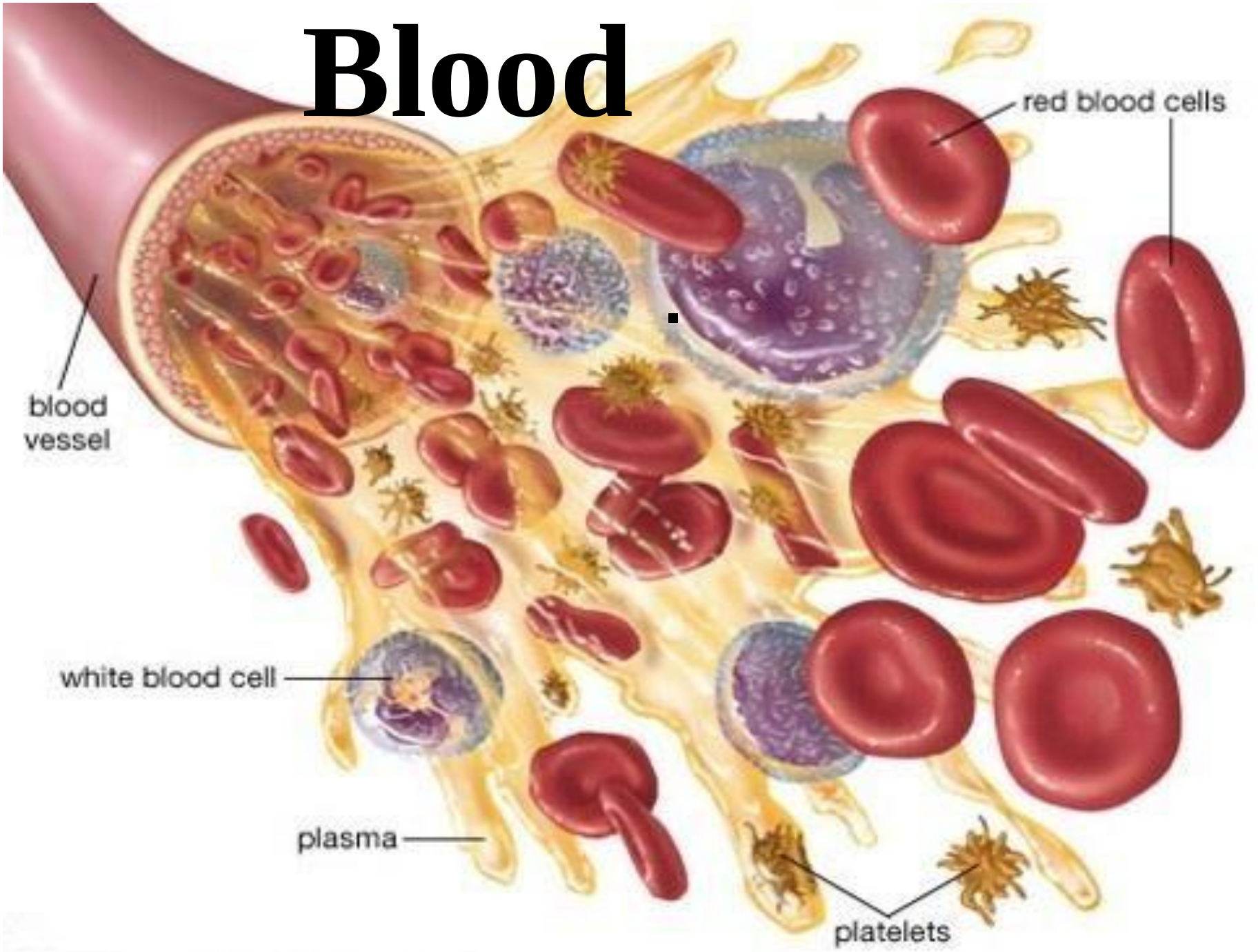
Blood


red blood cells
blood vessel
white blood cell
plasma
platelets

Connective Tissue

C.T. proper

Ground substance is jelly like

- Loose C.T.
- Adipose C.T.
- Reticular C.T.
- Dense C.T.
- Elastic C.T.
- Mucoid C.T.

Modified C.T.

Ground substance is modified

- **Solid nature = supporting C.T.**
  - **Cartilage)firm(**
  - **Bone)hard(**
- **Fluid nature (plasma(**
  - **Blood**

Blood
Modified CT

- Adult has ~ **5.5 -6 L**
- Circulate in **CVS**
- Considered **modified** connective tissue:

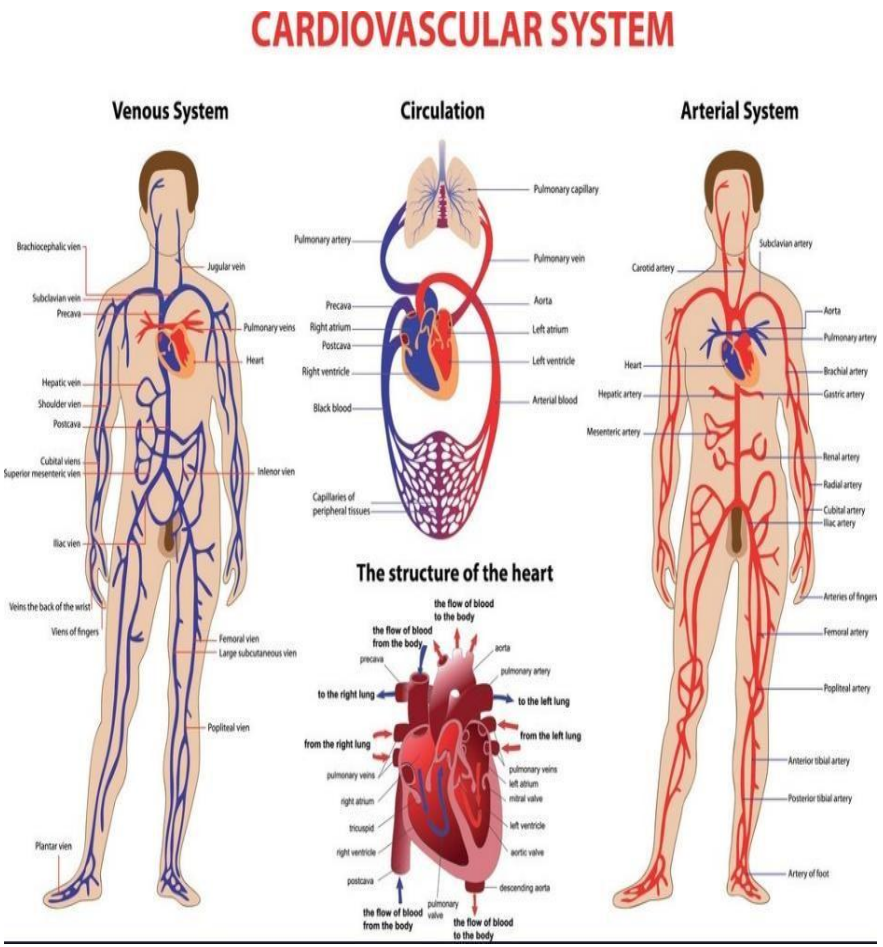
➢ Mesodermal in origin

➢ cells

➢ liquid ground substance (**called plasma**(

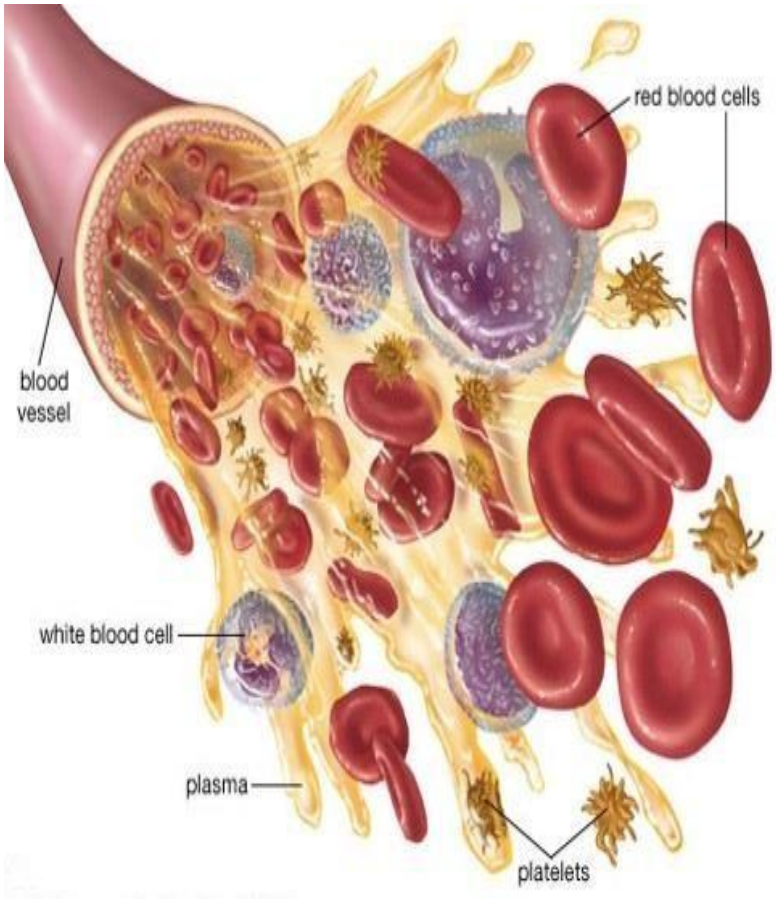
➢ dissolved protein fibers

(fibrinogen) ⟹ fibrin



BLOOD

Consists of liquid (plasma) and cellular components by a machine called a centrifuge.



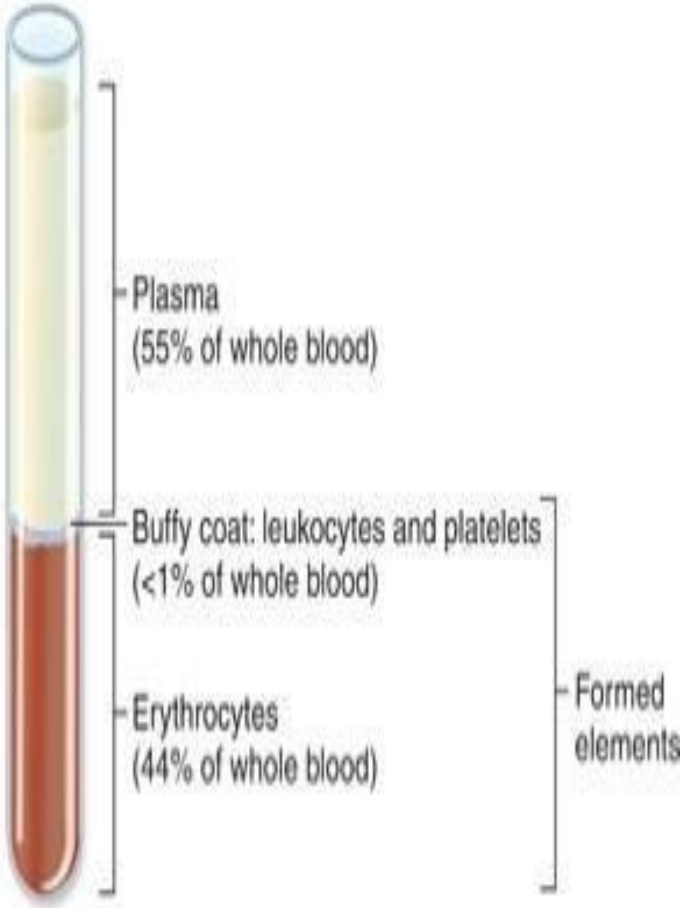
- **Plasma: 55%**

- **Cells = Formed Blood elements 45%**
  - **Originate in the red bone marrow**
  - **Blood formation = hematopoiesis**

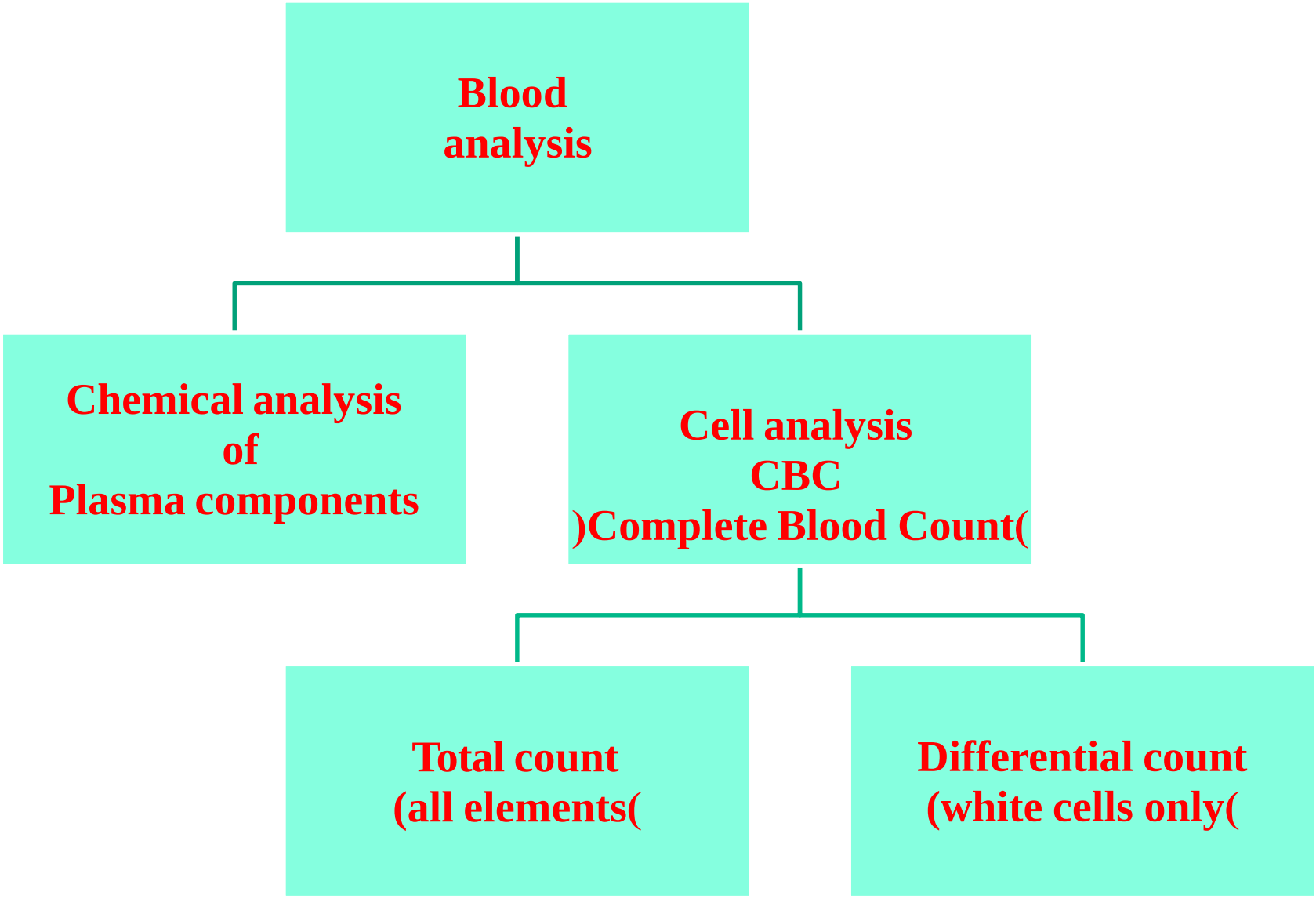
- **No aberrant fibers.**

(1) Withdraw blood into a syringe and place in a glass tube.

(2) Place the tube into a centrifuge and spin for about 10 minutes.



(3) Components of blood separate during centrifugation to reveal plasma, buffy coat, and erythrocytes.


Blood analysis
Chemical analysis of Plasma components
Cell analysis CBC)Complete Blood Count(
Total count (all elements(
Differential count (white cells only(

Plasma

%55of blood volume:

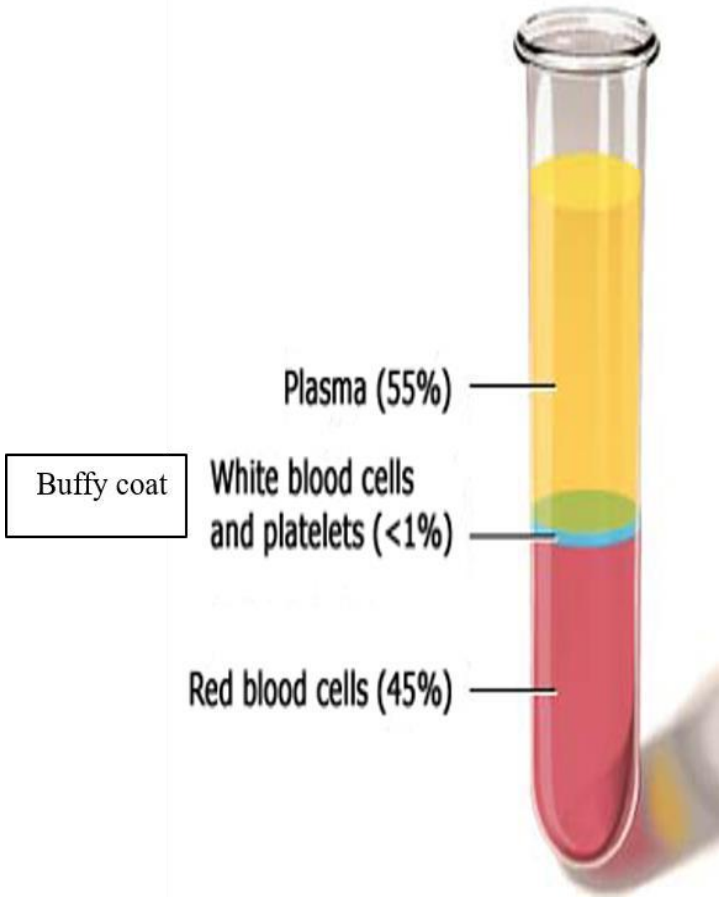
- **Water .92%**
- **Organic substances:% 7**
  - plasma proteins

)albumin, globulin, prothrombin and **fibrinogen**(

  - Hormones & enzymes.

- **Inorganic salts 1%**

)Na Cl, Bicarbonates, phosphates & calcium(



The Blood Film= Smear

Preparation of blood for laboratory study

•Why do we do a blood film ?

1.To study blood elements.

.2To make differential leukocytic count.

Steps:

- Put a small drop of blood
- Spread into a thin film

•Stain with Leishman or Giemsa stain

(methylene blue +eosin(

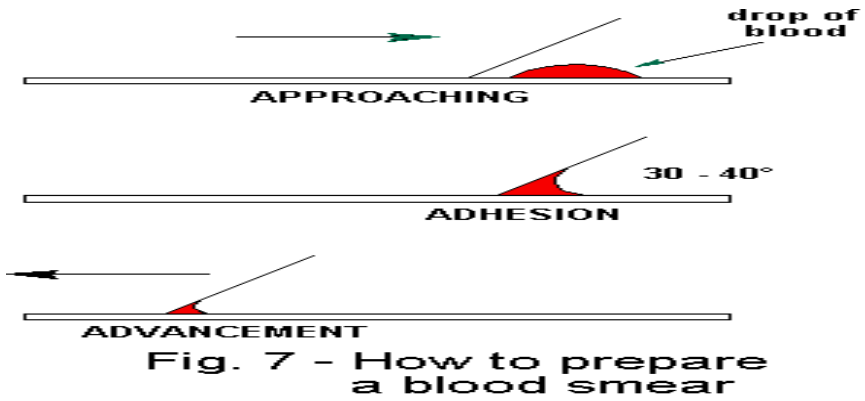
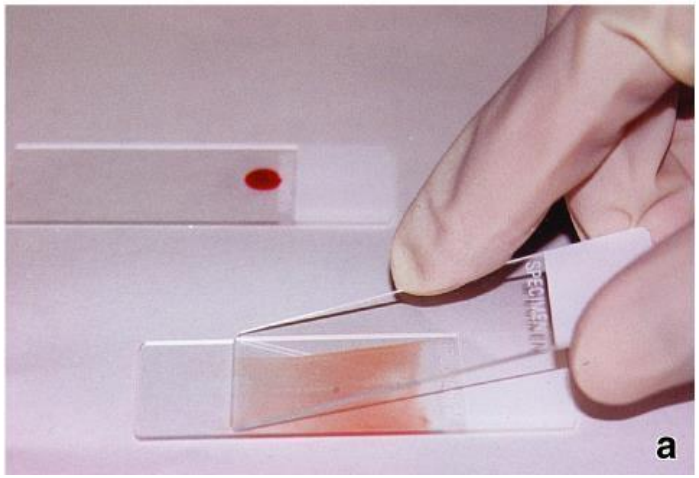


Fig. 7 - How to prepare a blood smear



Blood Film

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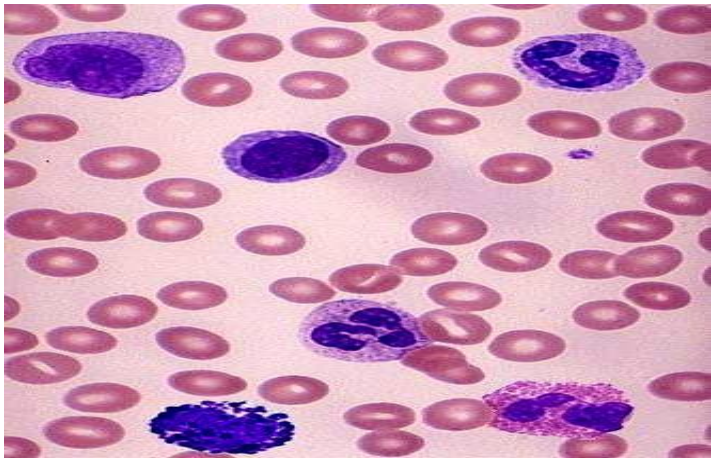
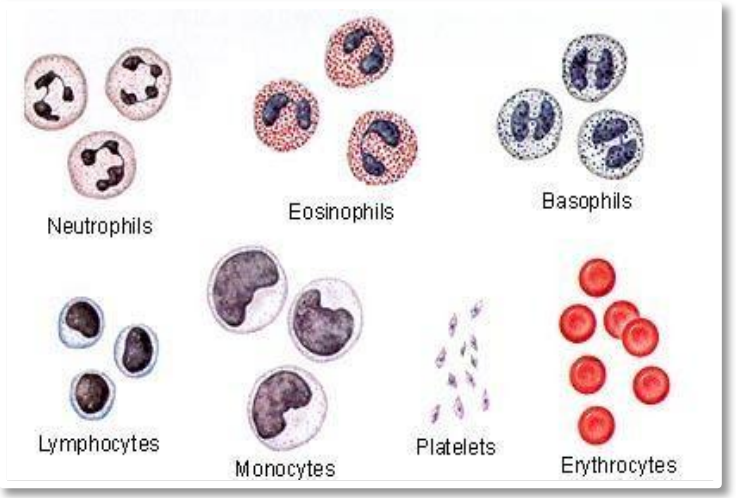
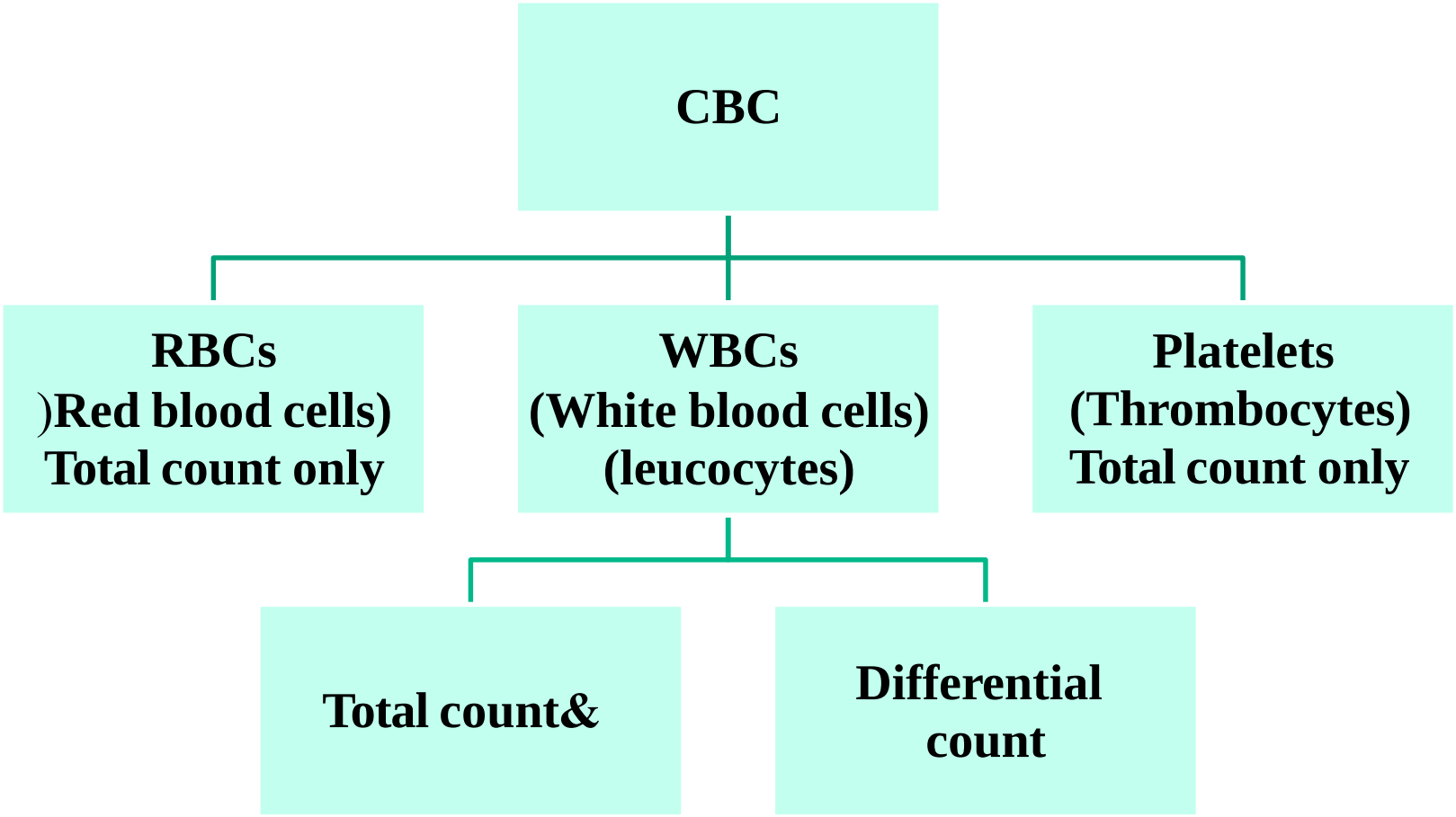




Giemsa's / Leishman's = **methylene blue + eosin**

- ►basophilic **(violet(**
- ►eosinophilic **(pink(**
- ►azurophilic **(red purple(**

Complete blood count (CBC)



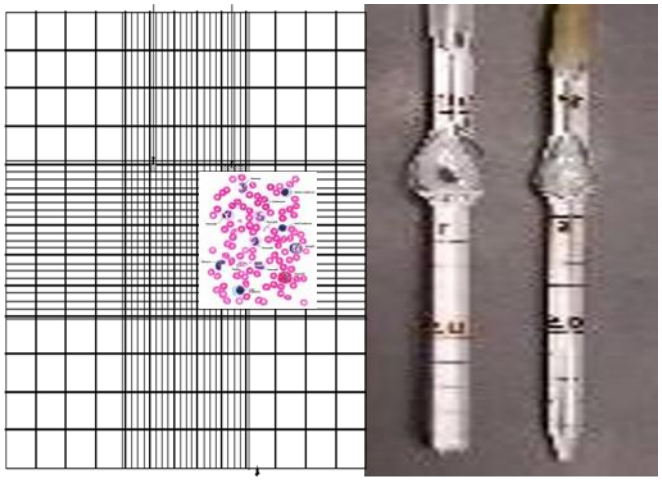
Complete blood count (CBC(

-1Total count:

It is the total number of blood elements (RBCs, WBCs, or Platelets) per cubic millimeter

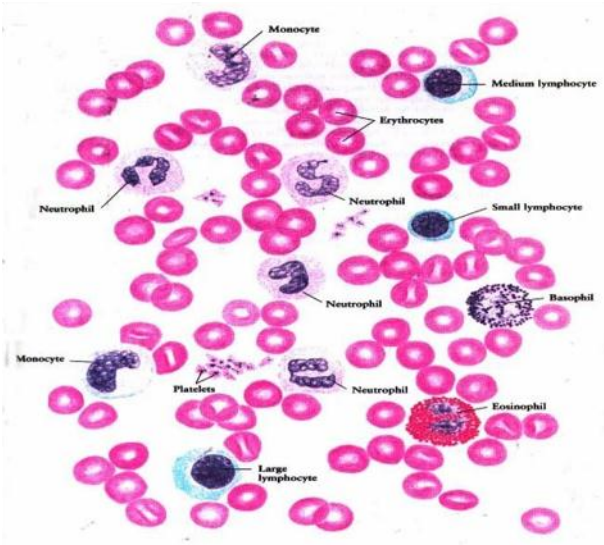
Measured by

- Hemocytometer
- Or Automatic counter

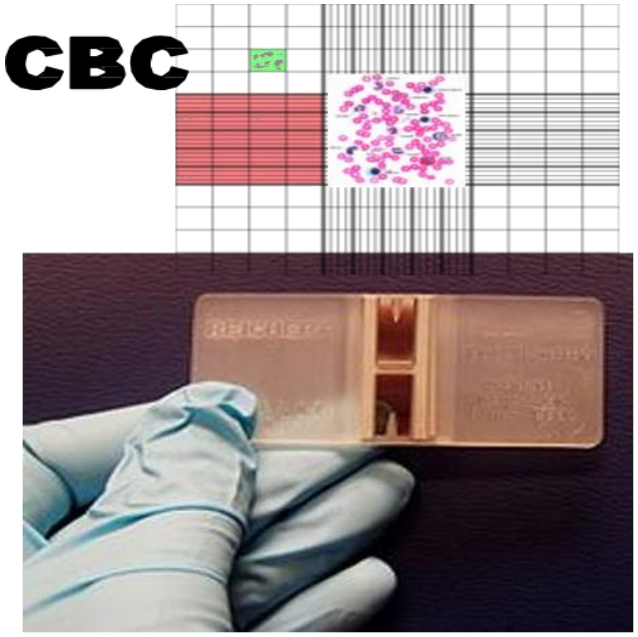


-2Differential leukocytic count

The percentage of each type of leucocytes to the total count



Blood cell count=



❖ **Manual method= Conventional**

=Hemocytometer= counting chamber.

❖ **Electronic method**

=automated hematology analyzer.

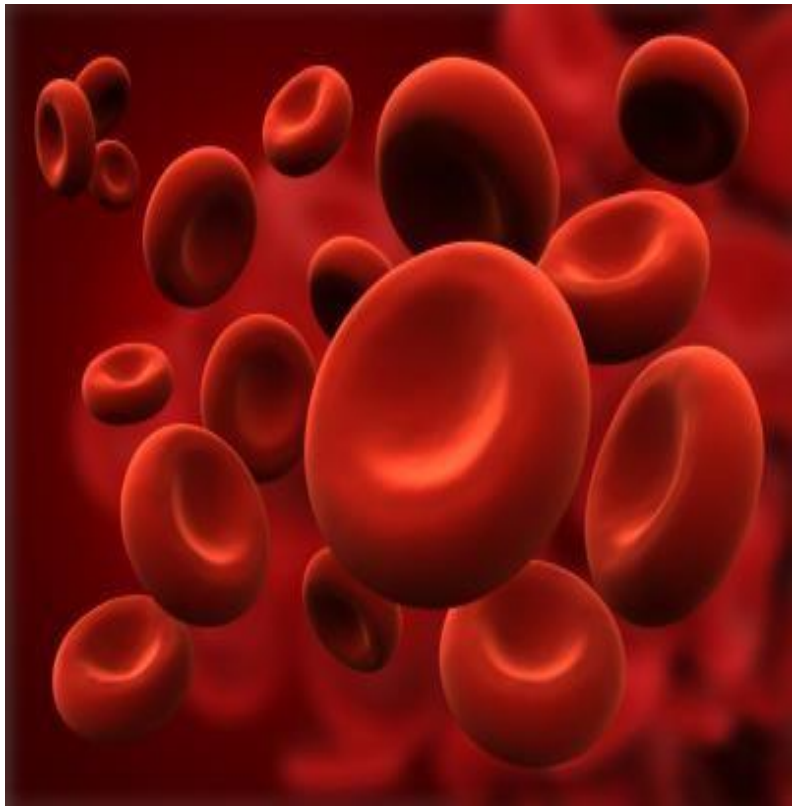
Total count

- RBC count **4.5-5** million/mm^3 in female
- Total leukocytic count -4,000 /11,000mm^3
- Platelet count 250,000- 350,000/mm^3

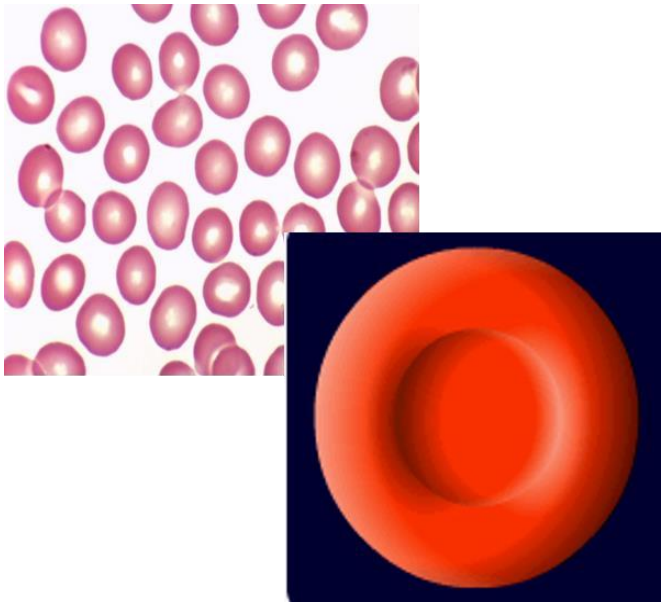
Differential leukocytic count

Blood cells

1. Total or Differential count
2. Shape & size
3. Structure (nucleus + granules(
4. Function
5. Life span
6. Abnormalities



Red Blood corpuscles



Normal RBCs total count:

- In **males** □ 5- 5.5 millions / mm^3 blood
- in **females** □ 4.5-5 millions / mm^3 blood
- LM of RBCs:

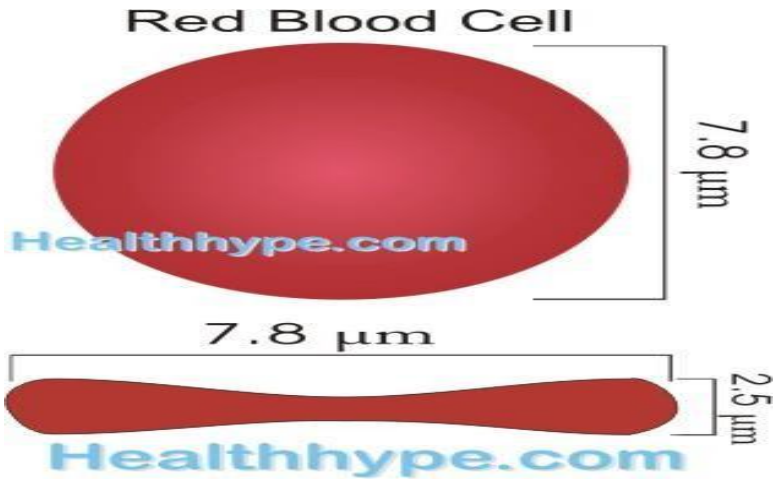
❖ **Shape:** - Biconcave discs.

- Mature RBCs are membrane- bound corpuscle.

❖ **Size:**

- -Diameter 7.5 □m
- -Thickness 1 □m

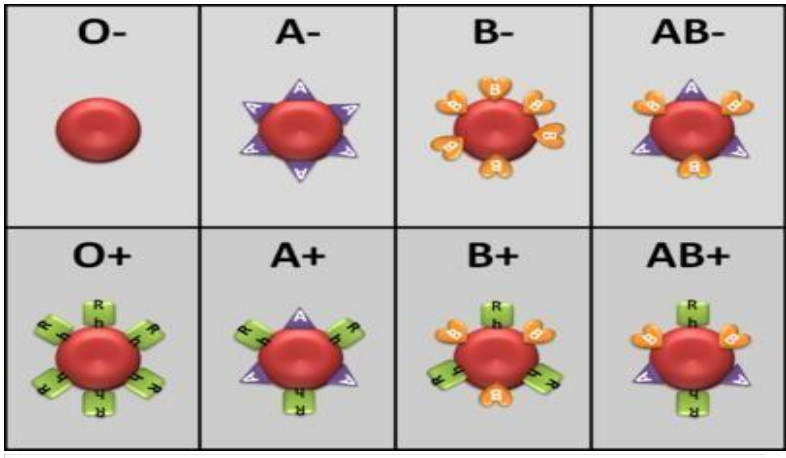
❖ **Structure : Nucleus----** anucleate.

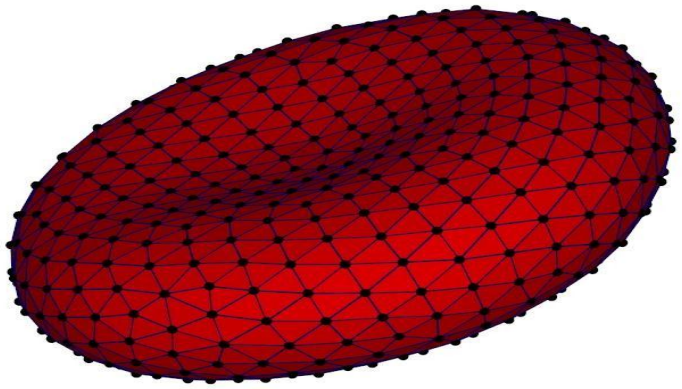


Cytoplasm 33% of the corpuscular volume is Hemoglobin ▬ heme "Fe"+ Globin 'protein'

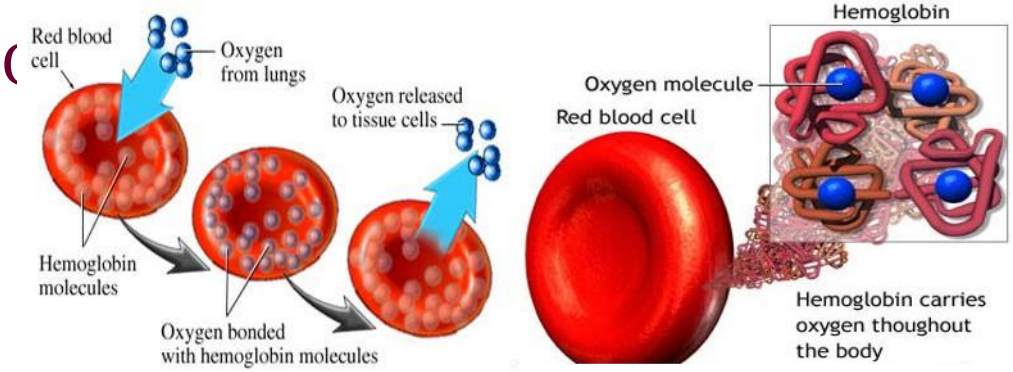
EM picture of RBCs:

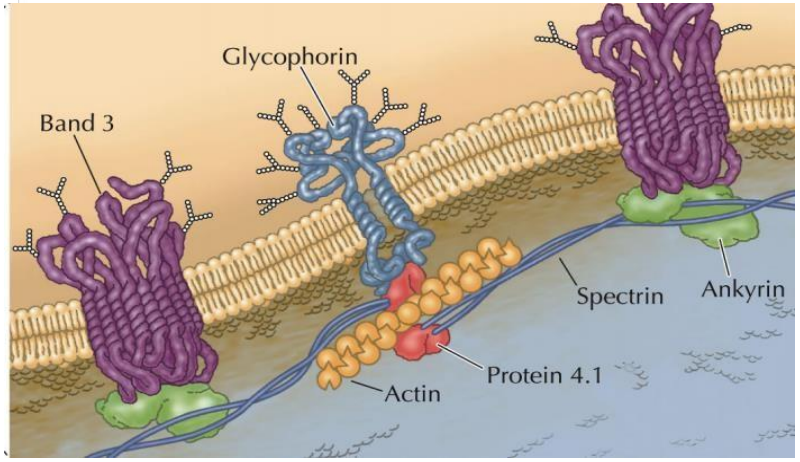
- **Glycocalyx**
- responsible for the **ABO/ Rh** blood group.
- **No** nucleus, **No** typical organelles.
- Only few mitochondria
- subplasmalemmal cytoskeleton
-)actin, spectrin & ankyrin) responsible for the flexibility of RBCs.





- Function of RBCs

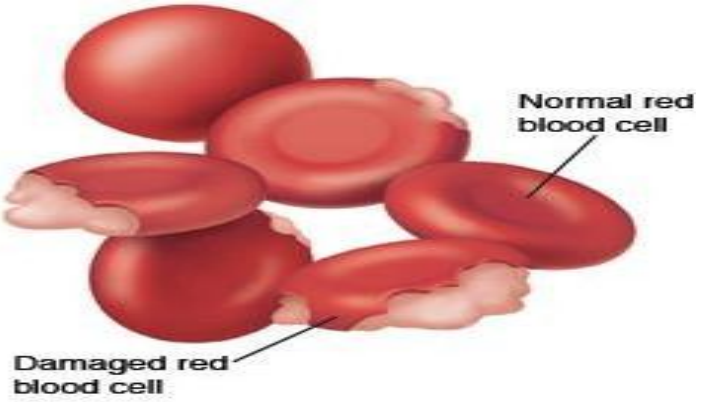




life span:

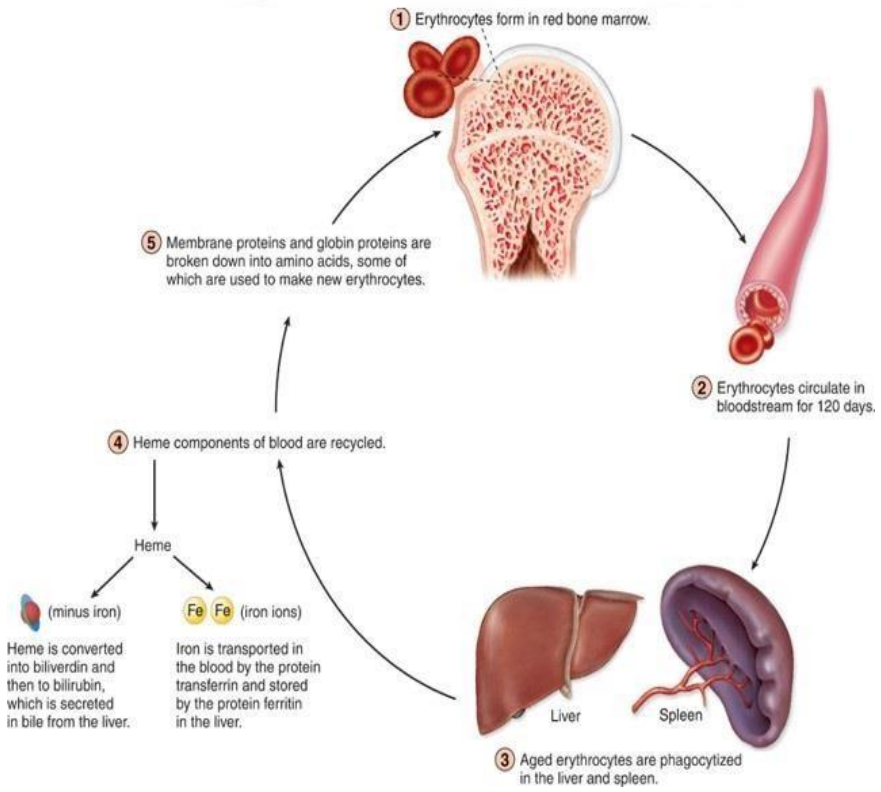
- **120-100days**

Then removed by **Macrophages** of **spleen and liver sinusoids**

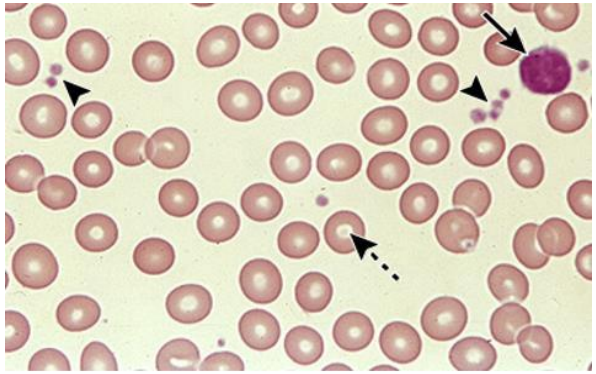


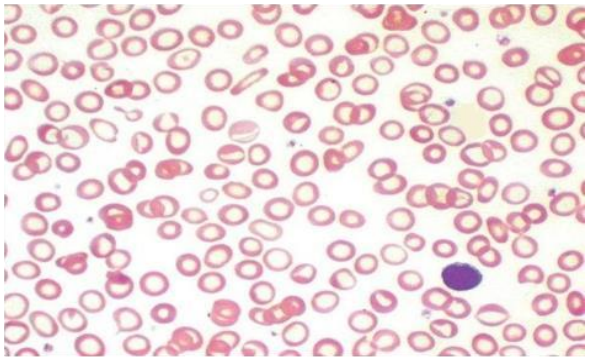
Adaptation to function

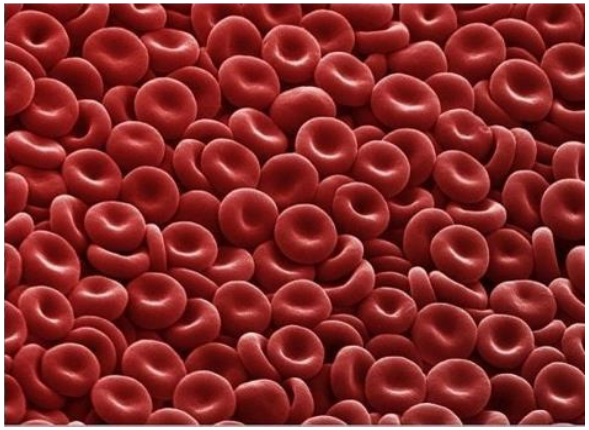
1. Glycocalyx well developed
2. ▲surface area (Biconcave(
3. ▲amount of HB
)no nucleus/ organelles(
4. ▲ ▲HB at the periphery
5. Selective permeability
6. Carbonic anhydrase
7. ▲flexibility to squeeze without damage (cytoskeleton(



Abnormalities of RBCs







Abnormalities of RBCs in number

- **Anaemia:**

Decrease ??? in the total number of RBCs.

- **Polycythaemia:**

increase in the total number of RBCs.

Causes: (decreased oxygen tension(

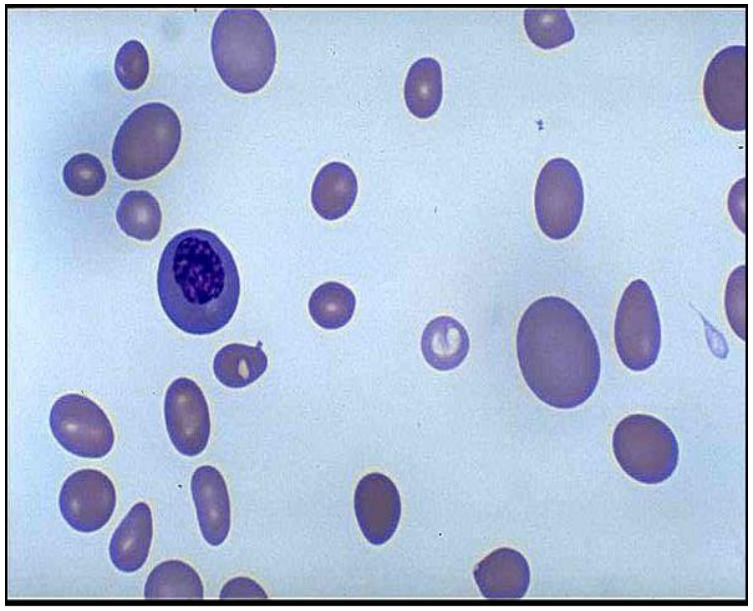
Physiological: newborns ,high altitude

Pathological: chronic lung and heart diseases.

Abnormalities of RBCs in size

- **Microcytosis**:

diameter of RBCs is **less than 6μm**.
(Microcytic anaemia(

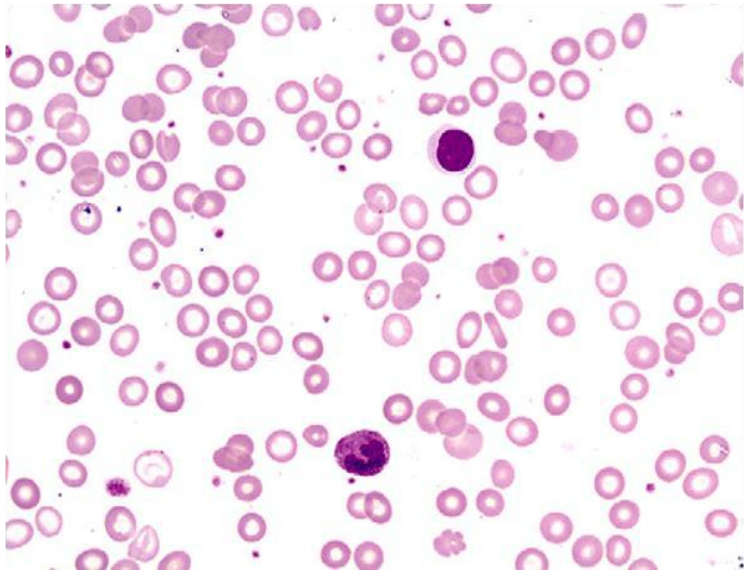


- **Macrocytosis**

diameter of RBCs is **more than 9μm.**
)Macrocytic anaemia(

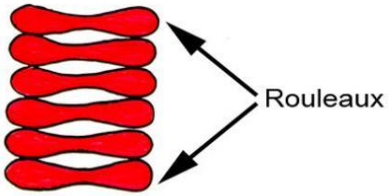
- **Anisocytosis**

Variable in size



Abnormalities of RBCs in shape

1.Rouleaux formation In slow circulation

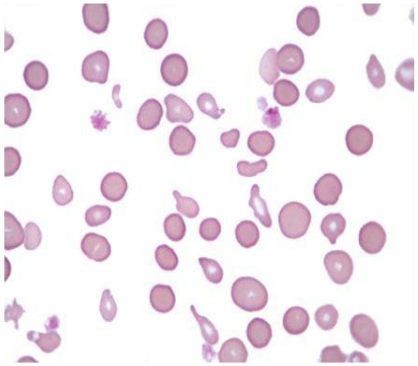


2. Poikilocytosis

Variable in shape

3. In hypertonic solution

►echinocytes(crenation(

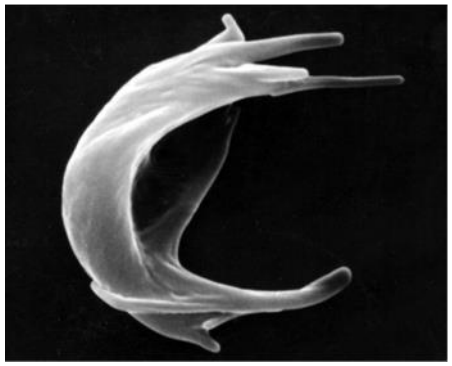


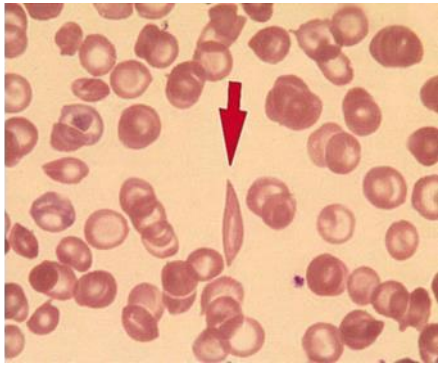
.4In hypotonic solution= swelling

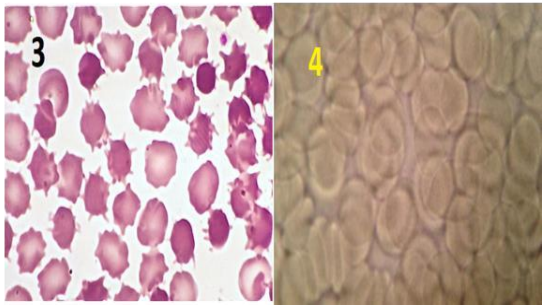
►Ghosts

.5Sickle Cell Anemia

)abnormal Hemoglobin





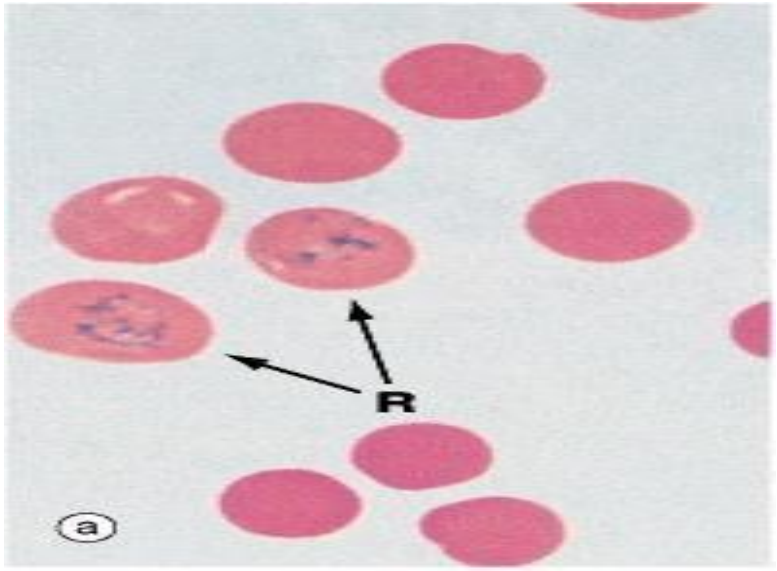


Reticulocytes = immature RBCs

- Reticulocytes represent 1% of all RBCs in normal blood film.
- Nucleated → No nucleus

differ than mature RBCs

- slightly larger (8µm.(
- Cytoplasm contains remnants of ribosomes.
- On staining with cresyl blue form a reticulate pattern.



Clinical significance:

An increase in this percentage indicates an

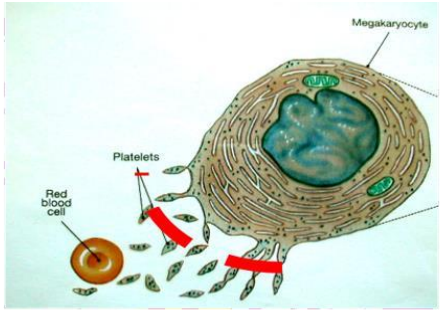
- accelerated rate of erythropoiesis.

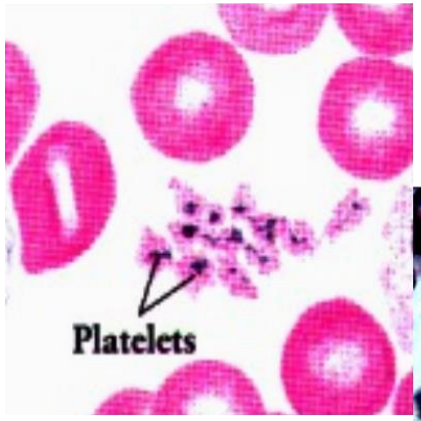
To compensate for anemia or severe hemorrhage.

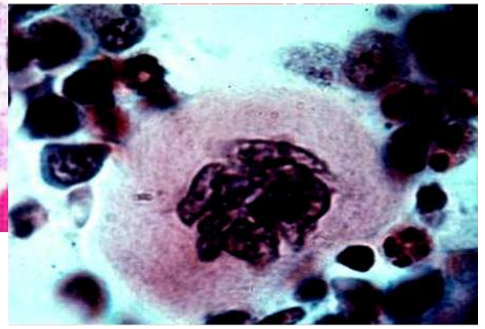
BLOOD PLATELETS

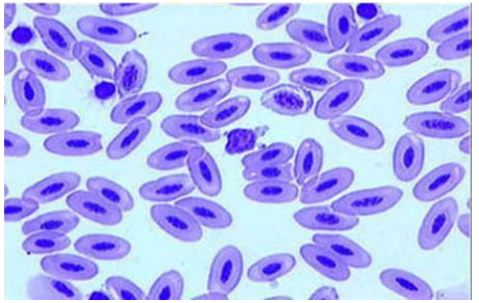
Origin: from megakaryocyte in the bone marrow.

- **Cell fragments of megakaryocyte.**
- **Thrombocytes.**
- **Thromboplastids**









❖ Normal Platelet Count

/350,000-250,000mm^3

(400,000-200,000)

Structure (L. M: (

- **Shape:** Anucleate, biconvex discs.
- **Diameter** :2-3 μm.

central granular zone **(granulomere(**

Granulomere,granular central region

&peripheral clear zone **(hyalomere(**

Hyalomere at the periphery, there is a pale basophilic zone

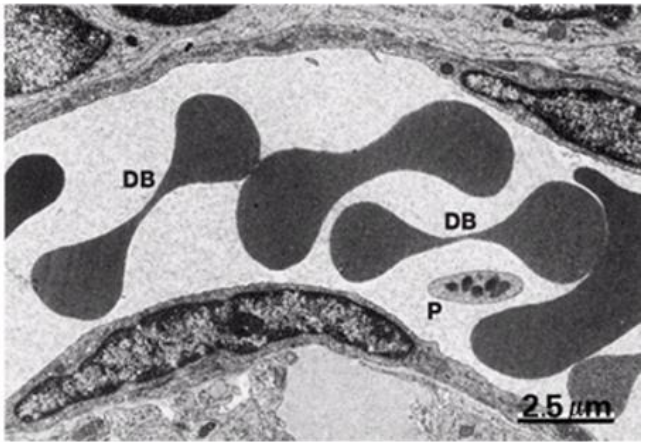
EM of the platelet:

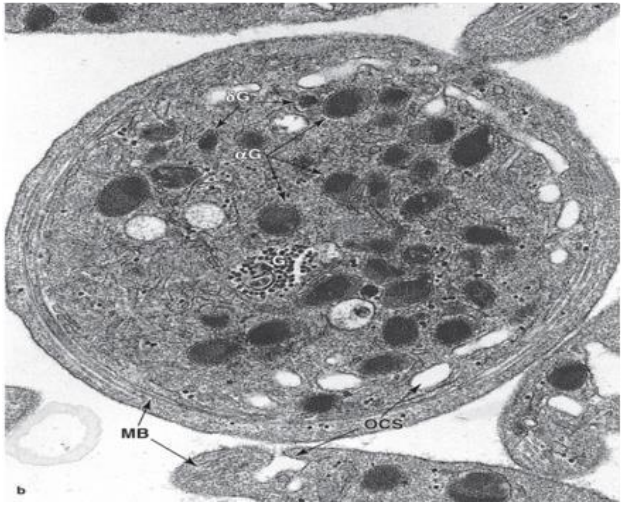
- Shape: Irregular, Pseudopodia.
- Size 3-2: □m.
- Shape: Anucleate, biconvex discs.
- Platelet membrane:

▲▲well developed cell coat glycoprotein for:

- Adhesion
- Aggregation

- Hyalomere &granulomere





Granulomere

- few mitochondria & ribosomes.
- scattered glycogen particles.
- 3types of granules:

❑ **Alpha (α)granules:**

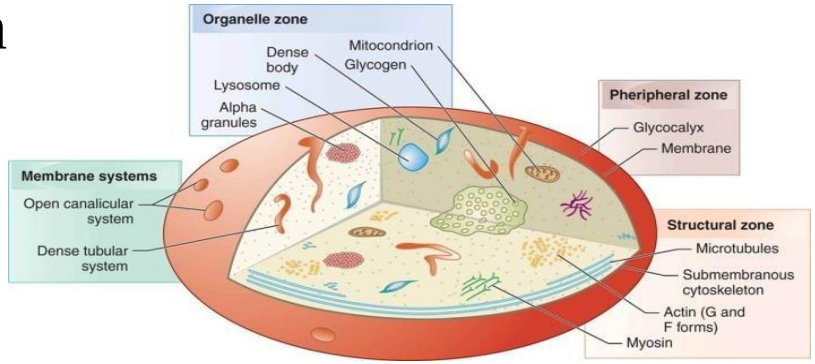
- Large, abundant, PD-GF, coagulation factors.

❑ Delta granules:

- Medium size, ATP, ADP, serotonin.

❑ Lambda(λ) granules:

h



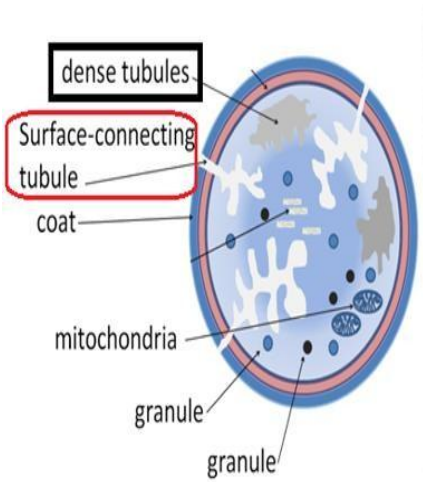
Hyalomere

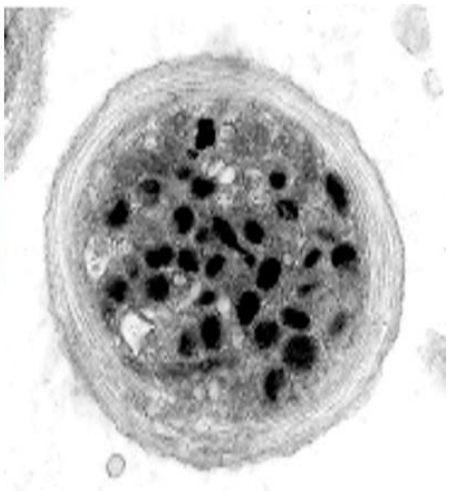
- Electron- lucent.
- Lacks organelles.
- It contains:

➢ **circumferential bundle of 10-15 microtubules ► ► discoid shape**

➢ **Actin & myosin ► ► motility + clot retraction**

➢ **Canalicular system =tubular**





Functions of platelets

- Platelet aggregation-→white thrombus
- Local blood coagulation-→ red thrombus
- Serotonin → Vaso-constristriction
- **Clot retraction** → by microfilaments
- Clot removal→ by **proteolytic enzymes**

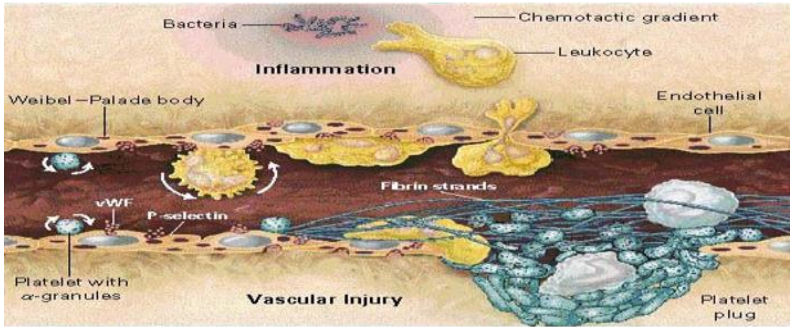
Life span: 10- 14 days in blood

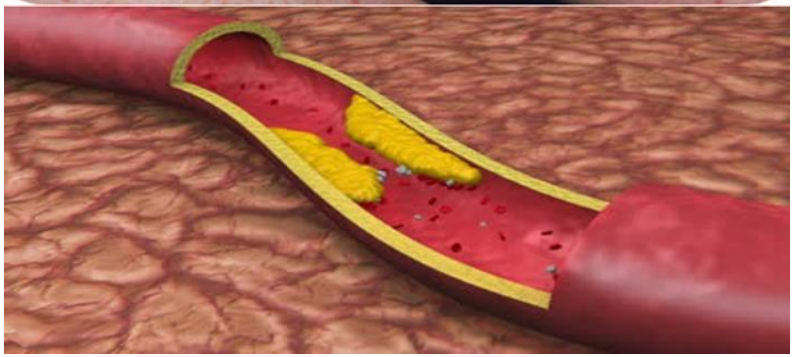
Abnormality of the platelets:

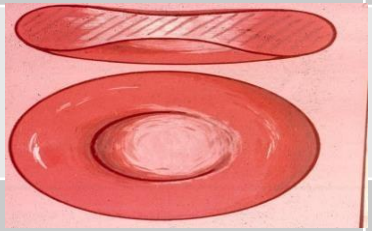
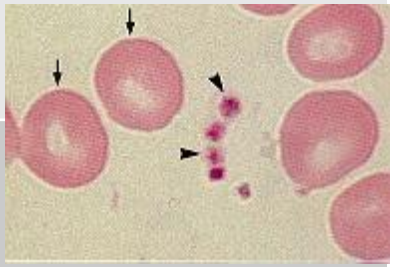
❑ **Thrombocytopenia▼ ▼ ▼**

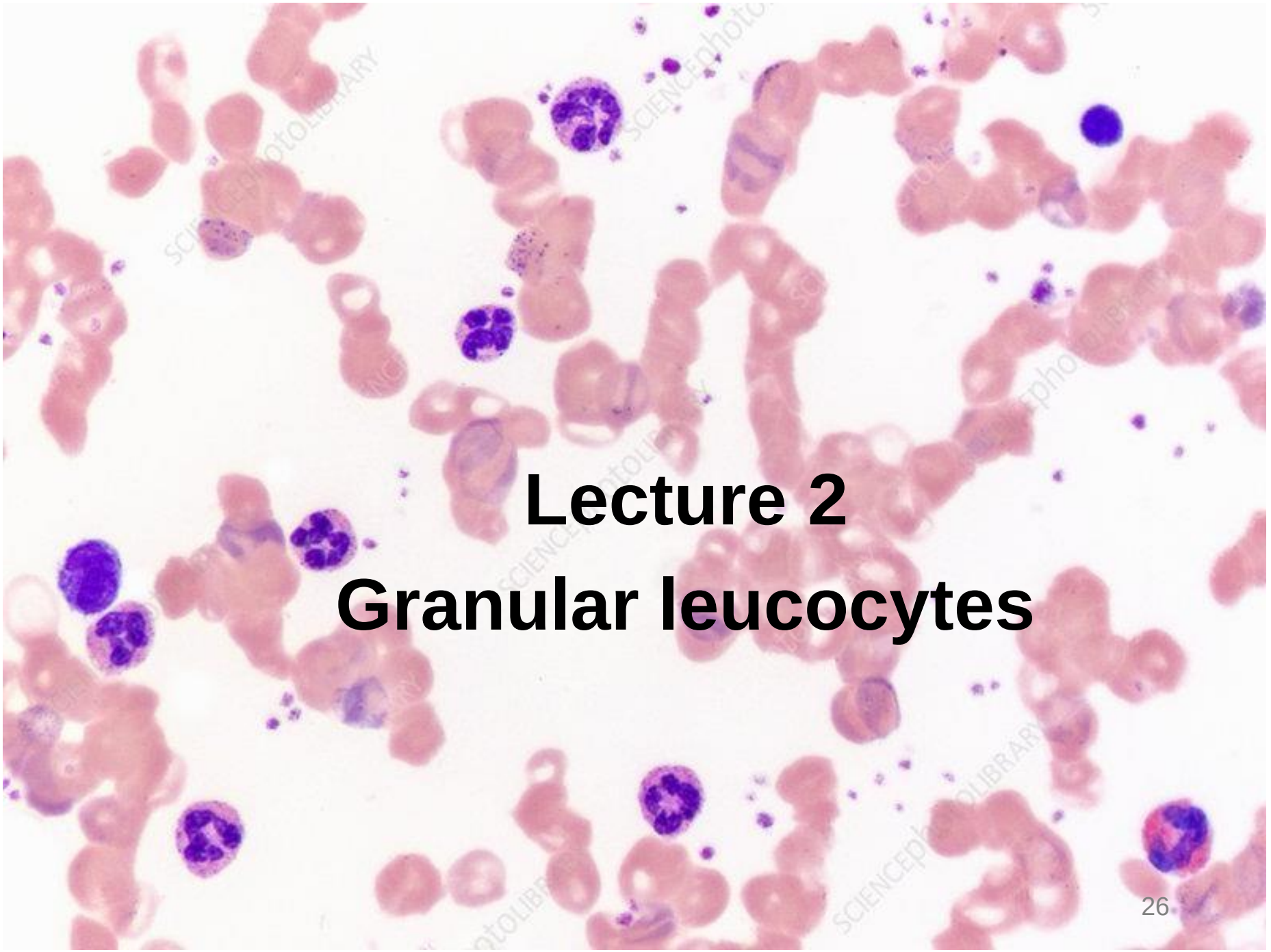
Thrombocytopenia (purpura(

❑ **▲ ▲ ▲Thrombocythemia**





	RBCs Red blood corpuscle Erythrocytes – Greek: “Red	Platelets Thrombocytes Thromboplastides
Number	***males*** **is 5 - 5.5 millions / mm³** ***females*** **it is 4.5-5 millions / mm³ blood.**	/350,000-250,000mm³ 400,000 -200,000
Size	8.5-7.5um **Macrocytes > 9 µm,** **Microcytes < 6 µm** **Anisocytosis = variation in si** 	3µm **5-2µm diameter** 
Shape	biconcave disc	**Biconvex**
Structure	no nuclei & other organelles only few mitochondria **Bag of Haemoglobin**	**Fragments of megakaryocyte** **Not true cell (Non-nucleated)** **Granulomere & Hyalomere**
Life span	**120-100days..**	**14 -10days in blood**
Function	**Carry O2 & Co2**	**-the process of thrombus formation (blood clotting) in response to any vascular endothelial injury to prevent excessive blood loss.** **-clot retraction and removal of the blood clot after healing of the vessel wall to re-establish the flow of the blood.**
Abnormality	**Polycythaemia: i.e. increase in the total number of R.B.Cs.** **Anaemia: i.e. decrease in the total number of R.B.Cs.** **Sickle Cell Anemia**	**INCREASE → Thrombosis** **Decrease → Bleeding**



Lecture 2
Granular leucocytes

The formed blood elements

Stains of blood film

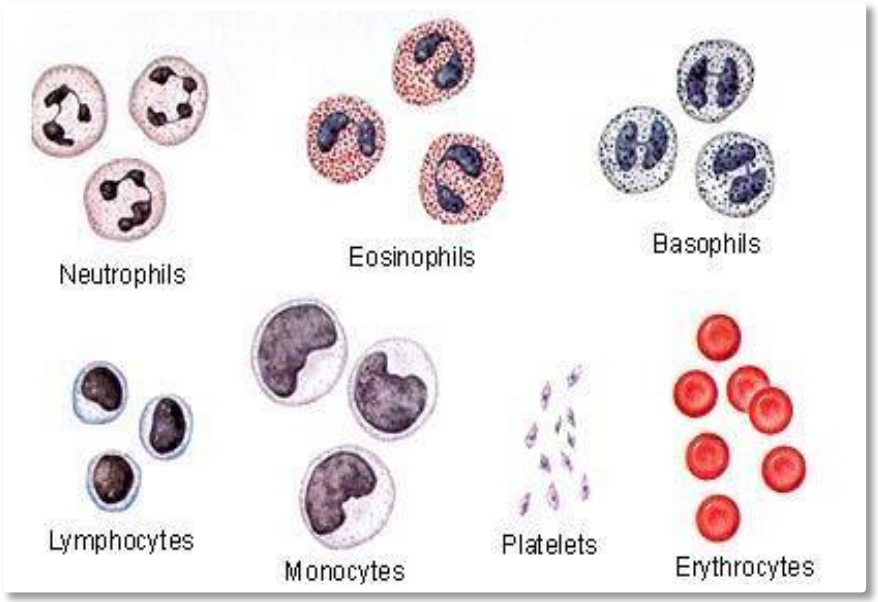
Giemsa's / Leishman's

=methylene blue+ eosin

►basophilic **(violet(**

►eosinophilic **(pink(**

►azurophilic **(red purple(**



Blood cells = 45 % of blood volume

- **Red blood corpuscles =Erythrocytes (RBCs(**
- **Blood platelets = Thrombocytes**
- **White blood cells =Leukocytes (WBCs:(**
  - **Granular leucocytes**

)neutrophils, eosinophils, basophils(

  - **Agranular leucocytes**

)lymphocytes, monocytes(

Leukocytes (WBCs(

Normal total Count

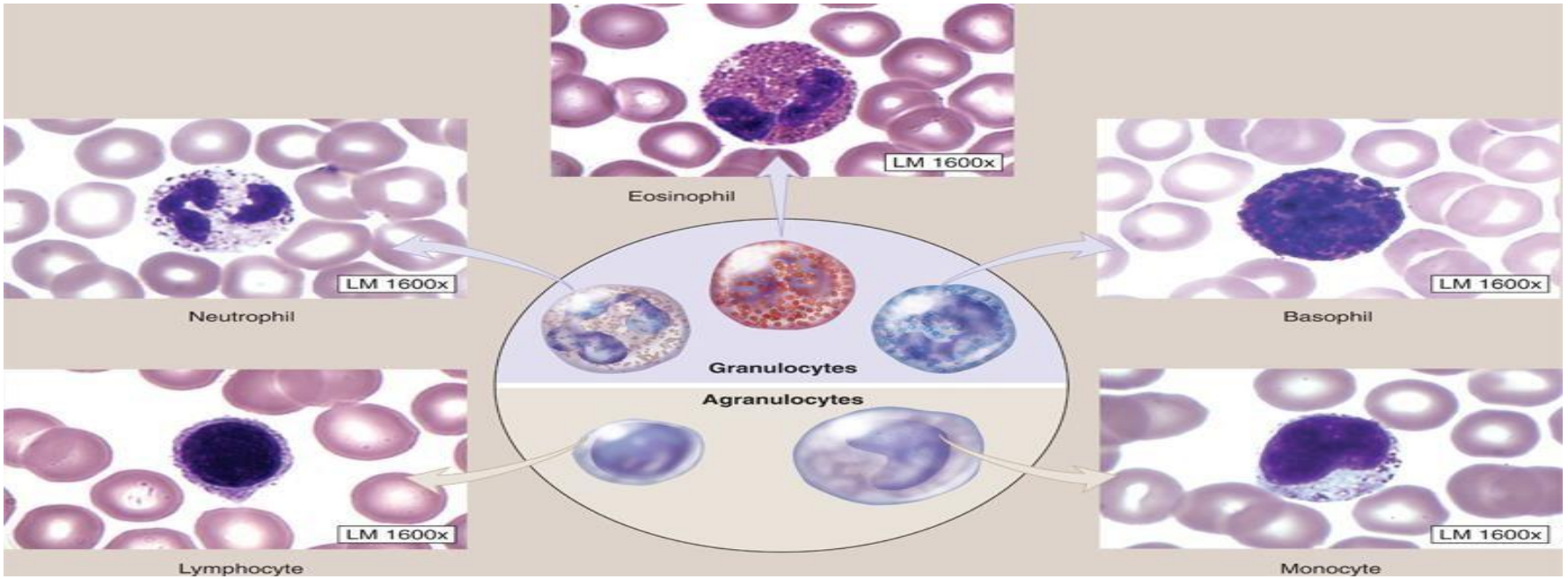
4000-11,000 / mm^3 blood.

I. Granular leukocytes:

- Neutrophils. %-60-70
- Eosinophils. 1- 4%
- Basophils. 1/2- 1%

Agranular leukocytes:

- lymphocytes.20-30%
- Monocytes. 3-8%



Difference between RBCs & WBCs

RBCs	WBCs
➢ 4,5- 5million / mm3	➢ /11000-4000mm3
➢ Biconcave	➢ Rounded
➢ No nuclei. / no organelles	➢ Contain (nuclei+ organelles(
➢ Bag filled with hemoglobin	➢ No hemoglobin
➢ Life span=120 days	➢ Life span= from **days** to years
➢ No ameboid movement	➢ Amoeboid movement
➢ Function : carry O2&CO2	➢ Defense & immunity

Neutrophils= Microphage (polymorphnuclear leukocytes

Differential count 60-70%

Size =10-12 microns

Shape: rounded

LM:

Nucleus : multilobulated = 2-8 lobes

Barr body ?? Condensed chromatin inactive **X- Chromosome in females**

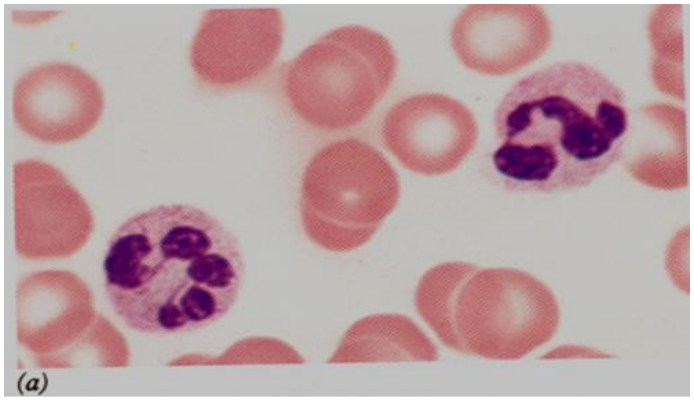
Cytoplasm: contains

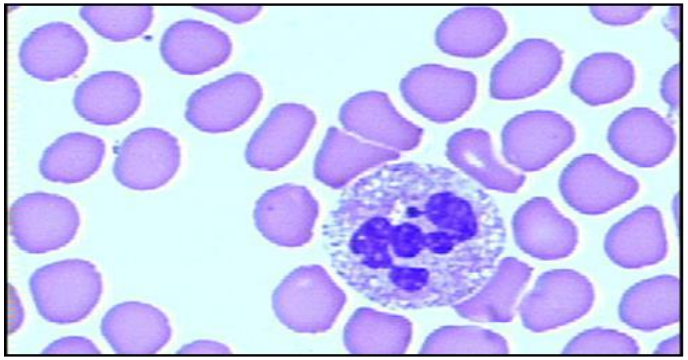
- Specific granules

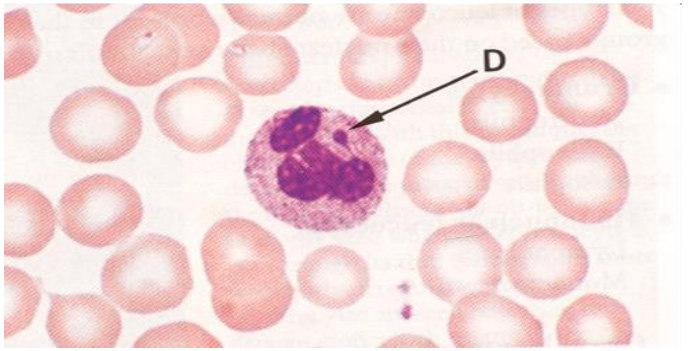
(neutral & small(

- Non specific:

azurophilic granules (few & large ,stained by **azure**(







EM of Neutrophils

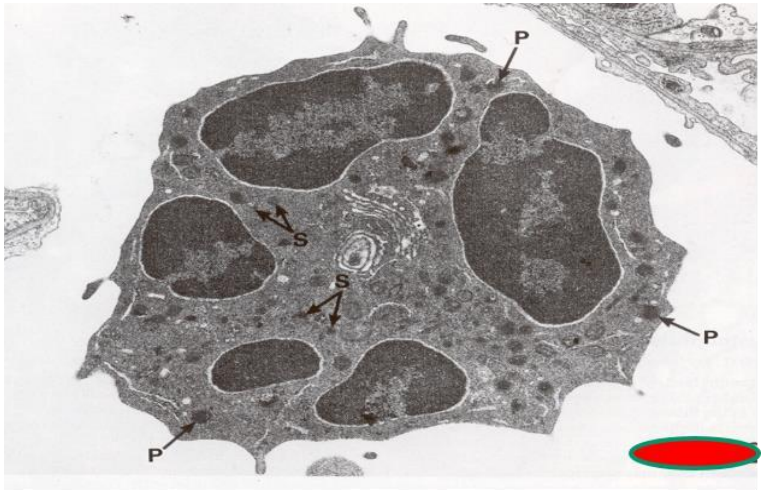
- Shape: irregular. When active
- Cytoplasm : Few organelles.
- **Granules.:**

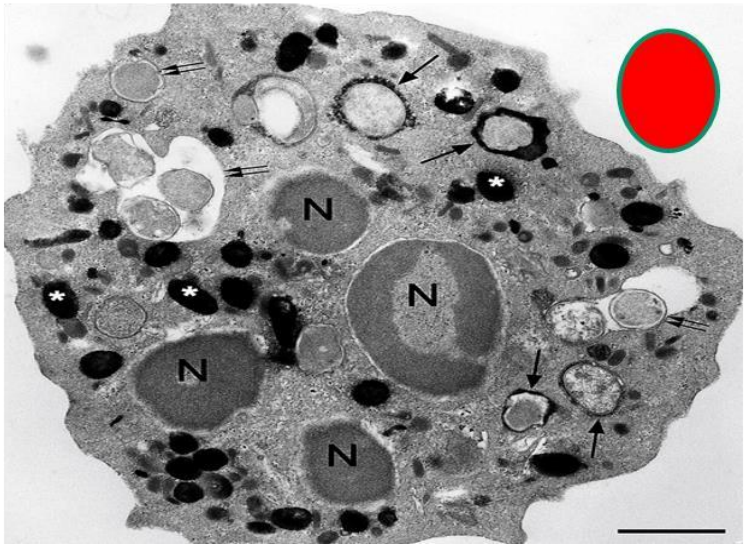
specific granules

Small , Numerous , **Rice grain** appearance , **functional enzymes e.g. Collagenase**

Non specific)Azurophilic(

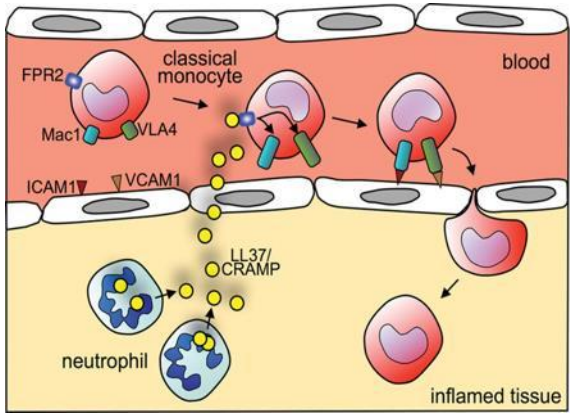
•Large , few , dense Contain lysosomal hydrolytic enzymes.

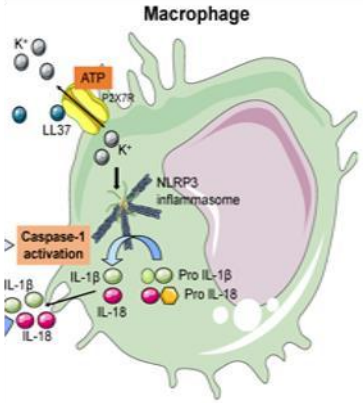




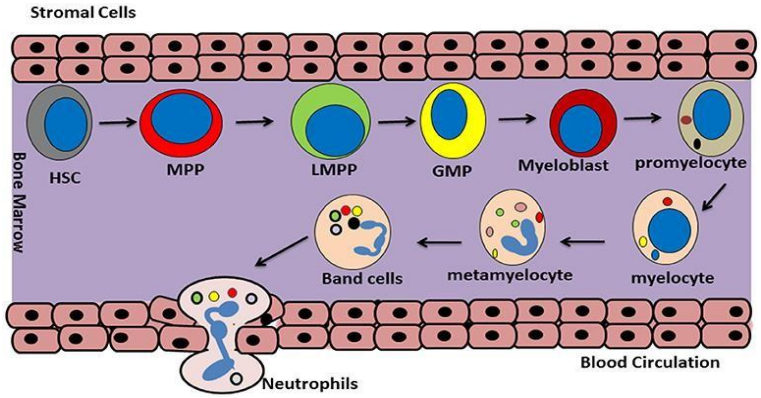
Functions

- The first line of defense.
- Micro-organisms in the C.T.
- Attraction of monocytes to the site of infection. ➡ Macrophages



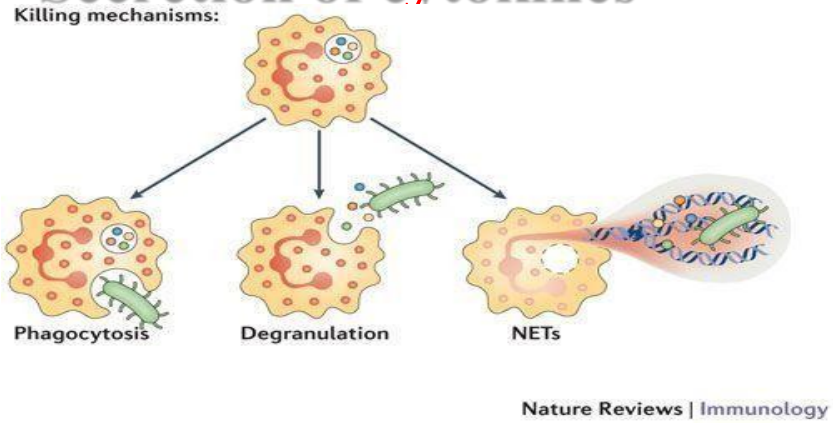


- Chemotaxis→ migration→

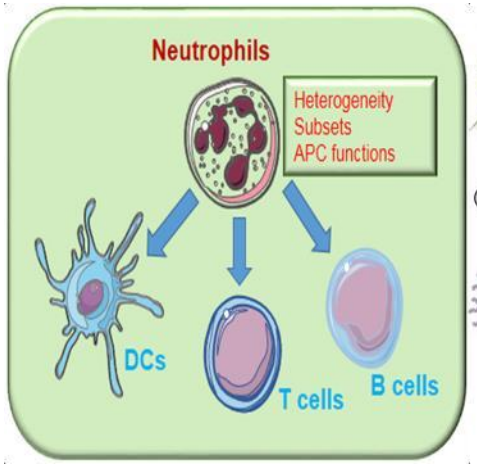


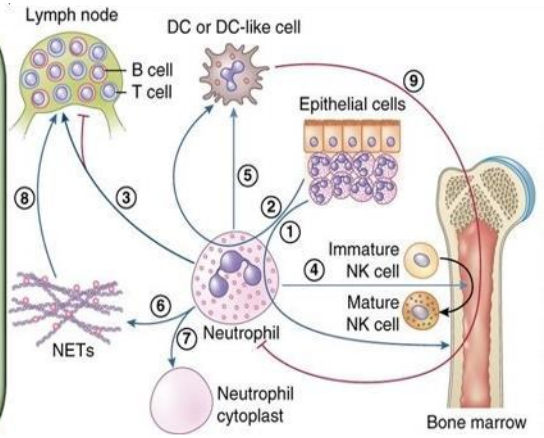
Phagocytosis → killing of bacteria by phagocytins **(specific secondary granules(**

→Secretion of cytokines



- Stimulation of bone marrow to form new neutrophils



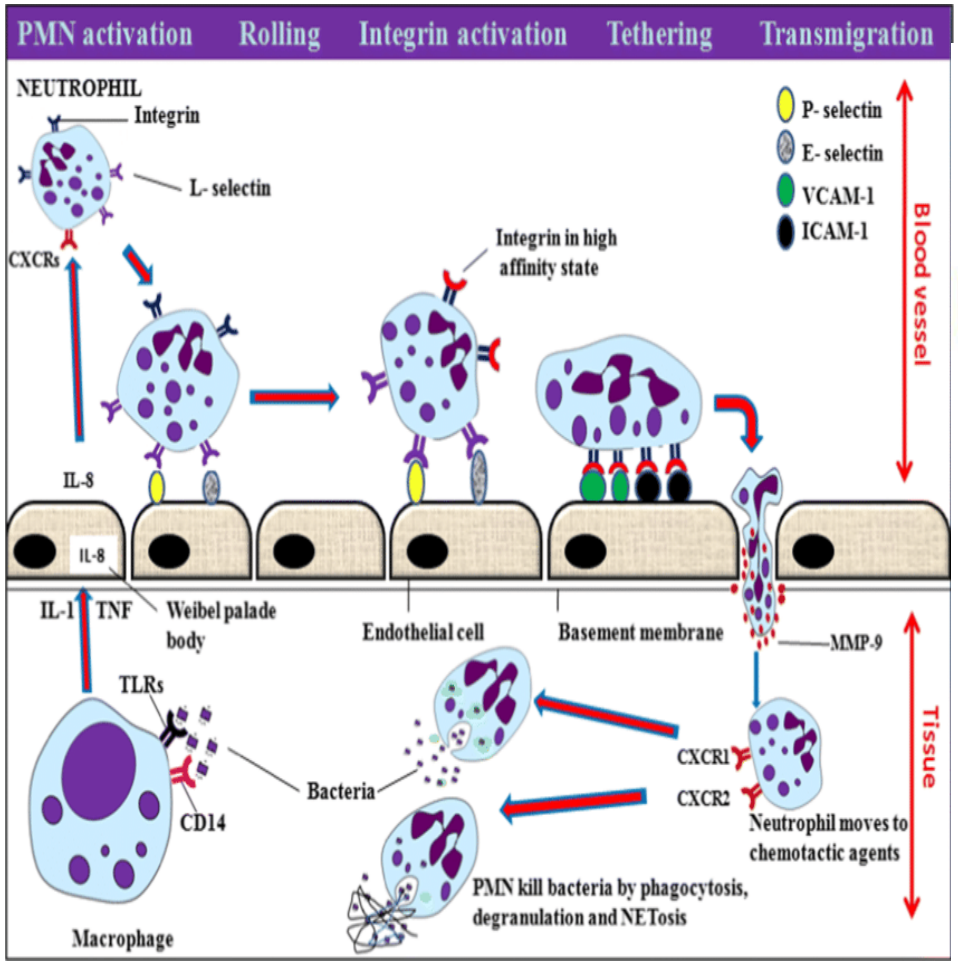


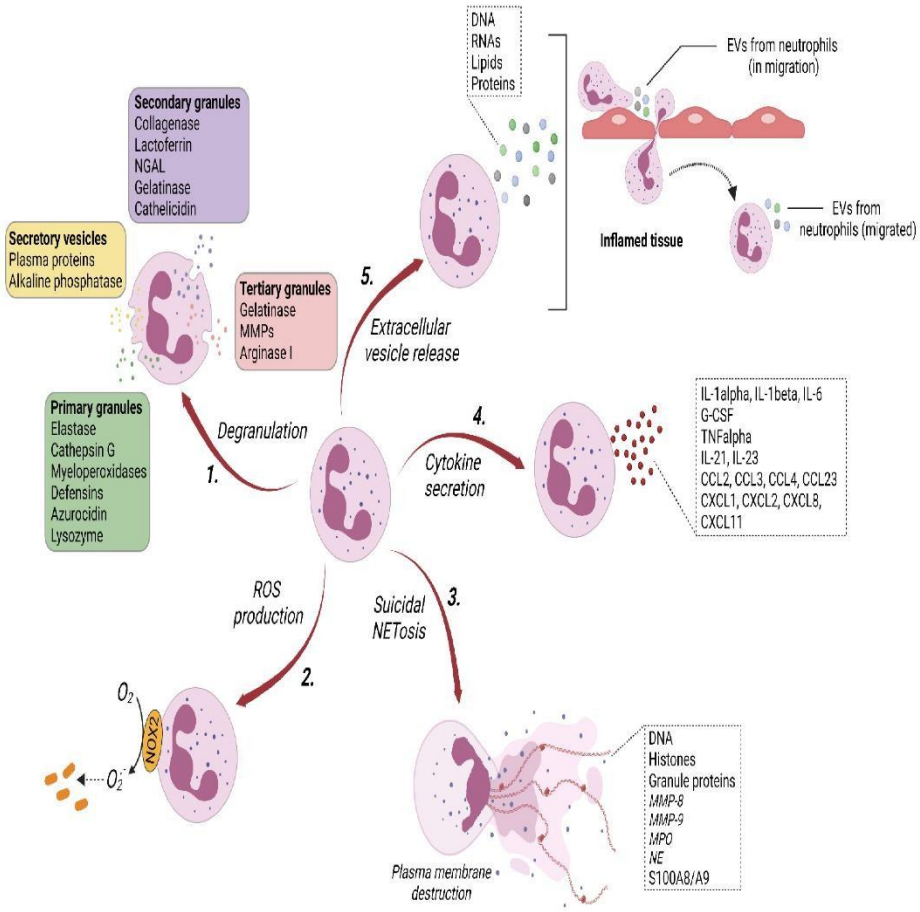
Life span: **1- 4 days** in blood

- digestion by lysosomal enzymes (1ry, azurophilic granules(
- destruction of invader & CT by Collagenase
- death of neutrophils Production of pus)**pus cells**(

Neutrophil and macrophage activation and migration at the site of inflammation.

The main phagocytic cells are macrophages in the tissues and neutrophils in the bloodstream. Initially, macrophages in the tissue sense the presence of invaders ----------
act on the endothelial cells (ECs) and cause the release of interleukin binds to receptors on neutrophil surface causing neutrophil activation.----------Activated neutrophil helps in transmigration. Chemokine receptors help neutrophils to move towards chemotactic gradients and after reaching its target, they attach, ingest and kill the foreign agent by various mechanisms





Abnormality of neutrophil count

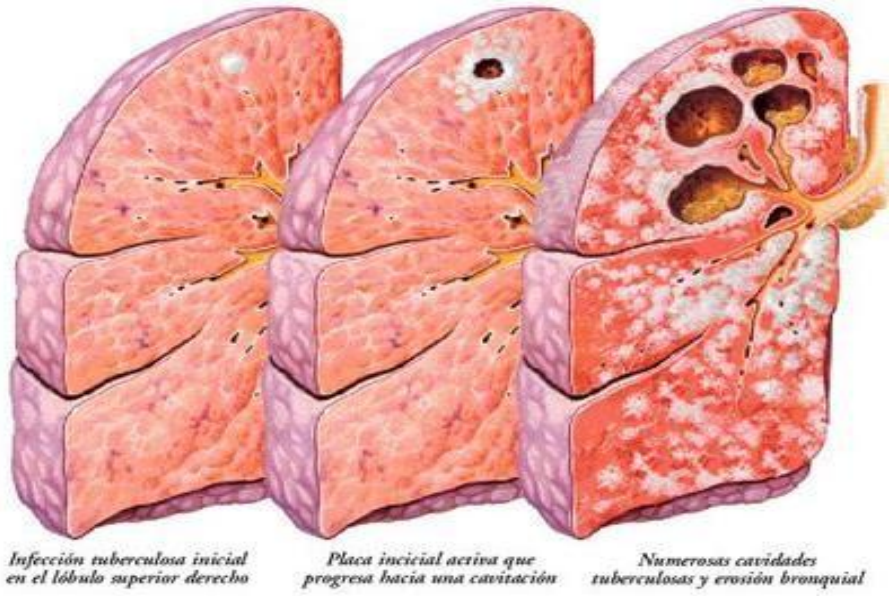
Neutrophilia ▲ ▲

in **acute** pyogenic **infection** = acute inflammations e.g.:

- ❖ Appendicitis
- ❖ Tonsillitis

Neutropenia: ⬇ ⬇

- ❖ Chronic infection e.g. TB
- ❖ Severe viral infection e.g. Influenza , Measles



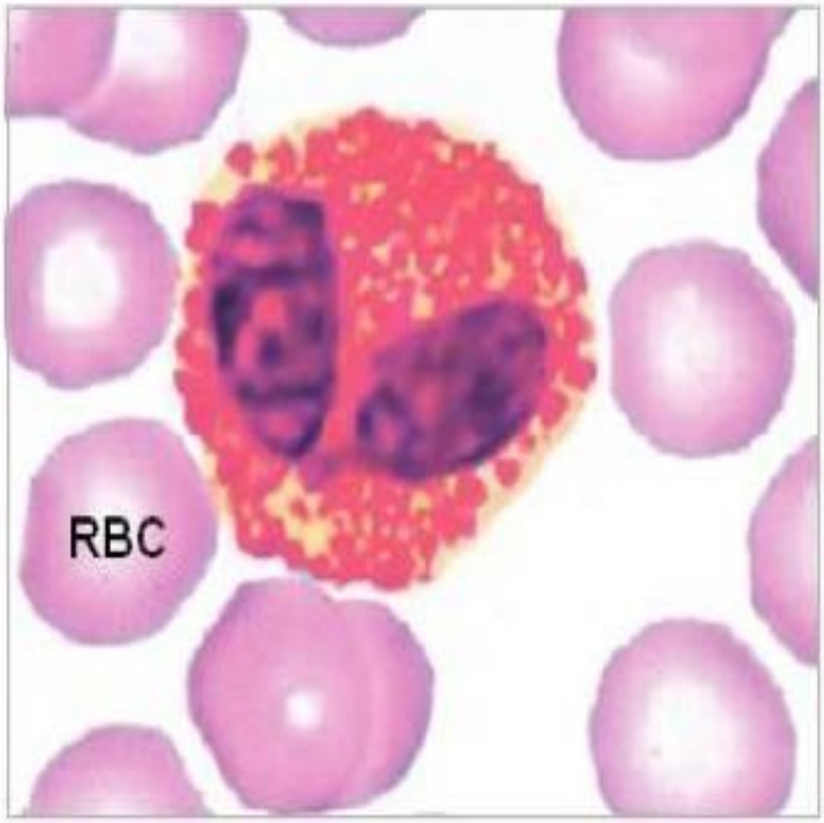
Eosinophils

- **Differential count :** 1- 4%
- **Size :** 12-15 microns.
- **Shape:** rounded
- **L.M:**

- Nucleus: bilobed C- shape

- Cytoplasm contains:

  - large specific acidophilic granules.
  - Few azurophilic granules

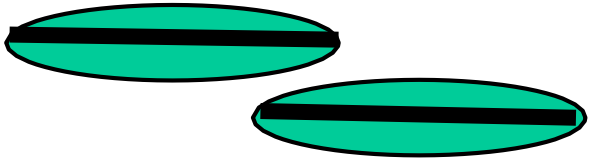


E.M:

- Bilobed C- shaped nucleus
- Cytoplasm contains
- Few organelles mitochondria, rER, & sER & glycogen
- **Specific granules** (Large, ovoid ,crystalloid core contain many hydrolytic enzymes histaminase , eosinophil peroxidase)
- Few non specific granules

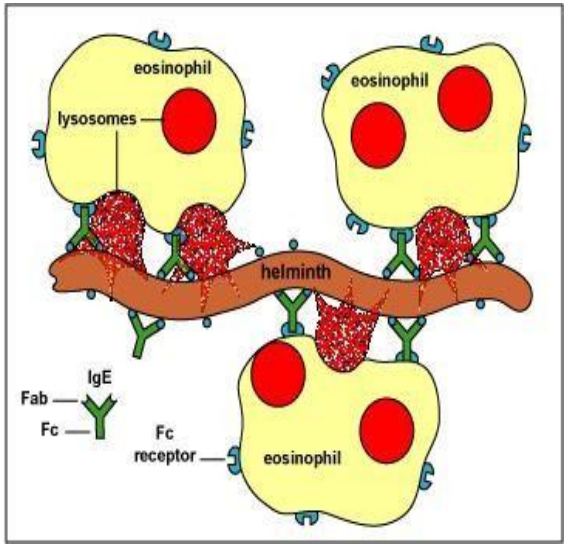
= azurophilic granules

Small , sphericalLysosomal hydrolytic enzymes



Function of Eosinophils

- Migrate to mucosa of GIT, respiratory, genito-urinary& skin.
- regulation of allergic reactions.
- Parasitic infection. (Not phagocytic)



Life span: several days up to week

Abnormal Eosinophil Count

❑ **Eosinophilia = increase** ▲ ▲

➢ **Allergic** reactions e.g. bronchial asthma, allergy , **parasitic** infections e.g. Bilharziasis.

❑ **Eosinopenia = decrease** ▼ ▼

➢ Steroid therapy. Bone marrow depression.

Basophils
Mast cell of the blood

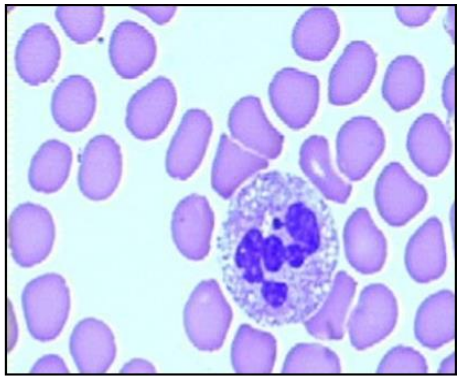
Differential count : ½ - 1%

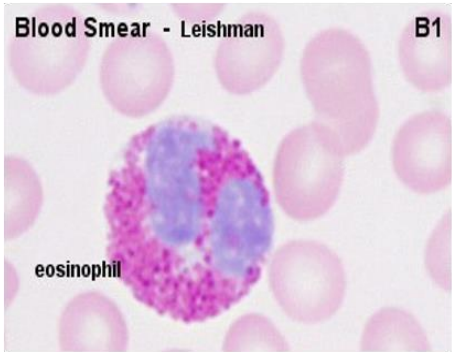
Size : 10 microns

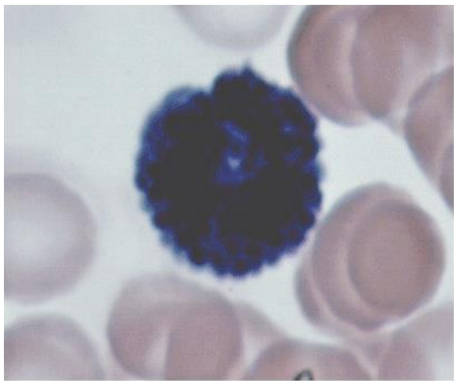
Shape : Rounded

LM:

- **Nucleus:** Bilobed, **(S-shaped(**
  - **obscured by large granules**
- Cytoplasm:
  - **abundant deep blue granules.**
  - **Metachromasia.**







E.M.

Nucleus : Bilobed S shape nucleus

Cytoplasm: mitochondria, ribosomes, glycogen

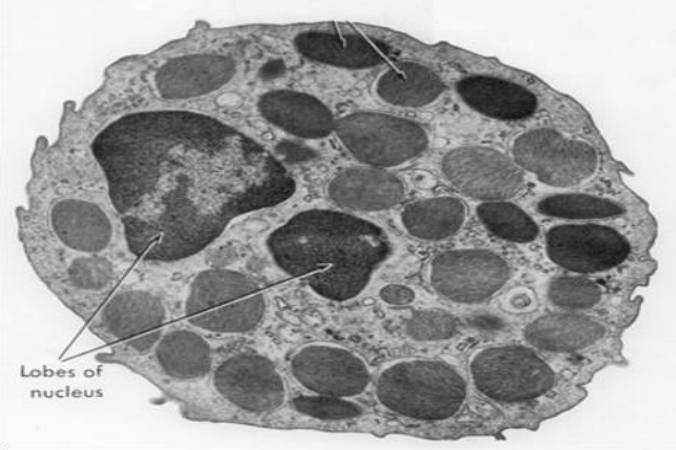
Granules :

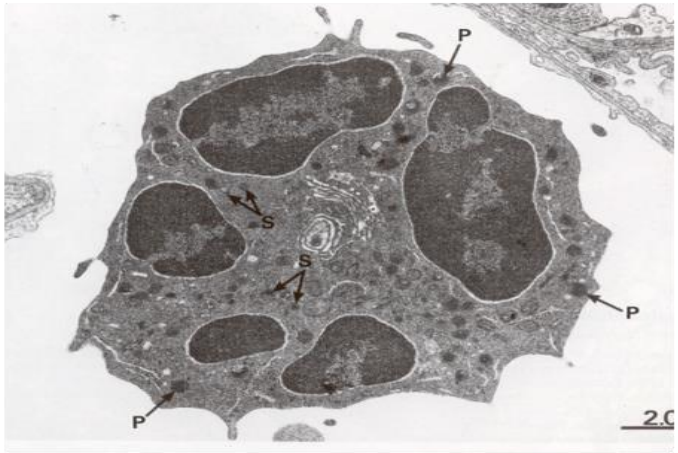
specific granules

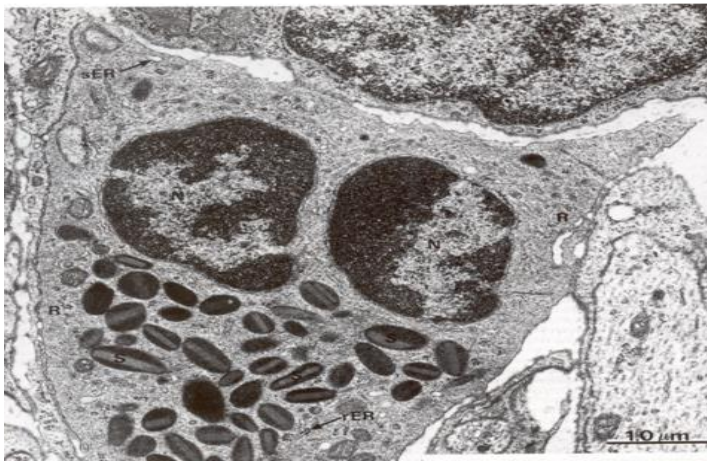
- Large, contain histamine, heparin

Non specific (azurophilic granules)

- Contain lysosomal hydrolytic enzymes.







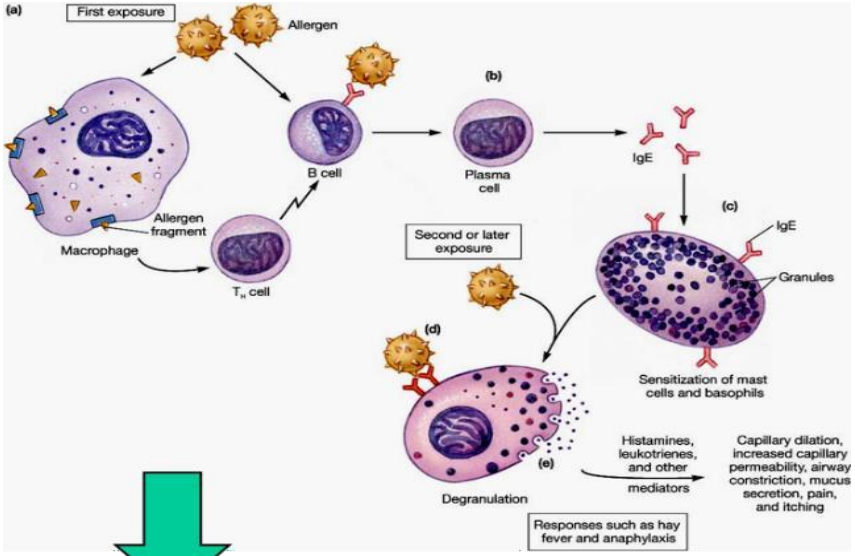
Functions

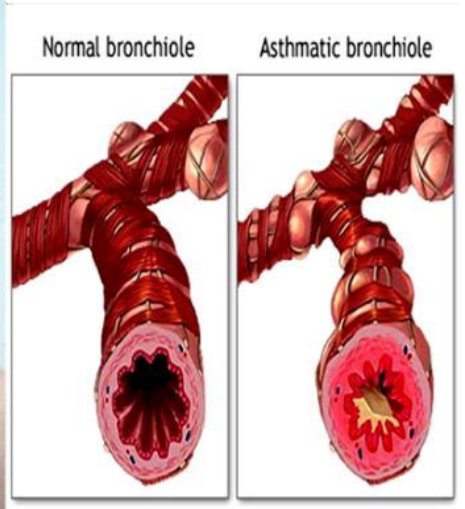
=Mast cell of blood=:

- **heparin:** anticoagulant
- **histamine:** **(anaphylaxis(**

- Secretion of histamine which initiates allergic reactions.
- Secretion of heparin which is a natural anti-coagulant.
- Secretion of eosinophil chemotactic factor to limit allergic reaction.

hypersensitivity reaction





Life span: **1-2** week

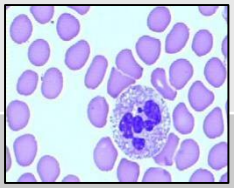
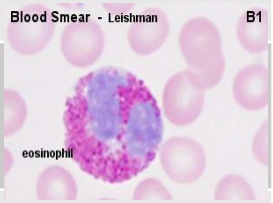
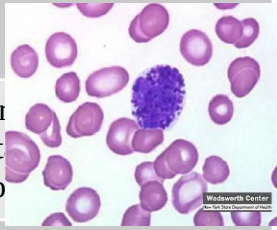
Abnormal count

Basophilia:increase ▲▲

- viral infections e.g.

small pox and chicken pox.

- **Systemic allergy**

	Neutrophils	Eosinophils	***Basophils*** **mast cell of the blood.**
Number	**%70-60of leukocytic count**	**%4-1of leukocytic count**	**%1-0of leukocytic count**
Size	**12-10**µm in diameter 	**larger than neutrophils (12-15 µm in diameter،**	**10)mm) in diameter،**
Shape	spherical in shape+ Neutral granules	spherical in shape+ Acidophilic granules	spherical in shape (basophilic) specific granules with heparin and histamine
Structure	multi-lobed nucleus human females may have **inactivated second X** chromosome (Barr body drum stick	bi-lobed nucleus C-shape or 	S-shape lobed nucleus, obscured by basophilic granules
Life span	lifespan 1-4 days in circulation؛	several days Up to week	2-1weeks 
Function	first line of defense against any invading micro-organism	• Kill parasites، • associated with allergic reactions	Basophils are r release of Hist allergic reactio
Abnormality	**Neutrophilia:** i.e. abnormal increase in the number of neutrophils. This is observed in acute inflammations e.g. appendicitis, tonsillitis. **Neutropenia:** i.e. abnormal decrease in the number of neutrophils e.g. in influenza, typhoid fever.	١*Eosinophilia:* i.e. abnormal increase in the number - Allergic reactions e.g. asthma, urticaria -Parasitic infections e.g. Bilharziasis. ٢*Eosinopenia:* i.e. l decrease in the number prolonged corticosteroid therapy.	Basophilia in systemic allergic reaction

Agranular leukocytes

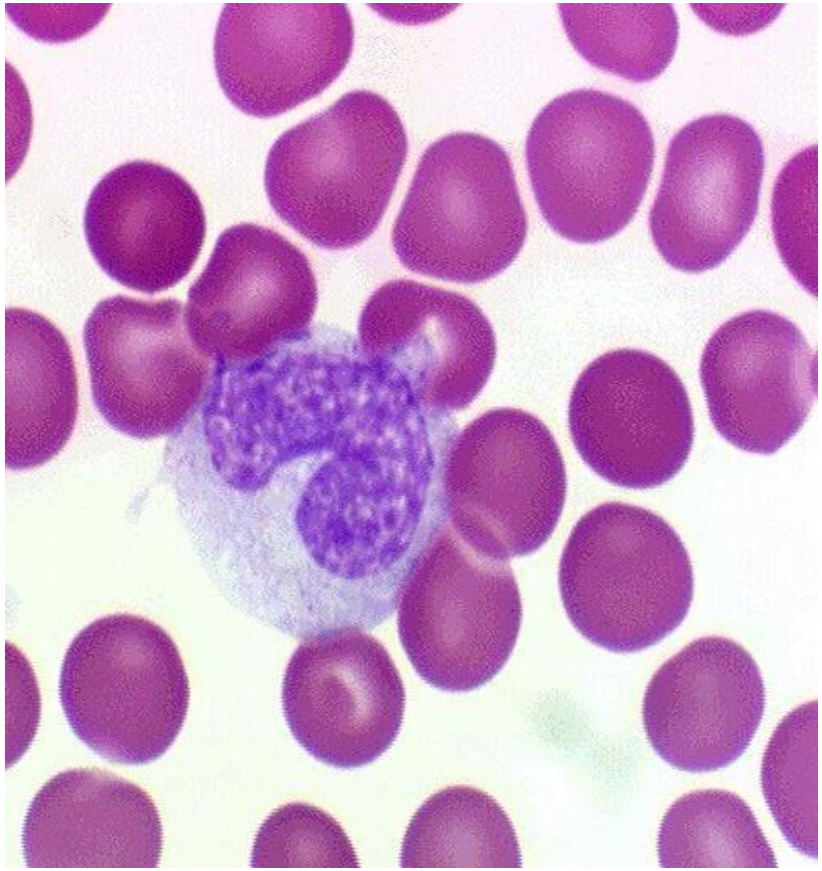
Monocyte

- **Differential count: 8% - 3**
- **Size :** 20microns = **Largest** in blood film
- **Shape : rounded**

LM:

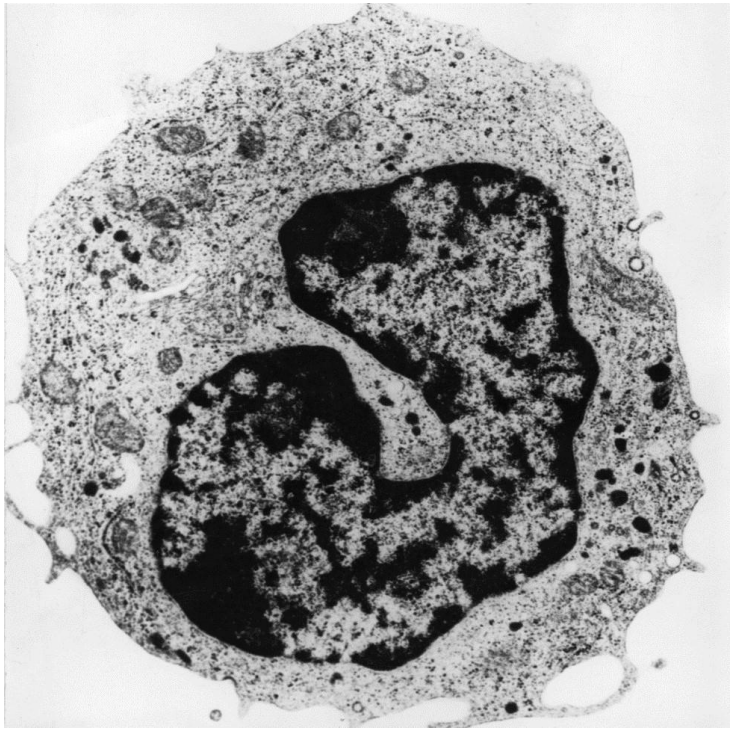
- **Nucleus:**
  - Large, eccentric , Kidney- shaped **)Indented(**
- **Cytoplasm:**
  - Finely granular, abundant pale basophilic non specific granules

=Azurophilic granules



EM:

- Irregular = Pseudopodia
- Nucleus: Large, eccentric kidney-shaped (Indented(
- The cytoplasm contains
  - a moderate amount of organelles.
  - Non specific (Azurophilic granules) few small dense granules containing lysosomal hydrolytic enzymes.

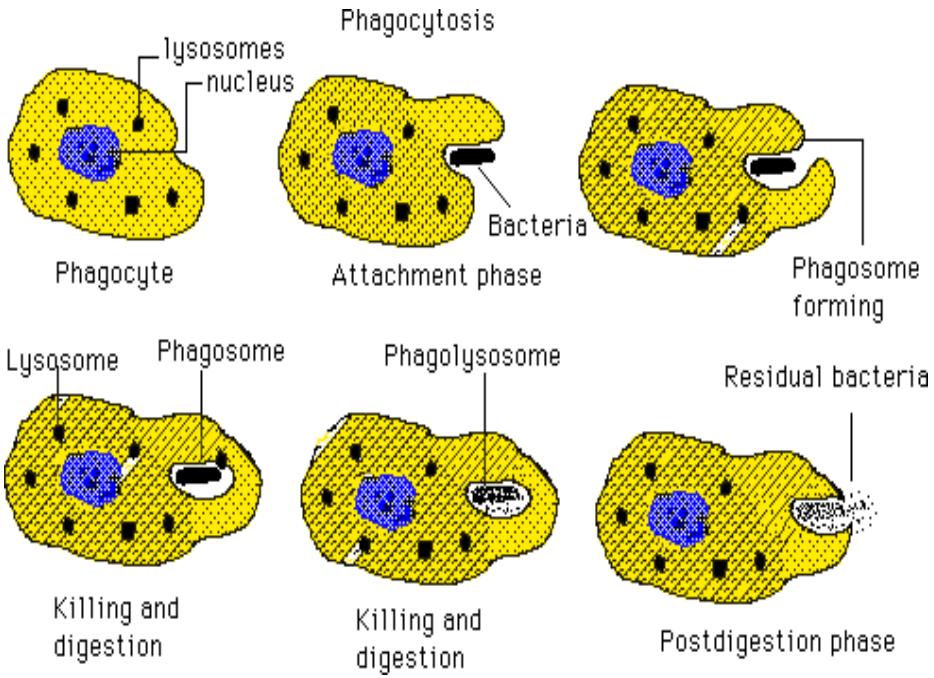


Function:

- Trans- migration & differentiation to tissue MACROPHAGE
- Immunologic function:

➢ Phagocytosis and intracellular digestion of bacteria, virus

➢ Ag- presenting cell



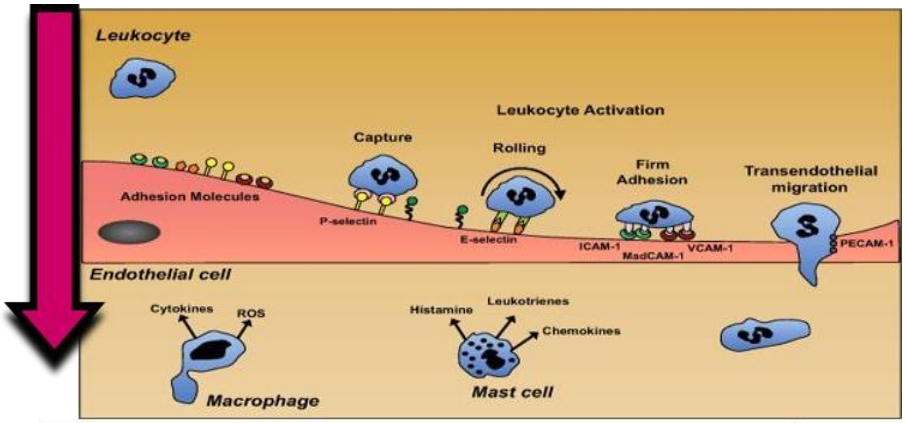
Life span : 1-2 days

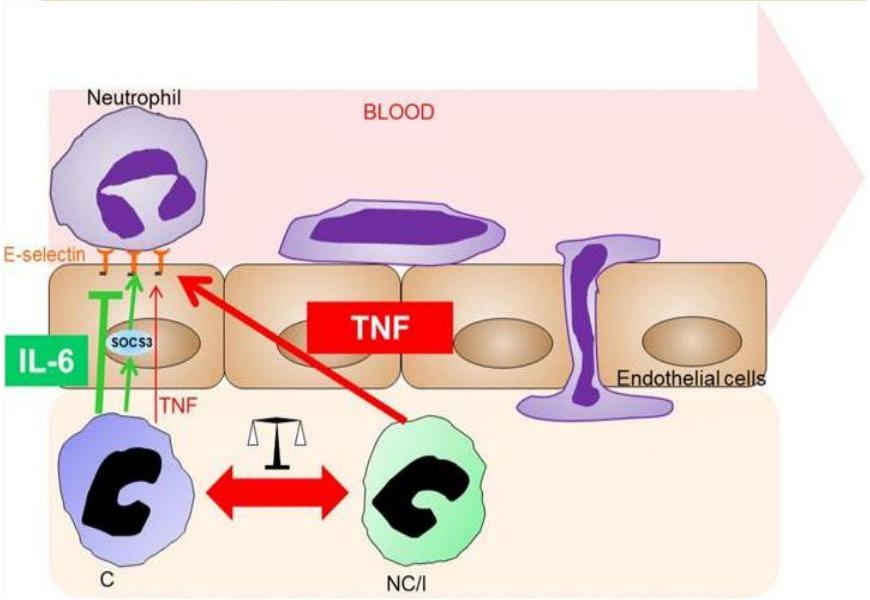
circulation in the blood, then enter the CT and trasform into macrophages

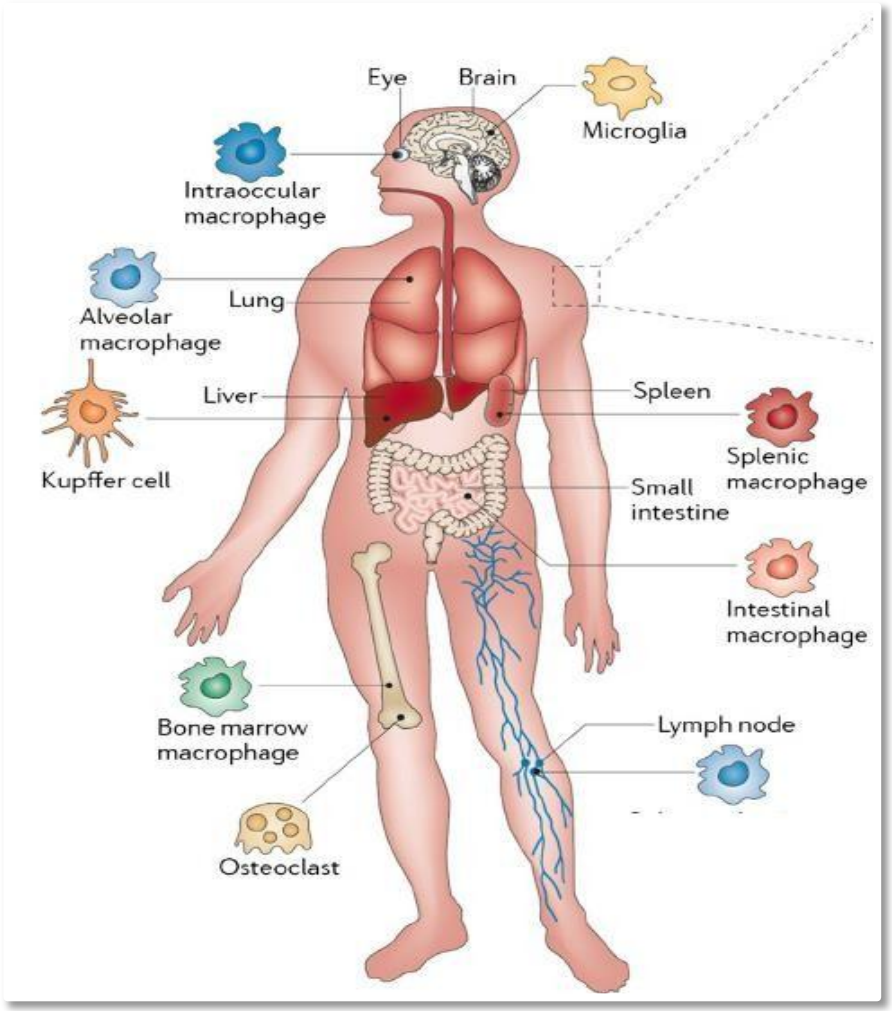
- Circulate from region to another & Function in CT=

Immunological function

Mononuclear phagocytic cells







Abnormal Monocyte count

Increase number = Monocytosis

Causes:

1 Malaria

2 Chronic infections (glandular fever , syphilis, T.B(.

3 Lymphomas & Leukemia.

⇓⇓ in number of **Monocyte**

Causes:

- **Bone marrow depression**
  - **drugs**
  - **Irradiation**
  - **Severe chronic diseases**

Lymphocytes

- Differential count: 20-30%
- Size : 9-12 microns
- According to the sizes:

➢ large lymphocytes.

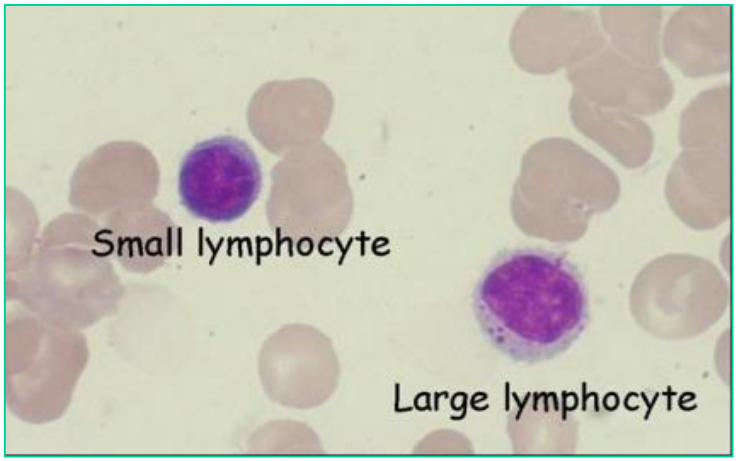
➢ Medium-sized lymphocytes.

➢ Small lymphocytes:

❖ Diameter = RBC.

❖ Most numerous.

❖ Functionally mature.



3functional types:

➢ T- lymphocytes:

- Start development in bone marrow.
- Differentiate in thymus.
- Cell-mediated IR.

➢ B-lymphocytes:

- Develop & differentiate in bone marrow.
- Humoral immune response.

➢ Natural killer cells = Null cells

➢ Develop in bone marrow.

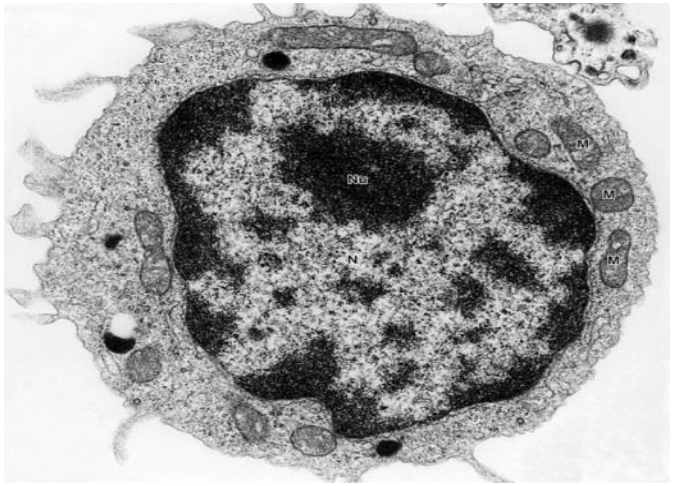
- Lack CDs of B or T.
- Are null cells(non B, nonT.(
- They don't enter the thymus to be competent.
- They act nonspecifically to kill virally infected cells &tumor cells

❖ LM:

- ➢ **Shape = rounded**
- Large nucleus, thin cytoplasmic rim
- ➢ No stained granules in the cytoplasm (except small **Azurophilic granules**
- **Small most common 90%**
- **Types: B**- and **T**-lymphocytes **(morphologically not distinguishable(**
- **Null-cells** (somewhat smaller size) Non B Non T

❖ EM:

- ➢ **Nucleus:** dense clumps.
- ➢ **Cytoplasm t**hin rim
- No specific granules Lysosomes= small & dense Azurophilic granules
- Many free ribosomes& few mitochondria + **2 centrioles**
- ▲▲The cell coat = **antigenic markers.**



Antigenic markers of lymphocytes

The cell coat: Large no. of cell receptors.

1. **Major histocompatibility complex (MHC)**
   Glycoprotein + specific a.a. sequence.

Tissue typing & antigenic recognition.

2. subclasses:

MHC I & MHC II.

2- The cluster of differentiation antigens (CDs):

- **Cell- surface glycoprotein + specific a.a. sequence.**
- **Expressed on different types of lymphocytes**
- **Marker proteins upon which** 

Functional types of lymphocytes.

Antigenic markers of lymphocytes
Major histocompatibility complex (MHC(

❖ MHC I:

- ➢ **On all nucleated cells.**
- **Glycoprotein + specific a.a. sequence.**
- **Tissue typing.**
- **Endogenous antigenic recognition:**
  - ➢ **virus- infected cells.**
  - ➢ **malignant cells.**

❖ MHC II:

- ➢ **Expressed on antigen-presenting cells.**
- **Glycoprotein + specific a.a. sequence.**
- **Tissue typing.**
- **Exogenous antigenic recognition:**
  - ➢ **Phagocytosed foreign Ags.**

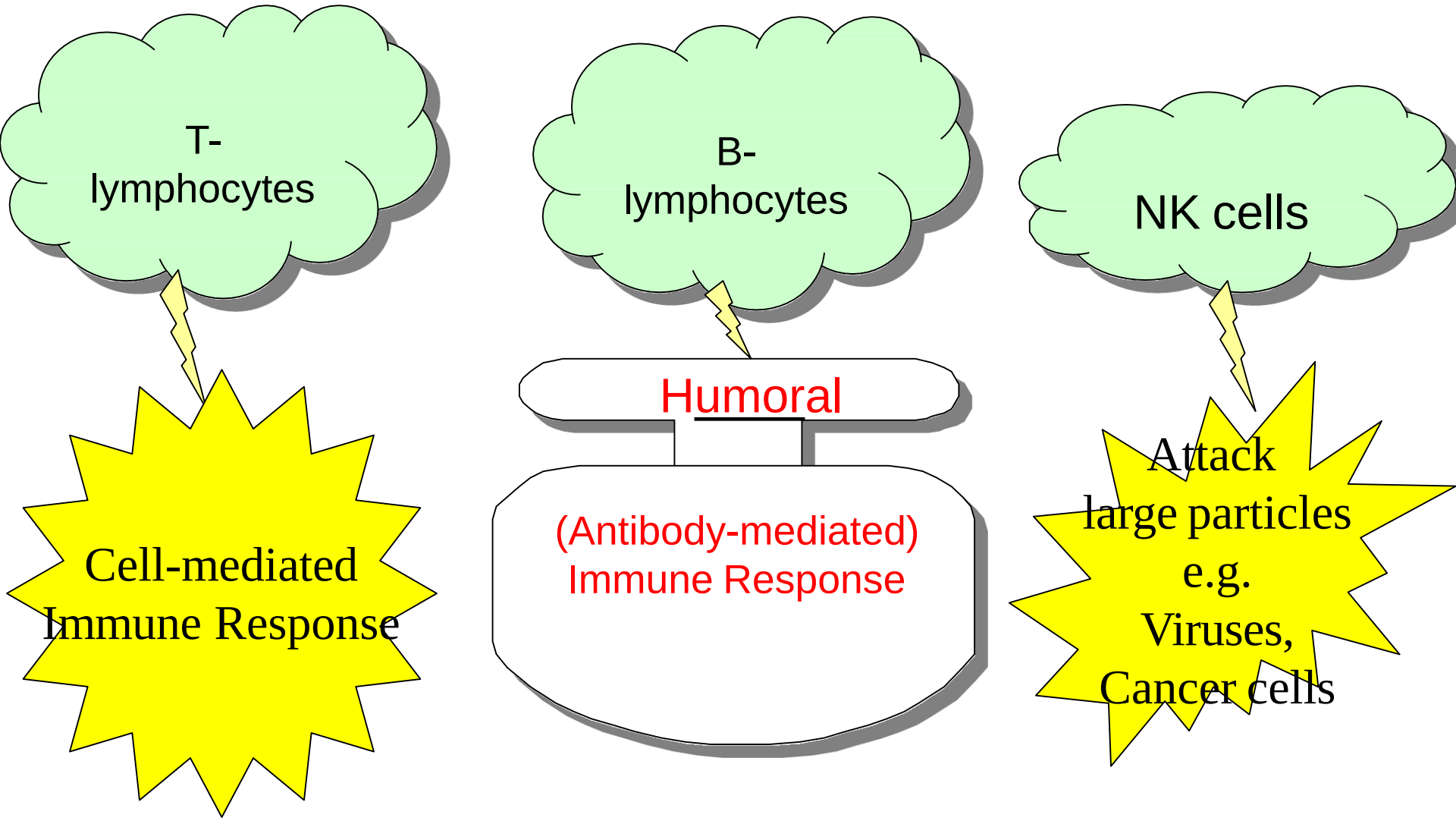
Function:

- After stimulation T-cells and B-cells become : Effector cells &Memory cells
- B cells form plasma cells, function in humoral immunity via immunoglobulins
- T cells function in cell-mediated immunity
- Effector T-cells: T helper cells, T suppressor cells, cytotoxic T cells
- Some T cells with “memory” of antigen exposure survive long periods; immunization
- Null Cells are composed of: Stem cells and Natural killer cells
- NK cells kill some foreign and virally alerted cells

❖ Life span:

- **months------ years**

Functions of Lymphocytes



Abnormal lymphocyte count

-1Lymphocytosis: ⬆ ⬆

Causes:

Physiological: in children

Pathological:

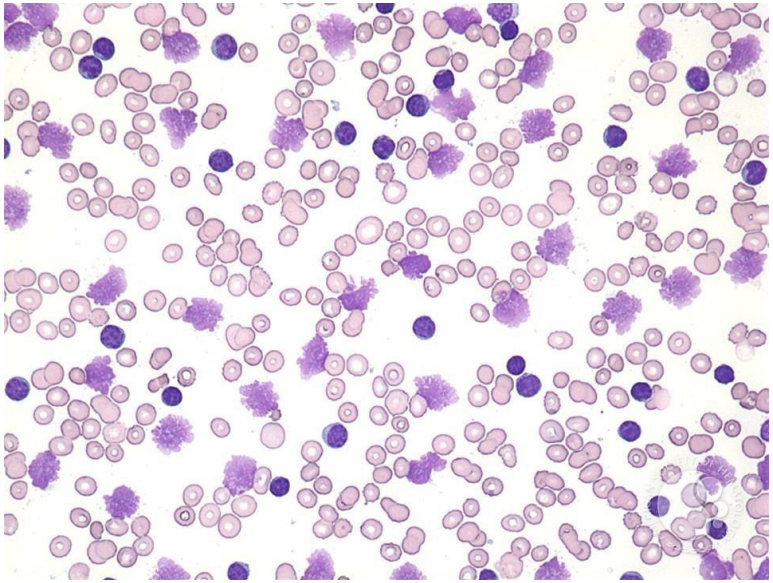
1chronic infections tuberculosis, syphilis،

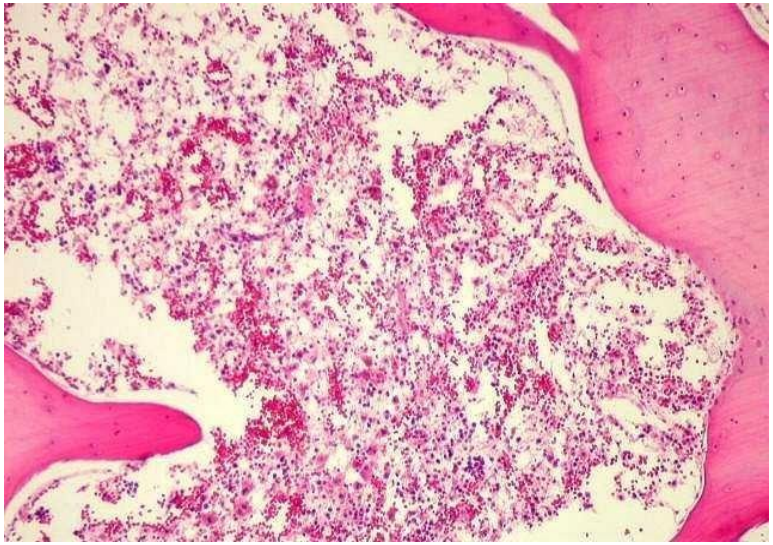
2 leukemia, Lymphoma.

-2Lymphopenia: ⬇ ⬇

Bone marrow depression.

- **drugs**
- **Irradiation**
- **Severe chronic diseases**

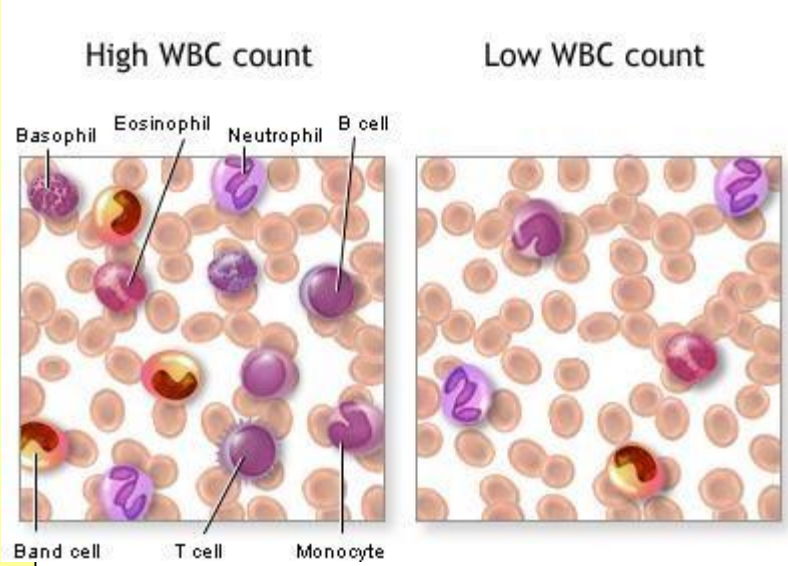




Abnormalities in leukocytic count

leukocytosis

- Infection
- Inflammations
- Allergic reaction
- Leukaemia

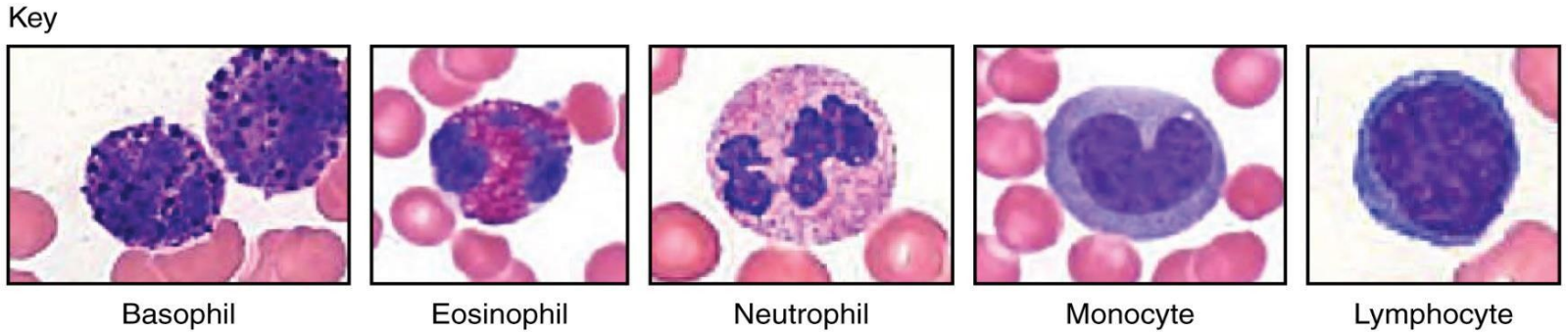


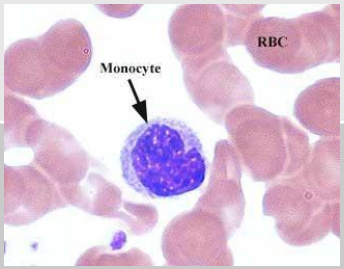
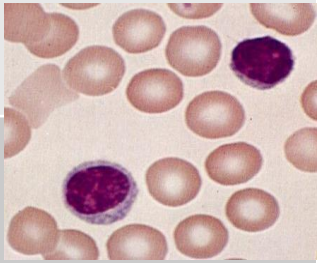
Leukopenia

- Bone marrow depression
  -drugs
  -Irradiation
  -Severe chronic diseases
- Typhoid fever
- Measles

Acquired Causes of decrease in number

Decreased Production	Increased Destruction	Shift to Marginating Pool
Bone marrow	Peripheral circulation	Move from the circulating pool to attach along the vessel wall
Medication: Chemotherapy Antibiotics, etc	Autoimmune diseases)Rheumatoid arthritis, SLE, etc(	Severe infection Endotoxin release Hemodialysis Cardiopulmonary bypass



	Monocyte	Lymphocyte **Subsets T, B, natural killer**
Number	**%**8-3**of WBCs**	**% 25-20of WBCs** **Next most common after neutrophils**
Size	**20-12µm** diameter 	11-9µm diameter Small , medium , large 
Shape	Spherical	Spherical
Structure	Spherical , Nucleus kidney-shaped No obvious granules	Spherical , Nucleus indented No obvious granules
Life span	Circulate for 3-4 days before enter into tissues and organs	variable life spans Month – years (memory cell(
Function	Precursor of <u>macrophages</u> in tissues Macro = "big"; phage = "eat" Phagocytic function	**B Cells i**nvolved in humoral immunity **T Cells** involved in cell-mediated immunity • T helper cells، • T suppressor cells، • cytotoxic T c & memory cell
Abnormality	*Monocytosis:* is an abnormal increase in the number of blood monocytes. It occurs in diseases	*Lymphocytosis:* It is an abnormal increase in the number of lymphocytes as in:

Bone marrow

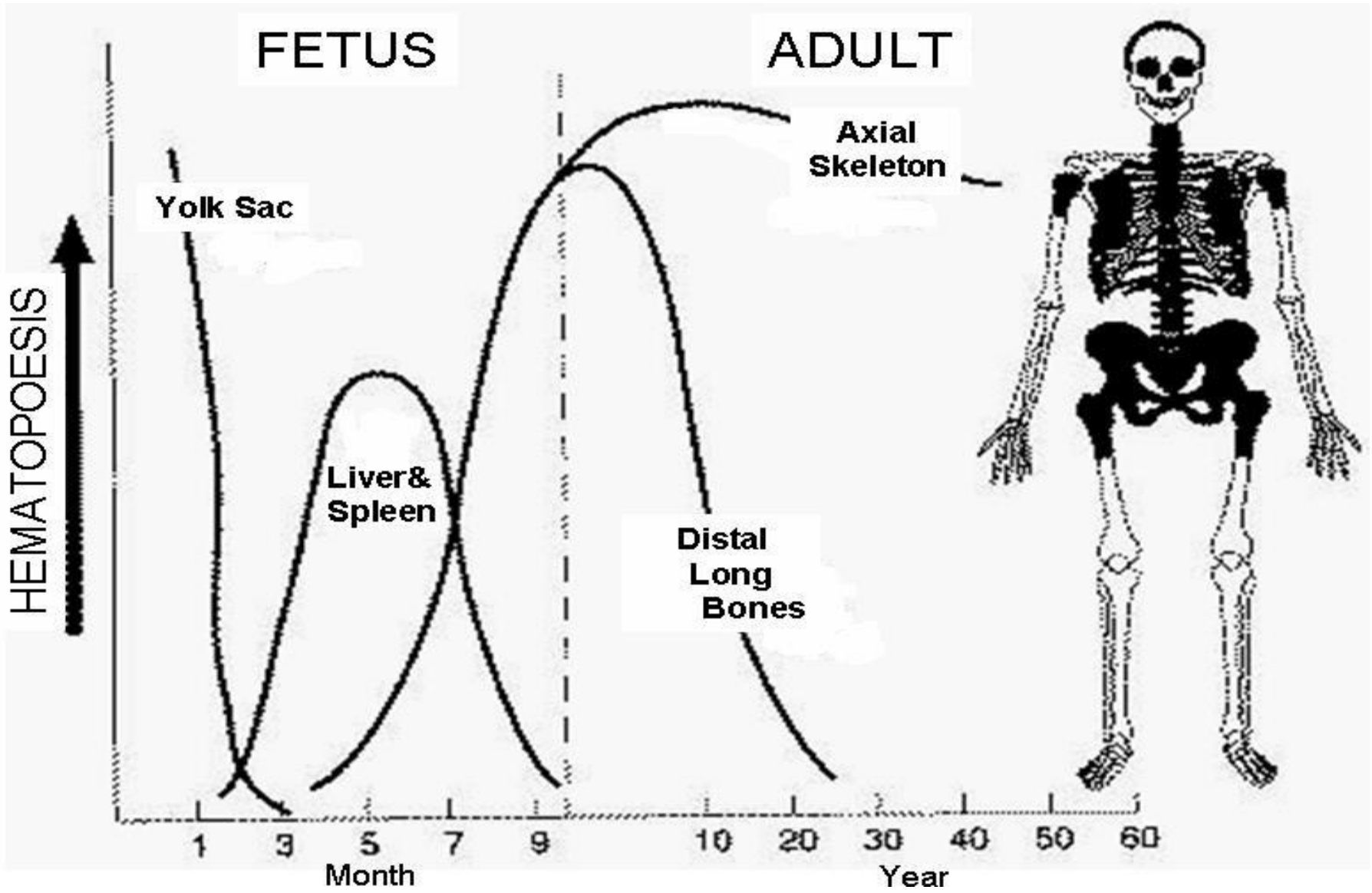
- **Def :** It is a semi-solid tissue . It is the primary site of new blood cell production or **hematopoiesis**
- Bone marrow is the site for other important activities in addition to hematopoiesis e.g. the removal of aged and defective erythrocytes and the **differentiation of B lymphocytes**. It is also the site of numerous **plasma cells**.

Site :

- **Yolk Sac: very early embryo**
- **Liver, Spleen: NEWBORN**
- **BONE**
  - **CHILDHOOD: AXIAL SKELETON & APPENDICULAR SKELETON BOTH HAVE RED (active) MARROW**
  - **ADULT: AXIAL SKELETON RED MARROW, APPENDICULAR SKELETON YELLOW MARROW**

- In adult humans, bone marrow is primarily located in the ribs , vertebrae ,sternum , and bones of the pelvis .

Blood Forming Organs



Types of bone marrow

The tissue responsible for **Hemopoiesis =** formation of balanced amounts of the different blood elements.

- daily formed = daily destroyed elements

1 **Red bone marrow:** active.

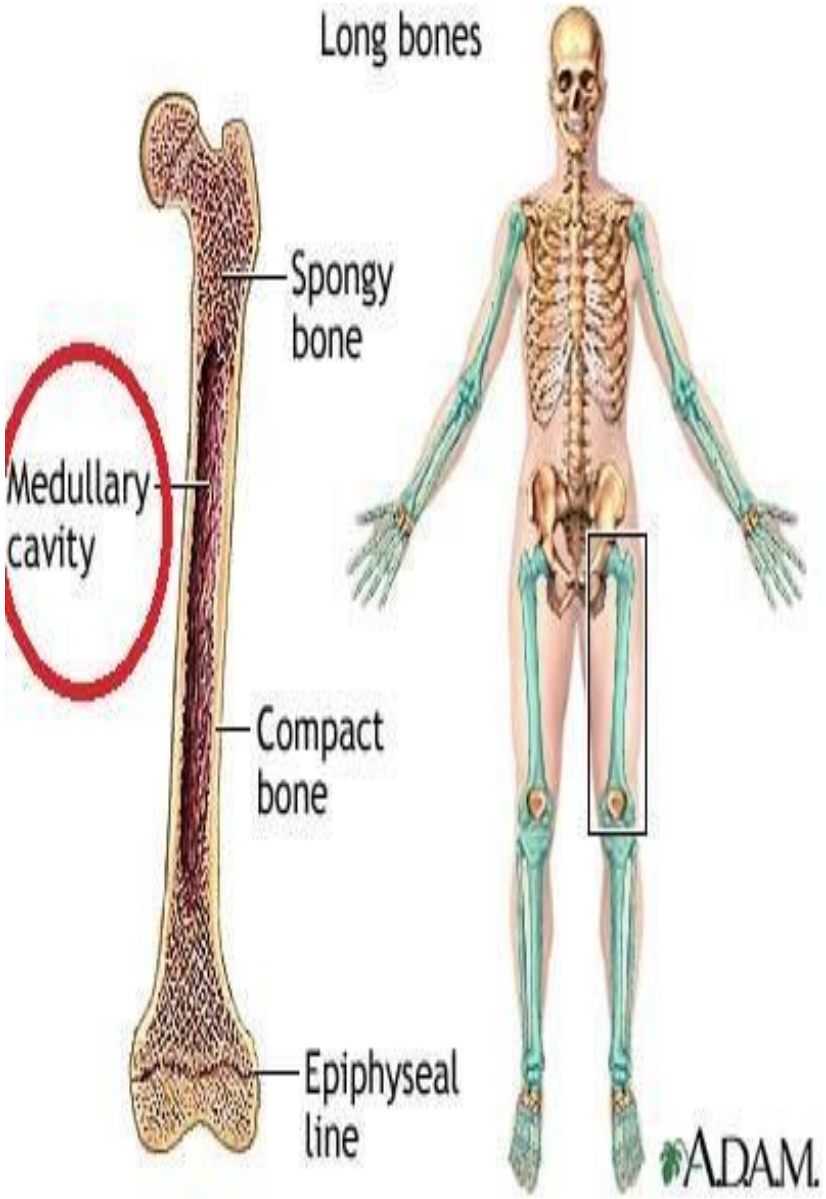
2 **Yellow bone marrow:**

- inactive. Yellow color ►large number of fat cells.
- can revert to the red type in **stress** as hemorrhage and anaemia.

Sites:

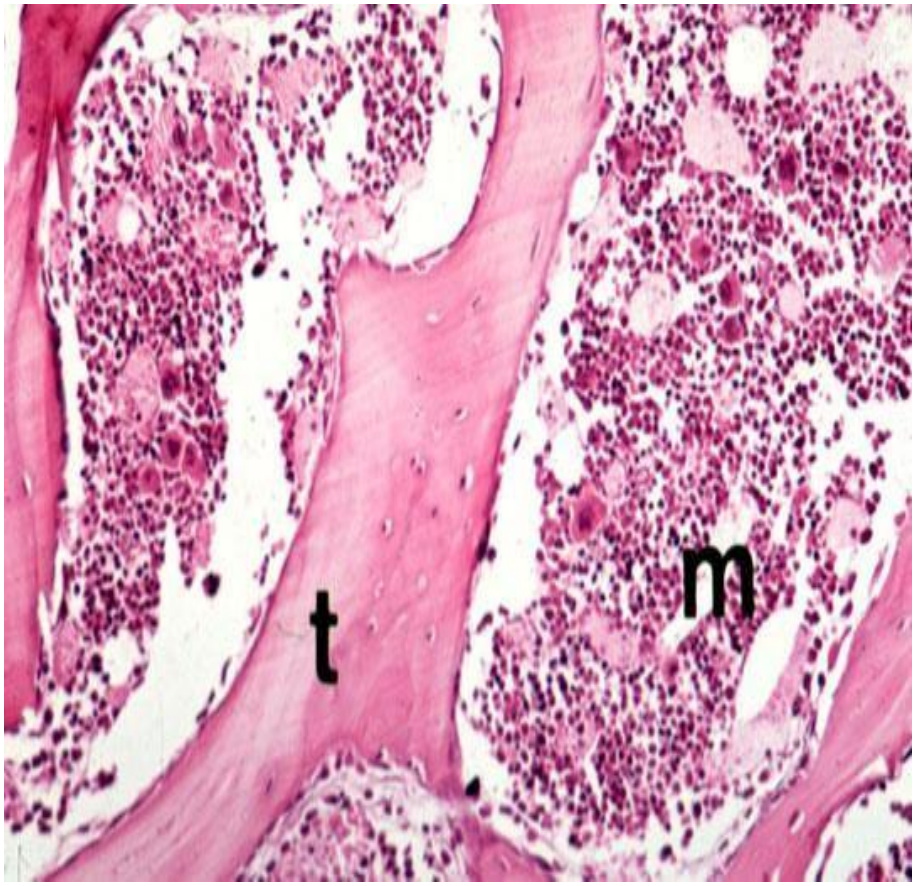
1. Central bone marrow cavity in long bones.

2.Multiple marrow cavities (Flat bone) between trabeculae of cancellous bone.

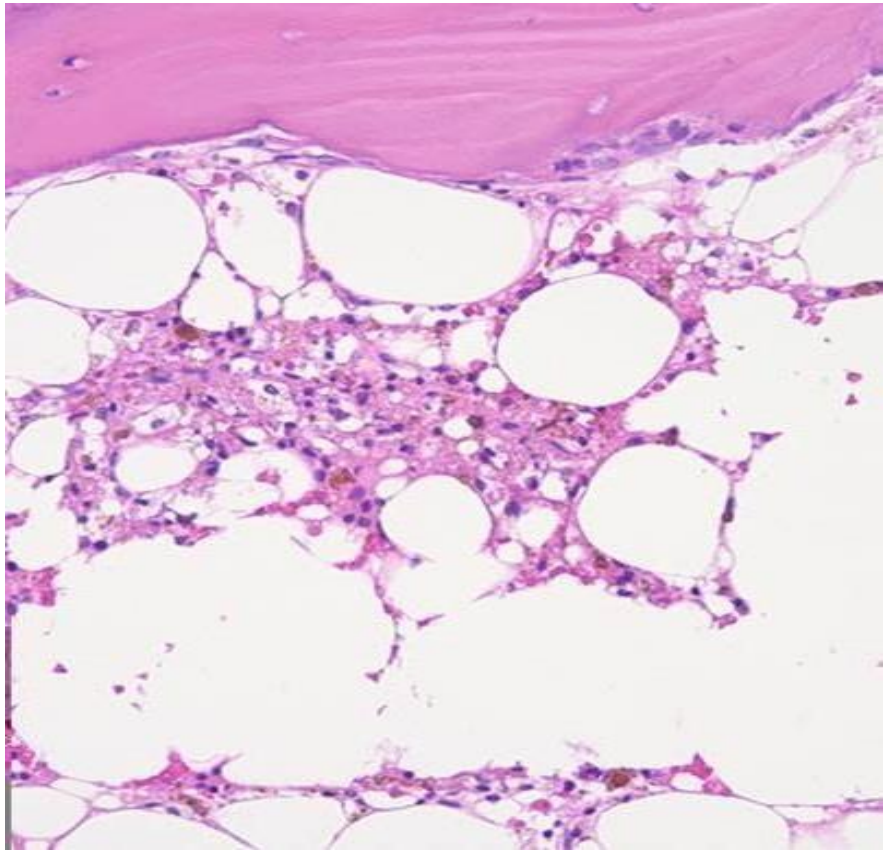


Types of bone marrow

Red bone marrow



Yellow bone marrow



Bone marrow examination

- is the pathologic analysis of samples of bone marrow obtained via **biopsy** and bone marrow **aspiration.**

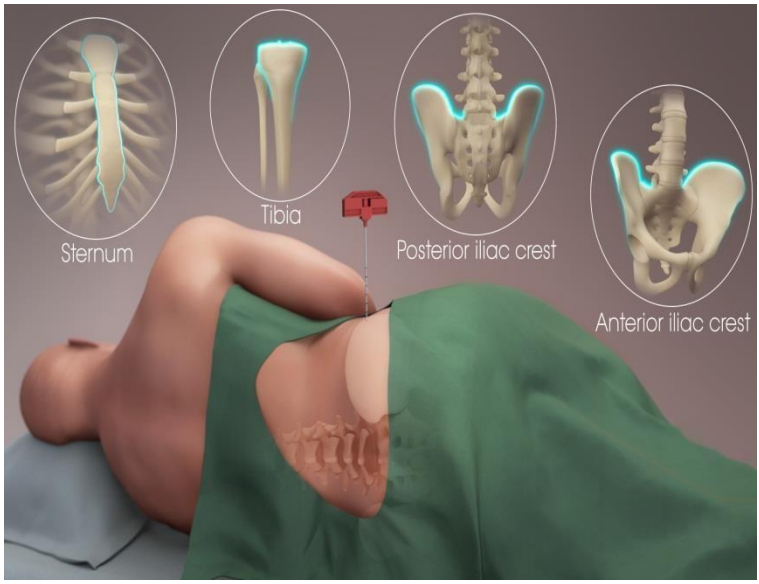
❑ The bone marrow produces the cellular elements of the blood, including **Platelets** , **RBCs** and **WBCs**.

❑ While much information can be obtained by testing the blood itself ،it is sometimes necessary to examine the source of the blood cells in the bone marrow to obtain more information on hematopoiesis; this is the role of bone marrow aspiration and biopsy.

❑ Bone marrow examination is used in the diagnosis of a number of conditions, including

leukemia, multiple myeloma, anemia , and Pancytopenia.

- The stem cells are typically harvested directly from the red marrow in the iliac crest, often under **general anesthesia**. The procedure is minimally invasive and does not require stitches afterwards. Depending on the donor's health and reaction to the procedure, the actual harvesting can be an outpatient procedure, or can require **1–2 days of recovery in the hospital**.



- **In adults**, bone marrow may also be taken from the sternum, while the tibia is often used when taking samples from **infants**. In **newborns,** stem cells may be taken from the umbilical cord .

- Another option is to administer certain drugs that stimulate the release of stem cells from the bone marrow into circulating blood. An **intravenous catheter** is inserted into the donor's arm, and the stem cells are then **filtered out of the blood**.

STRUCTURE & FUNCTION OF BONE MARROW

- The composition of marrow is dynamic, as the mixture of cellular and non-cellular components (connective tissue) shifts with age and in response to systemic factors.

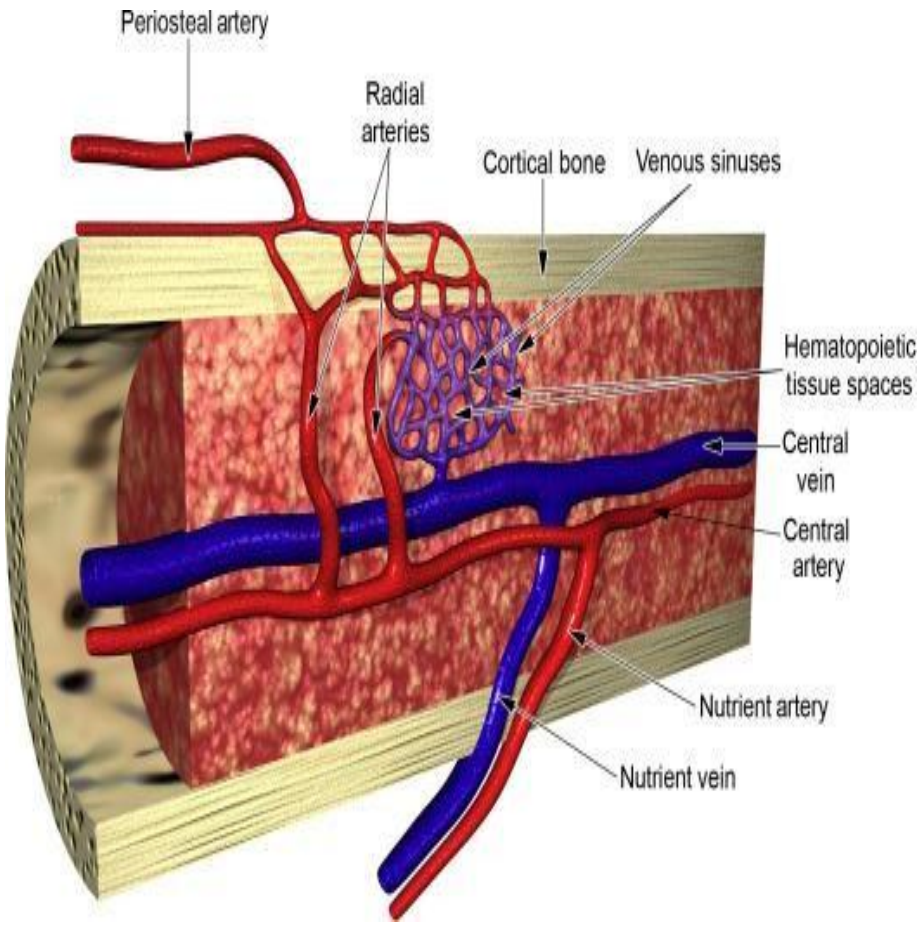
Bone marrow has:

- **vascular compartment**
- **Extravascular compartment.**

vascular compartment

The vascular compartment is supplied by

- a **nutrient** artery which branches into **central** longitudinal arteries which send out **radial** branches that eventually open into **sinuses.**
- These sinuses converge into a **central vein** that carries the blood out of the bone marrow into the general circulation.

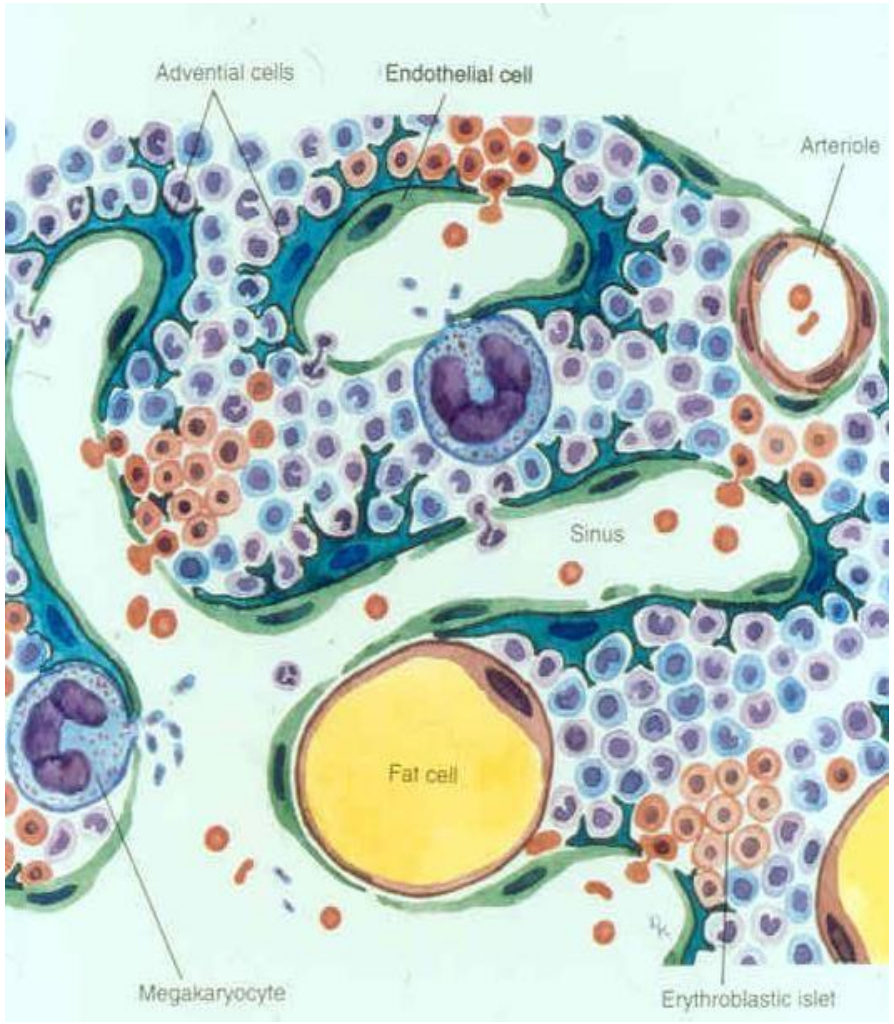


Extravascular compartment

- Hematopoiesis takes place in the extravascular compartment.
- The extravascular compartment

consists of:

- **a stroma** of reticular connective tissue
- **a parenchyma** of developing blood cells, plasma cell, macrophages and fat cells.
- Biological compartment is evident within the bone marrow, in that certain cell types tend to aggregate in specific areas.
- For instance, erythrocytes, macrophages, and their precursors tend to gather around blood vessels
- while granulocytes gather at the borders of the bone marrow.



Stroma

- **The stroma** of the bone marrow includes all tissue **not directly** involved in the marrow's primary function of hematopoiesis.
- Stromal cells may be **indirectly involved** in hematopoiesis, providing a microenvironment that influences the function and differentiation of hematopoeietic cells, they generate colony stimulating factors , which have a significant effect on hematopoiesis.

- **Cell types** that constitute the bone marrow **stroma include**:

- Fibroblast (reticular cell(
- Macrophages , which contribute especially to RBCs production, as they deliver iron for hemoglobin production
- Adipocytes
- Osteoblasts (synthesize bone(
- Osteoclast (resorb bone(
- Endothelial cells which form the sinusoids. These derive from endothelial stem cells، which are also present in the bone marrow

Hematopoietic components

- At the cellular level, the main functional component of bone marrow includes the progenitor cells which are destined to mature into blood and lymphoid cells.

❑ Marrow contains hematopoietic stem cells which give rise to the three classes of blood cells that are found in circulation: WBCs (leukocytes),RBCs)erythrocytes), and platelets)thrombocytes.(

❑ **The Pluripotent hemopoietic stem cells (PHSCs:(**

➢ great ability to divide.

➢ ½ Reserve other ½ becomes more differentiated.

❑ **Multipotent hemopoietic stem cells (MHSCs:(**

- Daughter cells of the PHSCs.
- Histologically, **larger**
- Cell divisions but are more

differentiated ►► cell colonies ►►**2** CFUs

CFUs►►► daughter stem cells more differentiated

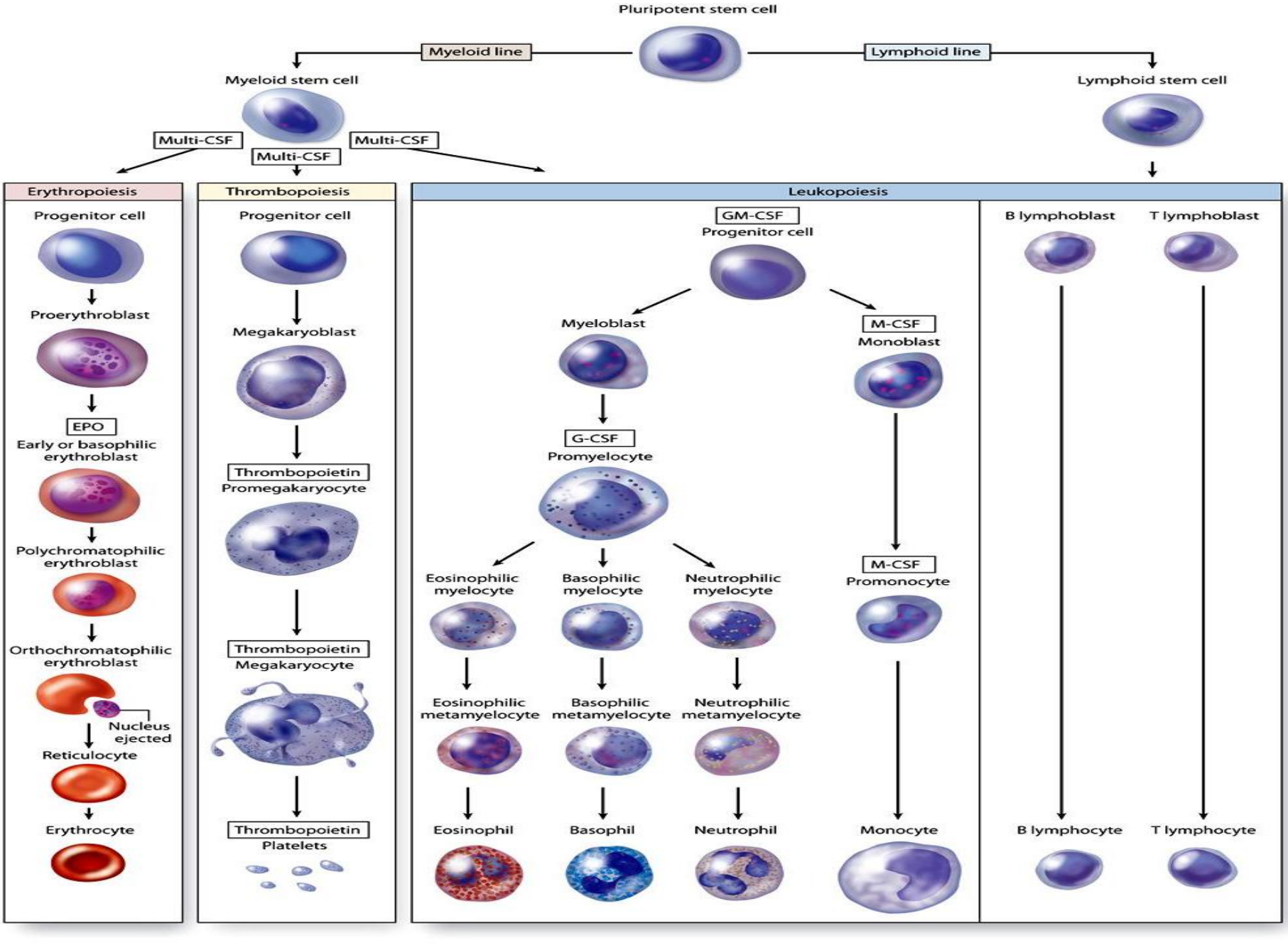
A- CFU- lymphocyte (CFU- Ly:(

Some migrate to the thymus, spleen and lymph nodes where lymphopoiesis is completed.

B- CFU- erythrocyte, megakaryocyte/ granulocyte-monocyte

►►unipotent progenitors

- CFU-Erythrocyte (CFU- E(
- CFU-Megakaryocyte (CFU-Meg.(
- CFU- Granulocyte /monocyte (CFU-GM‹(


Pluripotent stem cell
Myeloid line
Lymphoid line
Myeloid stem cell
Lymphoid stem cell
Multi-CSF
Multi-CSF
Multi-CSF
Erythropoiesis
Progenitor cell
Proerythroblast
EPO
Early or basophilic erythroblast
Polychromatophilic erythroblast
Orthochromatophilic erythroblast
Nucleus ejected
Reticulocyte
Erythrocyte
Thrombopoiesis
Progenitor cell
Megakaryoblast
Thrombopoietin
Promegakaryocyte
Thrombopoietin
Megakaryocyte
Thrombopoietin
Platelets
Leukopoiesis
GM-CSF
Progenitor cell
Myeloblast
G-CSF
Promyelocyte
Eosinophilic myelocyte
Basophilic myelocyte
Neutrophilic myelocyte
Eosinophilic metamyelocyte
Basophilic metamyelocyte
Neutrophilic metamyelocyte
Eosinophil
Basophil
Neutrophil
M-CSF
Monoblast
M-CSF
Promonocyte
Monocyte
B lymphoblast
T lymphoblast
B lymphocyte
T lymphocyte

Function

Bone marrow is the site for other important activities in addition to hematopoiesis.

These include:

Mesenchymal stem cells

- The bone marrow stroma contains mesenchymal stem cells (MSCs), also known as marrow stromal cells. These are multipotent stem cells that can differentiate into a variety of cell types. MSCs have been shown to differentiate, in vitro or in vivo , into osteolasts, chondrocytes,myocytes, marrow adipocytes

Bone marrow barrier

- The blood vessels of the bone marrow constitute a barrier, inhibiting immature blood cells from leaving the marrow. Only mature blood cells contain the membrane proteins, such as aquaporin and glycophorin, that are required to attach to and pass the blood vessel endothelium.
- Hematopoietic stem cell may also cross the bone marrow barrier, and may thus be harvested from blood.

Lymphatic role

- The red bone marrow is a key element of the lymphatic system , being one of the primary lymphoid organs that generate lymphocytes from immature hematopoietic progenitor cells. The bone marrow and thymus constitute the primary lymphoid tissues involved in the production and early selection of lymphocytes.

Hematopoiesis

Def : A process by which **blood cells** are **formed** by proliferation and differentiation of stem cells.

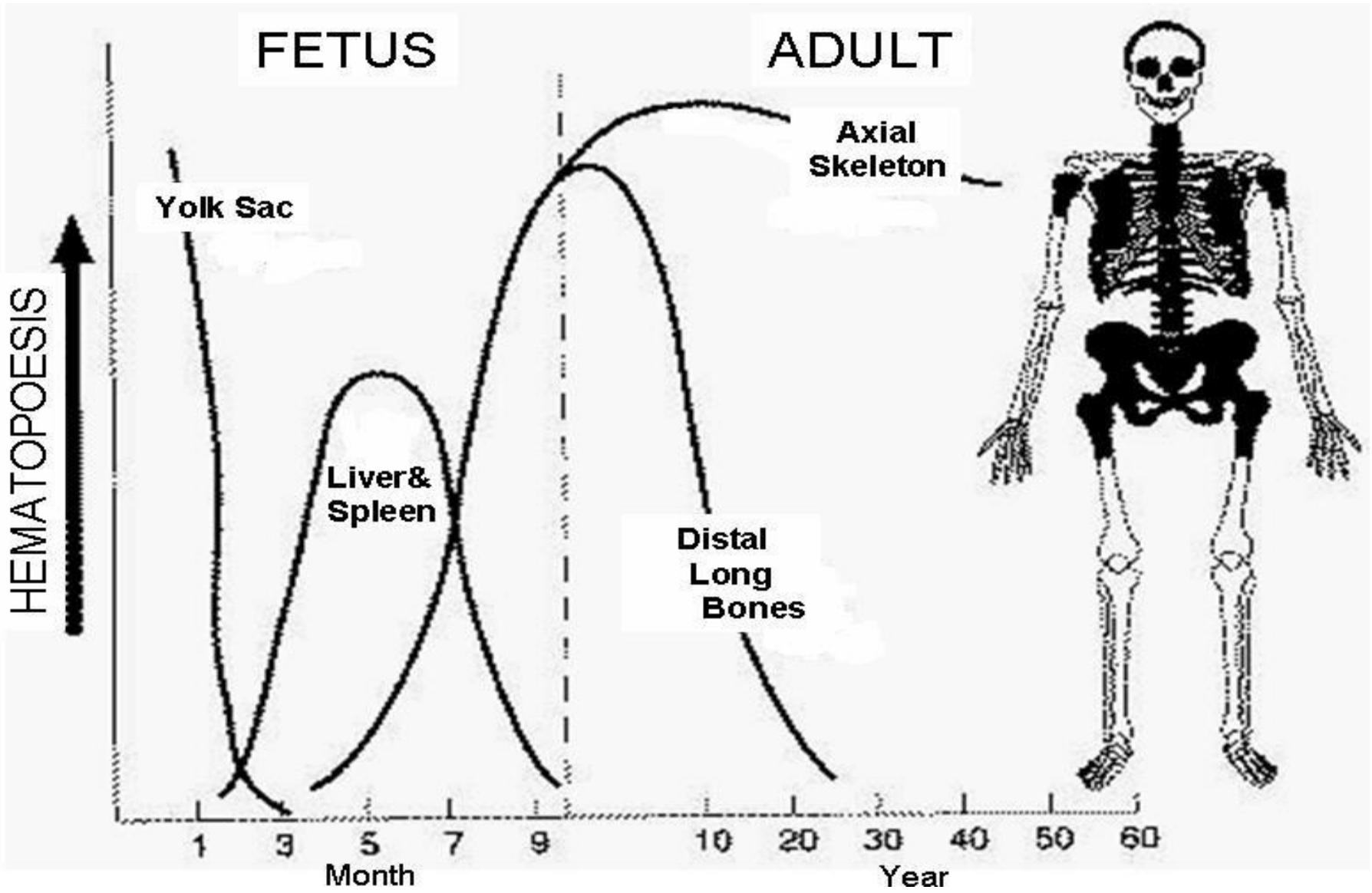
Prenatal hematopoiesis

- **Yolk sac (2-8 weeks(**
- **Liver & spleen (8- (28**
- **Bone marrow after (22 weeks(**

Postnatal Hematopoiesis

- **Prior to puberty:** skull, ribs, sternum, vertebrae, clavicles, pelvis, **and long bones.**
- **After puberty:** same bones except **no more shafts of long bones**.
- **Extra-medullary hemopoiesis:** liver and spleen continue to produce blood cells even after birth.

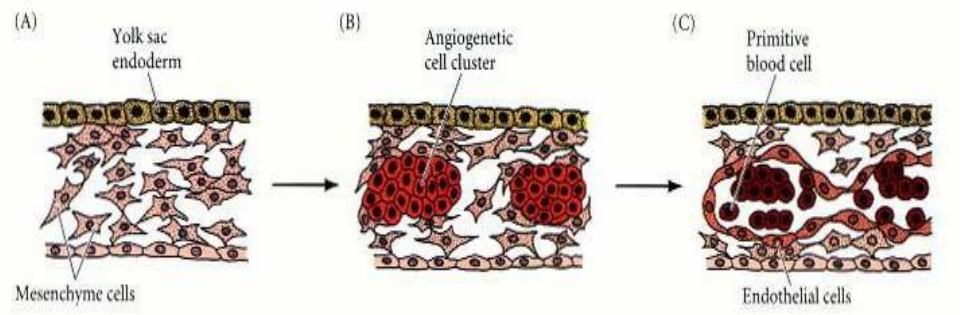
Blood Forming Organs



Prenatal hematopoiesis

-1Yolk Sac Hematopoiesis (blood islands) 2-8 weeks:

- **In the yolk sac,** mesenchymal cells differentiate to clusters of **hemangioblast** cells.
- **-1Peripheral hemangioblasts** further differentiate into **endothelial** cells&
- **-2Central hemangioblasts** give rise to **nucleated red blood cells ،no leukocytes** are formed in this phase.



- **-2Fetal Liver& spleen Hemopoiesis:** From **8 - 28** wks؛
- *Liver and spleen are colonized by definitive hematopoietic stem cells.
- ***Erythrocytes still have nuclei, leukocytes begin to appear**. All blood cell types **(except T cells)** can differentiate in the fetal liver & spleen.
- **extra-medullary hematopoiesis
- **-3Prenatal Myeloid phase:** Bone marrow is colonized late in embryogenesis (after **22 weeks**) by definitive hematopoietic stem cells **derived from the fetal liver &spleen.**
- All blood cell types **(except T cells(** can differentiate in the bone marrow.

Postnatal hematopoiesis

Prior to puberty:

skull, ribs, sternum،

vertebrae, clavicles, pelvis, **and shafts of long bones**..

After puberty:

same bones except **no more shafts of long bones**.

Extra-medullary hemopoiesis:

liver and spleen continue to produce blood cells even after birth

CFUs►►► daughter stem cells more differentiated

A- CFU- lymphocyte (CFU- Ly):

Some migrate to the **thymus, spleen and lymph nodes** where lymphopoiesis is completed.

B- CFU- granulocyte / monocyte, erythrocyte, megakaryocyte (CFU-GEMM): ►►**unipotent progenitors**

- CFU-Erythrocyte (CFU- E(
- CFU-Megakaryocyte (CFU-Meg.(
- CFU- Granulocyte /monocyte (CFU-GM،(

Cell potency

Cell potency is a cell ability to differentiate into other cell types

- **Totipotency** is the ability of a single cell to divide and produce all of the differentiated cells in an organism. Zygotes are examples of totipotent cells
- **pluripotency** refers to a stem cell that has the potential to differentiate into any of the three germ layers :endoderm ,mesoderm or ectoderm but not into extra-embryonic tissues like the placenta.
- **Multipotency** for example, a multipotent blood stem cell —and this cell type can differentiate itself into several types of blood cell like lymphocytes ،monocytes ،neutrophils **Oligopotency** is the ability of progenitor cells to differentiate into a few cell types

Examples of oligopotent stem cells are the lymphoid or myeloid stem cells.

- **Unipotency** one stem cell has the capacity to differentiate into only one cell type.

The Myeloid Cells

-1The Pluripotent hemopoietic stem cells (PHSCs:(

- great ability to divide.
- ½ Reserve other ½ becomes more differentiated.

-2Multipotent hemopoietic stem cells (MHSCs:(

- Daughter cells of the PHSCs.
- **larger**
- Cell divisions but are more differentiated ►► **cell colonies** ►► **2** CFUs

CFUs►►► daughter stem cells more differentiated

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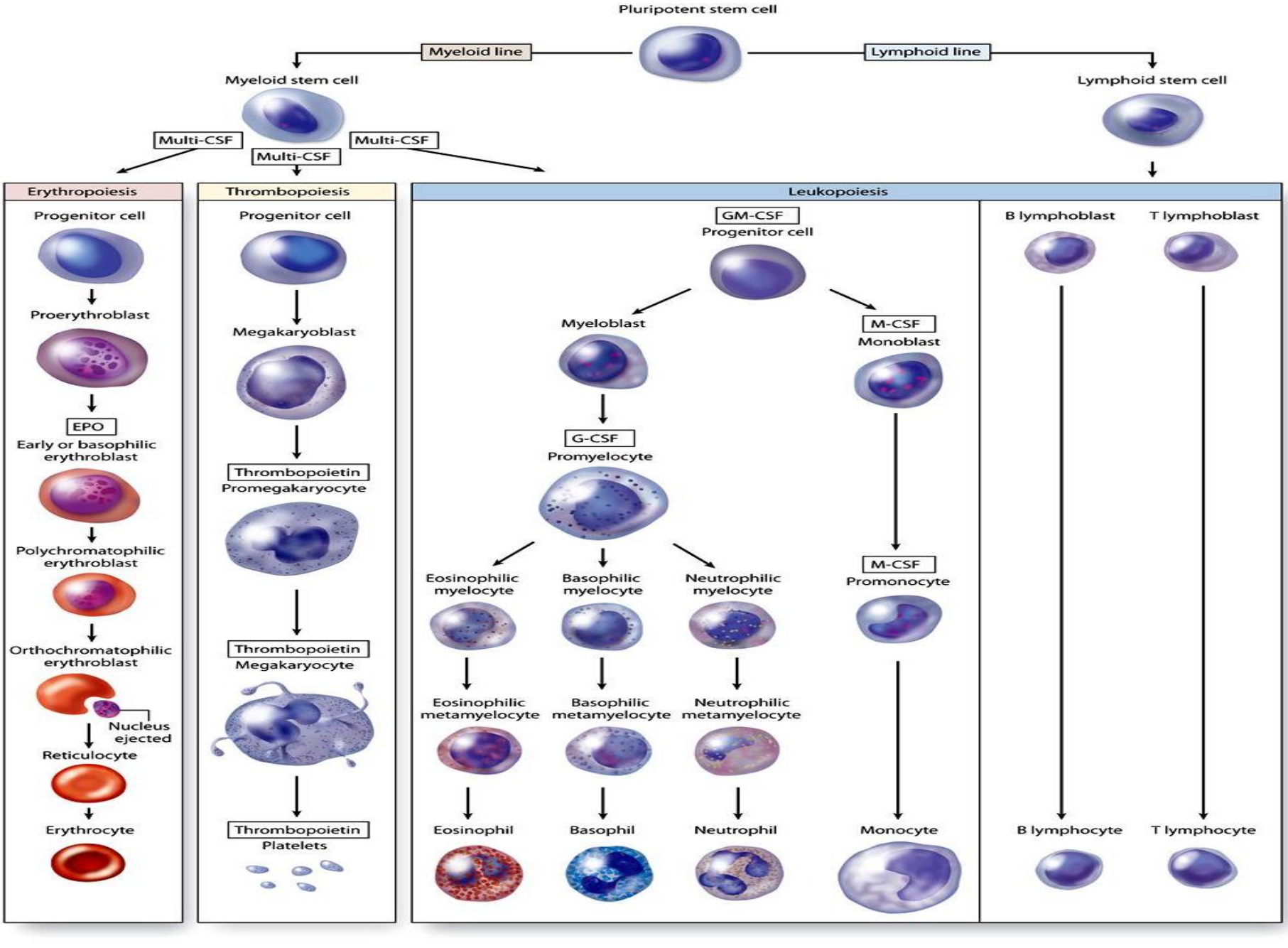
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Thrombopoietin
Megakaryocyte
Thrombopoietin
Platelets
Leukopoiesis
GM-CSF
Progenitor cell
Myeloblast
G-CSF
Promyelocyte
Eosinophilic myelocyte
Basophilic myelocyte
Neutrophilic myelocyte
Eosinophilic metamyelocyte
Basophilic metamyelocyte
Neutrophilic metamyelocyte
Eosinophil
Basophil
Neutrophil
M-CSF
Monoblast
M-CSF
Promonocyte
Monocyte
B lymphoblast
T lymphoblast
B lymphocyte
T lymphocyte

Erythropoiesis

Formation of RBCs –Takes about 7 days

1 **UMC**

2 **Pluripotential hemopoietic**

stem cells (**hemocytoblast(**

3**Restricted erythrocyte progenitor**

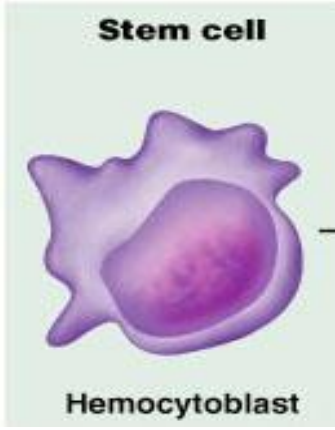
(Colony-forming unit erythrocytes **(CFU-E)**

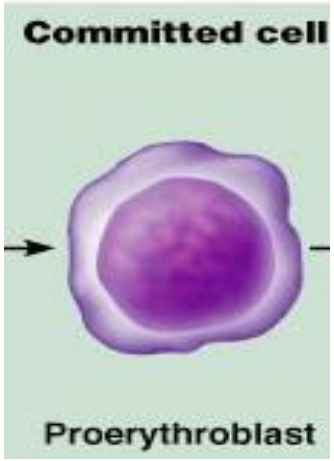
4- Pro- erythroblast:

- **Large.**
- basophilic cytoplasm with abundant Ribosomes.
- Large nucleus

-5Basophilic Erythroblast:

- **Most active in hemoglobin** synthesis.
- Ribosomes are ▲▲abundant.
- Cytoplasm is strongly basophilic





Erythropoiesis

-6Polychromatophilic Erythroblast

- hemoglobin.▲▲
- Ribosomes are still.▲▲
- Cytoplasm shows eosinophilic areas alternating with basophilic spots.
- **Last stage** in repeated cell **divisions**.
- Only **morphological maturation** of the erythroblasts.

-7Orthochromatophilic Erythroblast (Normoblast:(

- Synthesis of hemoglobin **is completed.**
- Ribosomes.▼▼
- **Nucleus:**
  - is condensed and reduced in size.
  - Gradually pushed towards the periphery ►►completely extruded from the cell.
  - Phagocytosed by the bone marrow macrophages.

Erythropoiesis

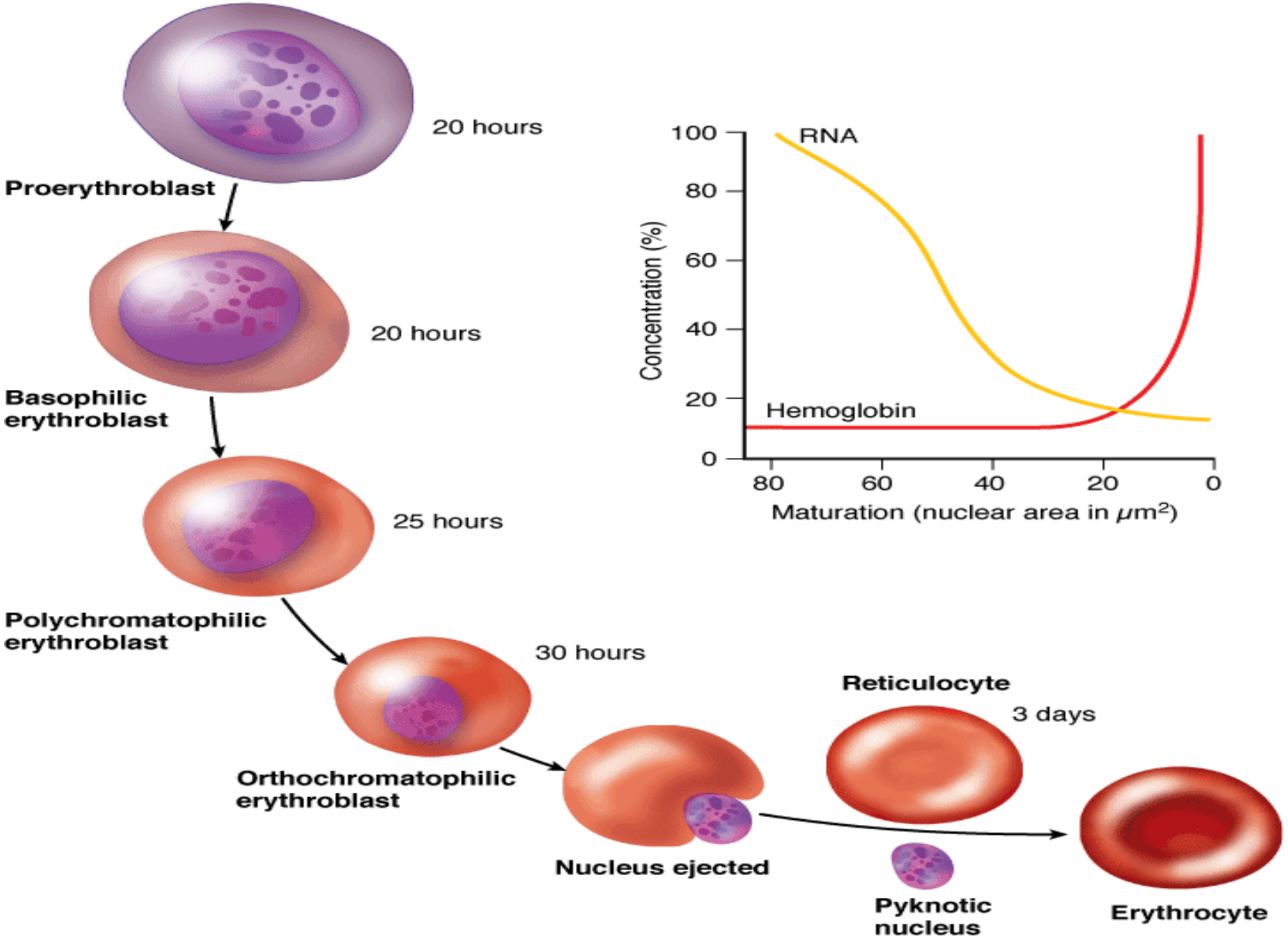
-8Reticulocytes

- immature RBCs
- non-nucleated
- **differ than mature RBCs**
  - slightly larger (8µm.(
  - Cytoplasm contains remnants of ribosomes.
  - On staining with **cresyl blue** form a reticulate pattern.
- Reticulocytes represent 1% of all RBCs in normal blood film.
- **Clinical significance:**

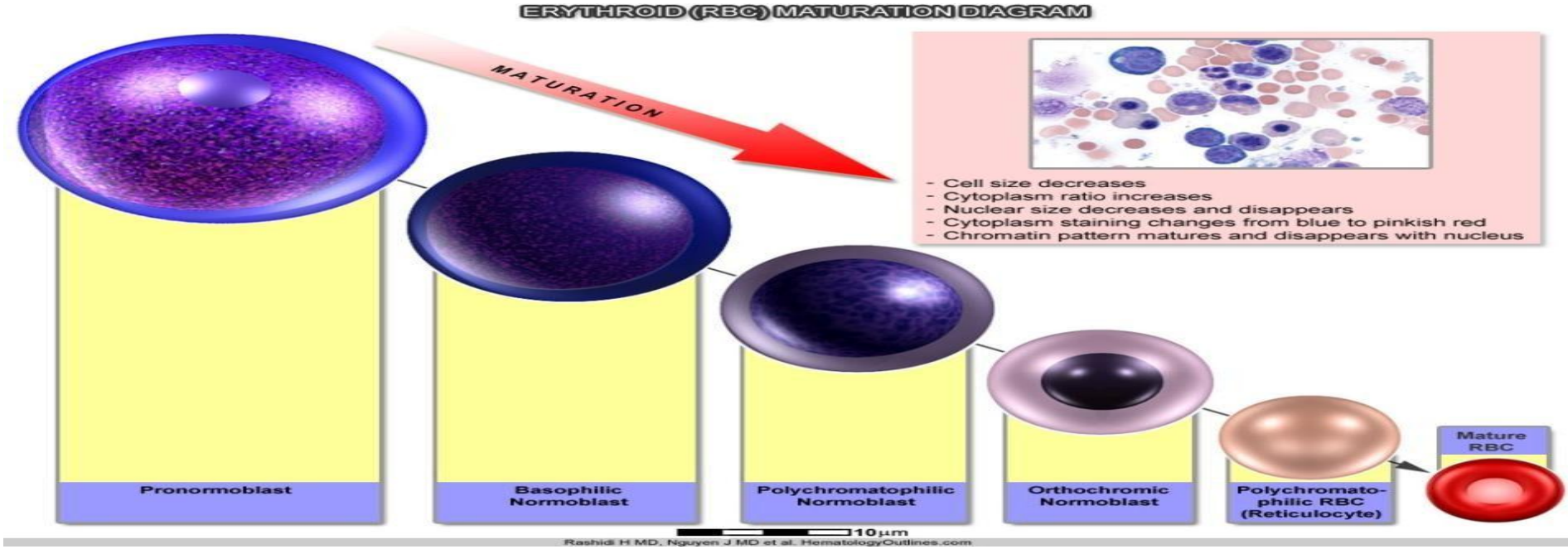
An increase in this percentage indicates an

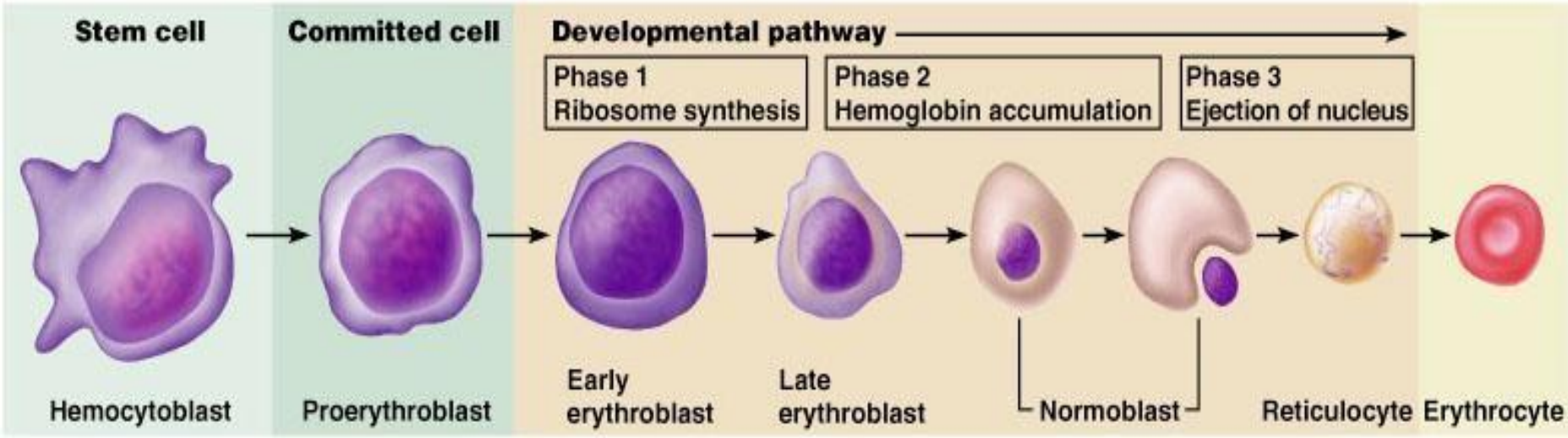
- **accelerated rate of erythropoiesis.**
- **compensate for anemia or hemorrhage.**

.9Mature RBCs



Erythropoiesis – Staining change





THROMBOPOIESIS

Formation of platelets
Takes about **10 days**
1-UMC.
-2Pluripotential hemopoietic stem cells
)hemocytoblasts.(

3 Restricted megakaryocyte progenitor
)Colony-forming unit (**CFU-Meg.(**

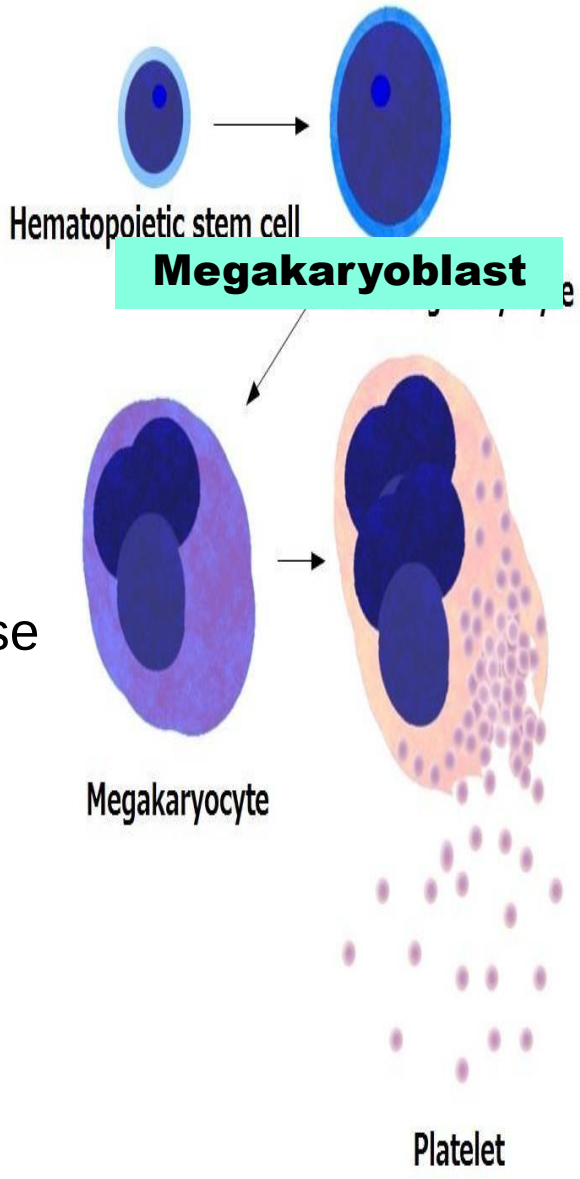
4Megakaryoblast: numerous nulceoli, multiplication of nuclear DNA **(polyploidy),** intense basophilic cytoplasm.

.5Promegakaryocyte: **lobulated nucleus** + multiple granules (clotting factors, lysosomes(

-6Megakaryocyte

→ demarcation membranes

→ **platelets.**



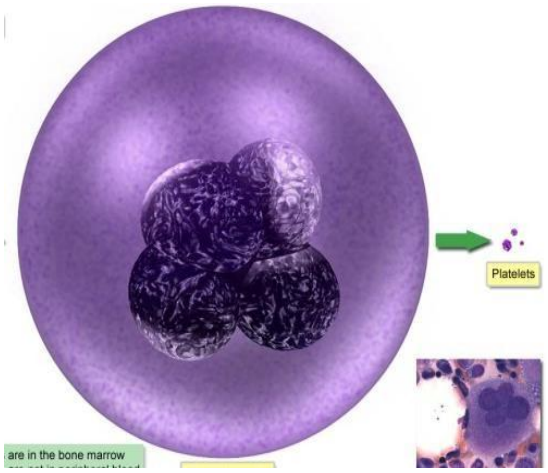
Megakaryocyte

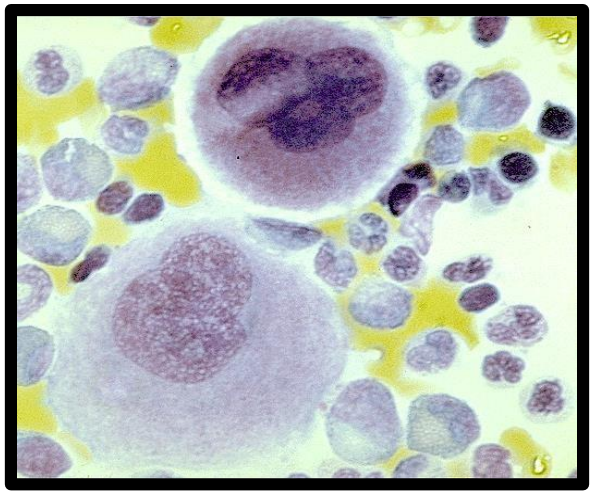
LM

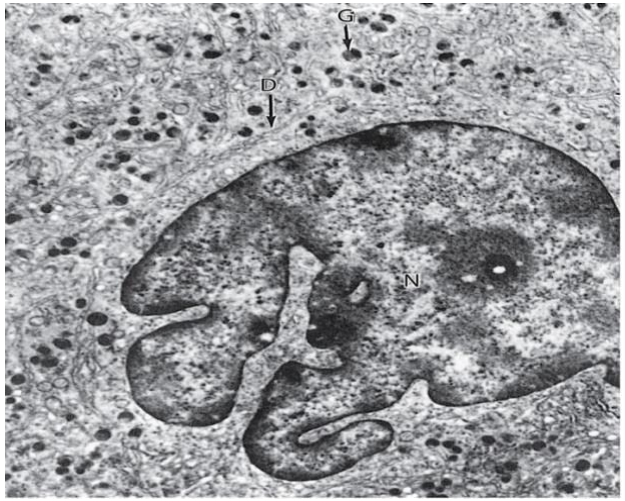
- **Giant cell (150µ.(**
- **Nucleus:**
  - **Lobulated.**
  - **Polyploid.**
- **Cytoplasm:**
  - **Filled with many organelles.**
  - **3types of granules.**

EM

- **Lobulated nucleus +numerous cytoplasmic granules (Alpha, Delta, Lambda(**
- **Membranous demarcation lines around the granules ▼▼**
- **Lines of cleavage.**





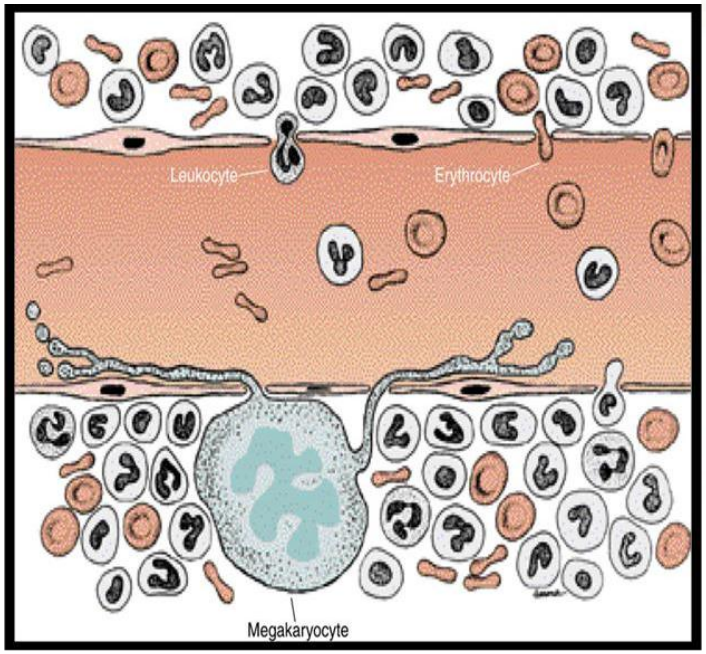


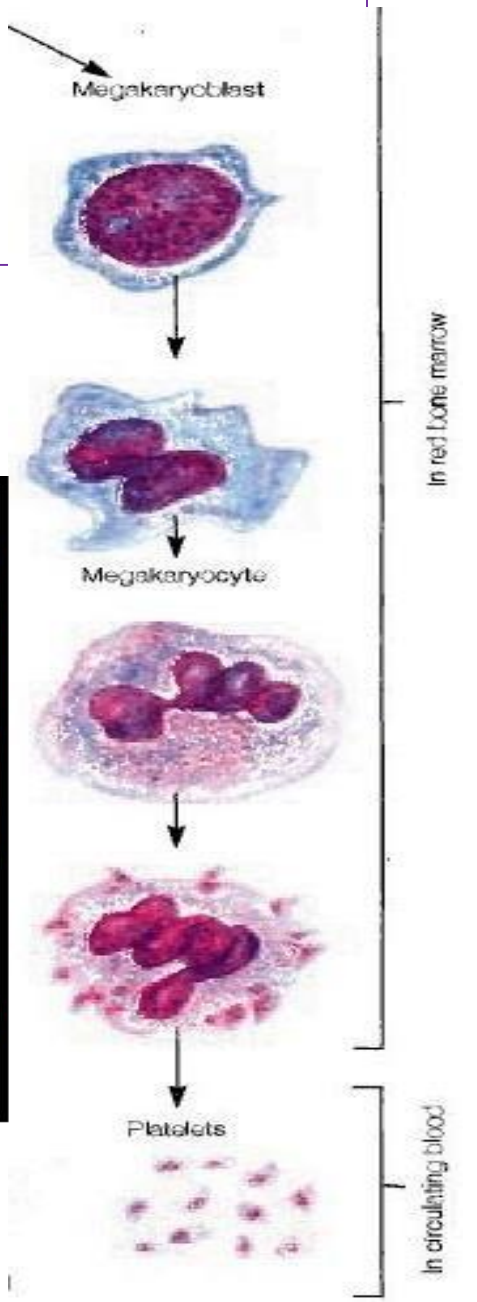
Megakaryocyte-release of platelets

- Megakaryocytes are located near BM sinusoids.
- Extend cytoplasmic processes:

▼▼

- release of platelets into blood stream.
- 1200 platelets / megakaryocyte





LEUKOPOIESIS

CFUs►►► daughter stem cells more differentiated

A- CFU- lymphocyte)CFU- Ly:(

Some migrate to the **thymus, spleen and lymph nodes** gland where lymphopoiesis is completed.

B- CFU- granulocyte/monocyte, erythrocyte, megakaryocyte (CFU-GEMM:(

►►**unipotent progenitors**

- CFU-Erythrocyte (CFU- E(
- CFU-Megakaryocyte CFU-Granulocyte /monocyte (CFU-GM‹(

Granulopoiesis

- begins from a hematopoietic stem cell .
- These are multipotent cells that reside in the bone marrow niche and have the ability to give rise to all heamatopoetic cells, as well as the ability of self renewal
- They give rise to either a common lymphoid progenitor or a common myeloid progenitor
- An oligopotent progenitor cell, that gives rise to the myeloid part of the heamatopoetic tree.
- The first stage of the myeloid lineage is a granulocyte - monocyte progenitor (GMP), still an oligopotent progenitor
- then develops into unipotent cells that will later on form a population of granulocytes, as well as a population of monocytes .
- The first unipotent cell in granulopoiesis is a myeloblast

Granulopoiesis

1 **UMC**

2 Pluripotential hemopoietic stem cells **(hemocytoblasts)**

3Restricted granulocyte progenitor, that are called (Colony-forming unit granulocytes **(CFU-G)**)

4 Myeloblast

5 Promyelocyte :(nonspecific granules)

6 Myelocyte :

(specific granules N,E,B…..?)

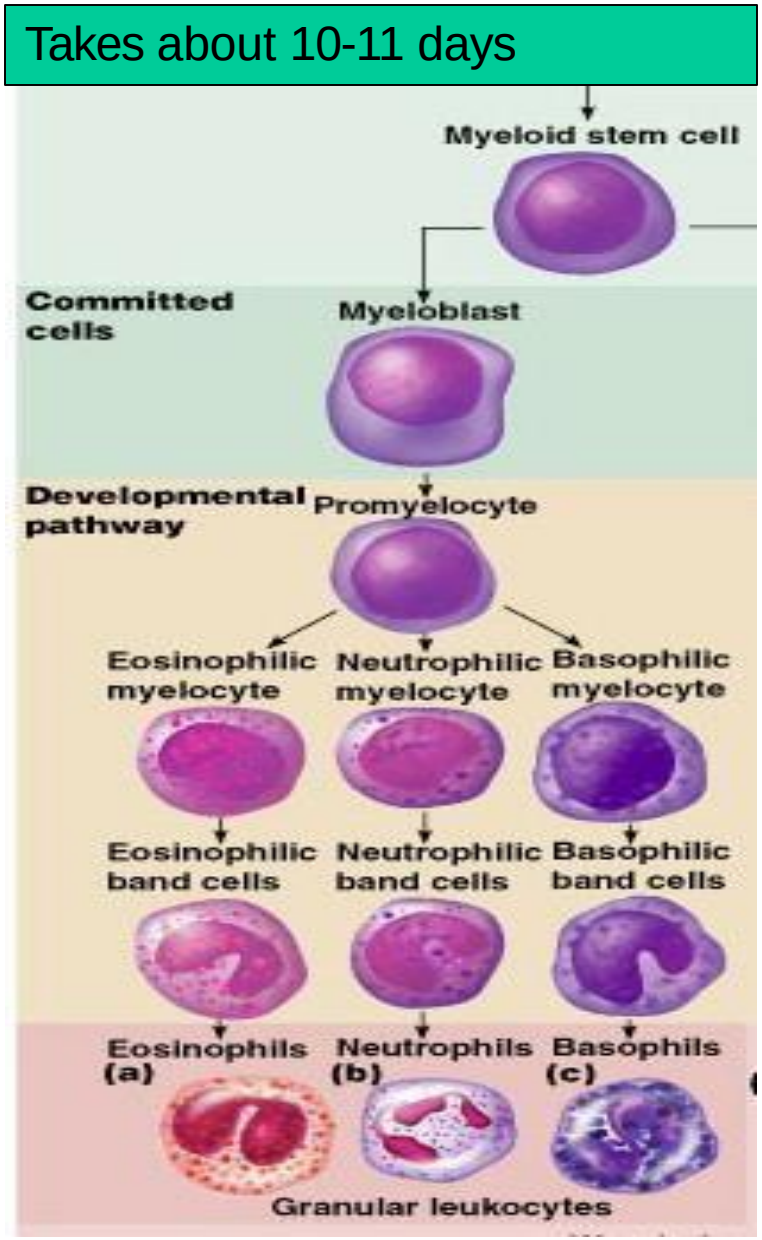
7 Metamyelocyte:

(specific granules N, E,B +**indentation of nucleus)**

8-Band cell

Smaller cells ,curved band nuclei ,**cannot divide**. May be present in peripheral blood.

9-Mature cells: (Neutrophils ,Eosinophils Basophils)



Monopoiesis

1 UMC

2Pluripotential

hemopoietic stem cells

(hemocytoblasts(

3 Restricted monocyte

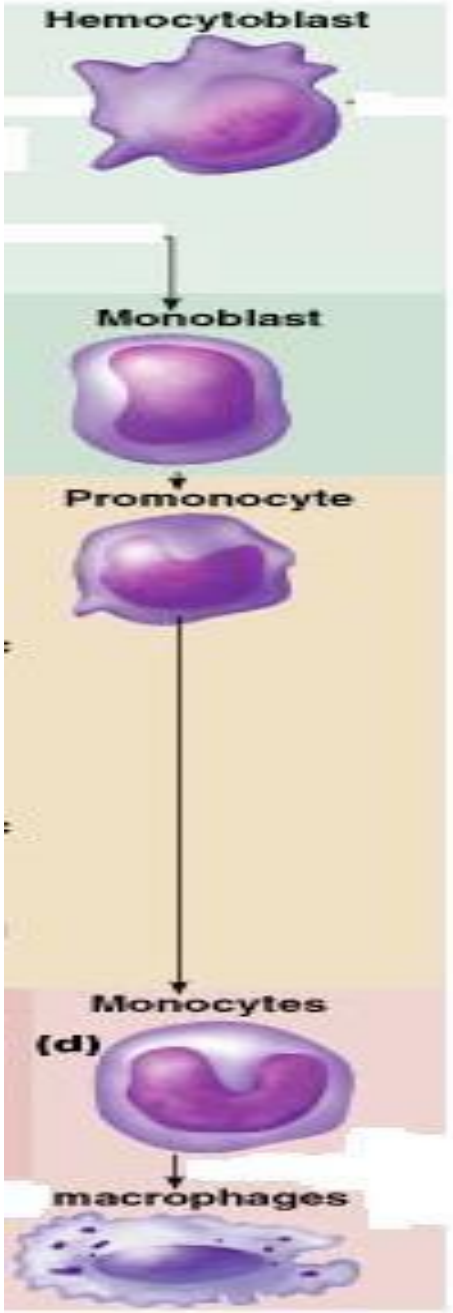
progenitor

)CFU-M) or with (CFU GM(

4 Monoblast.

5Promonocyte : indented nucleus + lysosomes.

6 Mature monocyte : 2 days in blood stream، then → tissue macrophages for several months.



Lymphopoiesis

Takes place in 1ry lymphoid organs

BM , Thymus

1 UMC

2Pluripotential hemopoietic stem cells

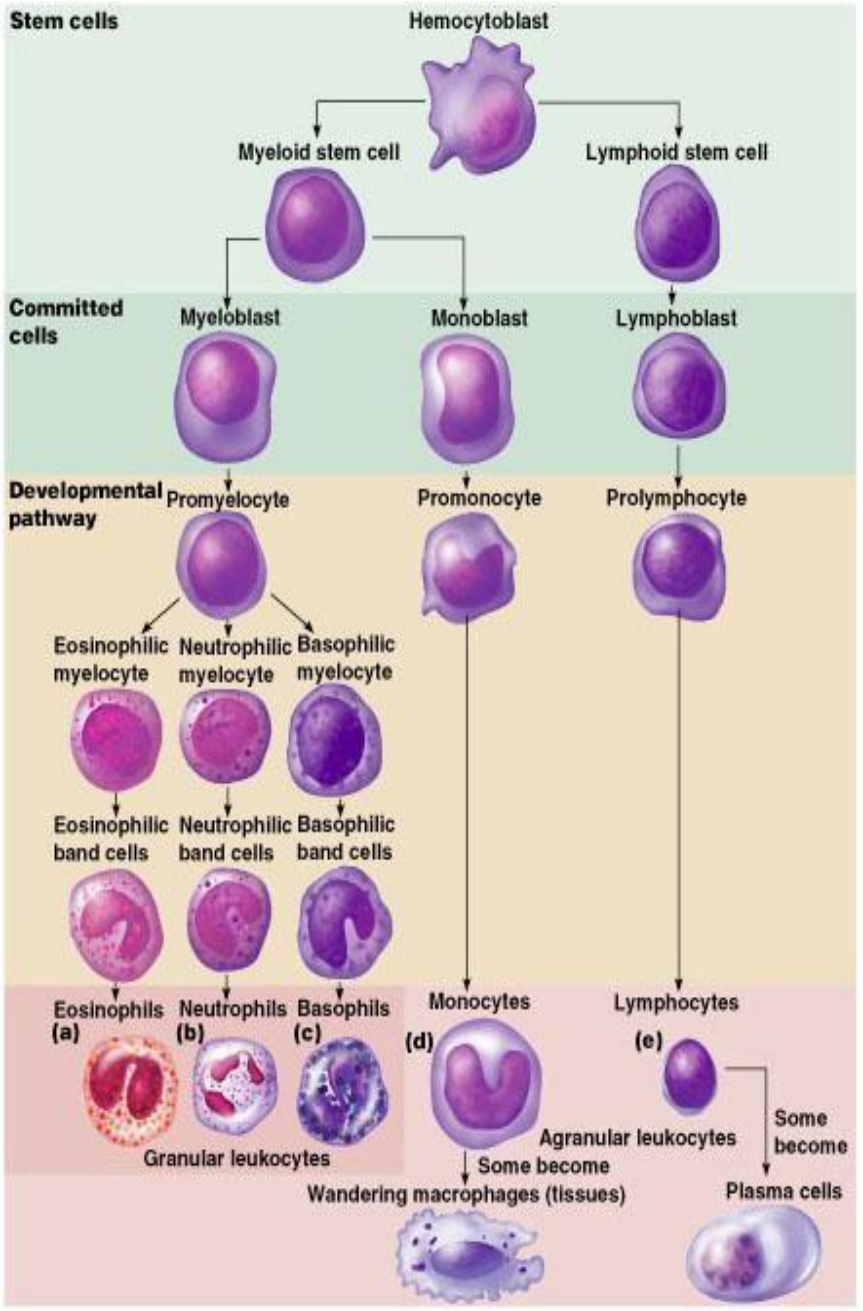
3Restricted lymphocyte progenitor (Colony-forming unit (CFU-L(

4 Lymphoblasts

5Prolymphocytes 6-

Lymphocytes……

)B, T (precursors) & Null cells(؟



LYMPHOPOIESIS

- Definition & sites.
- Involves the following:

1. PHSCs.
2. MHSCs.
3. CFU-Ly:

- Some daughters migrate to thymus
- ►►CFU- LY T, where:

❖ Reside in outer cortex►►

❖ T- lymphoblasts:

- ➢ Repeated mitosis.
- ➢ Azurophilic granules.
- ➢ Express surface markers.

❖ Thymus ---Mature T- lymphocyte--►►--peripheral lymphoid org

- Definition & sites.
- Involves the following:

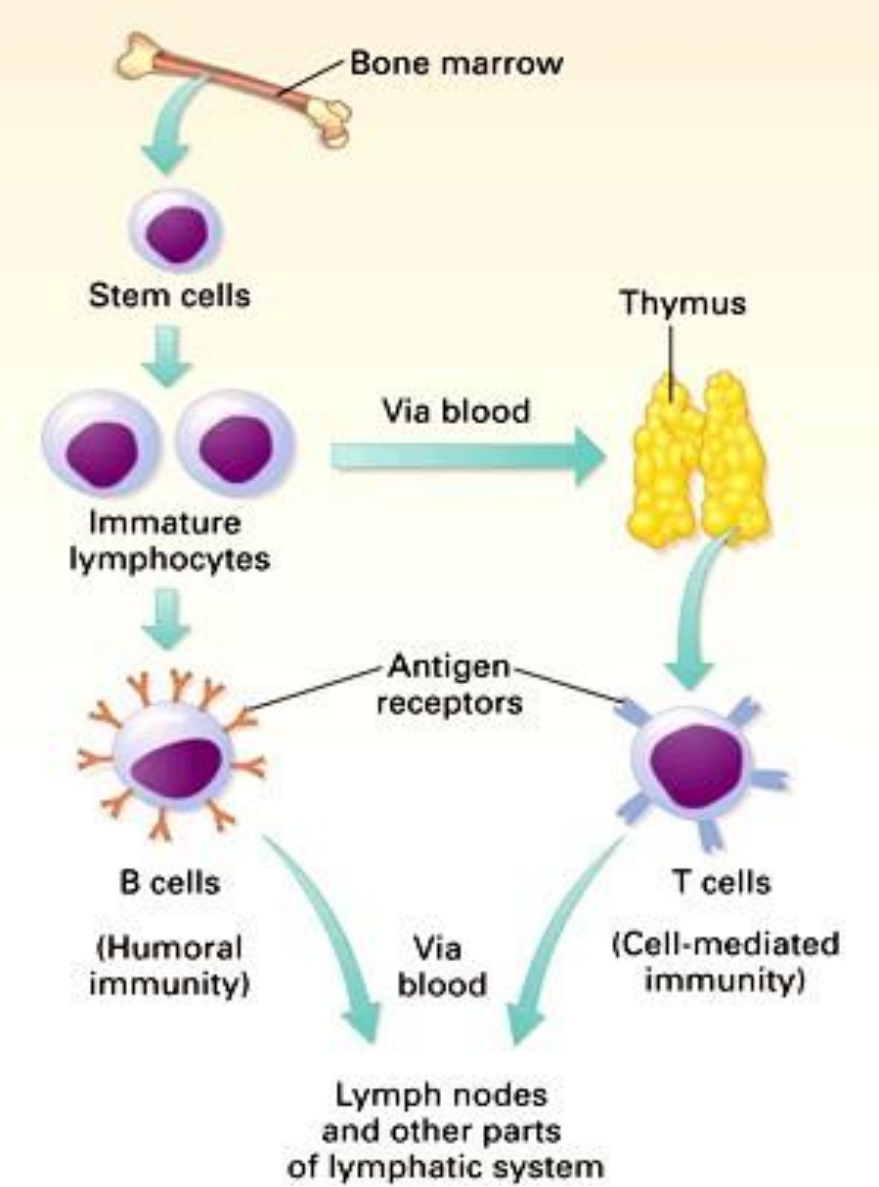
1. PHSCs.
2. MHSCs.
3. CFU-Ly:

- Some daughters remain in bone marrow
- ►►CFU- LY B, where: ►►

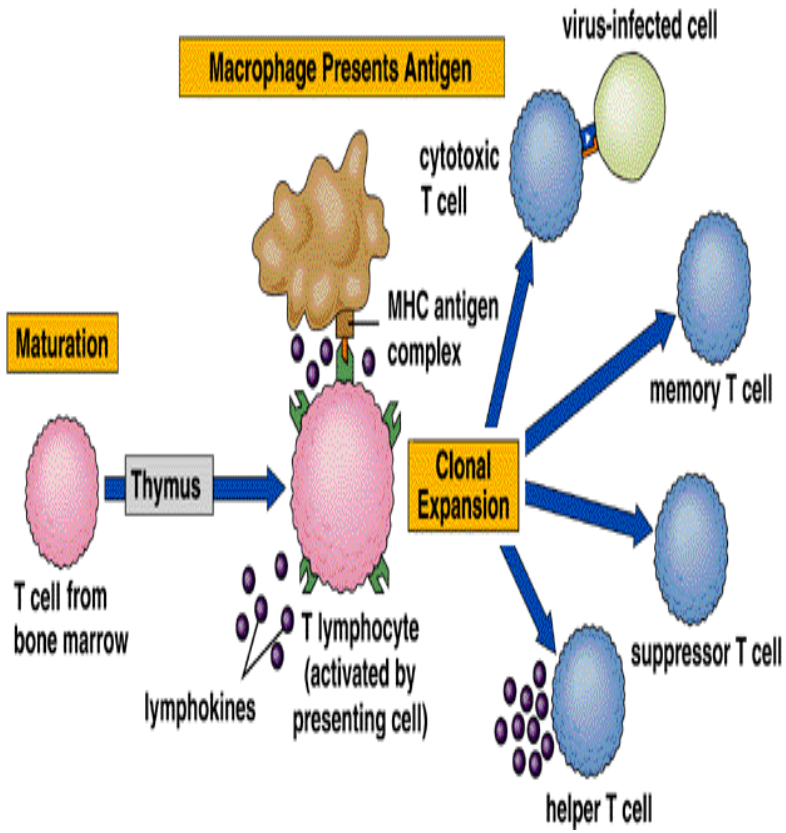
❖ B- lymphoblasts:

- ➢ Repeated mitosis.
- ➢ Azurophilic granules.
- ➢ Express surface markers.

❖ Mature B- lymphocyte►----►peripheral lymphoid organs.



T-Cell Activation and Diversity



FACTORS AFFECTING HAEMOPOIESIS

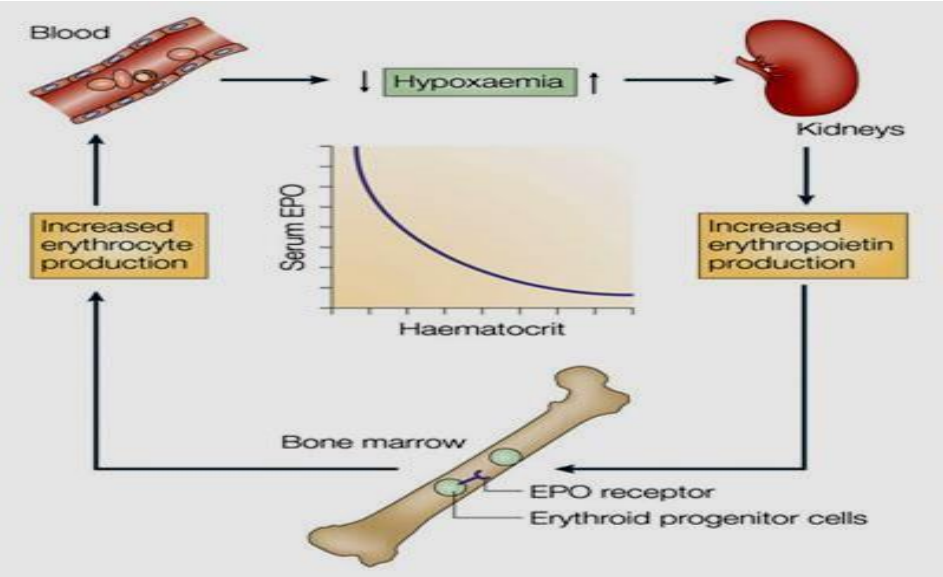
- **Stimulated by:**

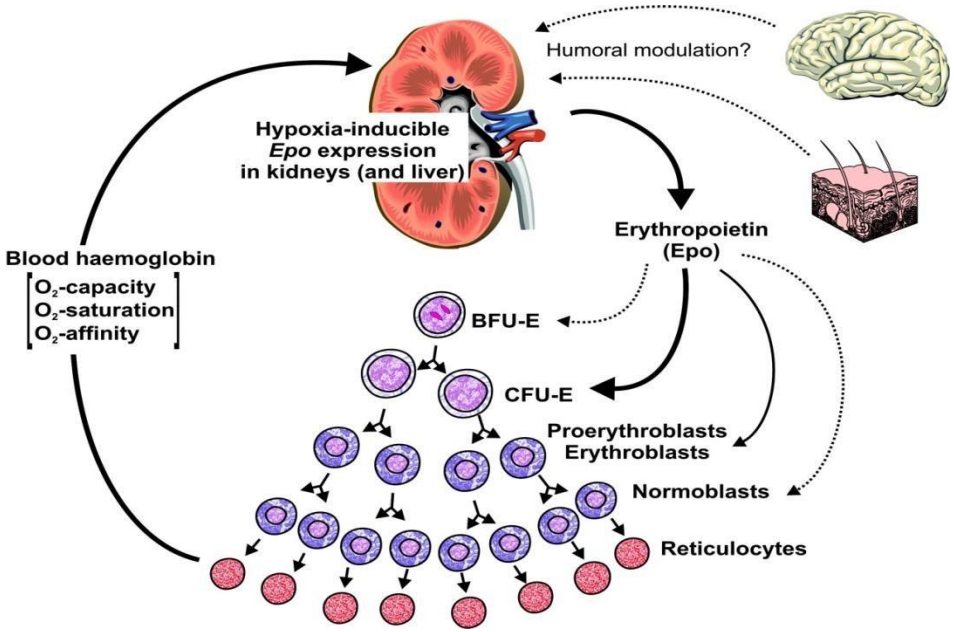
1. Erythropoietin.
2. Thyroxin.
3. Growth hormone.
4. Testosterone.

- **Inhibited by:**

1 Estrogen.

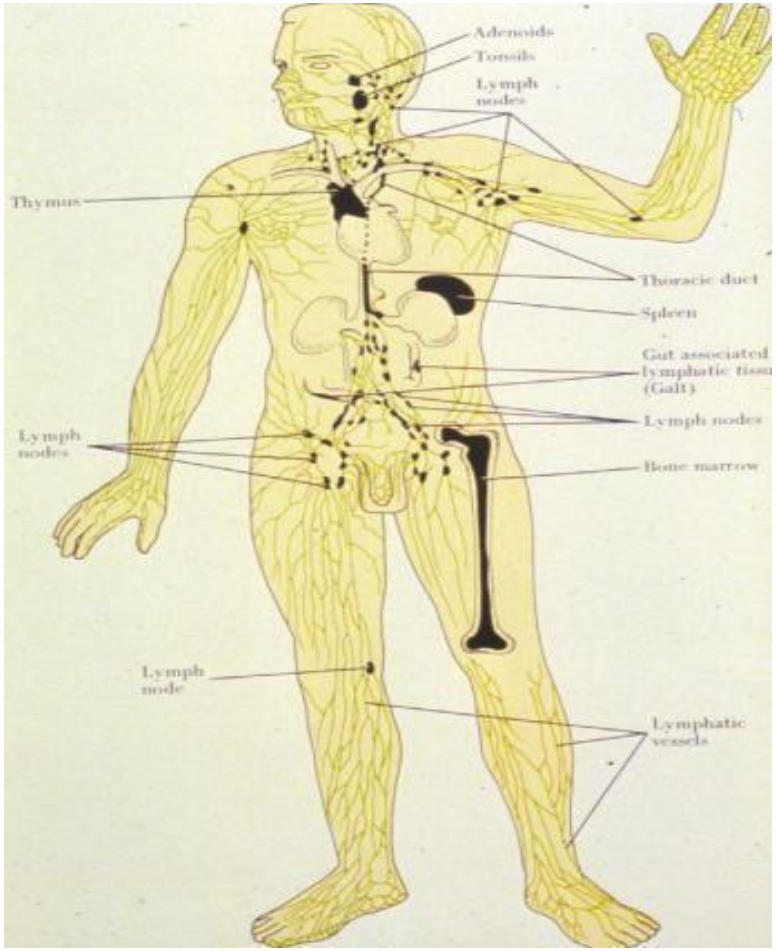
2 Nutritional deficiency.





immune system

- All cells and structures distributed throughout the body that Protect the body from invasion of micro-organisms or foreign substances



Body defense Mechanisms

1. **Surface protective mechanisms**
2. **The innate immune system**

➢ **Non –specific immune response**

➢ acts rapidly & has **no** immunological memory e.g.

❖ Complement system
❖ Phagocytic cells
❖ Natural –Killer cells

.3**The adaptive immune system**:
able to distinguish self from non-self

- **Specific immune response**
- specificity & diversity
- has memory،

Its contents are : T & B lymphocytes & APCs

- **Humoral immunity** …. Against antigens
- **Cell mediated immunity**…. Against tumor, transplant cells, virus infected cells & microorganisms

Lines of Defense

- Break the cycle of transmission

Physical Barrier

- **Skin: Stratum Cornium**
- **HCl In Stomach**
- **Mucus In Intestines**

First Line: Phagocytes to the Kill infectious agent

Neutrophils

Monocytes ⇨ macrophage

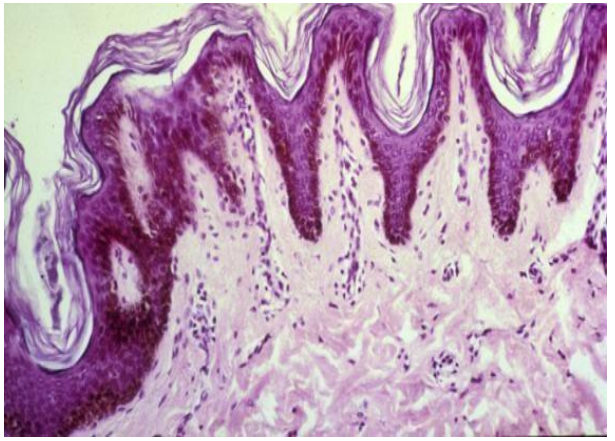
Increase host resistance

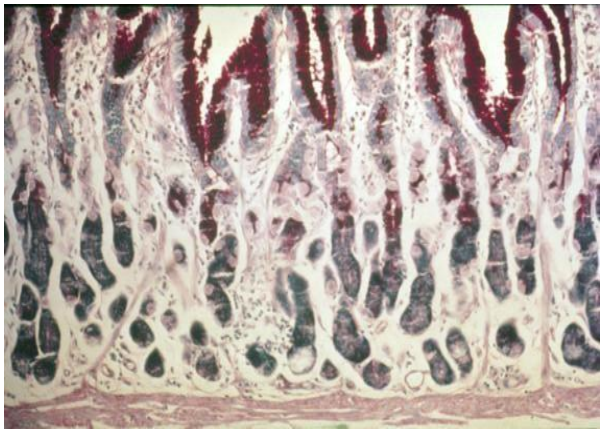
Characteristics of Immunity

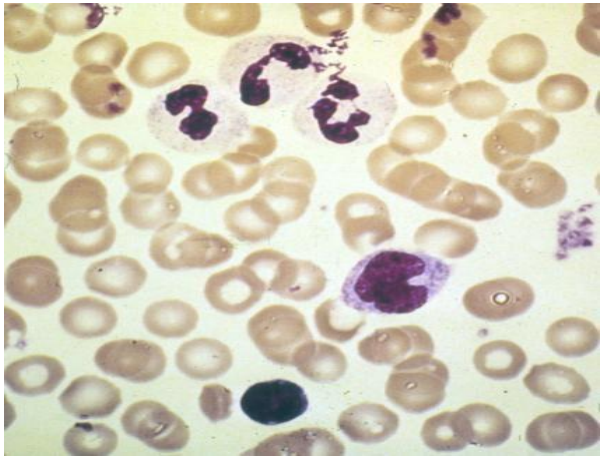
Acquired - requires exposure to antigens

Specificity - response is unique to exposure

Memory - remembers previous exposure







Immune system

Cells

❑ Fixed cells -

- **Reticular cells** - connective tissue cells that may secrete a fine matrix of reticular fibers that these cells extend cytoplasmic processes
- **Follicular dendritic cells (FDCs)** – appear similar to reticular cells in shape, but are really a type of macrophage - found in the germinal centers of lymph nodes. These cells bind foreign antigens and interact with lymphocytes as antigen presenting cells.

❑ Free cells

- 1. macrophages
- 2. various classes of lymphocytes (B and T)

Lymphoid organs

1ry = Central

- ❑ Bone marrow
- ❑ Thymus gland

2 -2ry = Peripheral

- ❖ Lymph nodes
- ❖ Spleen
- ❖ Tonsils
- ❖ MALT

Cells of the immune system

- **Macrophages**
- **Antigen – presenting cells**
  - Dendritic cells
  - Macrophages
  - B- lymphocytes
  - Epithelial reticular cells

Express **both MHC I &II** on their cell membrane

- **Granular** leucocytes(N,E,B(
- **Mast cell**
- **Lymphocytes (B ,T, natural killer(**

Lymphocytes

Arise in the red bone marrow, they protect the body against antigens

Types of lymphocytes

- **T-lymphocytes** (T cells): mature in the thymus, directly attack and destroy foreign cells
- **B-lymphocytes** (B cells): mature in the bone marrow, produce plasma cells that manufacture antibodies
- **NK (natural killer)** cells (non-speficic immunity) = they mature in the bone marrow

Lymphatic system

- It is part of the **circulatory** system and an important part of the immune system.
- It returns fluids that have leaked from the circulatory system back to the blood

Lymphatic system consists of:

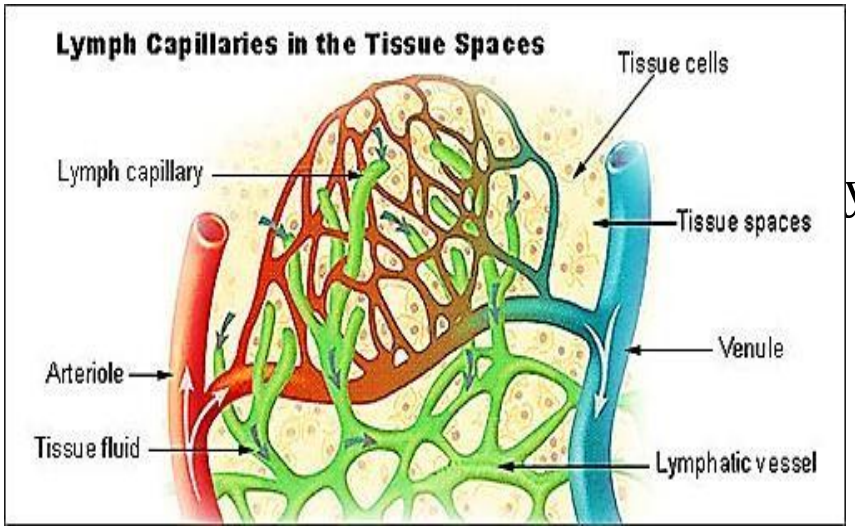
- ❖ Lymph vessels
- ❖ Circulating lymph
- ❖ Lymphoid tissues (organs(

Functions of lymphatic system

- ❑ Lymphatic system maintains the balance of fluid in the blood versus the tissues (fluid homeostasis(
- ❑ It facilitates absorption of fats and fat-soluble nutrients in the digestive system.
- ❑ It is part of the immune system and helping defend against foreign bodies such as bacteria
- ❑ Involved in production of lymphocytes and plasma cells

Lymphatics (lymphatic vessels(

- Lymphatic Vessels –Originate as lymph capillaries – Capillaries unite to form larger lymph vessels • Resemble veins in structure • Connect to lymph nodes at various intervals
- **lymphatic vessels**, conduct the lymph between different parts of the body. Lymphatics are resemble veins in structure except, that their coats are thinner and that these have numerous valves.



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Lymph is protein rich fluid that circulates throughout the lymphatic system.

- It is formed, when the interstitial fluid (the fluid which lies in the interstices of all body tissues) is collected through lymph capillaries, then transported through larger lymphatic vessels to lymph nodes, where it is cleaned by lymphocytes, before emptying ultimately into the right or the left **subclavian vein**, where it mixes back with the blood.

Lymphoedema is a long-term (chronic) condition that causes swelling in the body's tissues. It can affect any part of the body, bu usually develops in the arms or legs.

- It develops when the lymphatic system does not work properly. The lymphatic system is a network of channels and glands throughout the body that helps fight infection and remov excess fluid.

There are 2 main types of lymphoedema:

- **primary lymphoedema** – caused by faulty genes that affect the development of the lymphatic system; it can develop at any age, but usually starts during infancy, adolescence, or early adulthood
- **secondary lymphoedema** – caused by damage to the lymphatic system or problems with the movement and drainage of fluid in the lymphatic system; it can be the result of a cancer treatment, an infection, injury, inflammation of the limb, or a lack of limb movement

Lymphatic system organs

1. **-1The primary or central lymphoid organs**, that generate lymphocytes from immature progenitor cells.

1ry= central lymphatic organs

BM, Thymus

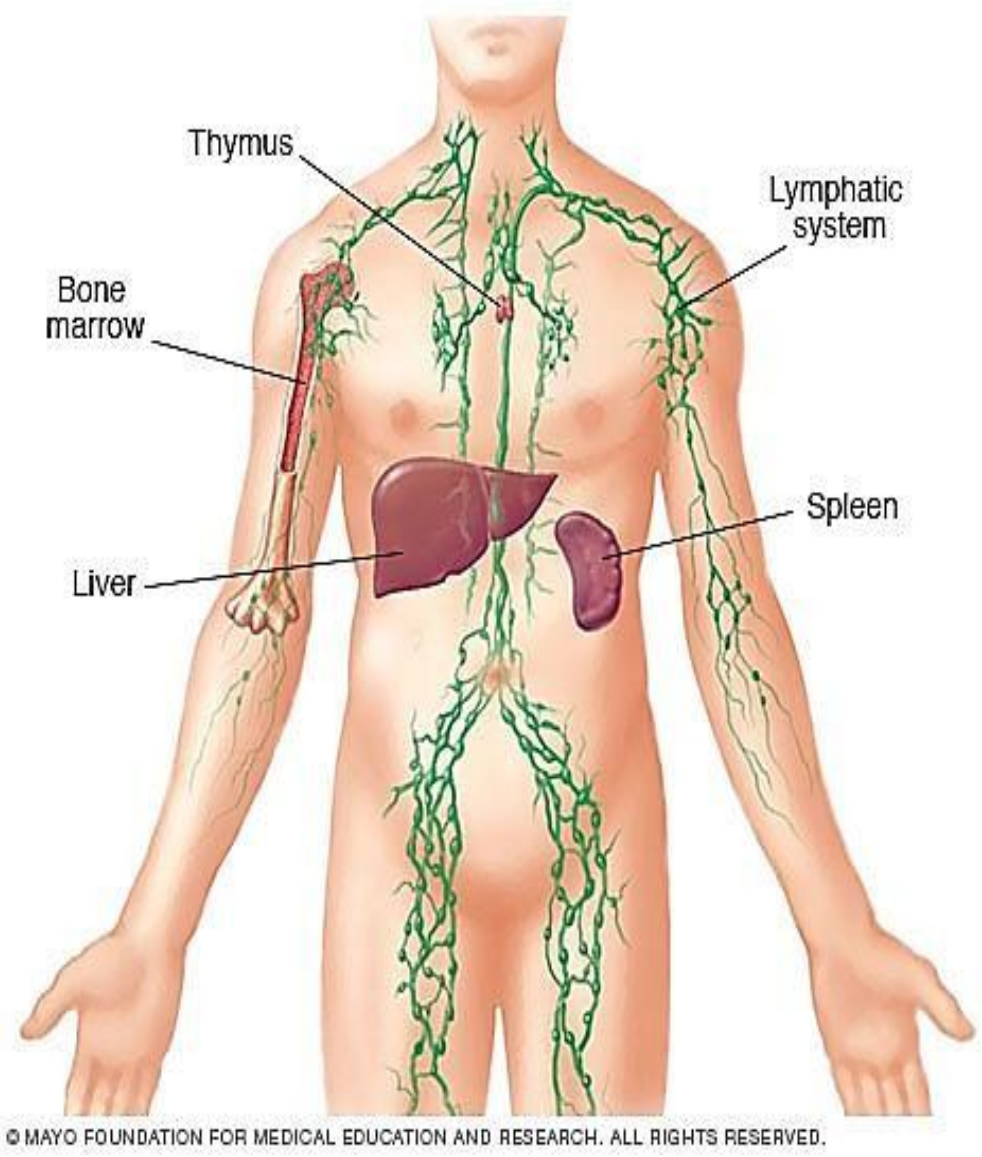
-2Secondary or **peripheral lymphoid organs**, which include:

2ry lymphatic organs

- **Lymph node**
- **Spleen**
- **Lymphatic nodules**

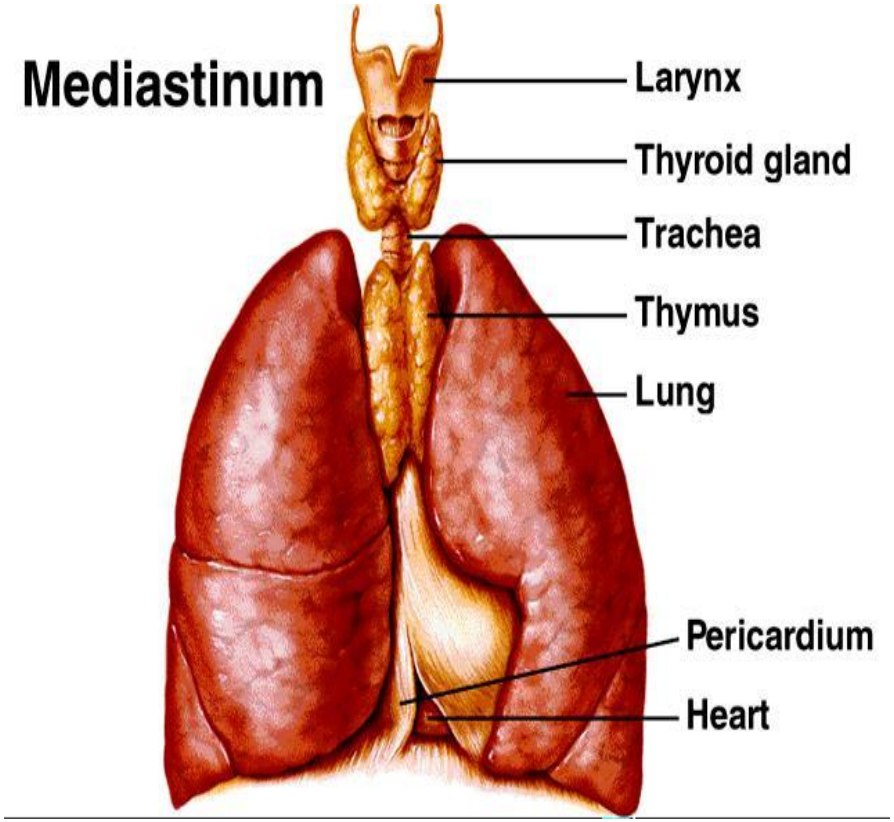
1. **Solitary**
2. **Aggregations**

- **Tonsil**
- **Peyer‘s patches**
- **Appendix**



Central lymphoid organs
Thymus gland

- The thymus is the site of maturation for T cells. The thymus increases in size from birth in response to **postnatal antigen stimulation.**
- **Basic structure of lymphatic organs:**
- **-1Stroma (Connective tissue component:(**
- capsule ,trabeculae (septa‹(**reticular C.T.**
- **-2Parenchyma (functioning component):** lymphocytes, macrophages (& or) epithelial cells with special arrangement.



Thymus gland

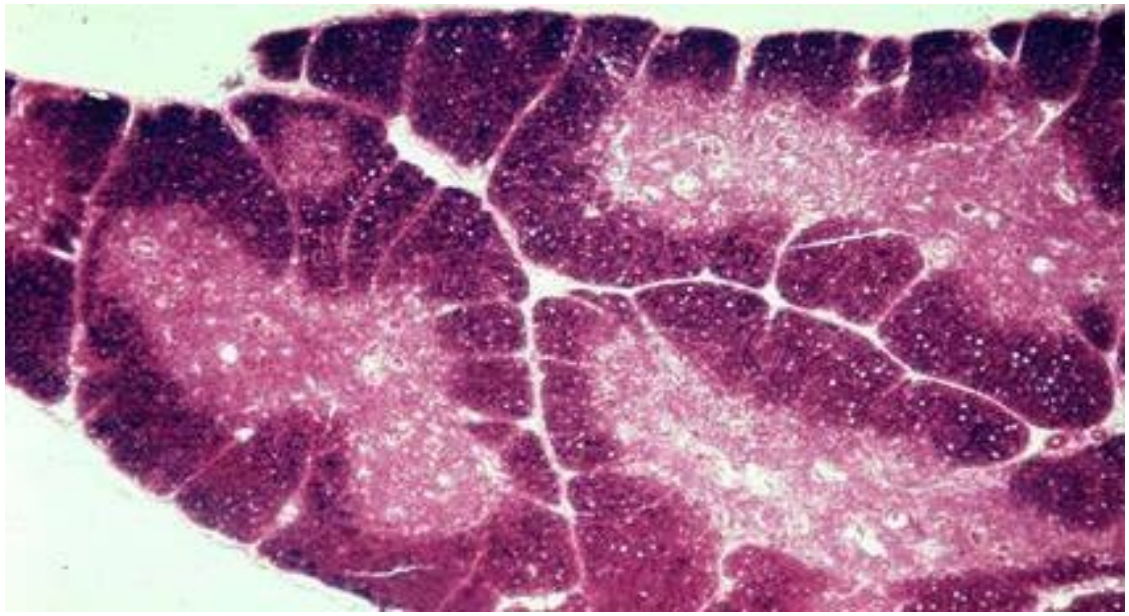
A-Stroma

1. **Capsule**
2. **Trabeculae**
3. **NO reticular F**

B- Parenchyma

1 Cortex

2 Medulla



Thymus gland

Structure:

-1Stroma: C.T component (capsule, trabeculae (septa)….lobes & lobules

No reticular fibers

The organ is highly lobulated and is invested by a loose connective tissue capsule.

*From the capsule, connective tissue septa containing blood vessels penetrate the substance of the organ, forming lobes.

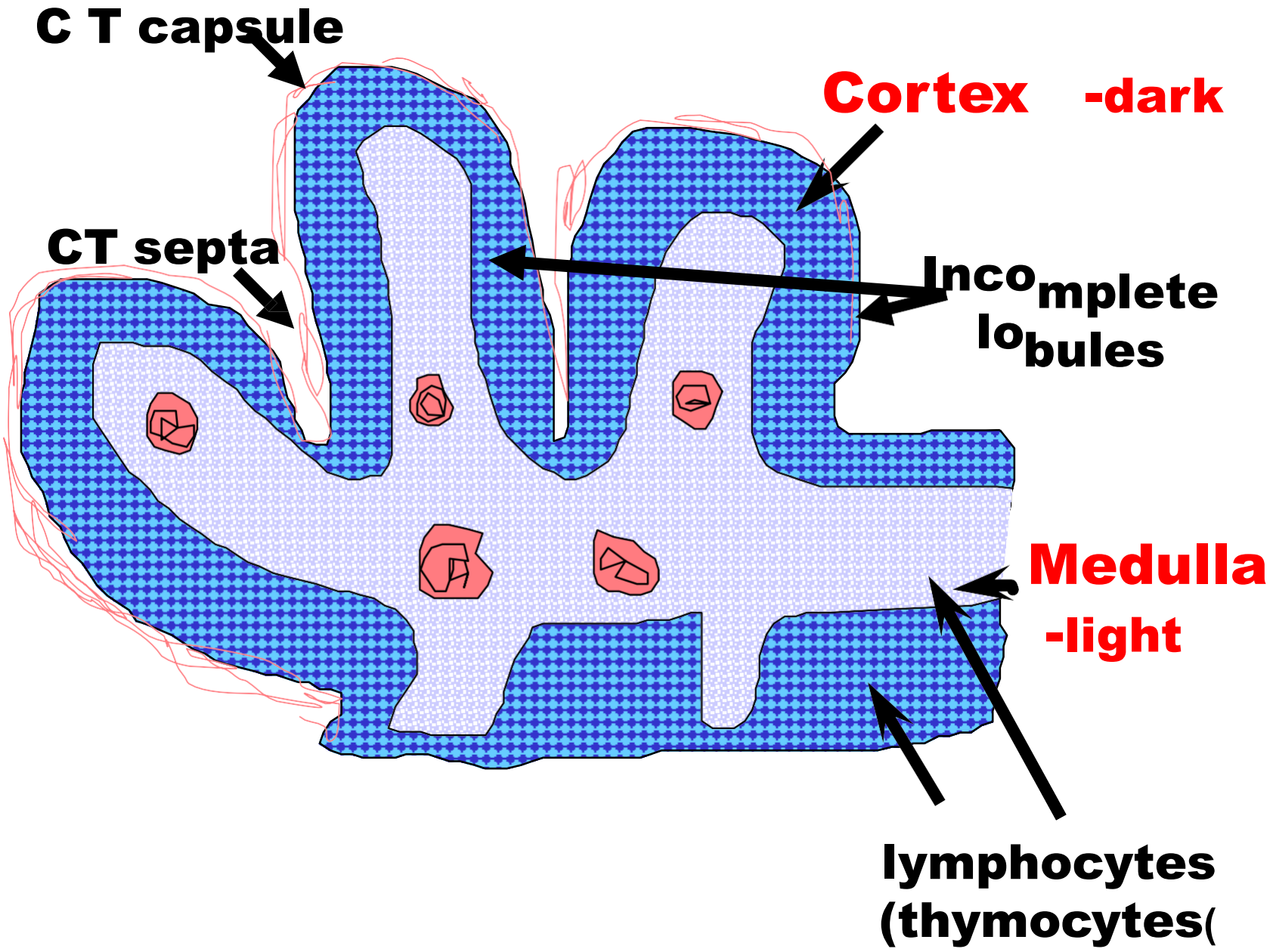
*Thin septa divide the lobes into incomplete lobules with common medulla.

-2Parenchyma: (functioning component(

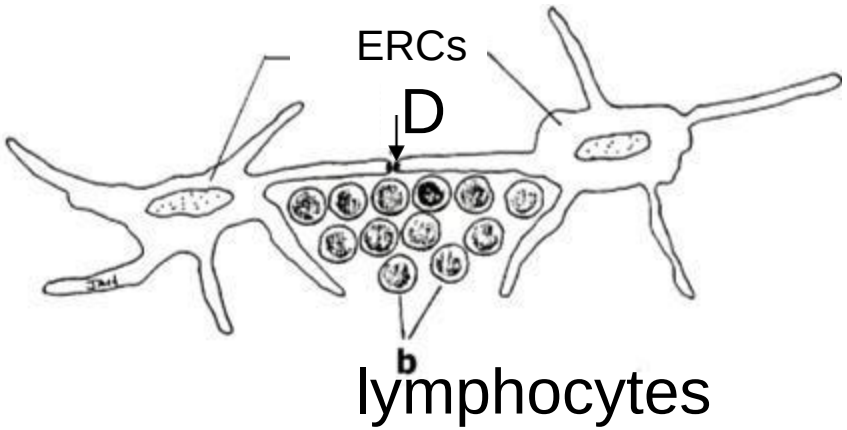
- -Lymphatic component.
- -Epithelial reticular cells.
- -Some macrophages.

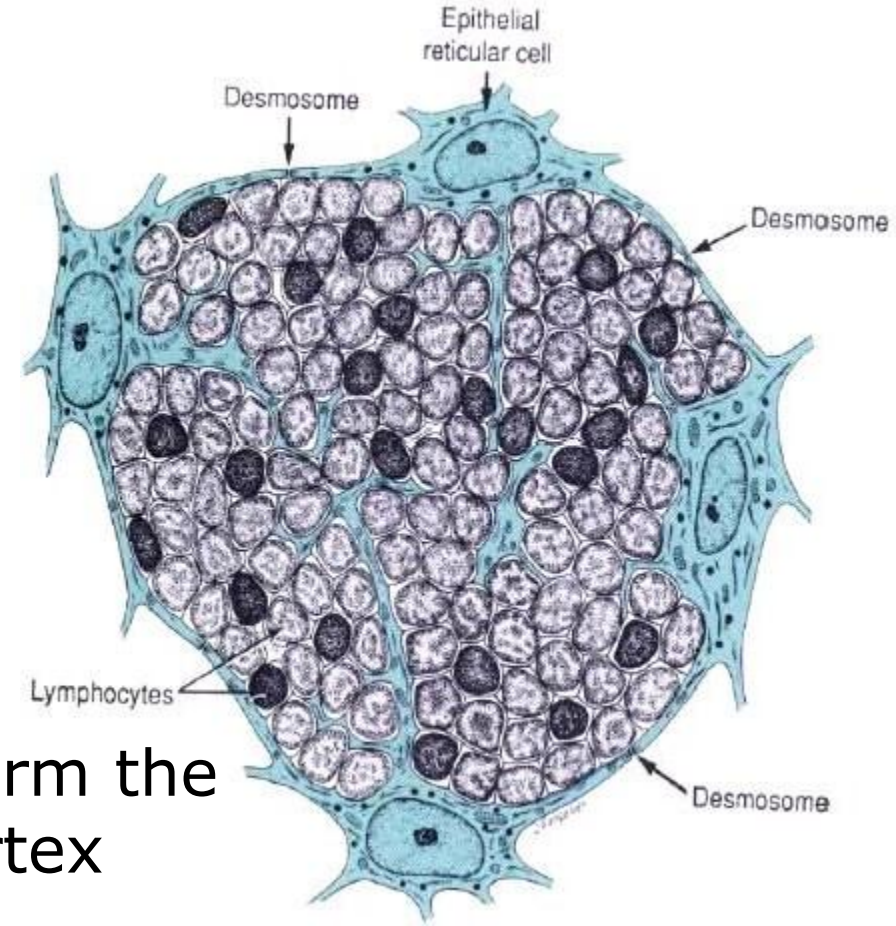
Each lobe has dark cortex and pale medulla.

Stroma


C T capsule
Cortex -dark
CT septa
Incomplete lobules
Medulla -light
lymphocytes (thymocytes(

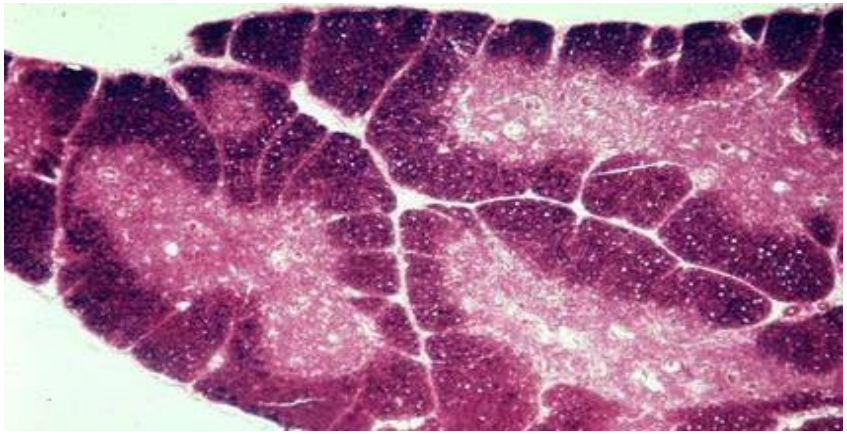
Cytoreticulum of the thymus





The epithelial reticular cells form the cytoreticulum dividing the cortex into lymphocyte filled compartments. So they provide a framework for the developing T

-2Parenchyma



A-Cortex

B-Medulla

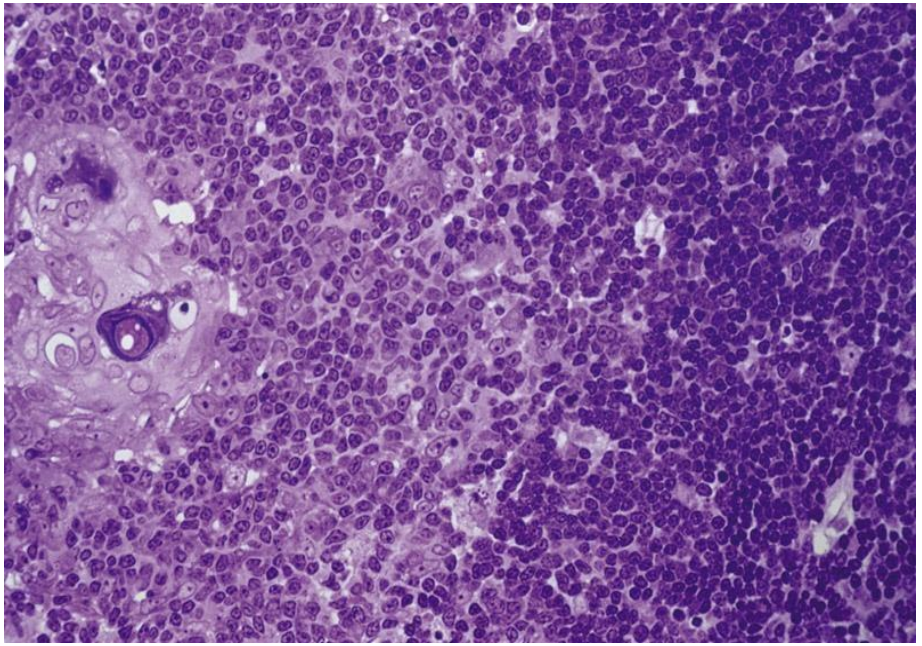
Both contain

-1T- Lymphocytes. No B- lymphocytes & plasma cell

2- Epithelial reticular cells.

3 Macrophages.

4 Blood capillaries.



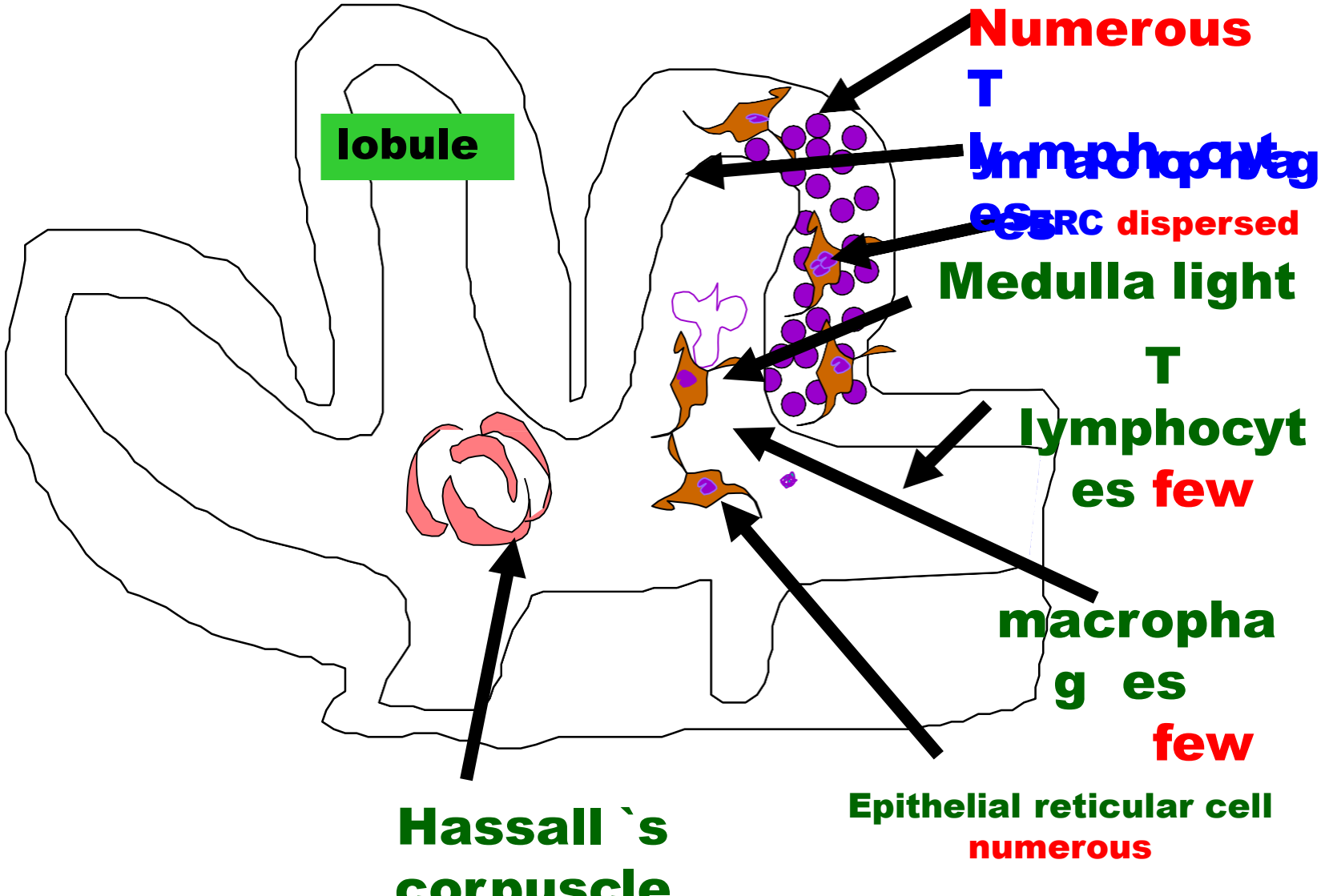
Cortex of thymus lobule

Peripheral dark-stained zone.

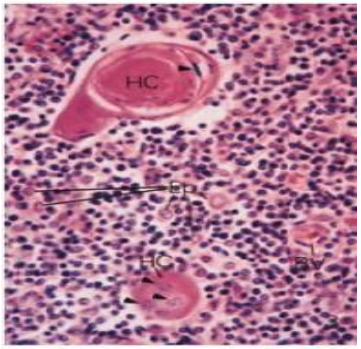
The cortex contain **densely packed** **T-** lymphocytes, epithelial reticular cells & macrophages.

Mature T lymphocytes leave the cortex to the medulla.

Parenchyma of thymus



Thymic medulla



*The thymic medulla contains primarily small, but fully mature, T lymphocytes.

* T lymphocytes leave the medulla **via venules**.

* These lymphocytes will populate specific regions of other lymphoid organs L.N., Spleen **)thymus dependant zones(**

- **Hassall's corpuscles**

Contains Hassall's corpuscles **(diagnostic feature),** which vary in size & are acidophilic in reaction.

*They consist of **concentric layers of epithelial reticular** cells, which are frequently **degenerate**, and may **calcify.**

Functions : Unknown

Epithelial reticular cells

Endodermal in origin.
*Branched cells with pale nuclei and acidophilic cytoplasm.
*Do **not** produce **reticular fibers**.

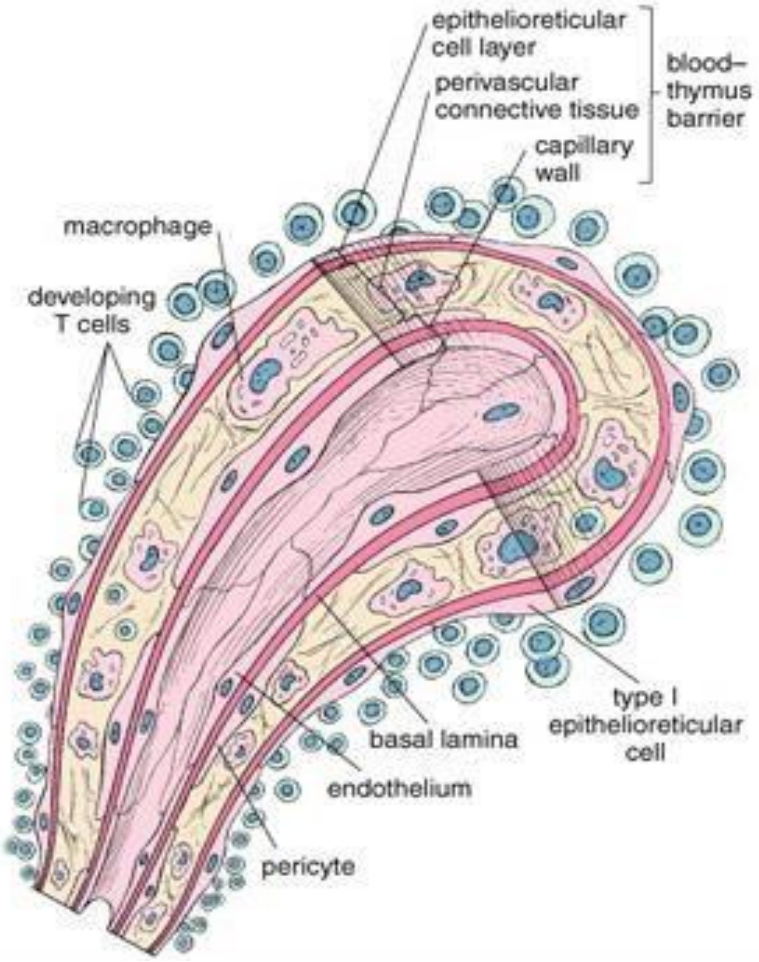
Functions of ERC

1. **Cytoreticulum**
2. **APC**
3. **Blood Thymus Barrier**
4. **Secretion of Growth factors (thymulin, thymosin, thymic humoral factor, thymopoietin) which regulate T cell maturation, proliferation, and function within the thymus and peripheral tissues.**

Blood thymic barrier

It is a barrier **between T cells and the lumen of the cortical vessels.**

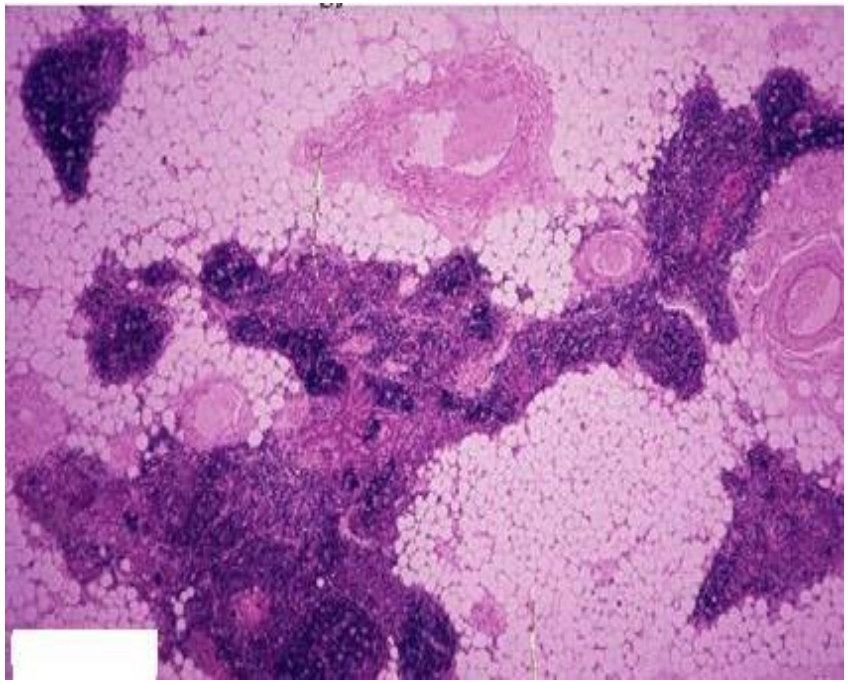
1. Continuous endothelium with tight junction
2. Thick basal lamina
3. Pericyte
4. perivascular space with macrophages
5. basal lamina of **Epithelial reticula cell** Epithelial reticular cells with tight junction



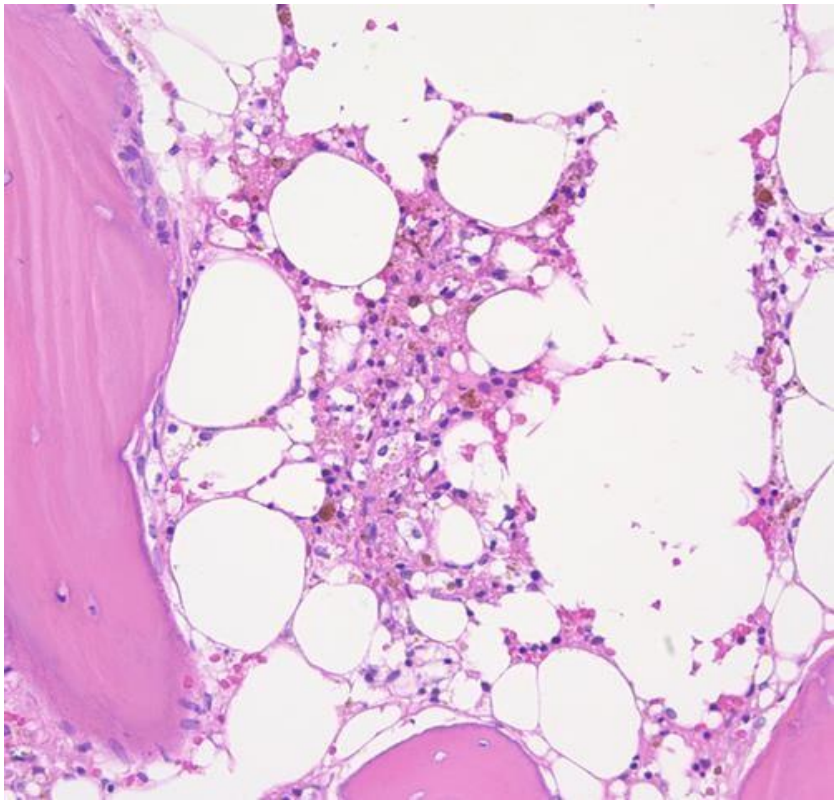
Thymus gland of adult

* Replaced by **Fibrous & adipose tissue.**
* Few lymphocytes, epithelial reticular cells&
* ⇧ Hassall's corpuscles.

Involution of thymus in adult



Yellow bone marrow



Specific structure of thymus

1. Undergo involution
2. No reticular fiber
3. No lymphatic nodule
4. No B- lymphocytes & plasma cell
5. Hassall ’s corpuscle
6. No afferent lymphatic

Cell in lymphoid organs

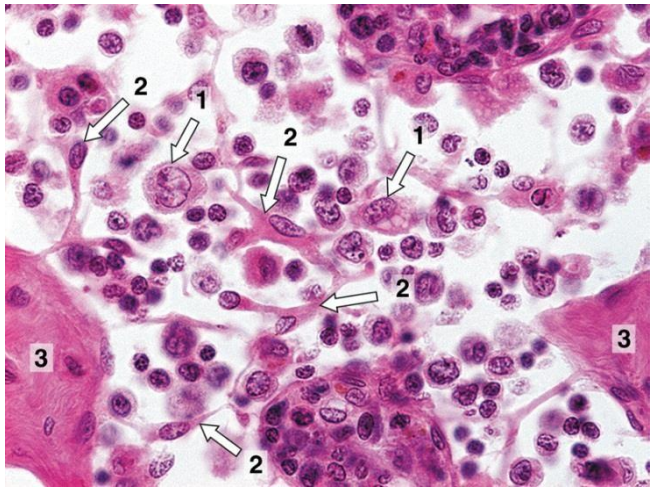
- **Macrophages**
- **Antigen – presenting cells**
  - Dendritic cells
  - Macrophages
  - B- lymphocytes
  - Epithelial reticular cells
- Granular leucocytes(N,E,B(
- Mast cell
- **Lymphocytes (B ,T, natural killer(**

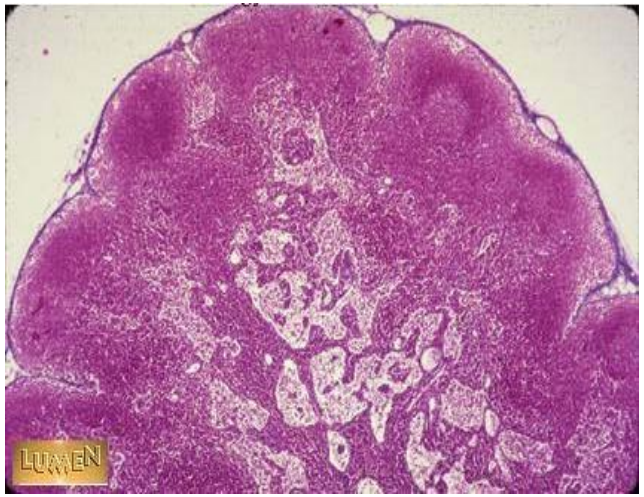
Diffuse = Loosely arranged

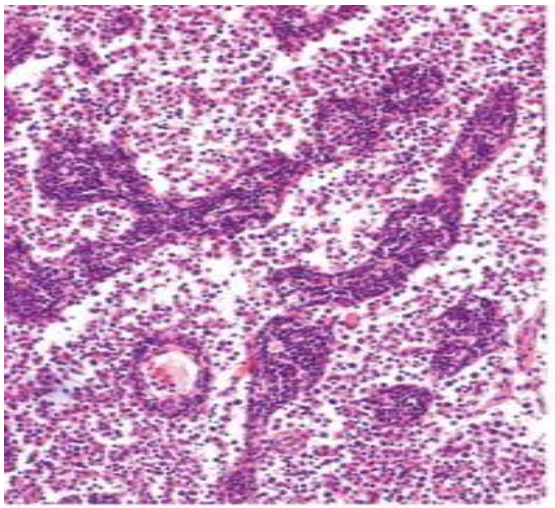
- Scattered in the lymphatic organ

Dense Aggregation

1. Lymphatic nodules = **follicles**
2. Lymphatic **cords**







Lymphatic nodules (follicles(

*Non-encapsulated collections of lymphocytes.
*Found in all lymphoid organs **except thymus**.

The lymphatic nodules are collection or spherical masses of lymphoid cells (B cell) which form either primary or secondary nodules

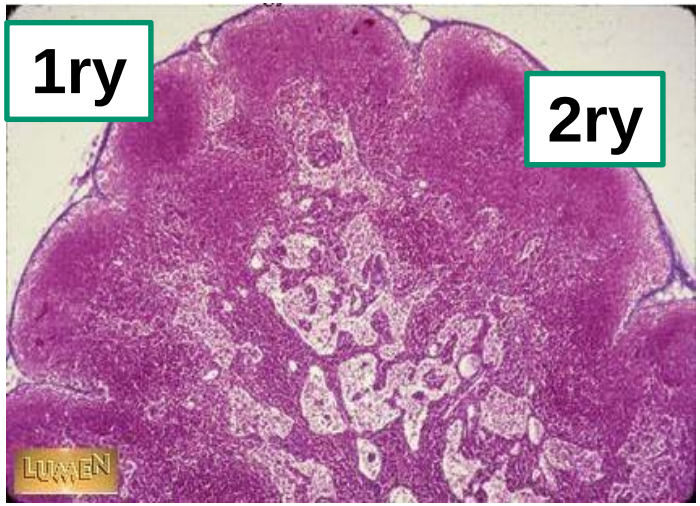
Primary nodule: mainly formed of small B- lymphocytes + macrophage.

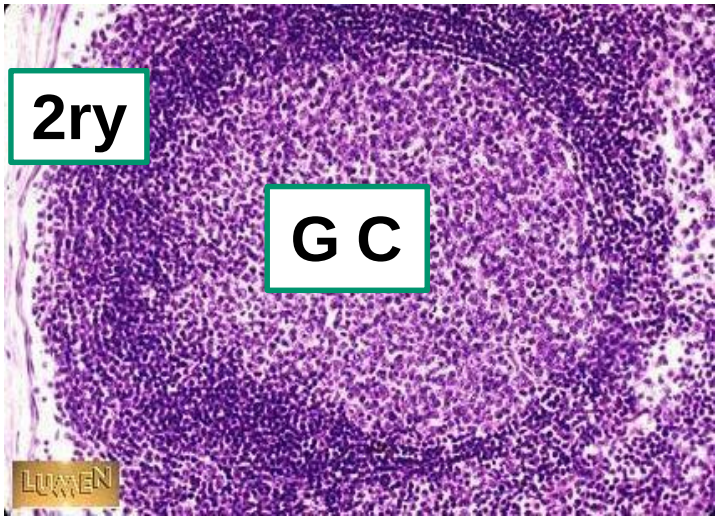
no germinal center.

Secondary nodule: it appears with paler area in the central part which is call germinal center or the reaction center

Contain lymphoblast + plasma cell

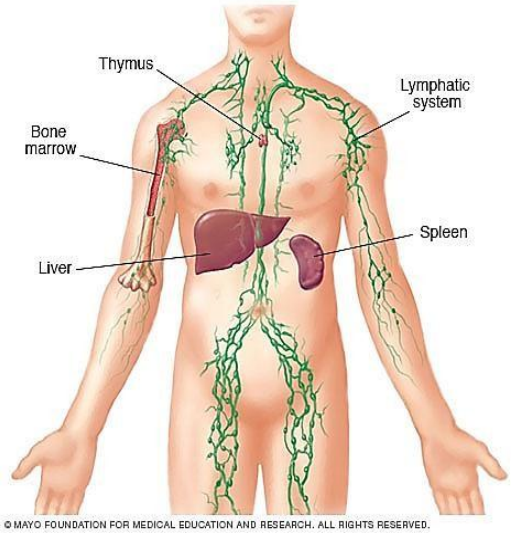
contains pale germinal center ,Mantle zone & peripheral zone





Structure of lymph node

- **Site:** along path of lymph vessels, most numerous in neck ,axilla , groin, along major vessels and in body cavities
- Small encapsulated oval bean shape structures. Serve as filter for removal of foreign bodies
- **Shape :** Each node is oval or bean shaped with fibrous capsule.
- It has a convex surface that is perforated by lymphatic vessels that have valves to pass lymph to the LN.
- It has concave surface **(hilum)** that is the site of entry and exit of artery and vein of LN. The lymph leave the node via efferent lymphatic vessels located in the hilum.



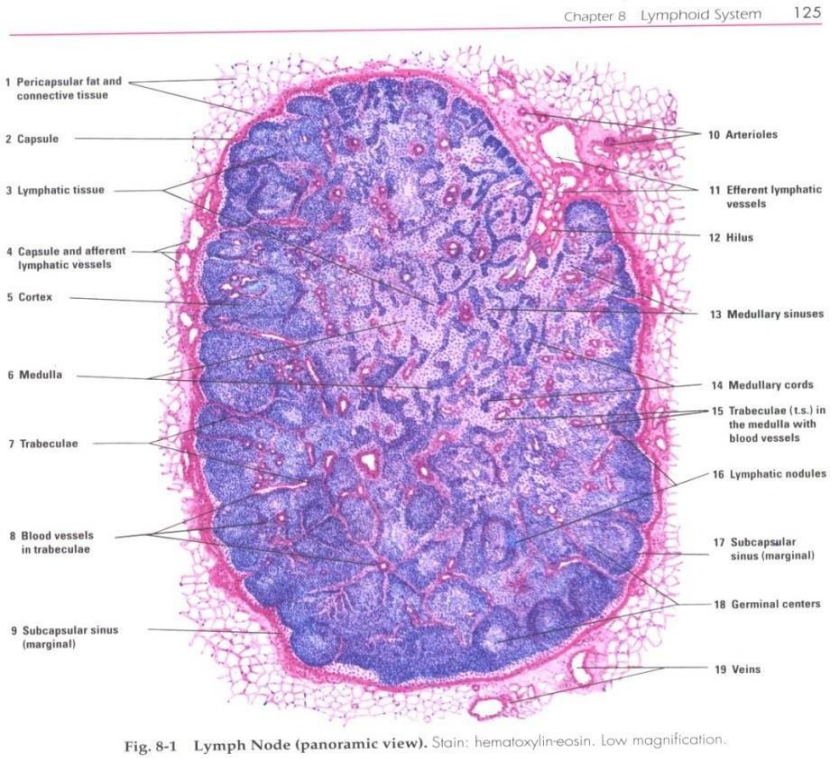


Fig. 8-1 **Lymph Node (panoramic view).** Stain: hematoxylin-eosin. Low magnification.

Histological structure of lymph node

STROMA

- **The coarse stroma:**
- **CT capsule**)complete fibroelastic(
- **Trabecuae in the cortex:** send perpendicular dividing the cortex into several incomplete compartments
- Thickened at the hilum
- It form sheath around the BV enter the LN at the hilum.
- **In medulla** the trabeculae runs in different direction forming a sort of network
- **Fine stroma:**
- Suspended from capsule and trabeculae
- in the form of **reticular fibers** and cells holding parenchymal cells in its meshes

Parenchyma

- **cortex** The outer part of the LN is highly cellular→
- superficial **(outer)** cortex
- Deep cortex = Paracortex **(inner cortex(**
- **Medulla**
- The inner part of the LN is
- less cellular→
- The cellular component of the LN which are T & B lymphocytes plasma cells and APCs are arranged into dense and loose arrangement.
- **Dense**→ cortical nodules
- medullary cords
- **Loose**→ loosely scattered B lymphocytes, plasma cells, macrophages and lymph sinuses

Lymph node stroma (CT skeleton(

Coarse stroma

Capsule

Afferent lymphatic

Trabeculae

Fine stroma

Reticular fibers

Suspended from the capsule and trabeulae

Efferent lymphatic

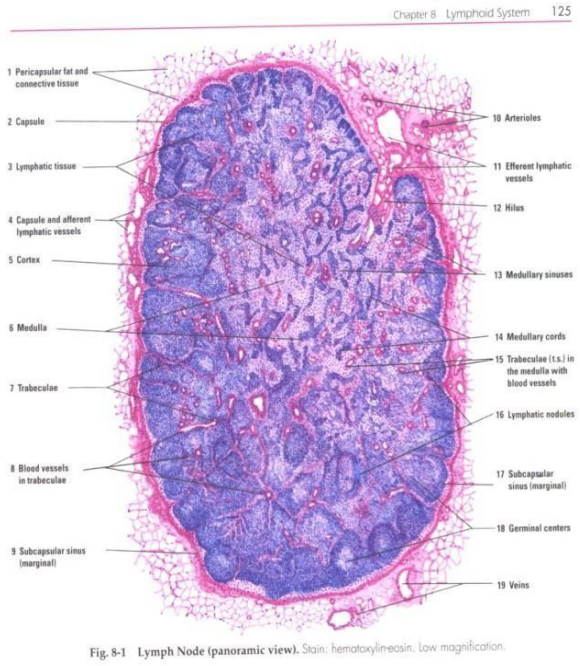
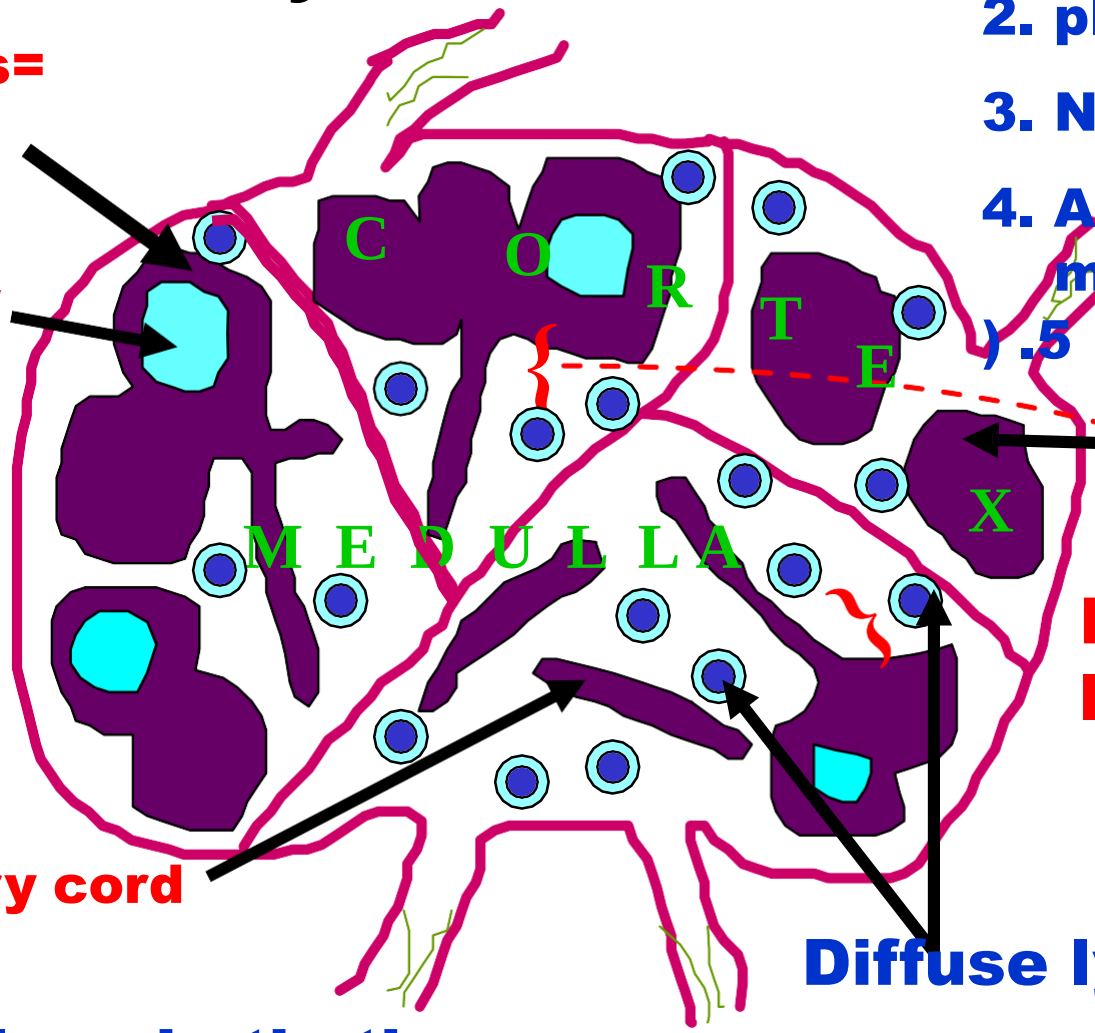


Fig. 8-1 Lymph Node (panoramic view). Stain: hematoxylin-eosin. Low magnification.

Parenchyma of LN

1. Lymphocytes B,T
2. plasma cells
3. Neutrophils
4. APCs macrophages( ) .5



Follicles= nodules

Secondary follicle Germinal center

primaryFollicle

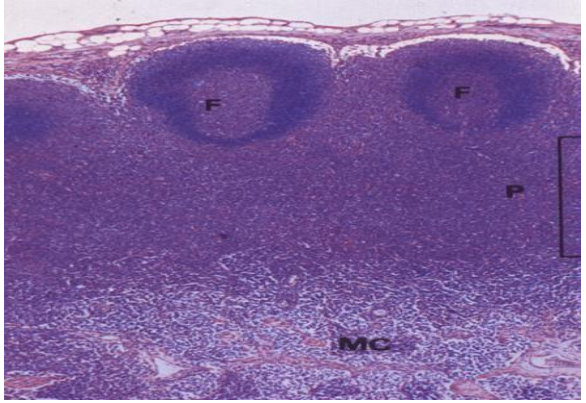
Paracortical zone

Medullary cord

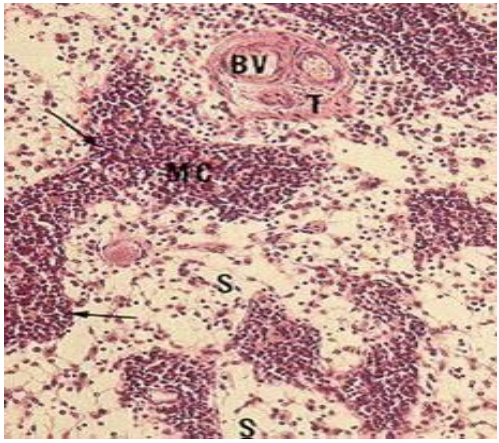
Diffuse lymphatic tissue

Lymphocytes, plasma cells, and macrophages.

Dense lymphatic tissue



Parenchyma



Cortex

❖ Outer cortex

Cortical nodule

- **Primary nodule**
- **B lymphocytes +macrophages**
- **Secondary nodule**
- **B lymphocytes +macrophages**
- **Lymphoblast (Germinal center(+macrophages**

❖ Inner cortex

) =thymus dependant area(

=Paracortical area is Formed of

- ❑ **T lymphocytes**
- ❑ **Macrophages**

❖ Medulla

1. Lymphatic sinuses
2. large blood vessels & supporting trabeculae
3. All are present in a framwork of reticular fibers
4. **medullary cords**

Contains:

- ❑ **B lymphocytes**
- ❑ **Numerous Plasma cells**
- ❑ **Marophages**

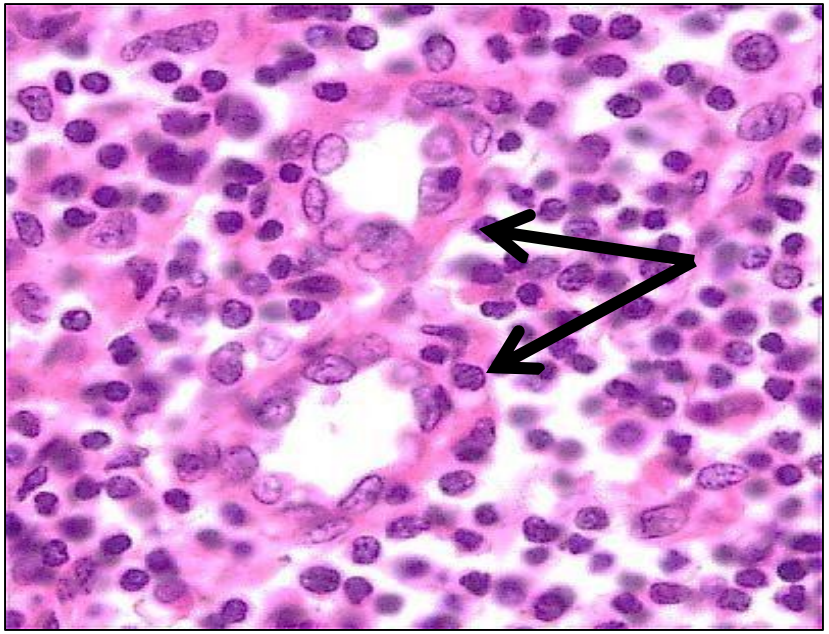
-2Paracortex)cortico-medullary:(

- between the cortex and medulla
- Is called the **Thymus dependent zone** of the lymph node, contains **T cells** have migrated from the thymus

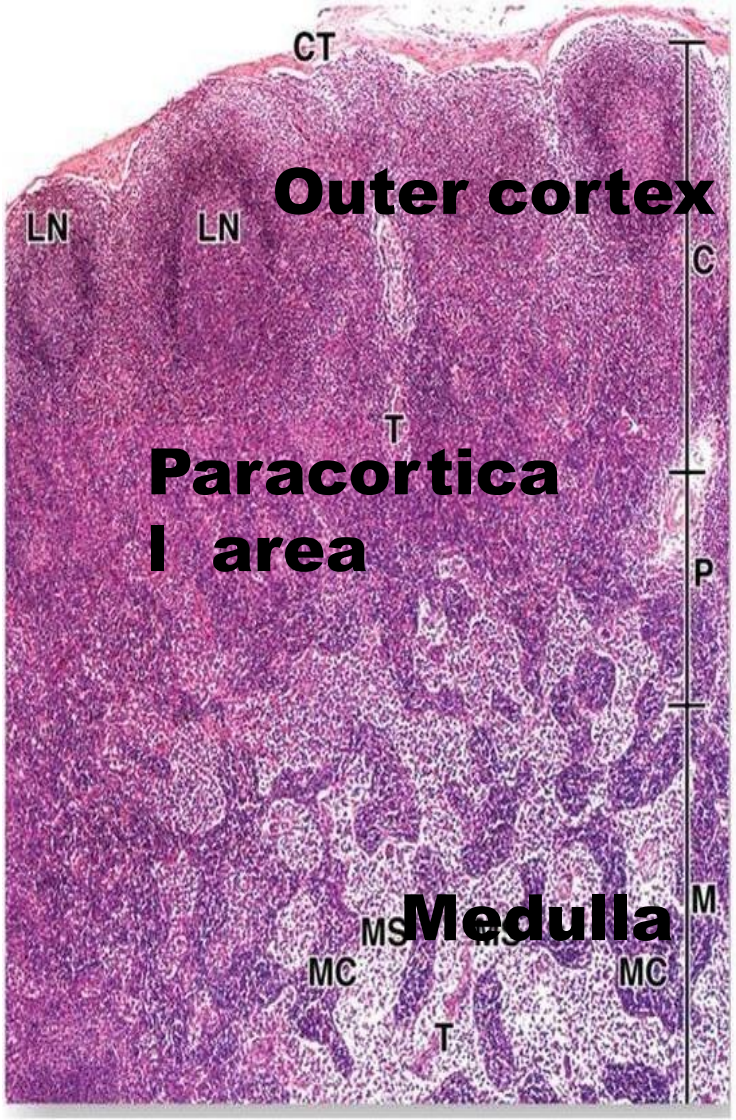
]T lymphocytes +High endothelial venules (HEV[(

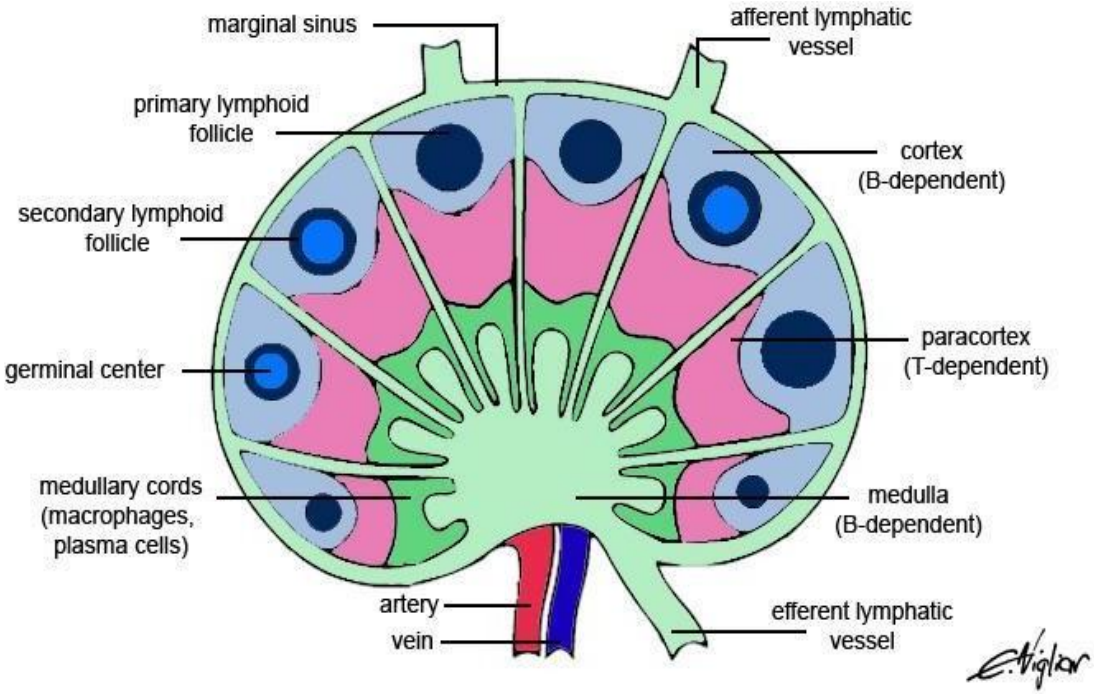
HEV:

- is the point of entry of T cells from blood to lymph node
- its endothelial lining is unusual
- is cuboidal to facilitate movement of T cells into LN



Three regions of LN

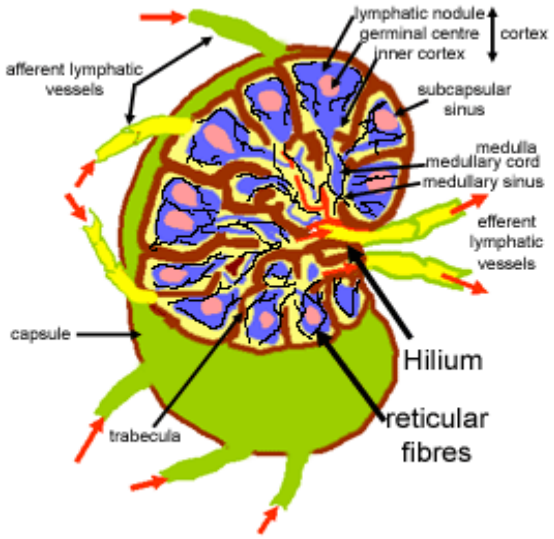


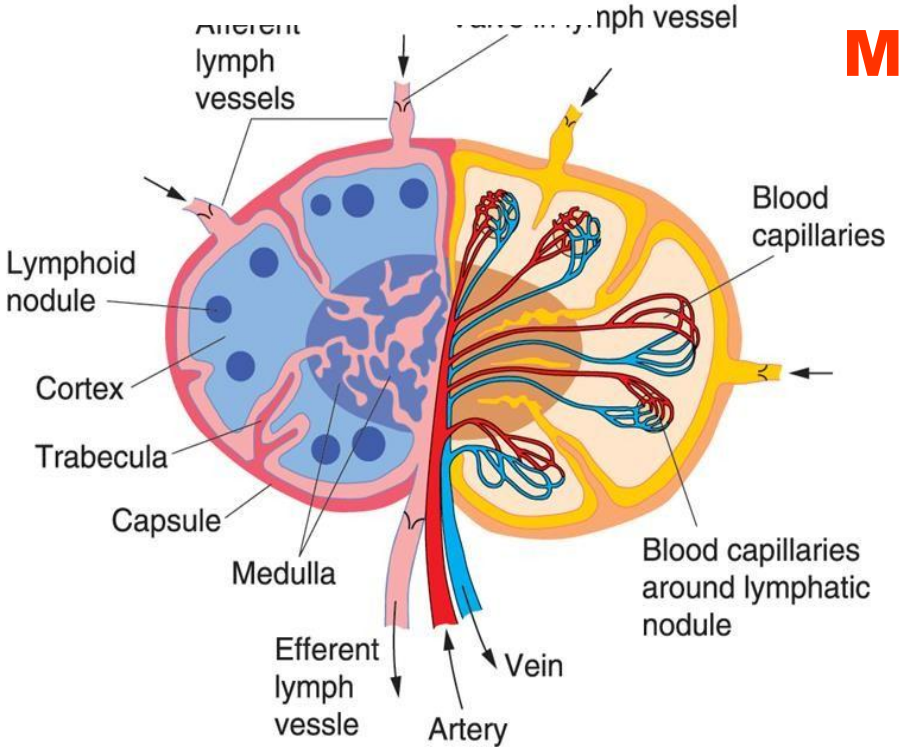


Function of lymph node

1. **The primary function of the lymph node is to filter the lymph which drains antigen from the tissues**
2. **production of B lymphocyte**

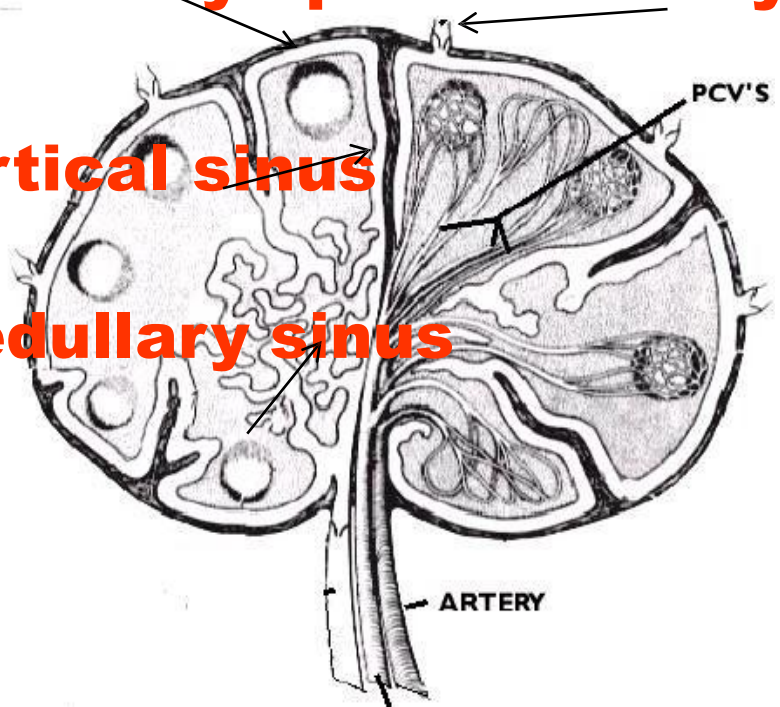
Lymphatic circulation





Subcapsula lymph

Afferent lymph



Cortical sinus

Medullary sinus

Efferent lymphatic

Structure of the spleen

A-Stroma.:

1 **Capsule:** **complete thick** rich in **collagenous** and **smooth muscle** fibers. **Covered by peritoneum**

2 **Trabecula:** Collagenous connective tissue projections from the capsule at the hilum . Branches repeatedly, and imperfectly divide the spleen into anastomosing chambers.

3 **Reticular CT:** reticular cells and fibers.

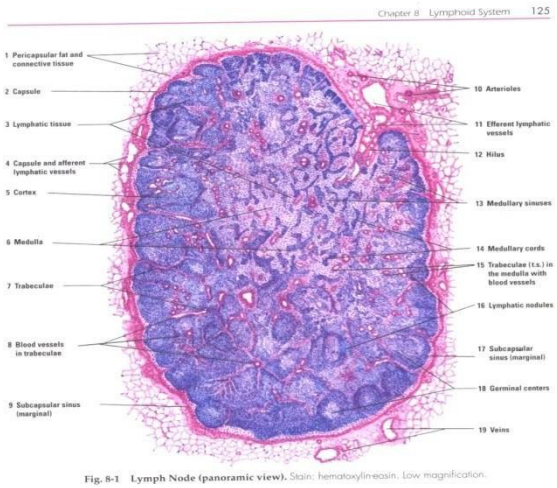
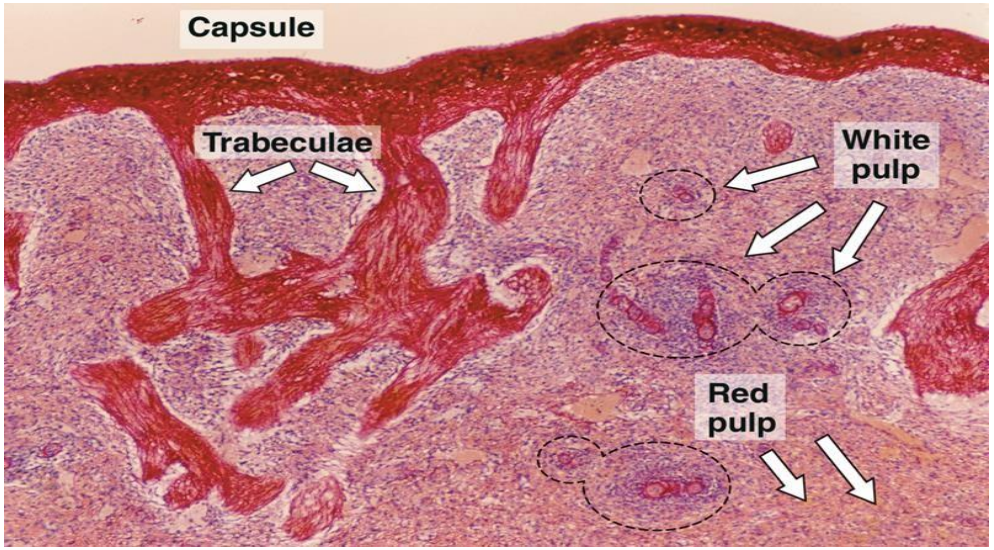
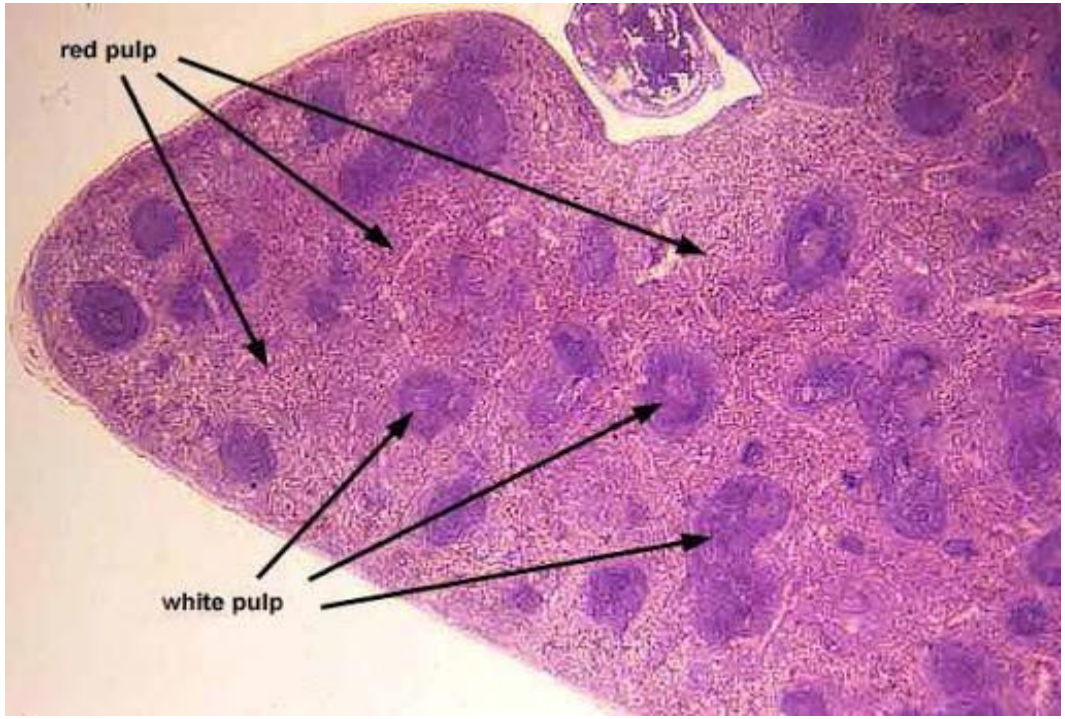
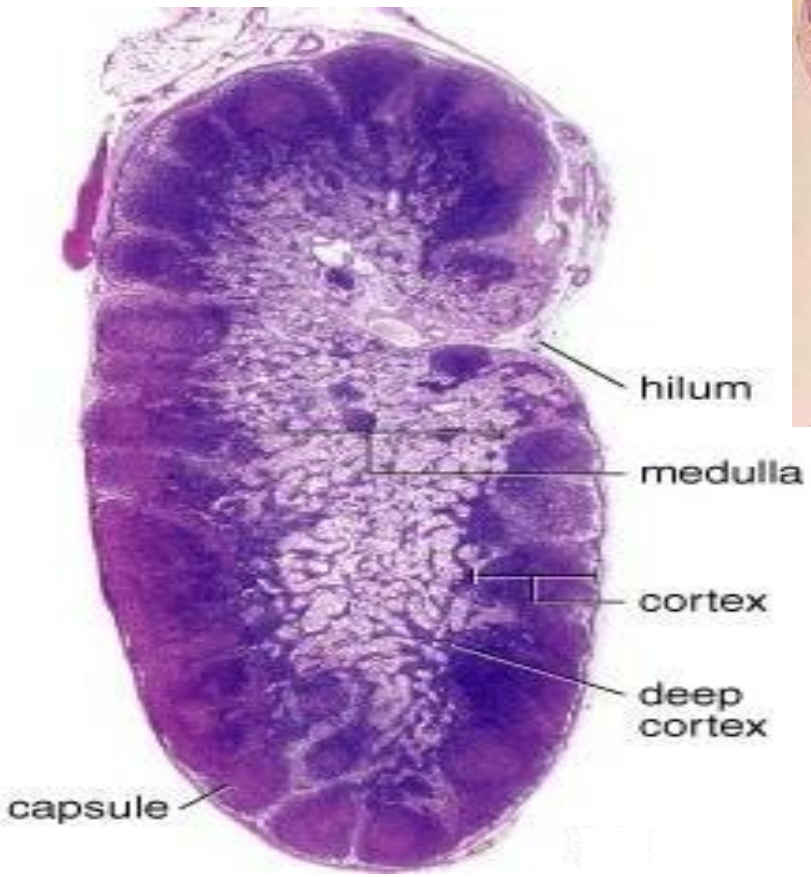


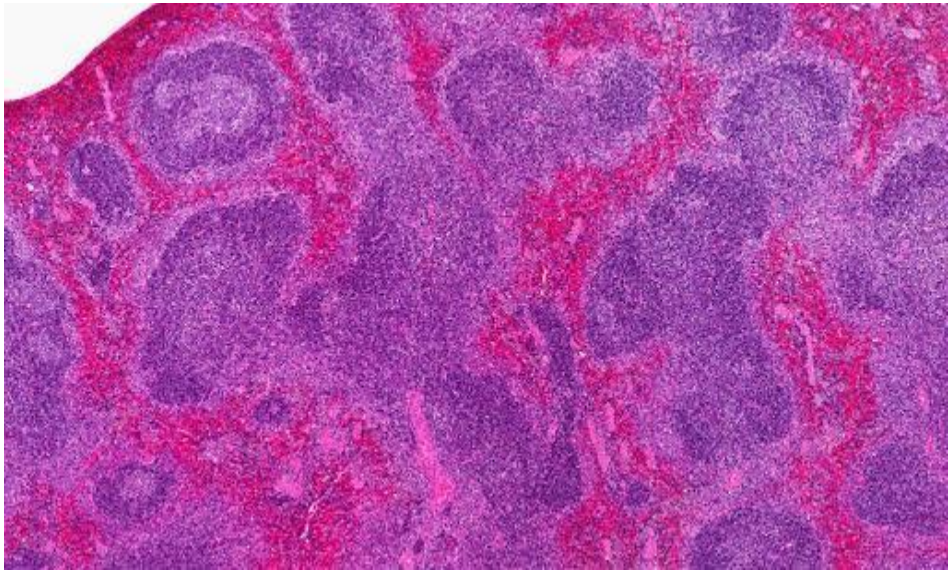
Fig. 8-1 Lymph Node (panoramic view). Stain: hematoxylin-eosin. Low magnification.



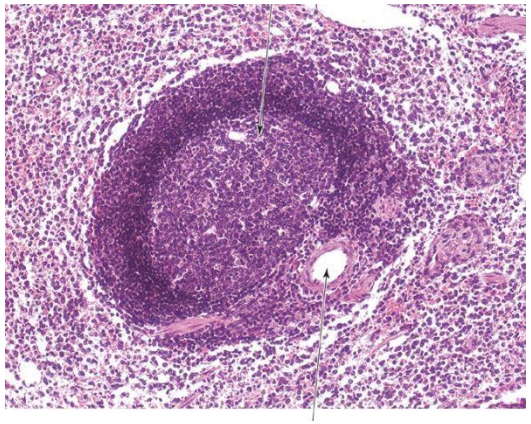
Spleen


red pulp
white pulp


hilum
medulla
cortex
deep cortex
capsule

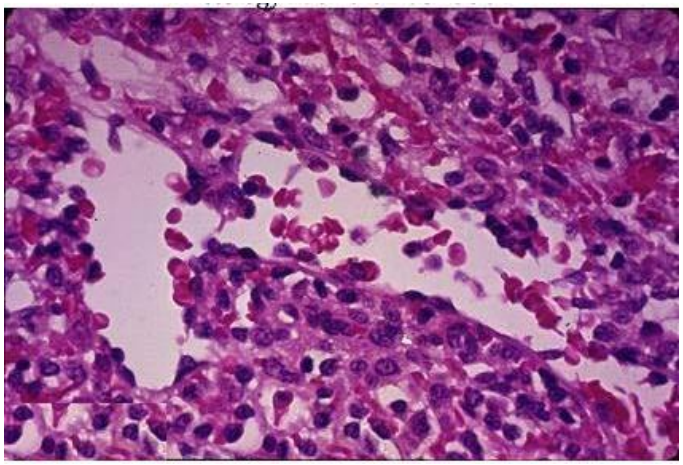


LN



Parenchyma

NO Cortex &Medulla



-1White pulp:

White pulp = lymphatic nodules)splenic Malpighian corpuscles): with pale germinal centers+mantle zone+ peripheral zone.

Central arteries : run at the periphery of the nodules (eccentric central). They are branches of splenic arteries and give numerous capillaries before leaving the white pulp to enter the red pulp.

Central arteries are ensheathed by T lymphocytes **(PALS(**

Thymus dependant zone: is the peri-arterial lymphatic sheath (PALS) of **T lymphocytes**

-2Red pulp:

So-called because of its color during life. Red color is due to abundant erythrocytes in and around blood sinusoids.

Consists of:

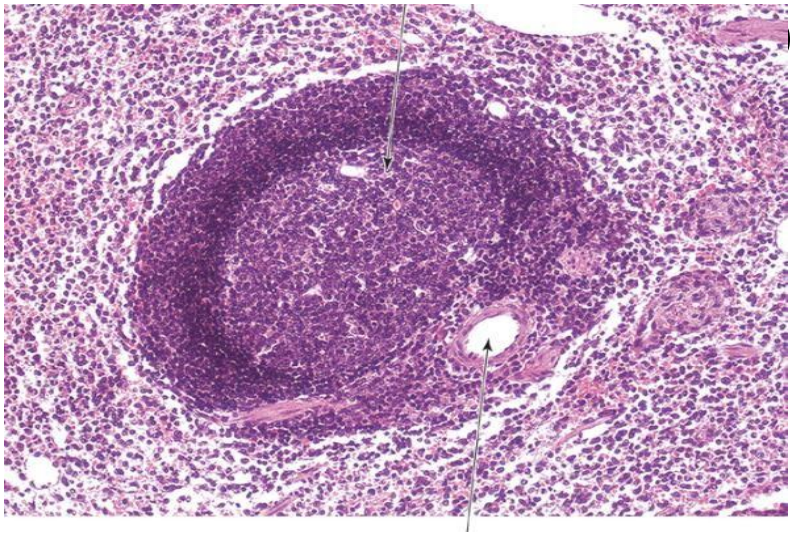
1 **Blood sinusoids**

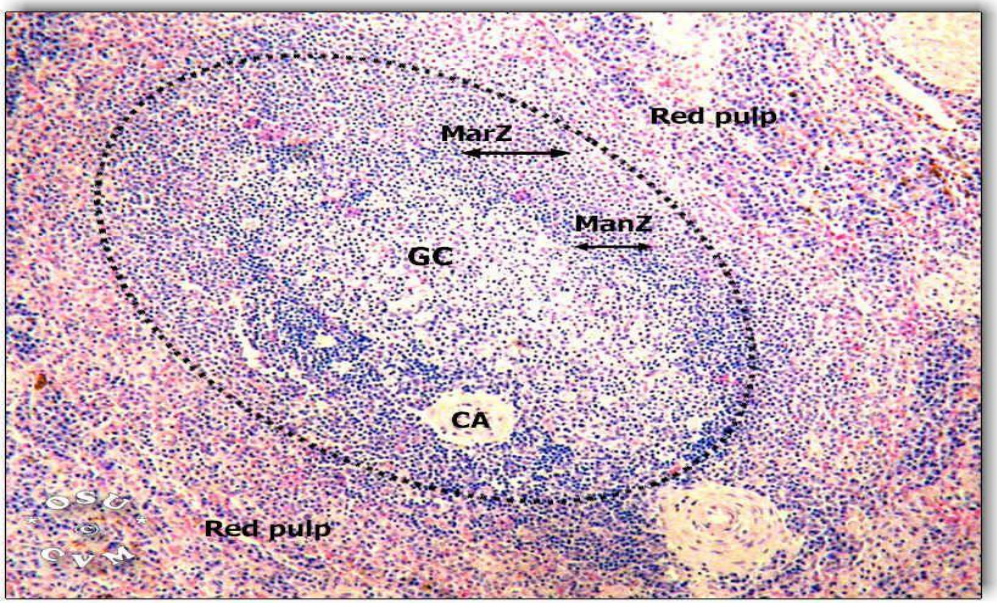
2 **Lymphatic tissue (Billroth cords):** Lymphatic tissue of the red pulp is not as compact as that of the white pulp.

- **+Marginal zone**

white pulp of spleen:

- **Periarteriolar lymphoid sheaths (PALS): mainly T** lymphocytes encircle the arteriole **)Thymus dependent zone of spleen(**
- **Germinal center** : lightly stained, contain B cells, activated B cells, plasma cells & macrophages are (located between PALS and marginal zone(
- **Manttle zone**: Dark stained, around germinal zone , mainly B cells
- **Marginal zone** at the peripl





Red pulp

)So-called due to its red color during life (↑ RBCs(

RBCs, platelets, WBCs, macrophages, B-lymphocytes, plasma cells،

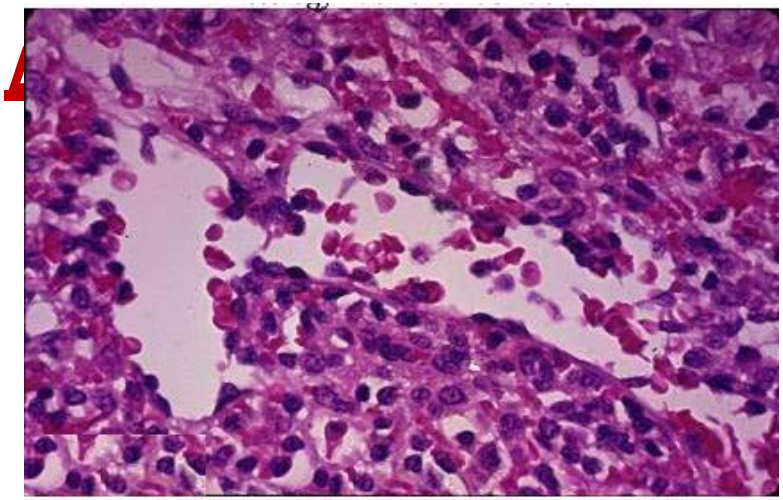
-1splenic cords (Billroth cords:(

- **Fibrils of loose CT within** blood sinusoids infiltrated with blood cells & plasma cells , macrophages

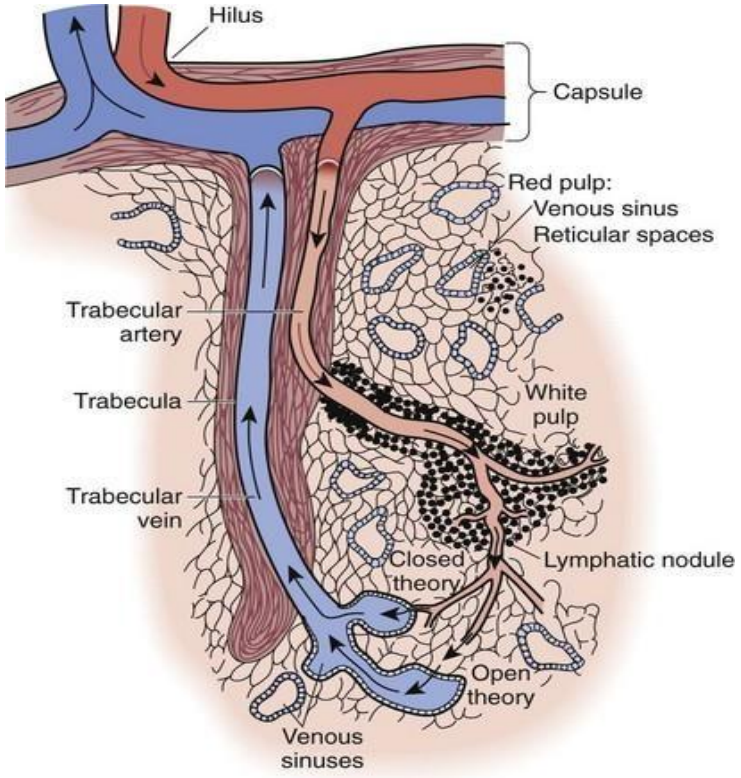
-2Blood sinusoids (venous sinuses:(

- wide spaces lined e fenestrated endothelium to allow passage of cells to the blood.

)Macrophages of spleen called A

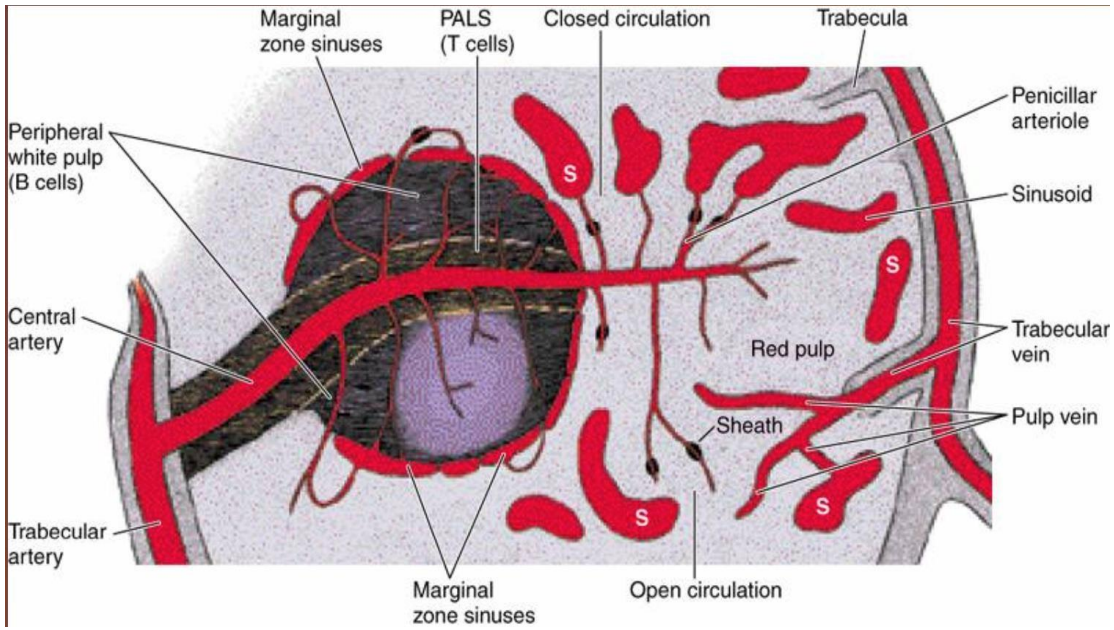


-1Open pattern.
2-Closed pattern.
-3Open and closed



Theories of splenic circulation:

1 Splenic artery.
2 Trabecular artery.
3 Central artery in white pulp.
4 Penicillar arterioles in red pulp
5 Sheathed capillaries surrounded by reticular cells and macrophages
6-Sinusoids (sinuses) of red pulp
7-Trabecular vein.
-8Splenic vein.



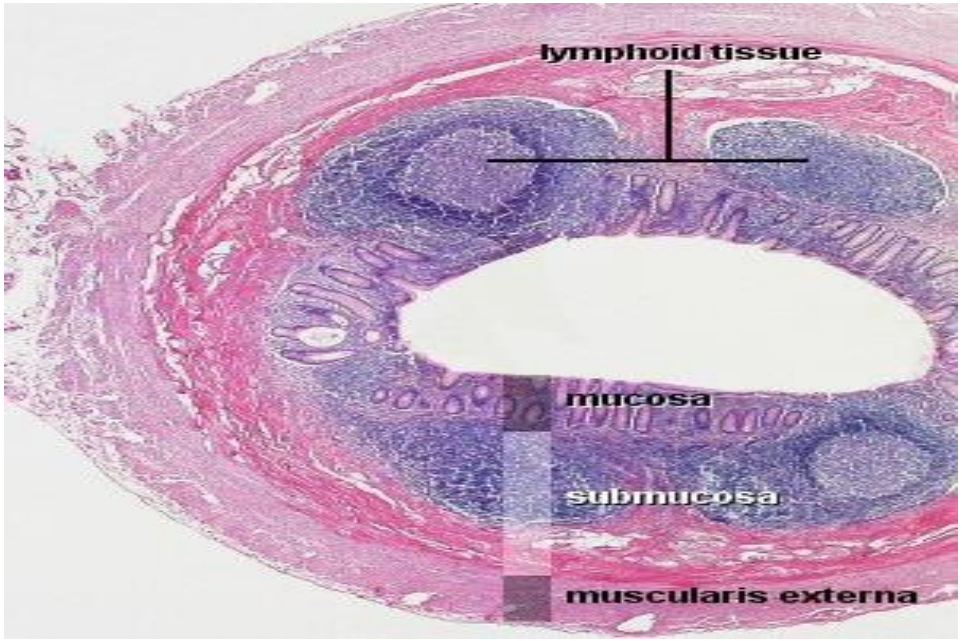
	LN	Spleen
Peritoneal covering	Absent	Present
Capsule	Capsule of collagen + elastic F	Capsule of collagen + elastic F +smooth M
Trabeculae	Thin regular from the cortex **not** contain smooth M	Thick irregular from the hilum contain smooth M
Parenchyma	Cortex + Medulla	White and red pulp
Dense lymphoid T	Cortical nodules + Medullary cords + thymus dependent area in deep cortex	Scattered white pulp with central artery +thymus dependent area in periarterial sheath
Loose lymphoid T	Scattered lymphocytes +plasma cells + macrophages + **Lymph sinuses**	Scattered lymphocytes + plasma cells + macrophages + + granulocytes + **Blood sinuses**
Function	❑ Filteration of lymph ❑ Immunological response	❑ Filteration of blood ❑ Immunological response

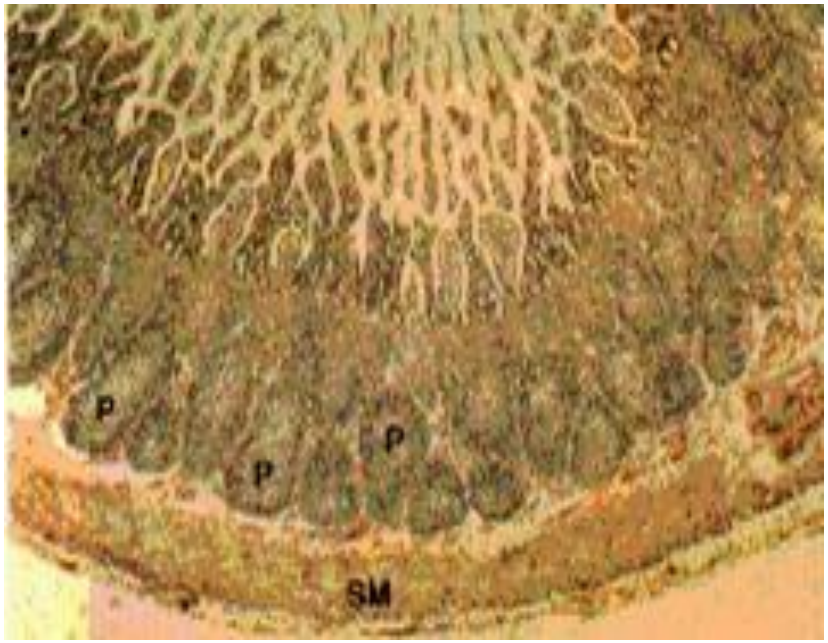
Aggregates of Lymphoid Follicles (MALT(

*Many bacteria permanently inhabit the digestive and respiratory tracts.

*To fight these invaders, MALT is especially abundant under the mucosa.

*Examples are: **Peyer's patches** of ileum and MALT of **appendix**.





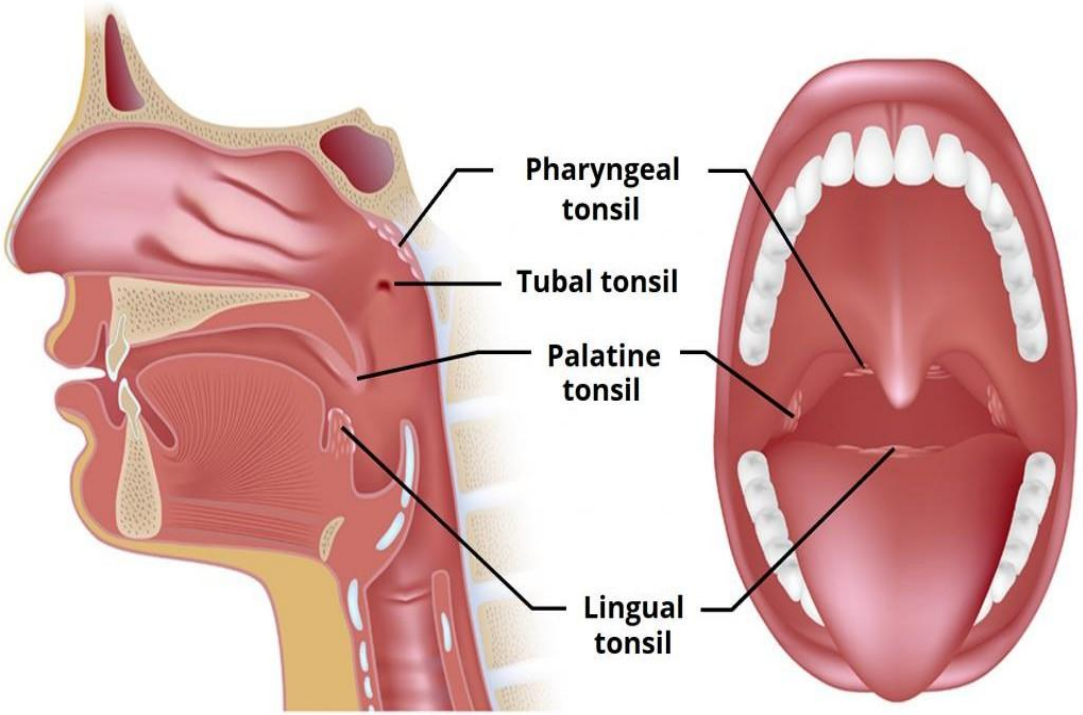
Tonsils

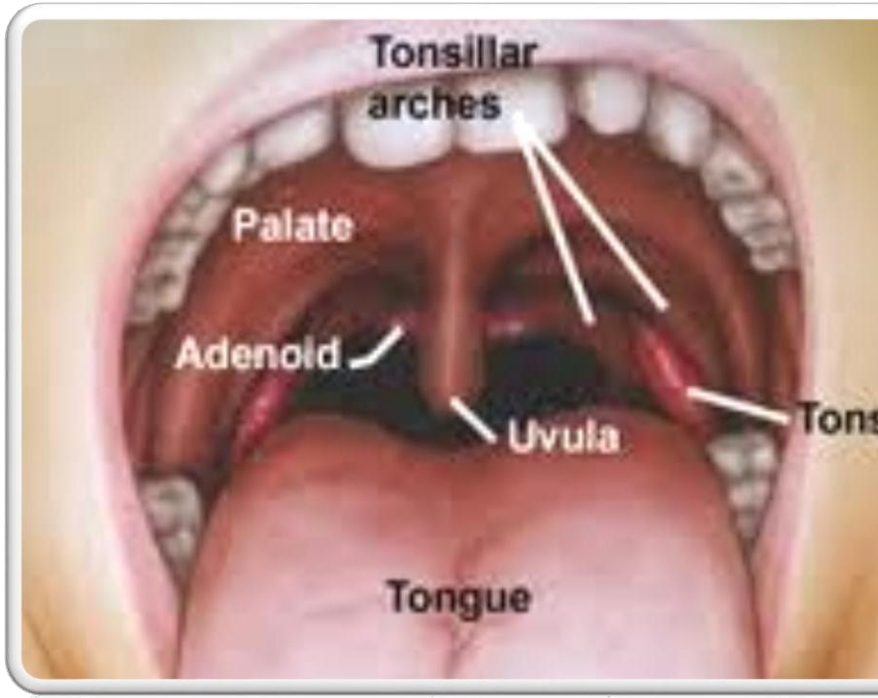
Partially encapsulated lymphoid tissue.

3types

- **Palatine**
- **pharyngeal**
- **lingual**

- Under the epithelium of initial portion of digestive system.
- Their function is to generate immune responses against foreign antigens that may enter the oral cavity





Palatine Tonsil

.1 Stroma

Incomplete Capsule

- **Anterior medial**

Epithelium of the oral cavity musosa (1ry crypt, 2ry crypt(

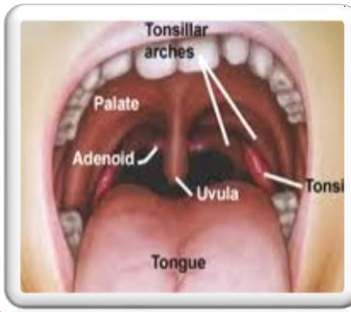
- **Posterior lateral**

C.T. capsule + palatine gland

-2Parenchyma:

1. Lymphoid follicles
2. Diffuse lymphoid tissue

Palatine Tonsil



Stroma

- The two palatine tonsils are located in the lateral walls of the oral part of the pharynx.
- **Each tonsil is characterized by:**

Incomplete capsule:

- **anterior and medial surfaces: covered by non ker str sq ep.**
- **Dips inside the parenchyma forming 1ry& 2ry crypts (15-.(20**
- **In the lumen of the crypt: desquamated epithelial cells, live and dead lymphocytes and bacteria.**
- **Posterior lateral : C.T. capsule**

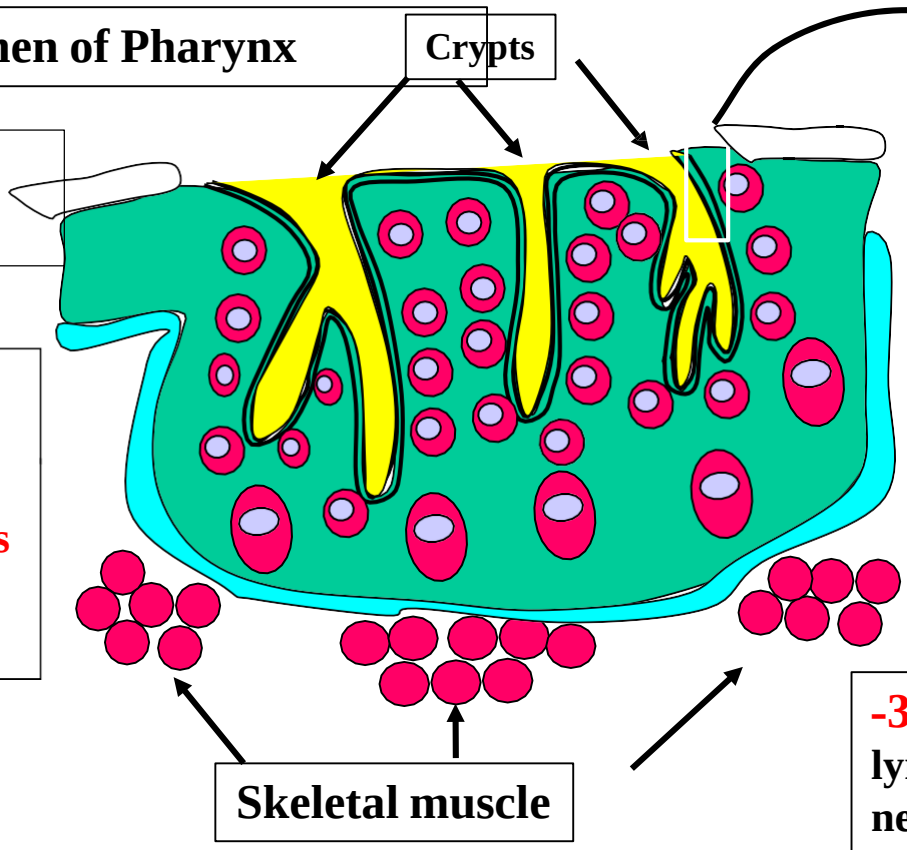
+palatine gland mucus secreting gland (palatine gland(

Parenchyma

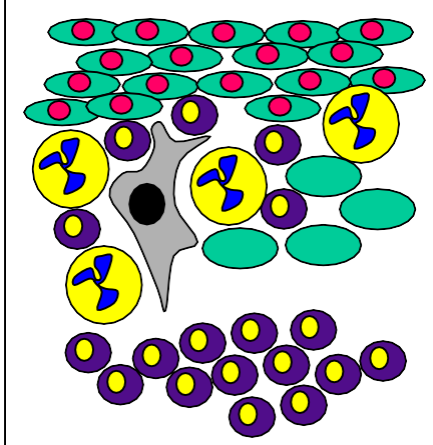
- **Lymphatic nodules:** present under epithelium and around the crypts.
- The **loose lymphoid** tissue consists of loosely arranged lymphocytes, plasma cells, leukocytes and macrophages.
- Present in between the lymphatic nodules.
- **No lymph sinuses** are present.

Palatine tonsils

Site: lateral wall of oropharynx



1- Epithelium at medial and anterior surfaces



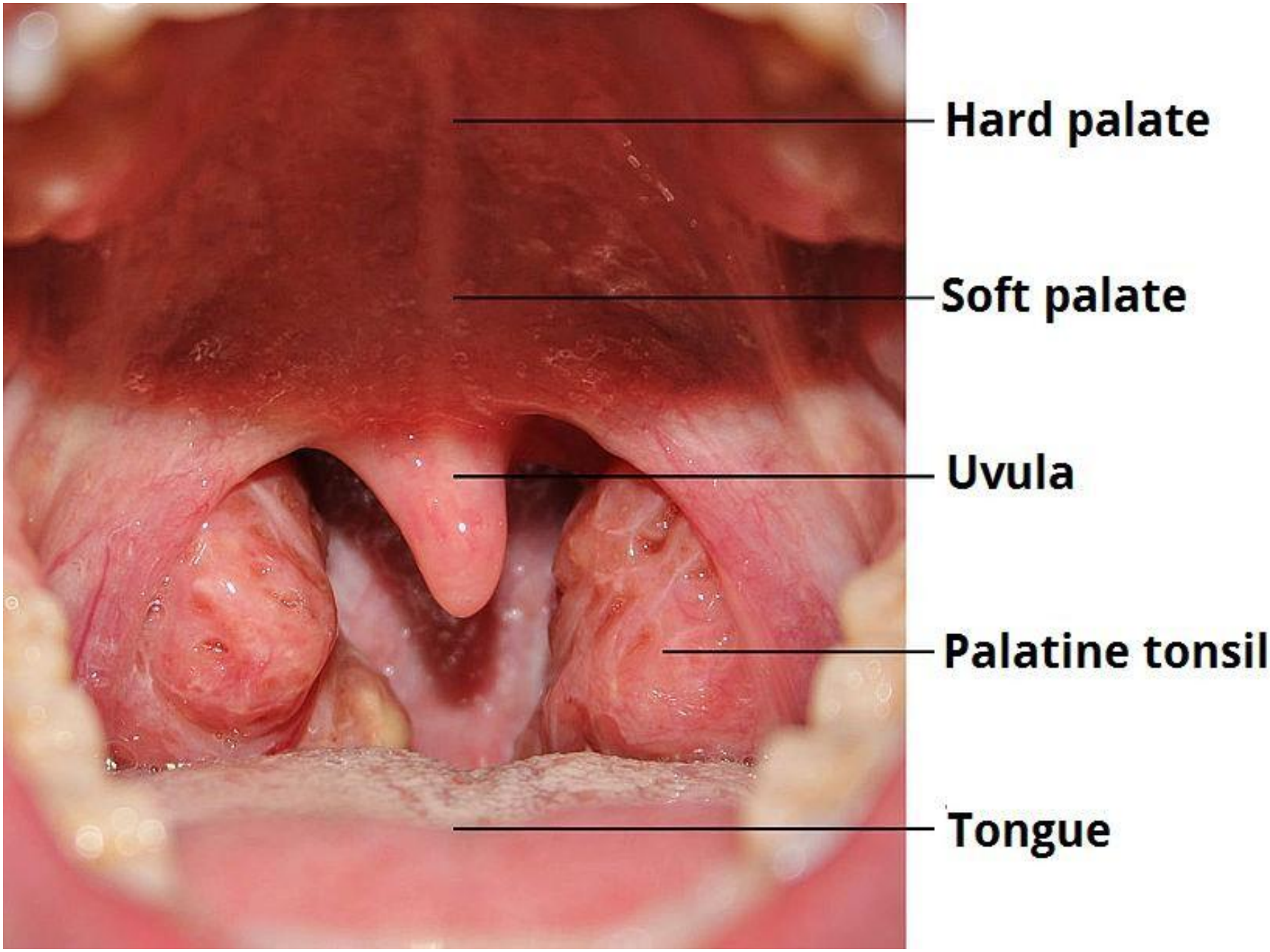
-2Lymphatic nodule

-4Capsule at the lateral and posterior surfaces

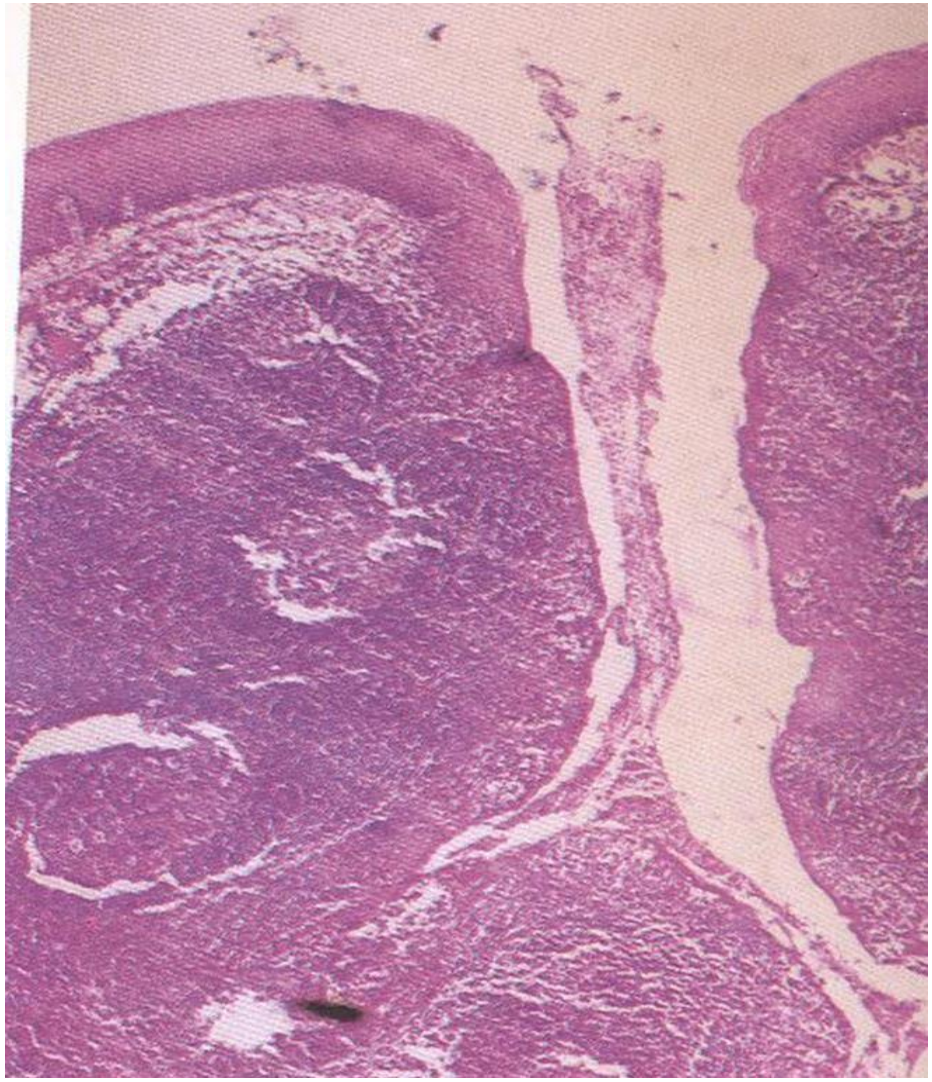
5- Contain mucous acini that do not open in the crypt

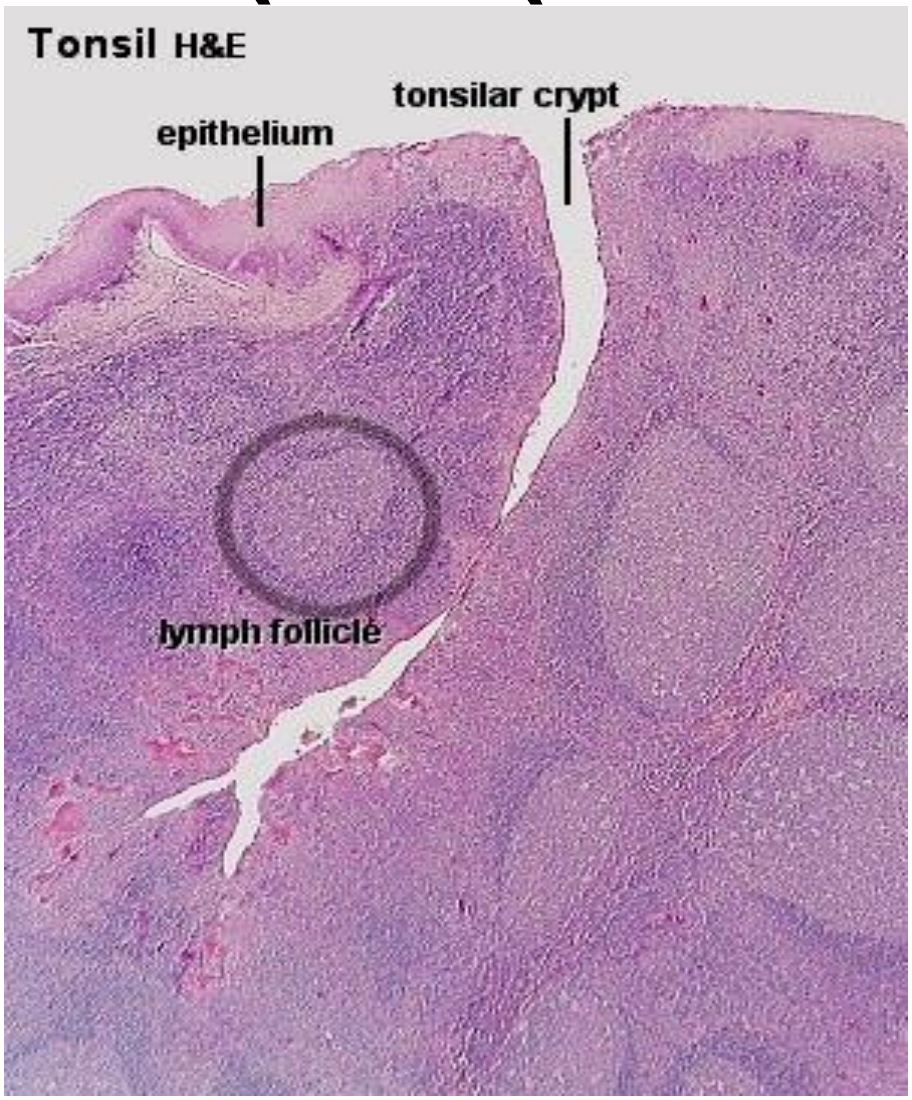
-3Diffuse infiltration of lymphocytes, plasma cell, neutrophils
APC, etc.

Capsule: Act as barrier against spread of infection Separate tonsil from surrounding tissue


Hard palate
Soft palate
Uvula
Palatine tonsil
Tongue

Palatine Tonsil (H&E(





Pharyngeal tonsil

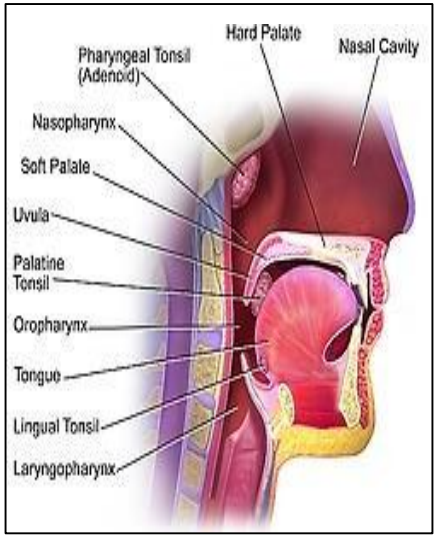
- **Single lymphoid mass**

Site: Under mucous membrane of nasopharynx pseudostratified ciliated columnar epithelium

- **No crypts but folds**
- **contain diffuse lymphoid tissue**

•Atrophy after 4 years old

Hypertrophy ------- Adenoid



Lingual tonsil

The posterior 1/3 human tongue

Covered e non keratinized stratified squamous epithelium.

contains lymphoid nodules + diffuse lymphocytes.