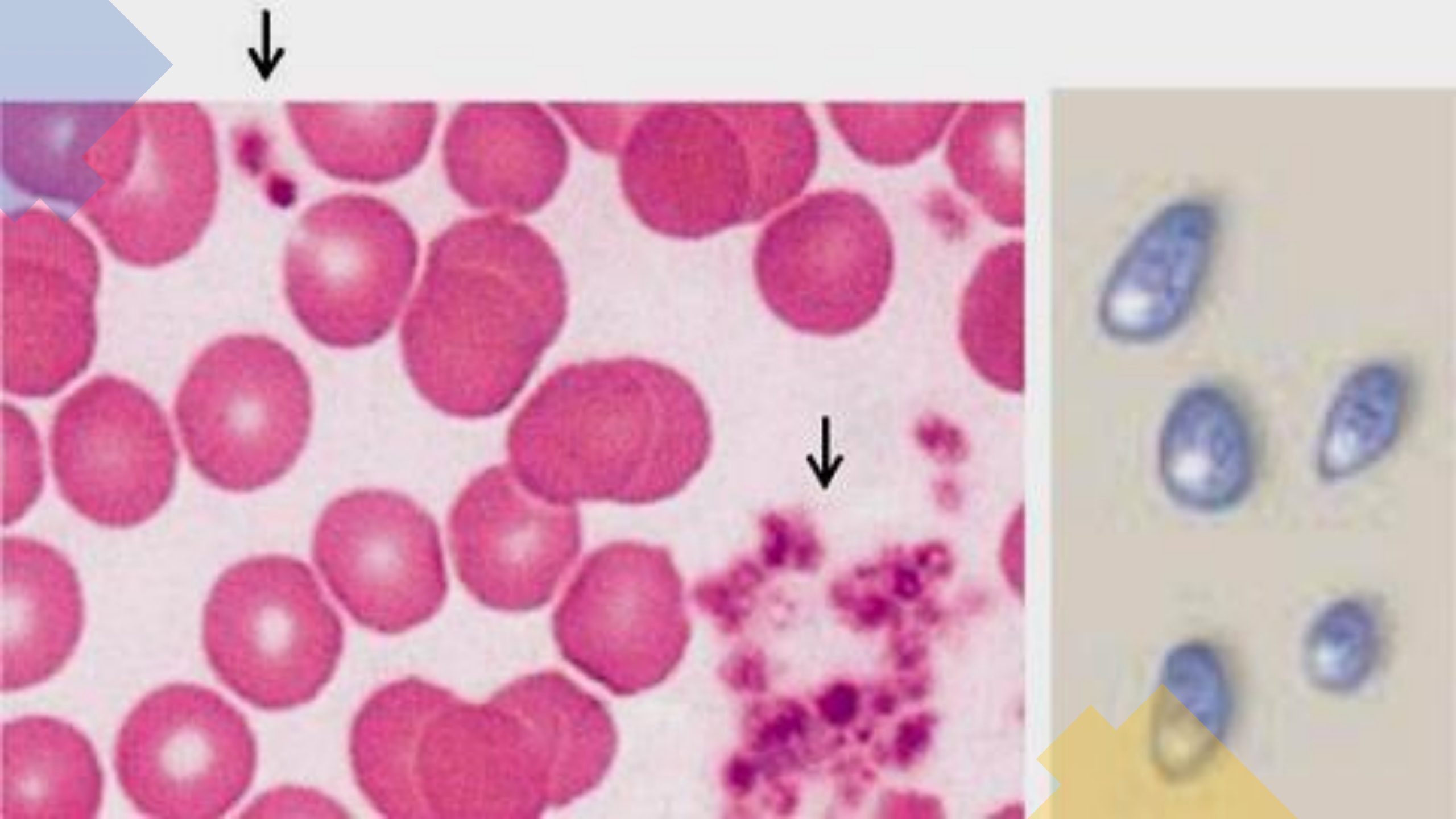
	RBCs	WBCs
Types:	▪ one type	▪ 5 types
Number:	▪ 4-6 million/^{3}mm	▪ 4-11 thousand/^{3}mm
Size:	▪ 6-9 (7.5) µm	▪ 6 to 18 µm
Shape:	▪ biconcave discs with rouleaux appearance	▪ spherical without rouleaux appearance
Color:	▪ greenish yellow	▪ colorless
Osmotic pressure:	▪ liable to hemolysis	▪ resist hemolysis
LM:	▪ corpuscles: – no nuclei – no cell organelles – contain hemoglobin	▪ true cells: – contain nuclei – contain cell organelles – not contain hemoglobin
Function:	▪ carrying O_2 and CO_2 inside blood vessels (so they have no amoeboid movement)	▪ phagocytosis outside blood vessels (so they have amoeboid movement)
Development:	▪ in red bone marrow	▪ in red bone marrow and in lymphatic tissues
Site:	▪ in blood	▪ in blood, in CT and in lymphatic tissues
Life span:	▪ 4 months	▪ few dyes to many years

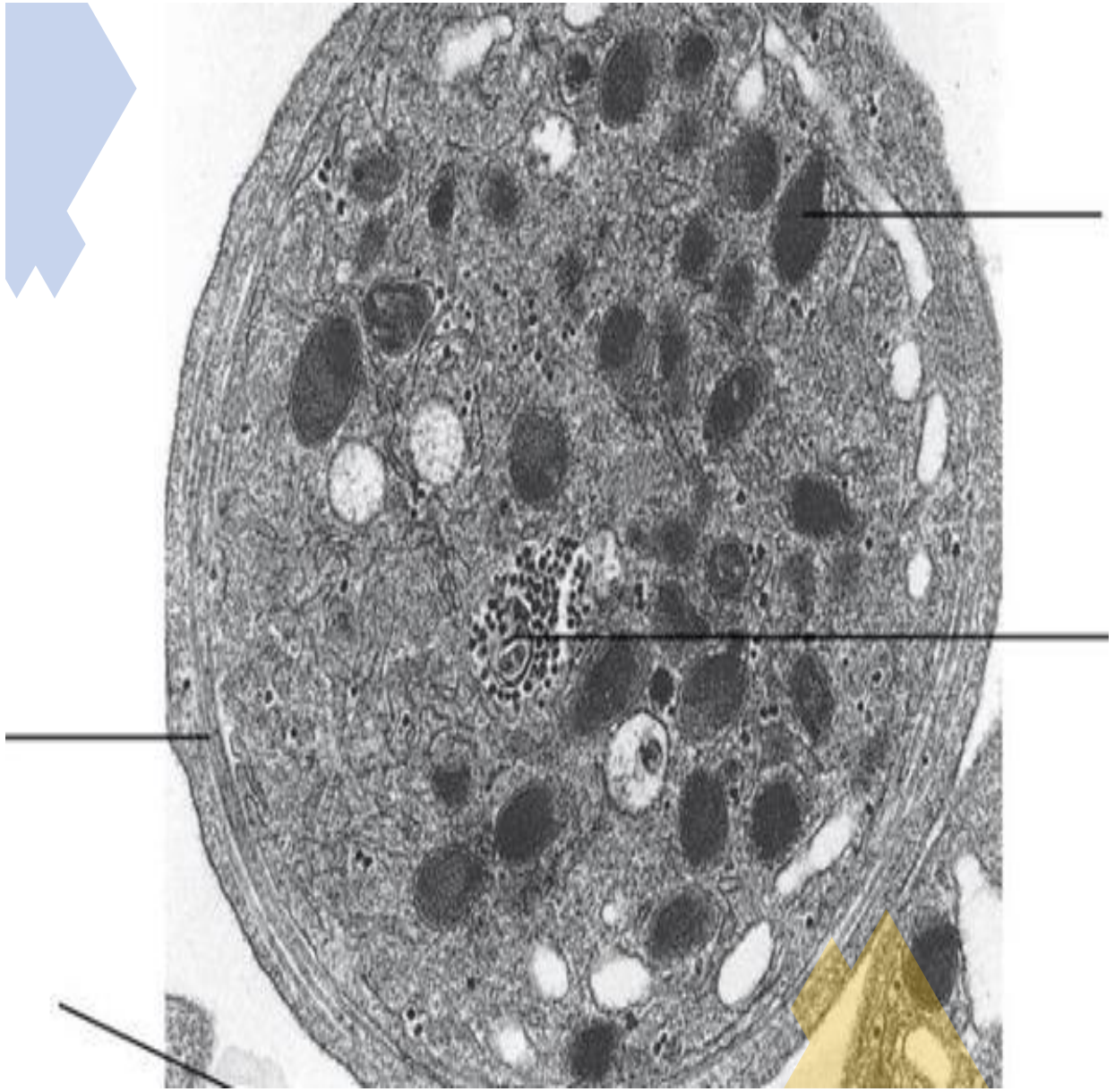
• Blood platelets or thrombocytes

- Platelets are not true cells (as they have no nuclei and cannot divide).
- Number: 150-400 thousand/3mm.
- The diameter of platelets is 2-4 µm
- and their life span is 5-10 days.

- LM: small rounded plates formed of peripheral pale hyalomere and central basophilic granulomere.

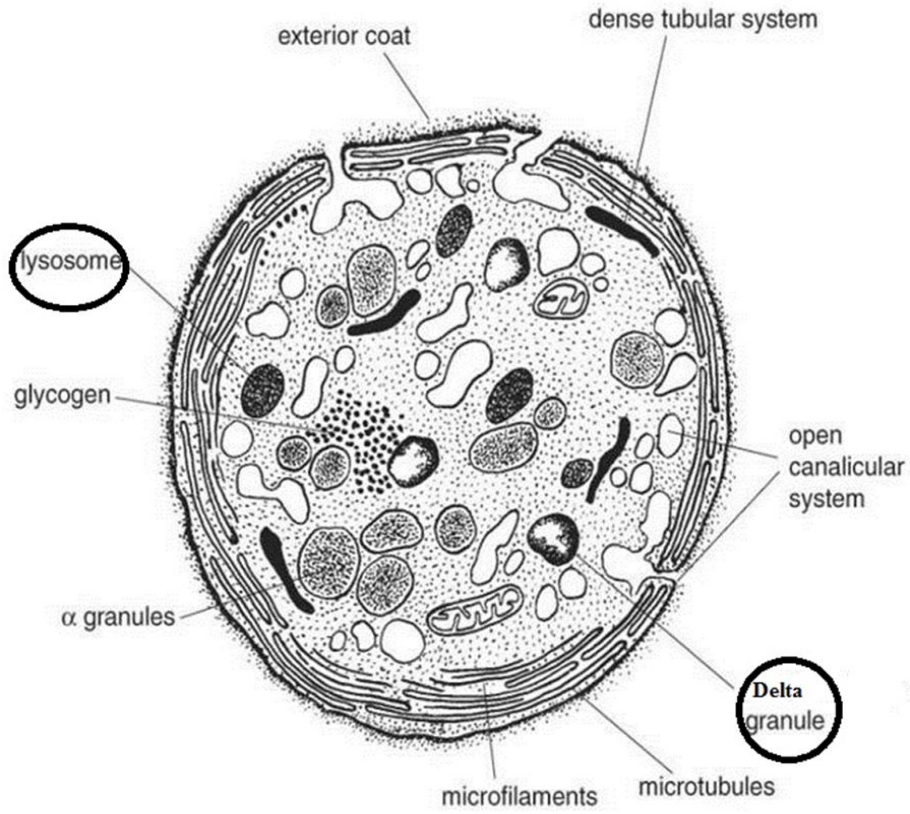
- EM:
- o Peripheral hyalomere is formed of:
- Marginal bundles (of microtubules and microfilaments).
- Open canalicular system (invaginations of cell membrane).
- Irregular tubular system (ER that stores Ca2+ ions).





Central granulomere is formed of:

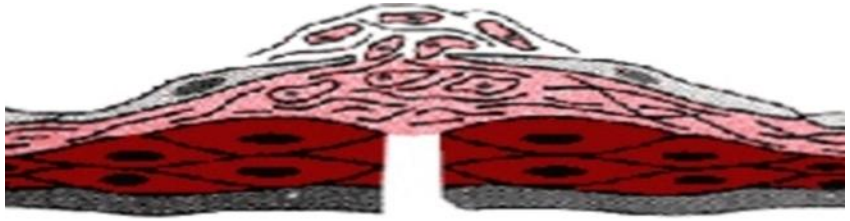
- **Alpha (α) granules (300-500 nm):** large and contain **(** fibrinogen and other coagulation factors) **platelet factor 4, platelet-derived growth factor and other platelet-specific proteins.**
- **Beta (β) granules (mitochondria).**
- **Delta (δ) granules (250-300 nm):** less abundant, medium- sized granules which contain histamine, serotonin, ATP, ADP.
- **Lambda granules (lysosomes):**few small dense granules that contain lysosomal hydrolytic enzymes.
- **Glycogen granules.**



- **Function of blood platelets:**

- **1. Blood agglutination: to form white thrombus (platelets + fibrin).**
- **2. Blood coagulation: to form red thrombus (platelets + fibrin + RBCs).**
- **3. Secretion of serotonin (vasoconstrictor).**
- **4. Clot retraction by contractile microfilaments.**

- **Thrombocytopenia (decrease number of platelets) causes increase in bleeding time.**



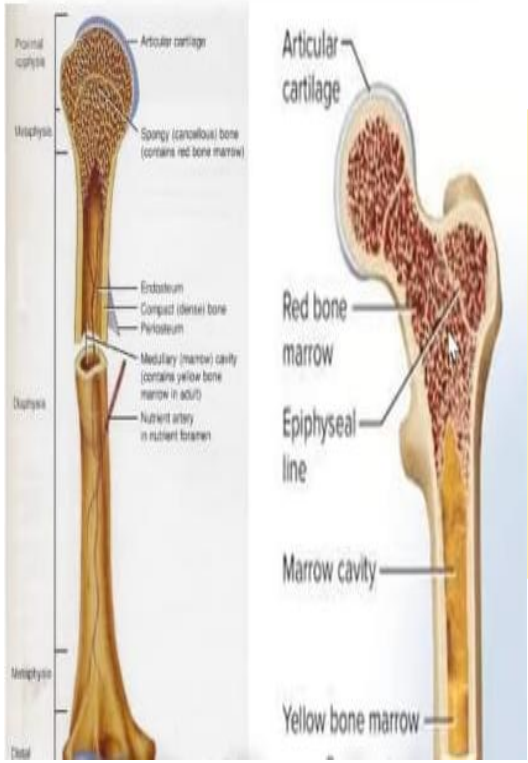
• Bone marrow (BM)

• **Blood cells are developed in:**

• **Myeloid tissue (bone marrow): that may be red active bone marrow or yellow inactive bone marrow.**

• **– Red active BM: present in all bones up to 7 years and in flat bones of adults.**

• **– Yellow inactive BM: present in long bones of adults and act as a reserve BM (that may change to red BM in sever blood loss).**



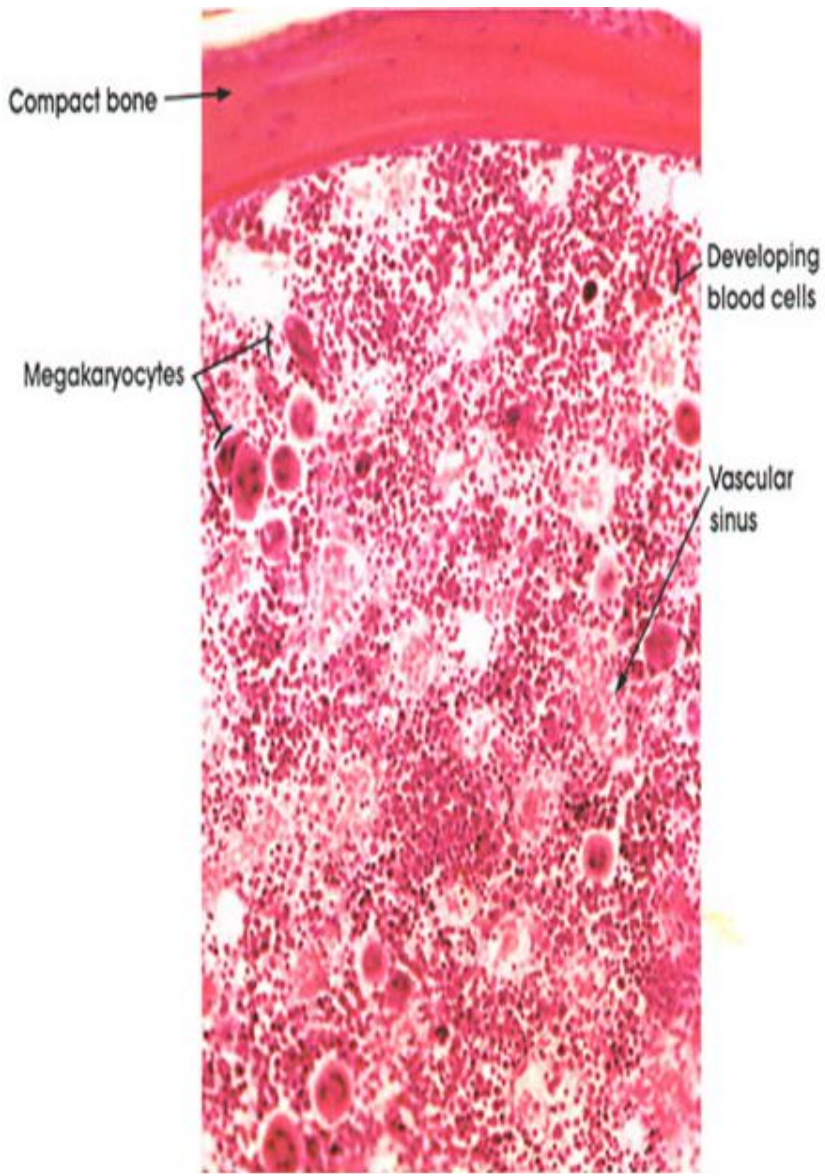
• **Lymphoid tissue: lymph node, spleen, tonsils and thymus.**

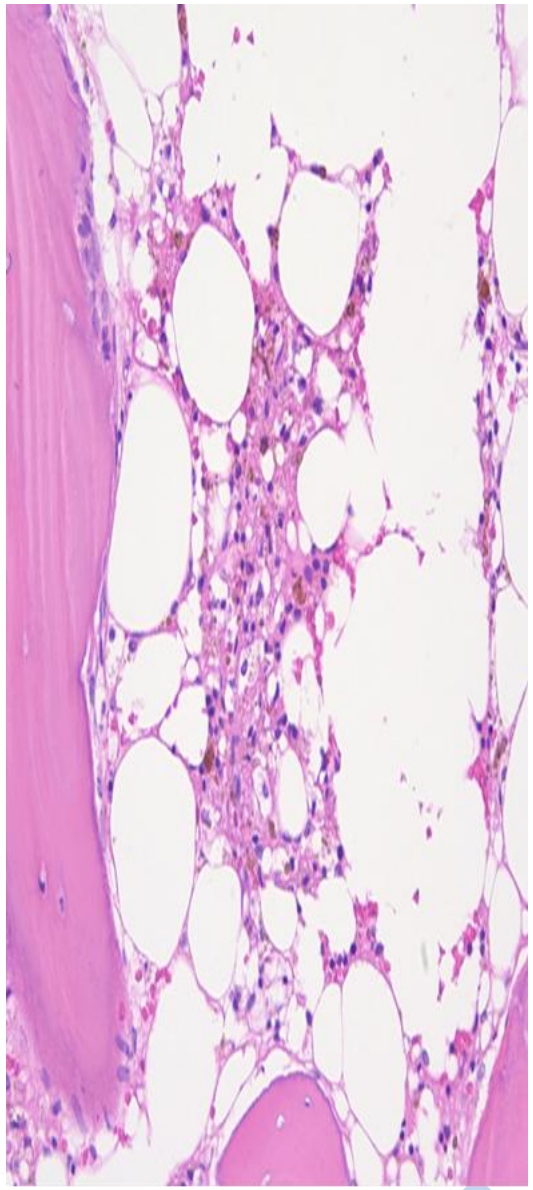
• **Histological structure of red active bone marrow: it is formed of:**

• **Stroma of fixed CT cells (reticular cells, fat cells, fixed macrophages, pericytes, endothelial cells and osteogenic cells).**

• **Blood sinusoids.**

• **Mature and immature blood cells.**


Compact bone
Developing blood cells
Megakaryocytes
Vascular sinus



- **NB:** myeloid / erythroid ratio (immature leucocytes / immature erythrocyte) = 5/1 (because life span of RBCs is grater 5 times than life span of WBCs).
- **Functions of red active bone marrow:**
- 1. Production of blood cells (depending on stem cells and erythropoietin hormone).
- 2. Phagocytosis of old RBCs by bone marrow macrophages.
- 3. Storage of iron in bone marrow macrophages.

Haemo-poiesis (formation of blood cells)

- All blood cells are formed in the red active bone marrow from mother stem cells named “pluri-potential hematopoietic stem cells”.
- These pluri-potential stem cells give rise to 2 types of stem cells:
- 1. Myeloid stem cells: that can differentiate to erythrocytes, thrombocytes, granulocytes or monocytes.
- 2. Lymphoid stem cells: that can differentiate to lymphocytes only.

Myeloid stem cells give rise to progenitor cells named “colony forming cells (CFCs)” which are small rounded basophilic cells (8-10 µm) with small rounded pale nuclei (containing fine chromatin).

- Progenitor cells (CFCs) differentiate to blasts, pro-cytes, cytes then mature RBCs, platelets or WBCs.
- Plurpotential stem cells , myeloid stem cells , colony forming cells, blasts, procytes, cytes, mature cells

haemo-poiesis	RBCs	platelets	granulocytes	monocytes	lymphocytes
(1) progenitors	erythrocyte-CFCs	megakaryocyte-CFCs	granulocyte-CFCs	monocyte-CFCs	lymphocyte-CFCs
(2) blasts	3 erythro-blasts	megakaryo-blasts	myelo-blasts	mono-blasts	B or T lymphobastes
(3) pro-cytes	normoblasts	pro-megakaryocytes	pro-myelocytes	pro-monocytes	B or T pro-lymphocytes
(4) cytes	reticulocytes	megakaryocytes	2 BEN myelocytes		B or T small lymphocytes
(5) mature cells	erythrocytes	platelets	BEN	monocytes	B or T large lymphocytes

• Erythro-poiesis:

- **Development of RBCs depends on presence of: progenitor cells (colony forming cells) - erythropoietin hormone - iron, folic acid, vitamin B12 and amino acids.**
- **It takes 7 days during which:**
- **nucleoli and mitochondria disappear - nucleus extract - hemoglobin increase.**
- **Pluri-potential hematopoietic stem cells ➡ myeloid stem cells ➡**
- **1. progenitor cells (erythrocyte-colony forming cells) ➡**
- **2. blasts: – Pro-erythroblasts (12 µm) with 2 nucleoli**
- **– Basophilic erythroblast (11 µm) without nucleoli**
- **– Poly-chromatophilic erythroblasts (10 µm) with hemoglobin ➡**
- **3. pro-cytes: ortho-chromatophilic erythroblasts "normoblasts" (9 µm) that characterized by extraction of pyknotic nucleus**

4. **cytes: reticulocytes (8 µm) with basophilic reticulum of polyribosomes ?**

5. mature erythrocytes (7.5 µm) filled with hemoglobin without nucleus.

NB: reticulocytes increase in peripheral blood (> 1% of RBCs) during hemorrhage or hemolysis.

- **Erythropoisis**
- **Erythrocyte maturation involves hemoglobin synthesis and formation of a small, enucleated, biconcave corpuscle. Several major changes take place**
- **1. Cell and nuclear volumes decrease, until the nucleus finally extruded from the cell.**
- **2. There is a gradual decrease in the number of polyribosomes (basophilia), with a simultaneous increase in the amount of hemoglobin (a highly eosinophilic protein).**
- **3. Mitochondria and other organelles gradually disappear.**

- **The development of red blood corpuscles (erythrocytes) takes the following stages:**

- **1- Pluripotent Hemopoietic Stem Cells**
- **2- Myeloid stem cells for erythrocytes.**
- **3- CFU-erythrocytes (CFU-E)**
- **4-blast: Proerythroblast.**
- **Basophil erythroblast.**
- **Polychromatophil erythroblast.**
- **5- procyte :ortho-chromatophilic erythroblasts “normoblasts”**
- 6- reticulocyte
- **7- Erythrocyte (the mature RBCs)**

Myeloid stem cell

Progenitor cell
(CFC)

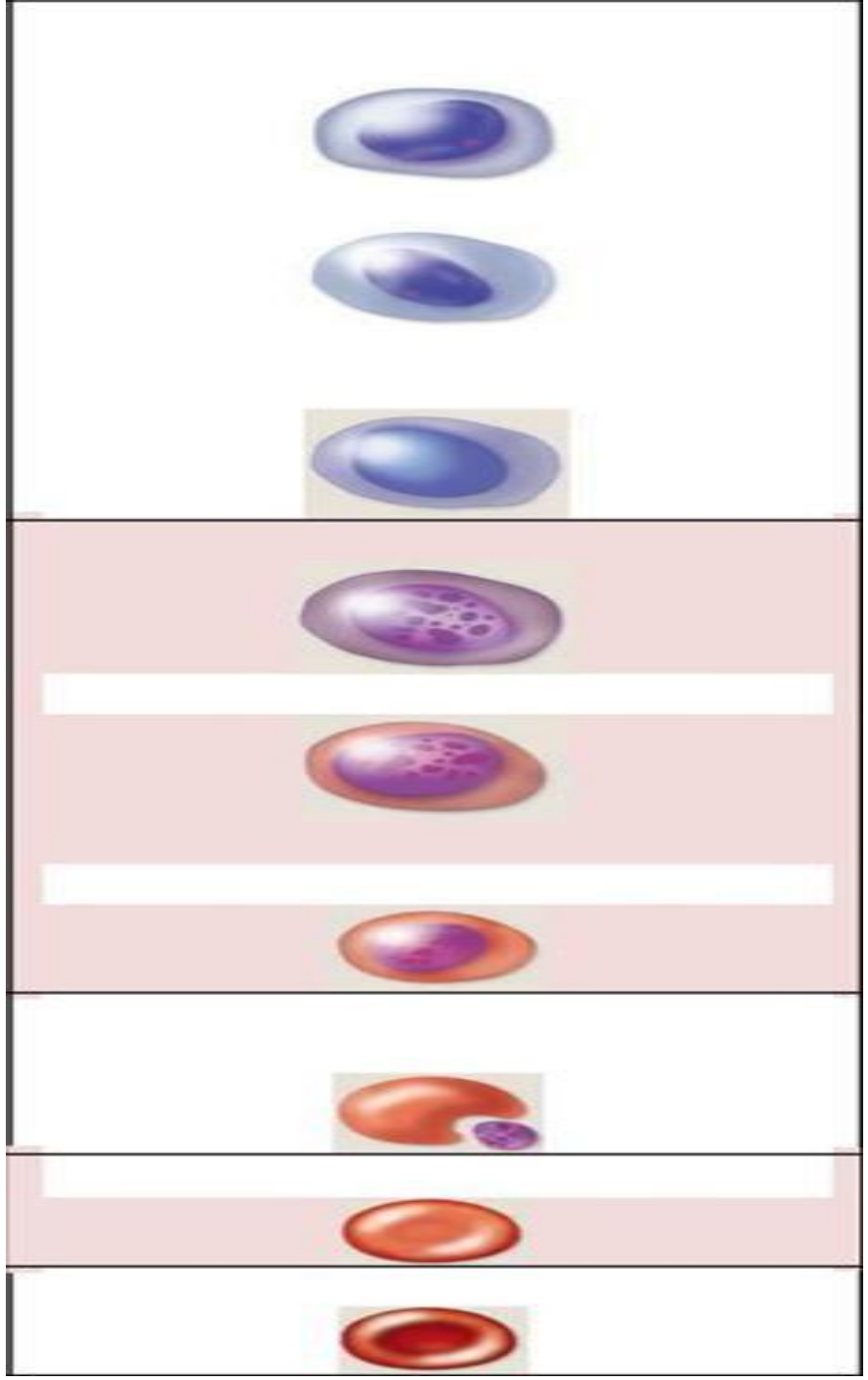
Pro-erythroblast

Basophilic erythroblast

Poly-chromatophilic erythroblast
(10 µm)

Ortho-chromatophilic
erythroblast (9 µm
Reticulocyte (8 µm)

Erythrocyte (7.5 µm)



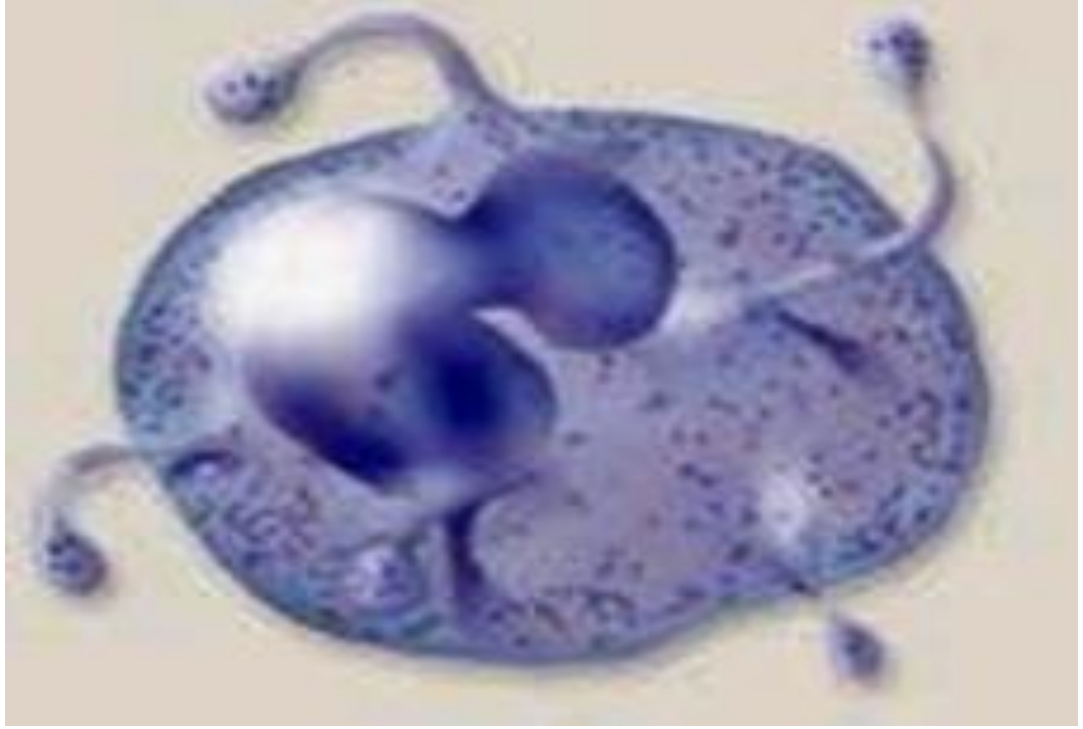
• Thrombopoiesis;

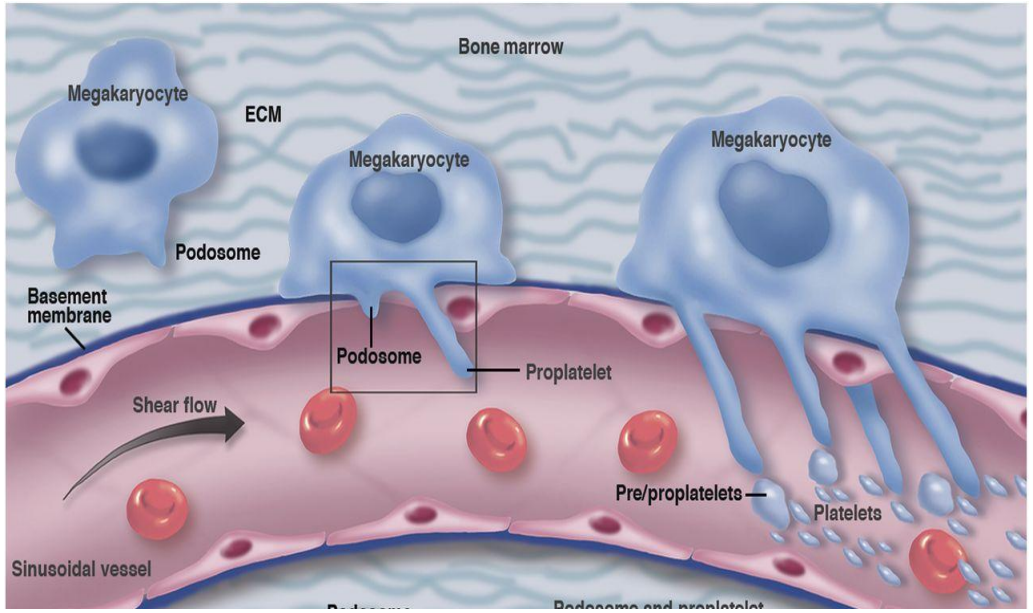
- The stages of thrombopoiesis are
- 1. Pleuripotent stem cells.
- 2. Myeloid stem cells.
- 3. Colony forming unit for megakaryocytes (CFU-Meg)
- 4. Megakaryoblasts
- 5. Megakaryocytes.
- 6. Blood platelets.
- Megakaryocytes are giant cells, up to 150 µm in diameter, with large, irregularly lobulated polyploid nuclei.
- Their cytoplasm contain numerous mitochondria, well developed RER, and an extensive Golgi apparatus from which arise the specificgranules of platelets .
- Many long, branching pseudopodia-like projections called proplatelets extend from megakaryocytes and pinched off forming platelets

- Thrombo-poiesis:
- Pluri-potential hematopoietic stem cells ⟹ myeloid stem cells
- 1. progenitor cells (thrombocyte-colony forming cells)
- 2. blasts: megakaryoblast is a large cell (25-50 µm) with several nucleoli
- 3. pro-cytes: pro-megakaryocyte is a larger cell with highly poly-ploid nucleus (where endomitosis 64 N or >30 times more DNA than in a normal diploid cell)
- 4. cytes: megakaryocyte is characterized by:
- Very large size (up to 150 µm) with multi-lobed poly-ploid nucleus (without nucleoli), many mitochondria, well-developed rER and many Golgi apparatus.
- To form platelets megakaryocyte extends several processes called pro-platelets that penetrate sinusoidal endothelium and expose to circulating blood.

Each megakaryocyte produces few thousand platelets then undergoes apoptosis and removed by macrophages.

- Pro-platelet is >100 µm long and 2-4 µm wide and has a framework of actin filaments and loosely bundled microtubules along which vesicles and specific granules are transported
- 5. mature platelets (2-4 µm).





Thrombo-poiesis

Pluri-potential stem cell

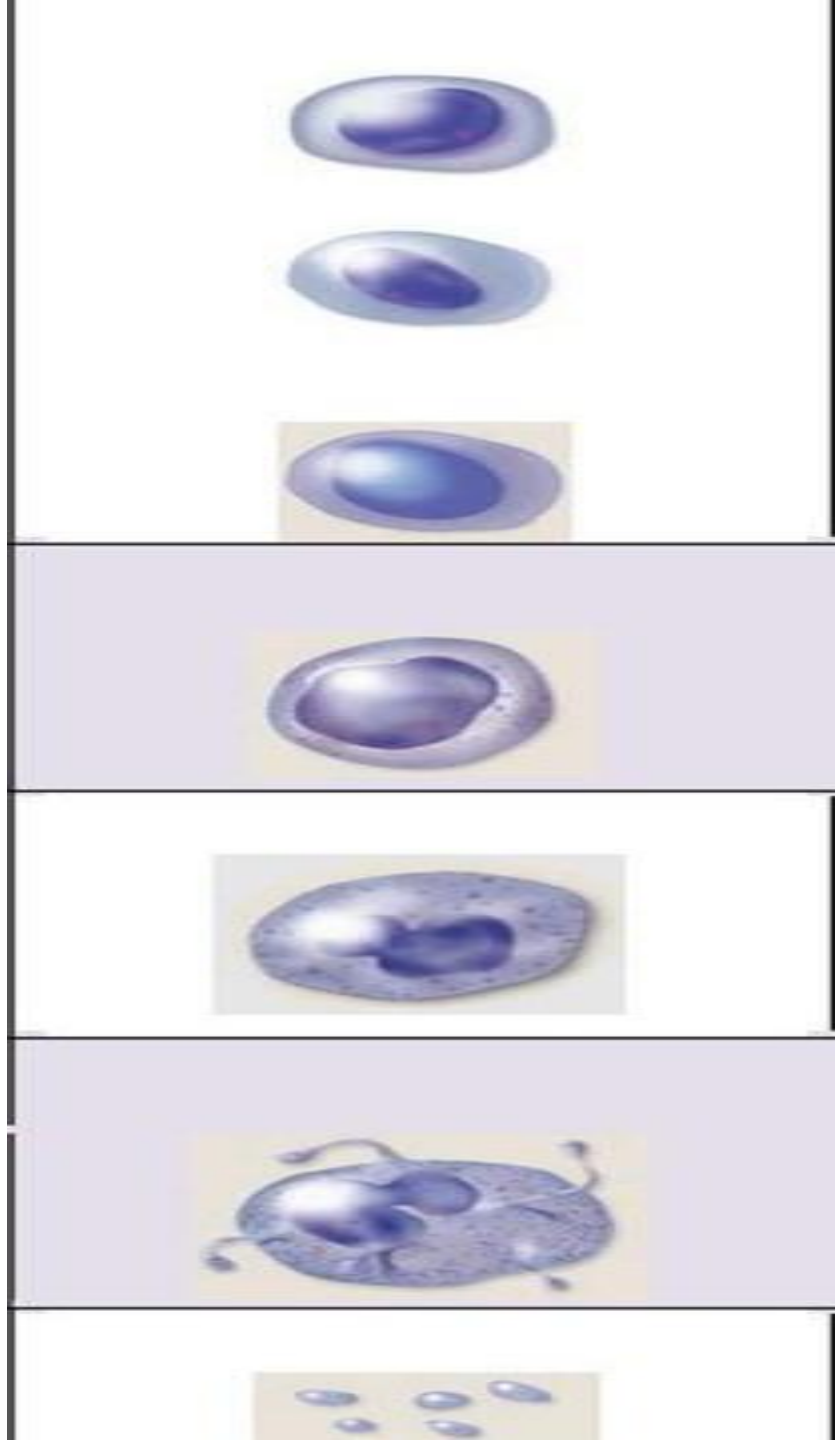
Myeloid stem cell

Progenitor cell (CFC)

Megakaryoblast (25-50 µm)

Pro-megakaryocyte

Megakaryocyte (up to 150 µm)



- **Granulopoiesis**
- **Granulocytes maturation involves cytoplasmic changes dominated by synthesis of proteins for the azurophilic granules and specific granules .This process includes the following steps**
- **1. Pluripotent Hemopoietic Stem Cells**
- **2. Myeloid stem cells for granulocytes**
- **3. Colony forming unit for granulocyte series (CFU-GM).**
- **4. Myeloblast.**
- **5. Promyelocyte.**
- **6. Myelocyte.**
- **7. Metamyelocyte.**
- **8. Granular leucocyte**

Granulo-poiesis:

- Pluri-potential hematopoietic stem cells myeloid stem cells
- 1. progenitor cells (granulocyte-colony forming cells)
- 2. blasts: myeloblasts (without granules) - they have 2 nucleoli
- 3. pro-cytes: pro-myelocytes (with undifferentiated granules)
- 4. cytes:
- – BEN myelocytes (with differentiated granules)
- – BEN meta-myelocytes (with specific granules and rod shaped nuclei)
- 5. mature basophils, eosinophils and neutrophils (with specific granules and characteristic nuclei).
- NB: Neutrophilic metamyelocytes "juvenile neutrophils" Mono-poiesis
- (with kidney-shaped nucleus) staff neutrophils qq
- Pluri-potential stem cell
- (with bend-rod nucleus) that increase with acute
- infection (> 2% of neutrophils in peripheral blood).

- **Agranulopoiesis**

- The precursor cells of monocytes and lymphocytes do not show specific cytoplasmic granules or nuclear lobulation
- The development of monocytes takes the following stages
- 1. Pluripotent stem cells
- 2. Myeloid stem cells for monocytes
- 3. Colony forming unit for monocytes series (CFU-GM).
- 4. Monoblast 5. Promonocyte. 6. Monocyte
- The Development of Lymphocytes takes the following stages
- 1. Pluripotent stem cells
- 2. Lymphoid stem cells which remain in bone marrow in the case of B-cell development OR migrates to the cortex of the thymus gland for T-cell development .
- 3. Lymphoblasts.
- 4. Lymphocytes.

Mono-poiesis:

hematopoietic stem cells → myeloid stem

Pluri-potential

cells →

1. progenitor cells (monocyte-colony fo rming cells)

→

2. blasts: monoblasts →

[redacted]

3. pro-cytes: pro-monocytes →

4. cytes: mo[redacted] with kidney-shaped

nuclei).

Lymphopiosis

- Pluri-potential hematopoietic stem cells
- lymphoid Monocyte stem cells
- 2 types of progenitor cells (lymphocyte-colony forming cells).


I love Histology!

REFERENCES:

JUNQUEIRA'S BASIC HISTOLOGY (TEXT AND ATLAS) (2018) 15 TH EDITION.

ELSEVIER'S INTEGRATED HISTOLOGY (2007) 1ST EDITION.

Choose the correct answer

١. The circulating blood contains:

a. All the immature formed elements of the blood.

b. Megakarocytes.

c. All the mature formed elements of the blood.

d. Colony forming unit.

٢. In the ultrastructure of eosinophils, the specific granule show:

a. Only electron dense material.

b. Ribosomes.

c. Crystalloid.

d. Only SER.