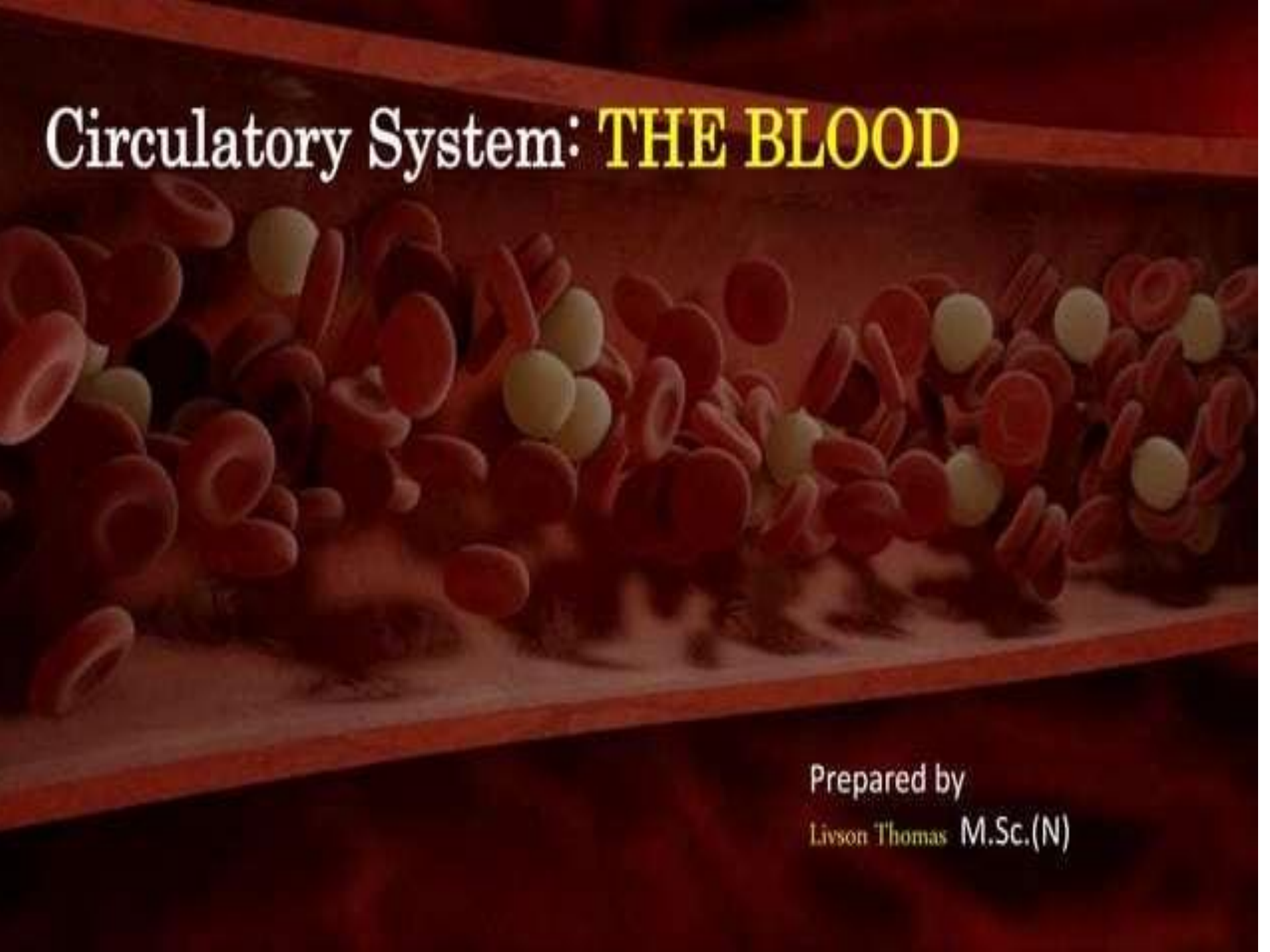
# Circulatory System: THE BLOOD



Prepared by

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# THE BLOOD

- Blood is a fluid connective tissue.

The **main** function:

- Blood is the fluid that transports oxygen and nutrients to the cells and carries away carbon dioxide and other waste products.

# Characteristics

- Viscous (thicker) and sticky
- Temperature: 100.4°F (38°C)
- pH: **7.35-7.45** (Slightly alkaline)
- Colour: Varies with oxygen content
  - With $O_2$ **bright red**
  - Less $O_2$ **dark red**
- Volume:

  Adult male: **5-6 L**

# Functions of Blood

## 1. Transportation:


Lungs --> **$O_2$** --> Body cells

Body cells --> **$CO_2$** --> Lungs

GI Tract --> **Nutrients** --> Body cells

Endocrine glands --> **Hormones** --> Body cells

Blood also transports heat and gathers waste products from various organs for elimination from the body

## 2. Regulation:

- Circulating blood helps maintain homeostasis of all body fluids
- Blood helps in maintaining the pH
- Blood helps in adjusting the body temperatures like water.
- Blood osmotic pressure influences water contents of cells and

# 3. Protection

- Blood clotting protects from excessive bleeding.
- WBCs protects against infection
- Blood proteins, including antibodies, interferons and complement help protect from diseases

# Blood plasma : A straw coloured fluid

Blood plasma is made up of:

**Proteins (7%)**

- Albumin (54%)
- Globulins (38%)
- Fibrinogen (7%)
- Other proteins (1%)

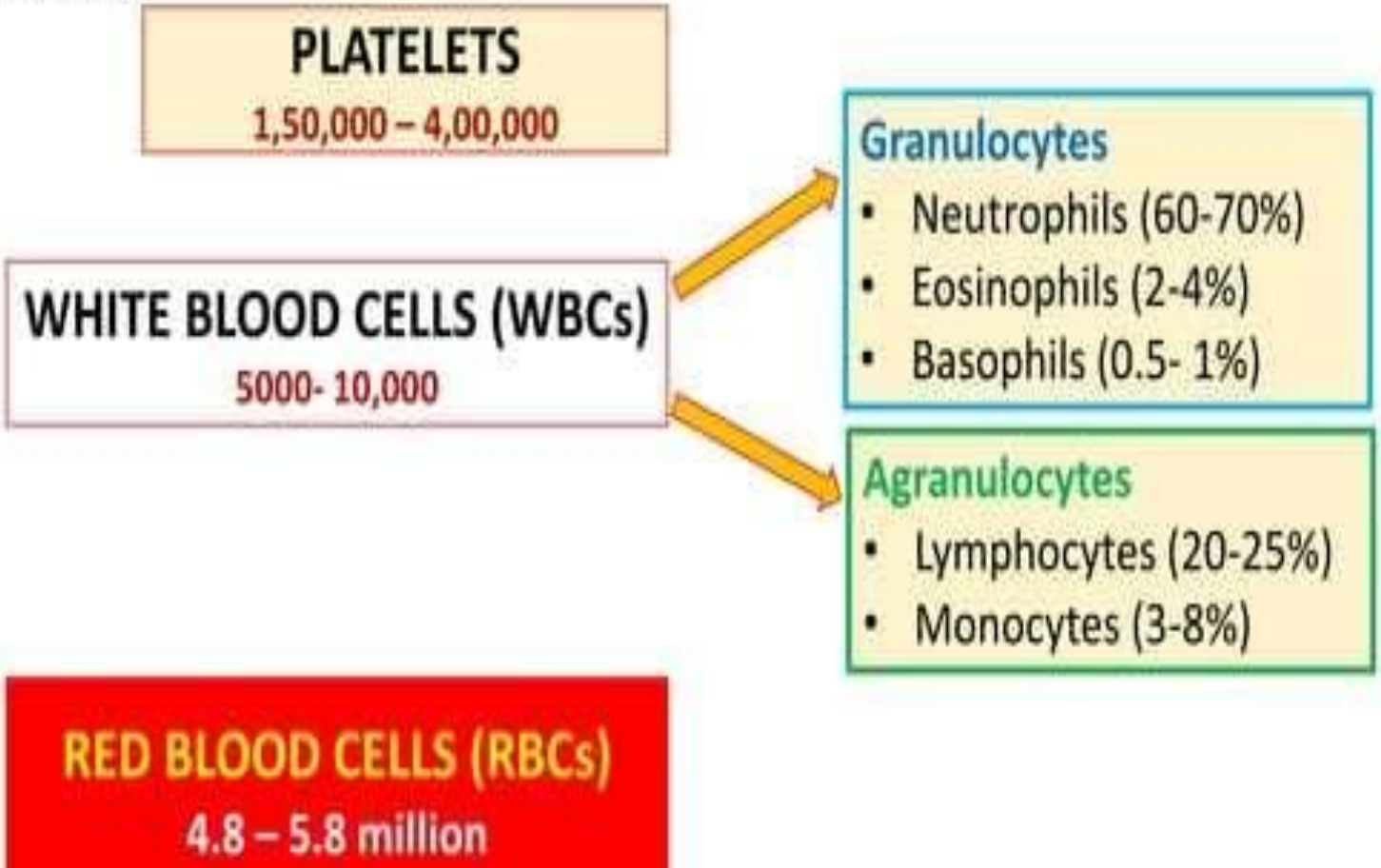
**Water (91.5%)**

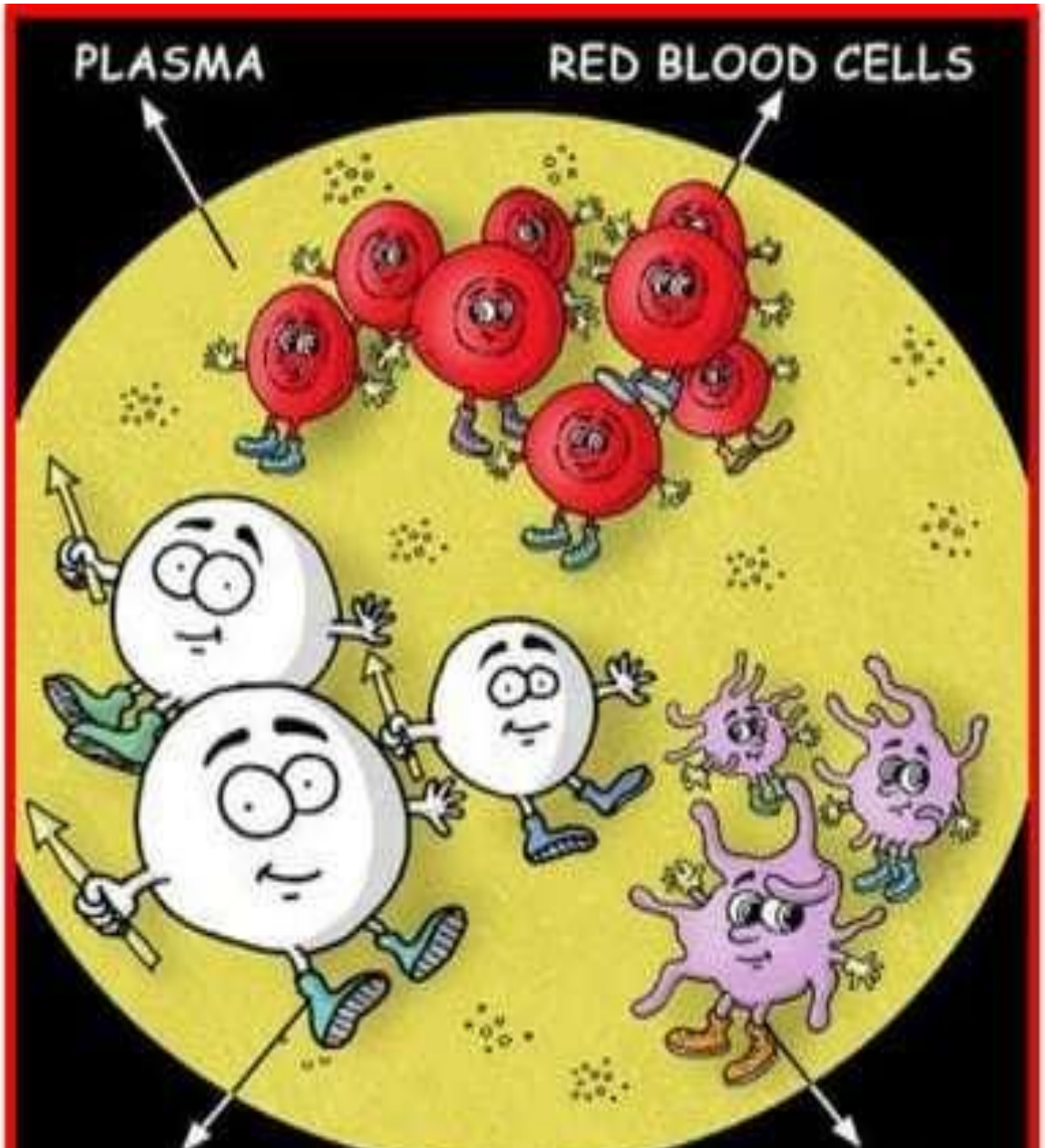
**Other Solute (1.5%)**

- Electrolytes
- Nutrients
- Gases
- Regulatory substances

# Formed Elements

- It consists of:



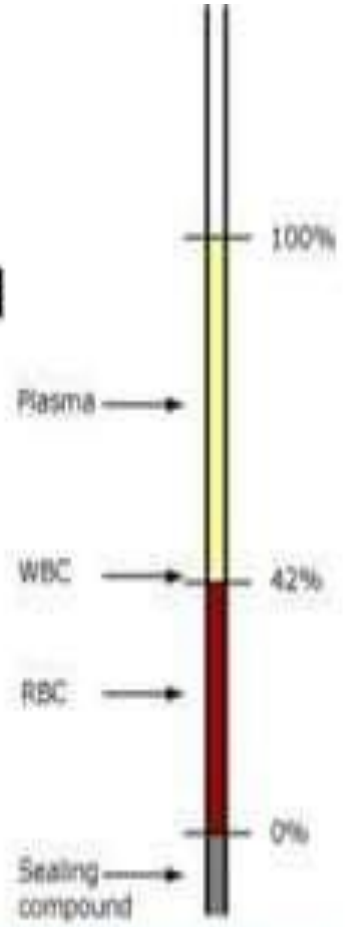

PLASMA
RED BLOOD CELLS

# Hematocrit

- The percentage of total blood volume occupied by RBCs is called the hematocrit.

- If hematocrit is 40, it indicates 40% of the volume of blood is composed of RBCs.

- Normal range
  - Adult Female: **38-46%**
  - Adult Male: **40 – 54%**




# Formation of Blood Cells

- The process by which the formed elements of blood develop is called **hemopoiesis** or **haematopoiesis**

**Kindly click on the link for the video about hemopoiesis:**

https://www.youtube.com/watch?v=cm8IK24RRvA

https://www.youtube.com/watch?v=uXolwWiaFpM

# RED BLOOD CELLS *(Erythrocytes)*

- These blood cells contain the oxygen carrying protein **hemoglobin**, which is a pigment that gives whole blood its red color.

- Shape: **Biconcave discs**
- Diameter: **7-8 µm**
- RBCs have **NO NUCLEUS**
- The cytosol of RBCs contains hemoglobin molecules

# RBC Physiology

- Highly specialized for their oxygen transport function.
- Due to no nucleus, lot of internal space is available for oxygen transportation.
- RBCs don't have mitochondria and generate ATP anaerobically (without oxygen)
- The biconcave disc shape also increases the surface area for diffusion of gas molecules into and out of RBC
- Each RBC contains about 280 million hemoglobin molecules

# Hemoglobin (Hb)

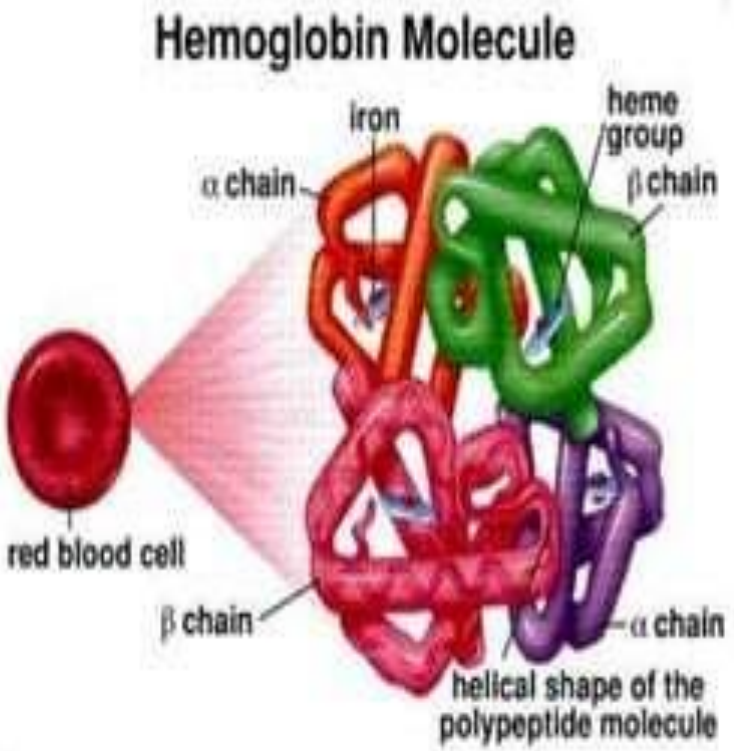
It is the iron containing protein in the blood.

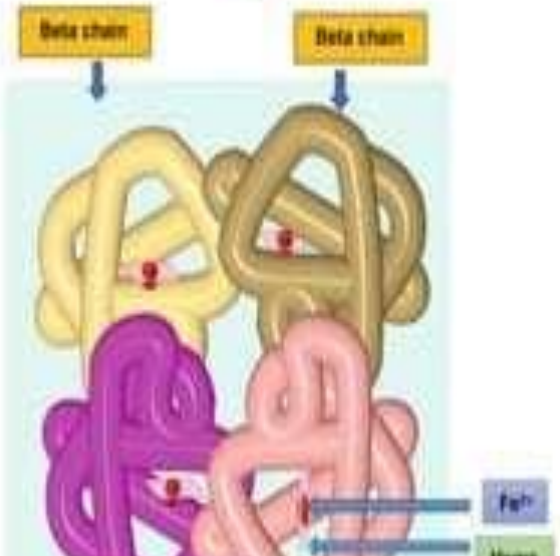
**Normal Hb value:** 13 to 17gm/dl (male)

12 to 15 gm/dl (Female)

**Structure:**

- Hb molecule consist of a protein called **globin**.
- Hb has **four polypeptide chains** ( 2 alpha and 2 beta chain)
- The four chains are bound by non-protein pigment called **heme.**
- Each heme ring has an **iron ion** ($Fe^{2+}$)






RED BLOOD CELL (Erythrocyte)

Hemoglobin (Protein)

Four Polypeptide Chain

- 2 Alpha Chain
- 2 Beta Chain

Four Heme pigment

**Structure of RBC**

- Heme – Oxygen molecule bond is reversible
- As blood flows through tissue capillaries Iron- Oxygen reaction reverses
- Oxygen is released first into interstitial space and then cells.
- Hemoglobin also transports 23% of the total carbon dioxide from metabolism.

Blood flowing through tissue capillaries pick up carbon dioxide, some of which combines with amino acid in the globin chain.

As blood flows through lungs the carbon dioxide is released from hemoglobin and

- Hemoglobin also plays a role in the regulation of blood flow and blood pressure.

Gaseous hormone **Nitric Oxide (NO)** produced by endothelial cells that line blood vessels binds to hemoglobin.

Under some circumstances **Hb** releases the **NO**, which causes ***vasodilation***, which is an increase in blood vessel diameter that occurs when the smooth muscles in the vessel walls relaxes.

Vasodilation improves blood flow and enhances oxygen delivery to cells near the site of Nitric Oxide release

- RBCs also contain the enzyme **Carbonic Anhydrase (CA),** which catalyses the conversion of carbon dioxide and water to carbonic acid, which in turns dissociates into $H^+$ and $HCO_3^-$ .

$$CO_2 + H_2O \xleftrightarrow{CA} H_2CO_3 \longleftrightarrow H^+ + HCO_3^-$$

<u>This reaction is important for two reasons:</u>

**1.** It allows about 70% of $CO_2$ to be transported in blood plasma from tissue cells to the lungs in the form of $HCO_3^-$

**2.** It also serves as an important buffer in extracellular fluid.

*(Buffer: It is a solution which resists changes in pH when acid or alkali is added to it)*

# RBC Life Cycle

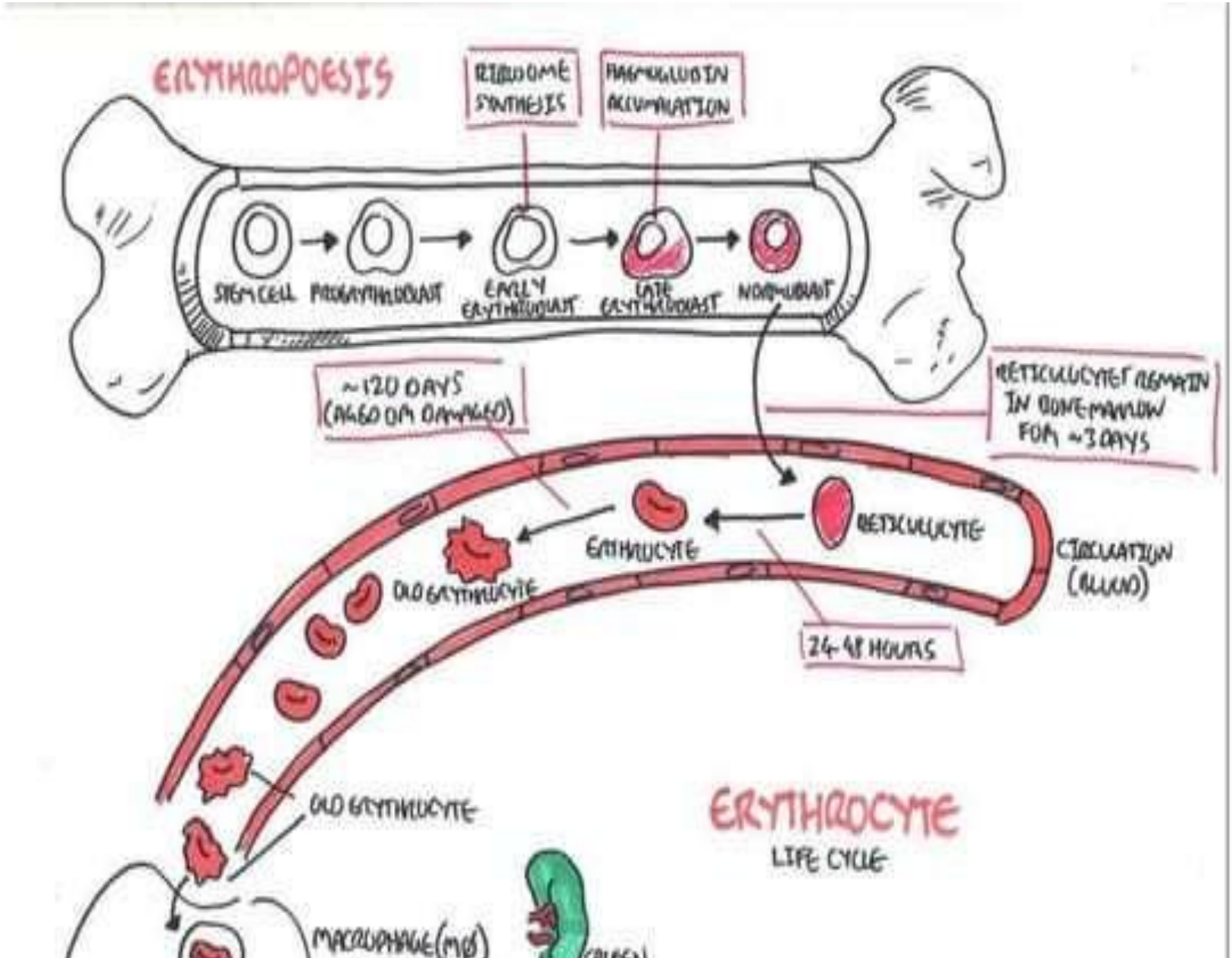
- RBCs live for only about **120 days**, due to the wear and tear they undergo while passing through capillaries.
- Without nucleus and other organelles, RBCs cannot repair themselves.
- Damaged RBCs are removed from circulation and destroyed by fixed phagocytic macrophages in the spleen and liver.
- The breakdown products are recycled and used in various metabolic processes.

# Erythropoiesis and destruction/ recycling of RBCs

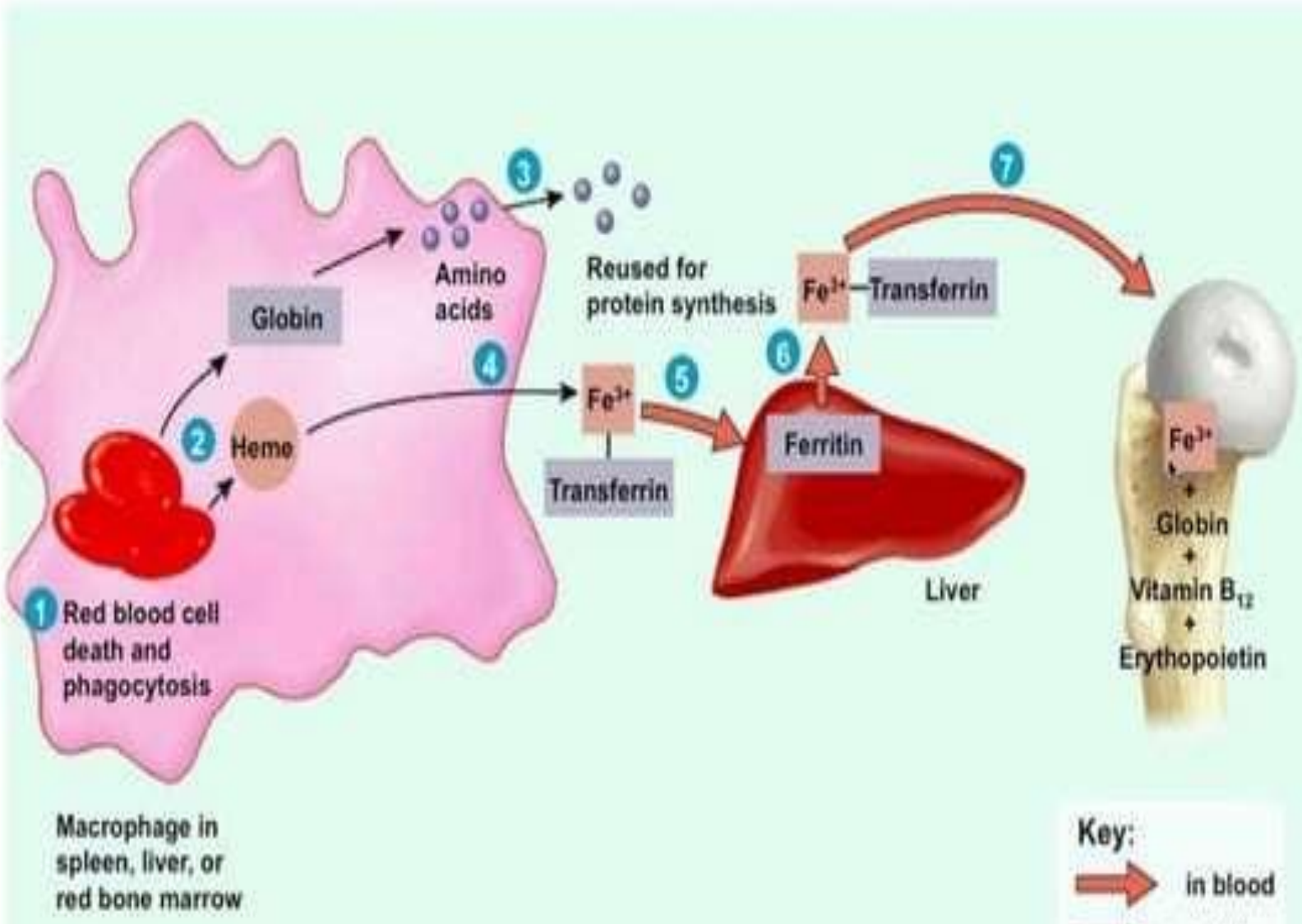
- **Erythropoiesis**: The production or formation of RBCs in the red bone marrow.
- **Erythropoietin**: Hormone that regulate RBCs production
- Removal of damaged RBCs take place in **Spleen, Liver** and **Bone marrow**
- Macrophages are specialized cells involved in phagocytosis of damaged or old RBCs

Click on the link below for explanation:

- https://www.youtube.com/watch?v=cATQFei6oAc


ERYTHROPOESIS
RIBOSOME SYNTHESIS
HAEMOGLOBIN ACCUMULATION
STEM CELL
PROERYTHROBLAST
EARLY ERYTHROBLAST
LATE ERYTHROBLAST
NORMOBLAST
~120 DAYS (AGED OR DAMAGED)
RETICULOCYTES REMAIN IN BONE MARROW FOR ~3 DAYS
ERYTHROCYTE
RETICULOCYTE
CIRCULATION (BLOOD)
OLD ERYTHROCYTE
24-48 HOURS
OLD ERYTHROCYTE
MACROPHAGE (MØ)
ERYTHROCYTE
LIFE CYCLE

# Destruction and Recycling of RBCs



# WHITE BLOOD CELLS

- White blood cells are also called **Leukocytes**

- WBCs have nuclei and a full complement of other organelles but they lack hemoglobin.

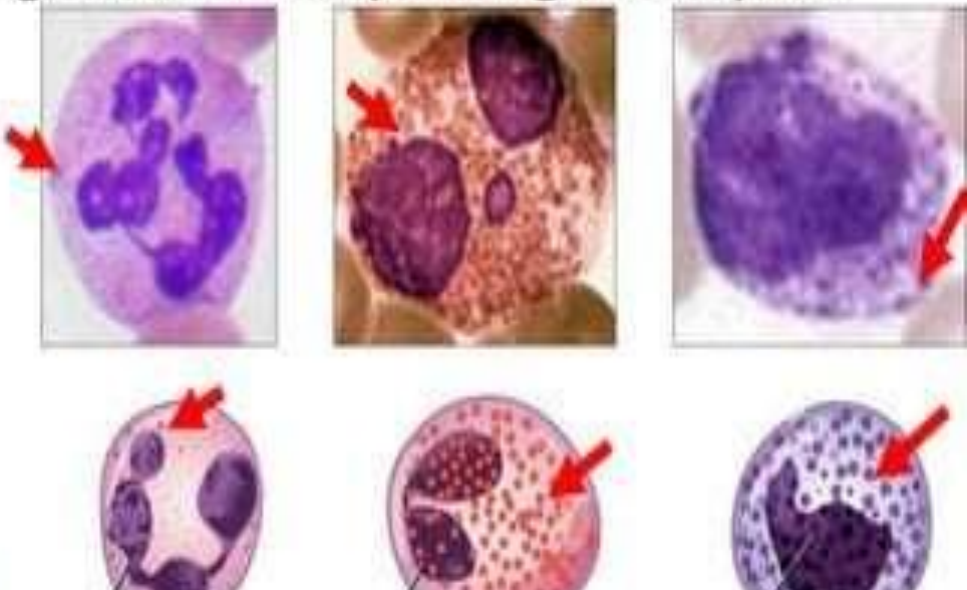
- WBCs are classified into two:
  - i. Granular leukocytes or Granulocytes
  - ii. Agranular leukocytes or Agranulocytes

# Granular Leukocytes

- **Staining** with **Leishman's stain** makes it possible to easily identify different types of leukocytes.

- Leukocytes with clearly visible granules with distinctive colouration that can be recognized under a light microscope are granular leukocytes or granulocytes.

- **Three** type:
  - Neutrophil
  - Eosinophil
  - Basophil

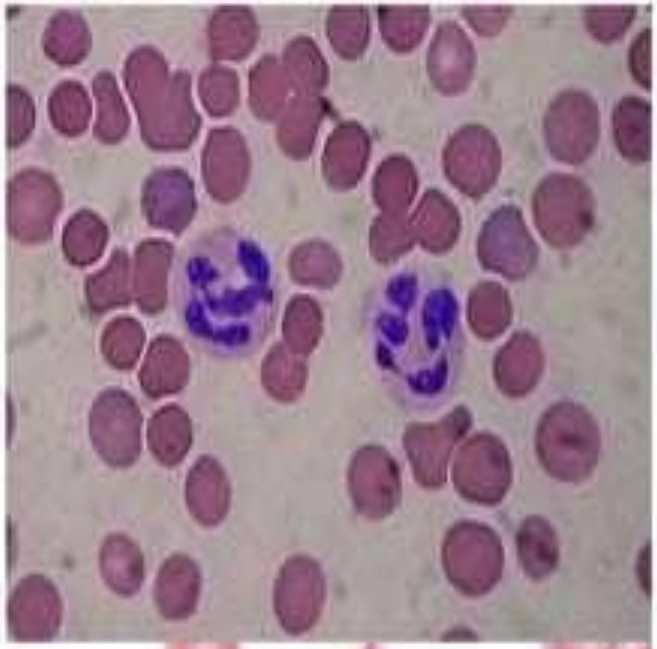


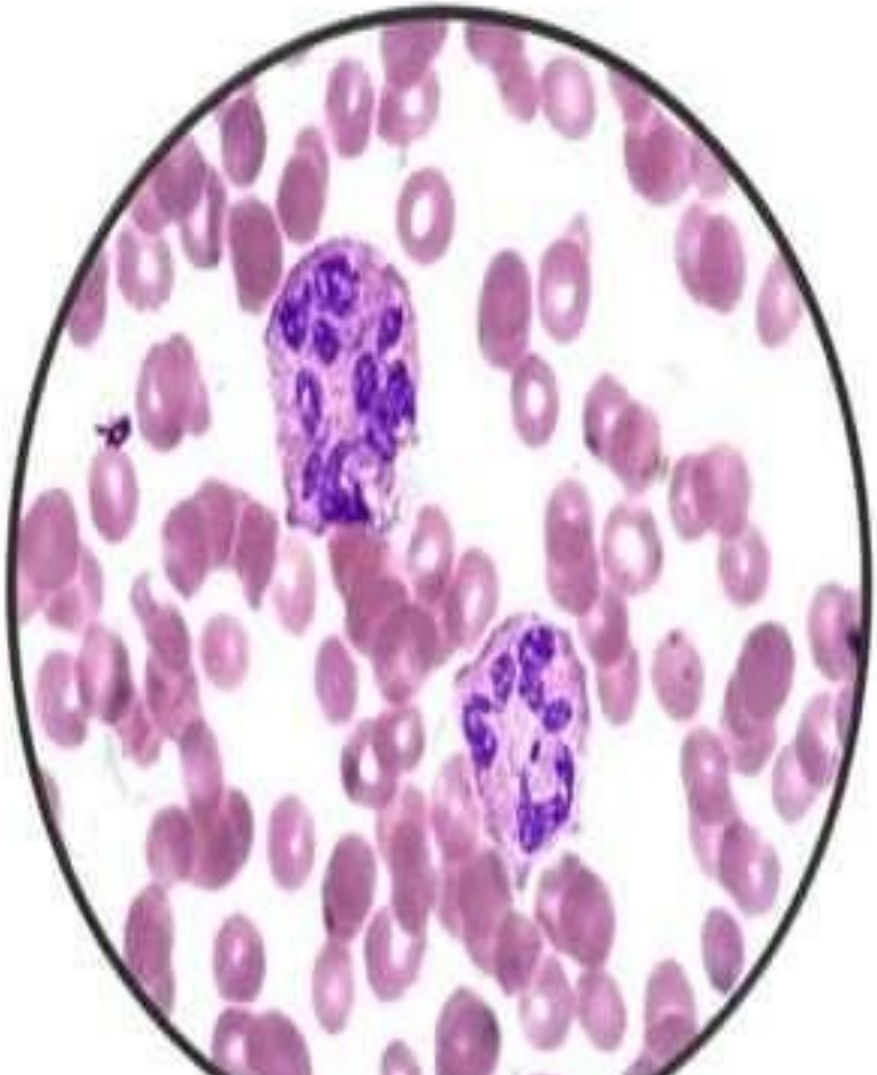
# Neutrophil

- The granules of neutrophil are smaller than those of other granulocytes.
- They are stained pale lilac.
- The nucleus have **2 to 5 lobes** connected by thin strands.
- Granules consist of ***lysosomes*** with enzymes for phagocytosis.
- They are attracted to area with infection by chemicals called ***chemotaxins.***
- Life span: Average **5 days**
- Neutrophils count = **2500-8000 per $mm^3$** (55-70%)

- **Function**: Small, fast and active scavengers
  - Protect the body against bacterial infection.

# Neutrophils under a Microscope





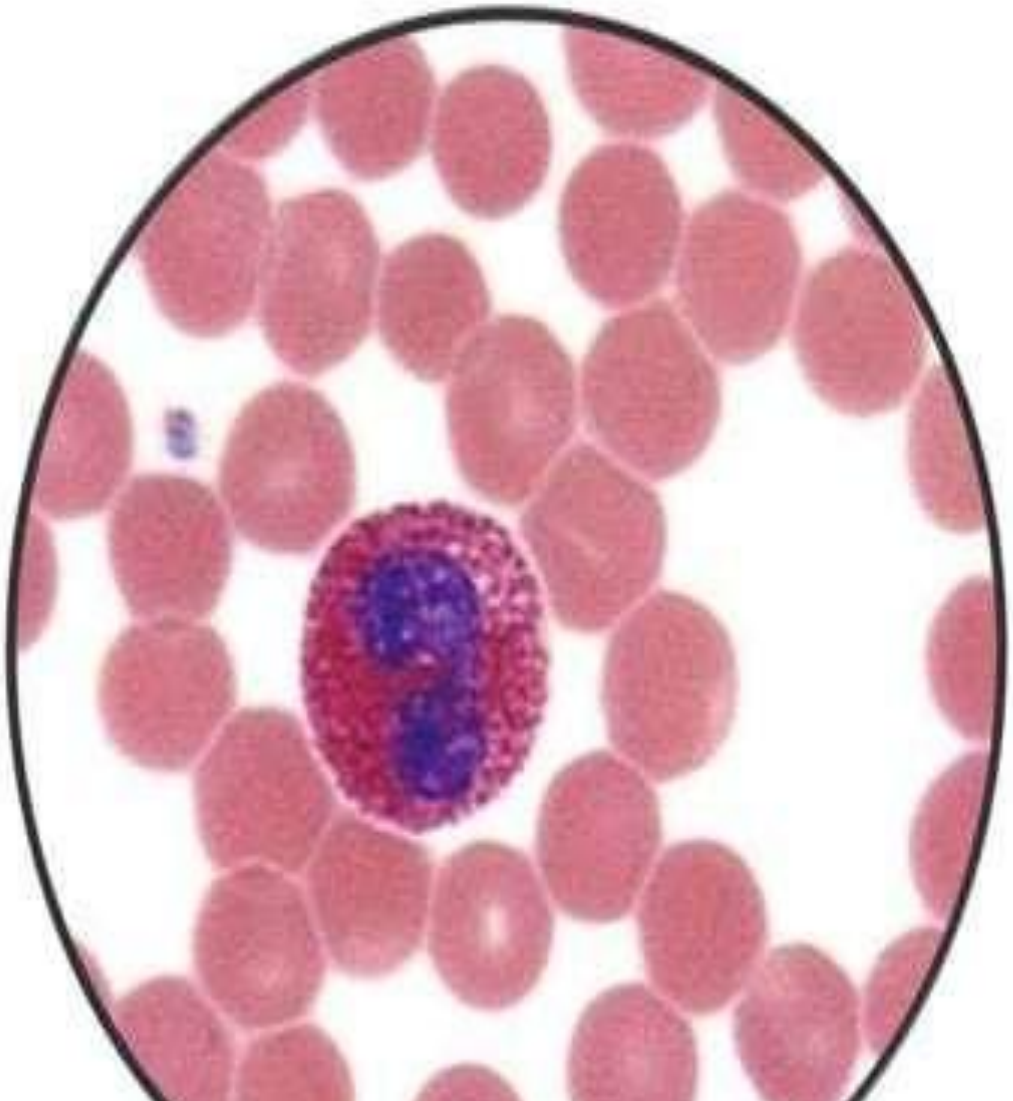
# Eosinophil

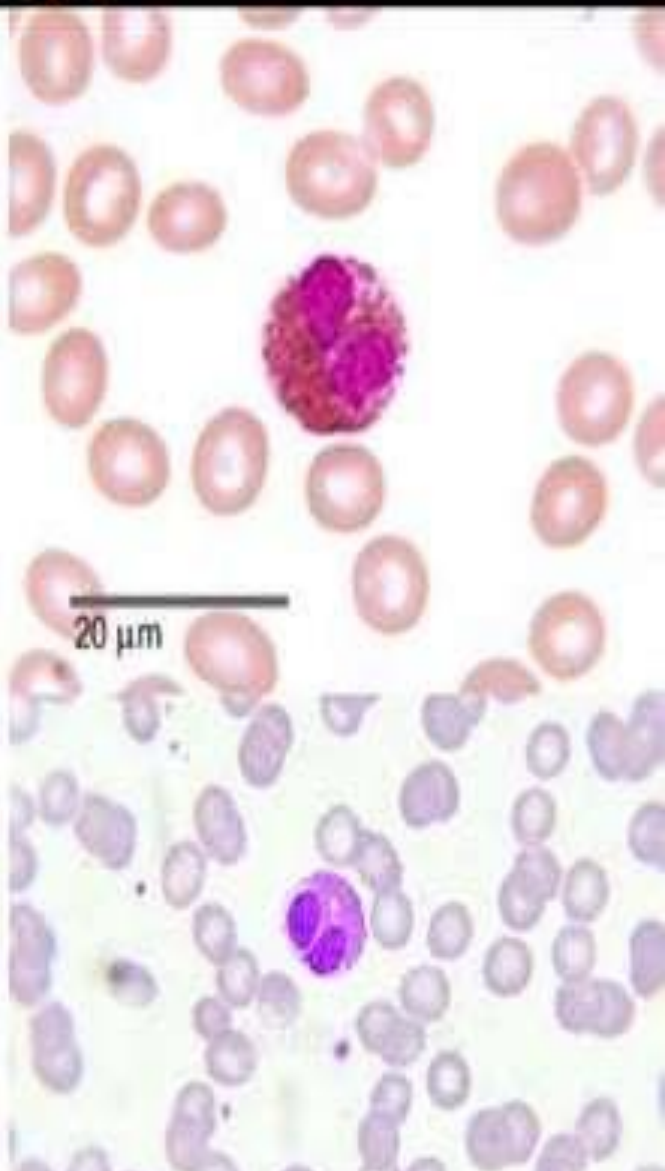
- Consist of large uniform sized granules.
- They stain Red-orange with acidic dyes.
- Nucleus often has **two lobes** connected by thick strands of chromatin.
- Count: **30-500 per $mm^3$** **(2-4%** of total WBCs)

- **Function:**

- Elimination of parasites like worms, using toxic chemicals stored in the granules.
- Accumulation of eosinophil occurs in allergic reactions **(hypersensitivity)**. Eosinophils helps in controlling inflammation. (e.g. Mosquito bite, asthma, skin allergy)

# Eosinophil under a microscope





# Basophil

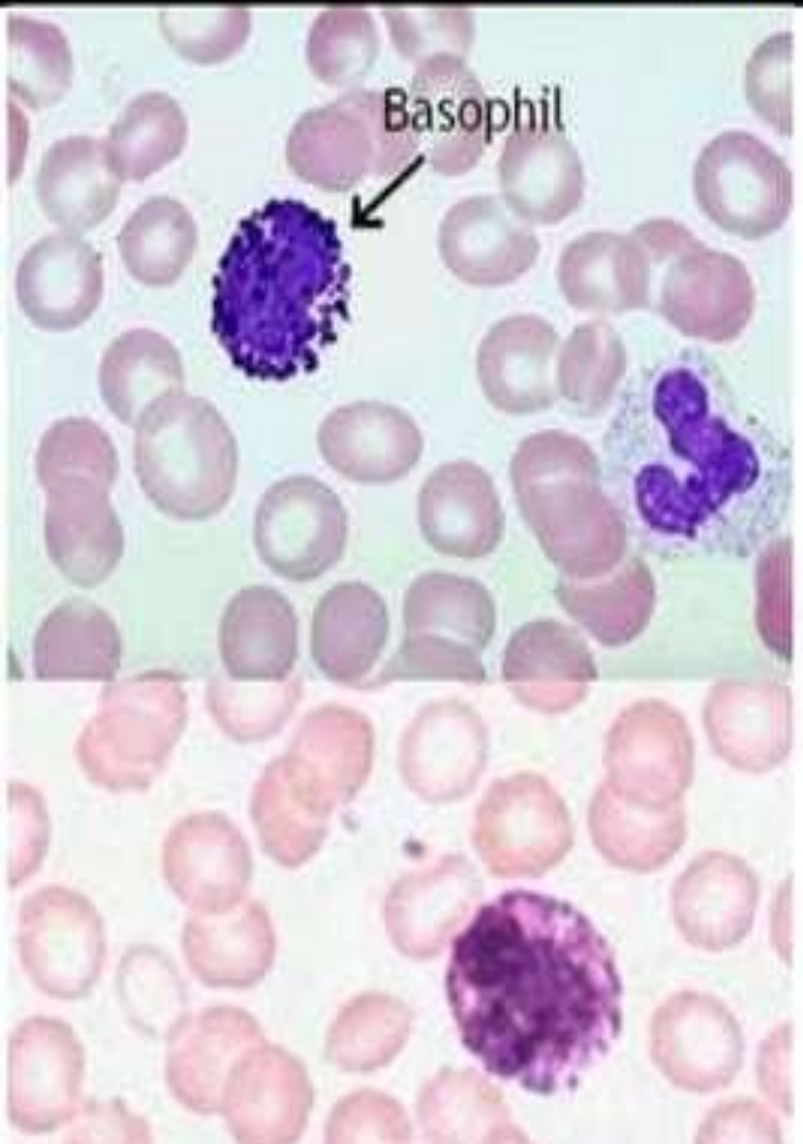
- Granules are round with various sizes.
- They stain **blue-purple** with basic dyes.
- Nucleus has **two lobes**
- Cytoplasmic granules are packed with **heparin, histamine** and other substances that promote inflammation.
- Count: **0.5 - 1%** of total WBCs.

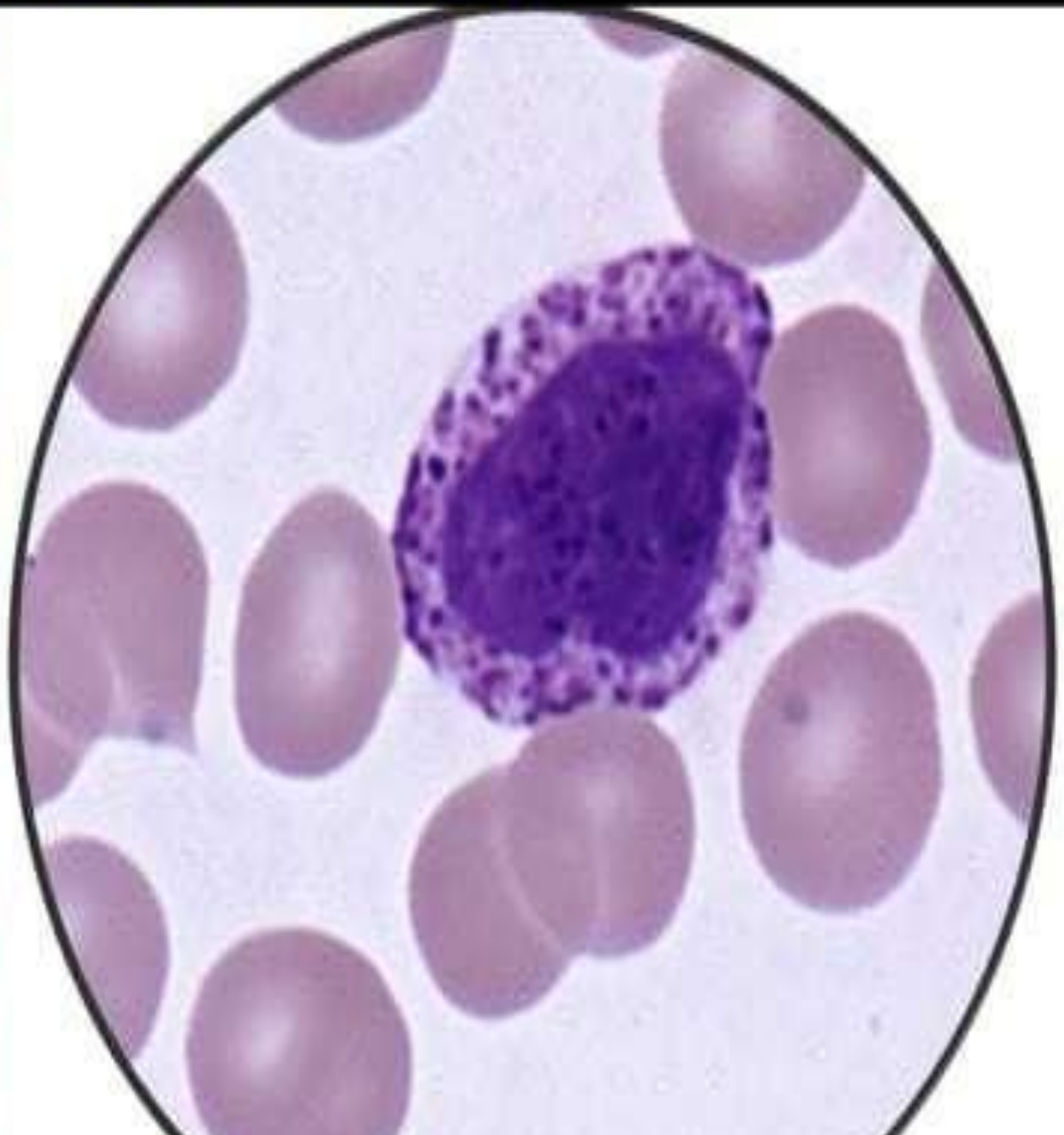
- **Functions**

- Contains the anti-coagulant heparin, which prevents blood from clotting.

- They also contain histamines which are released during an allergic reaction to enable inflammation

# Basophil under a microscope



# Agranular Leukocytes

- Even though they are called agranular, they have some amount of granules that are not visible under a microscope.
- 20-50% of WBCs are agranulocytes.
- They are of t

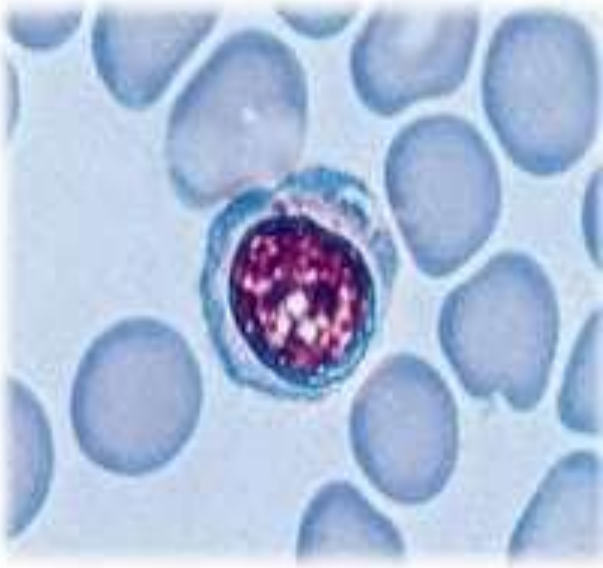
Lymphocyte

Monocyte

# Lymphocyte *(T-Cell, B-Cell, Natural Killer cell)*

- The nucleus stains dark and is round or slightly divided.
- The cytoplasm stains sky blue
- The larger the cell more cytoplasm is visible.
- Two types according to cell diameter

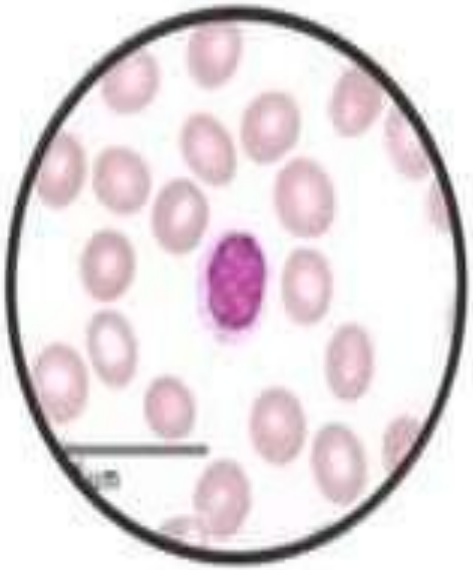
  - Small: 6-9 µm  - Large: 10-14 µm
- Count: 20- 40% of all WBCs (**1000 – 4800 in 1µl of blood**)

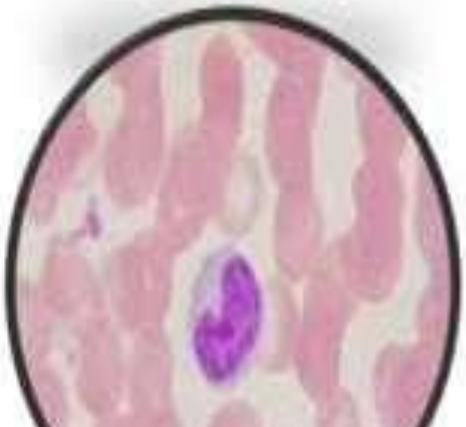


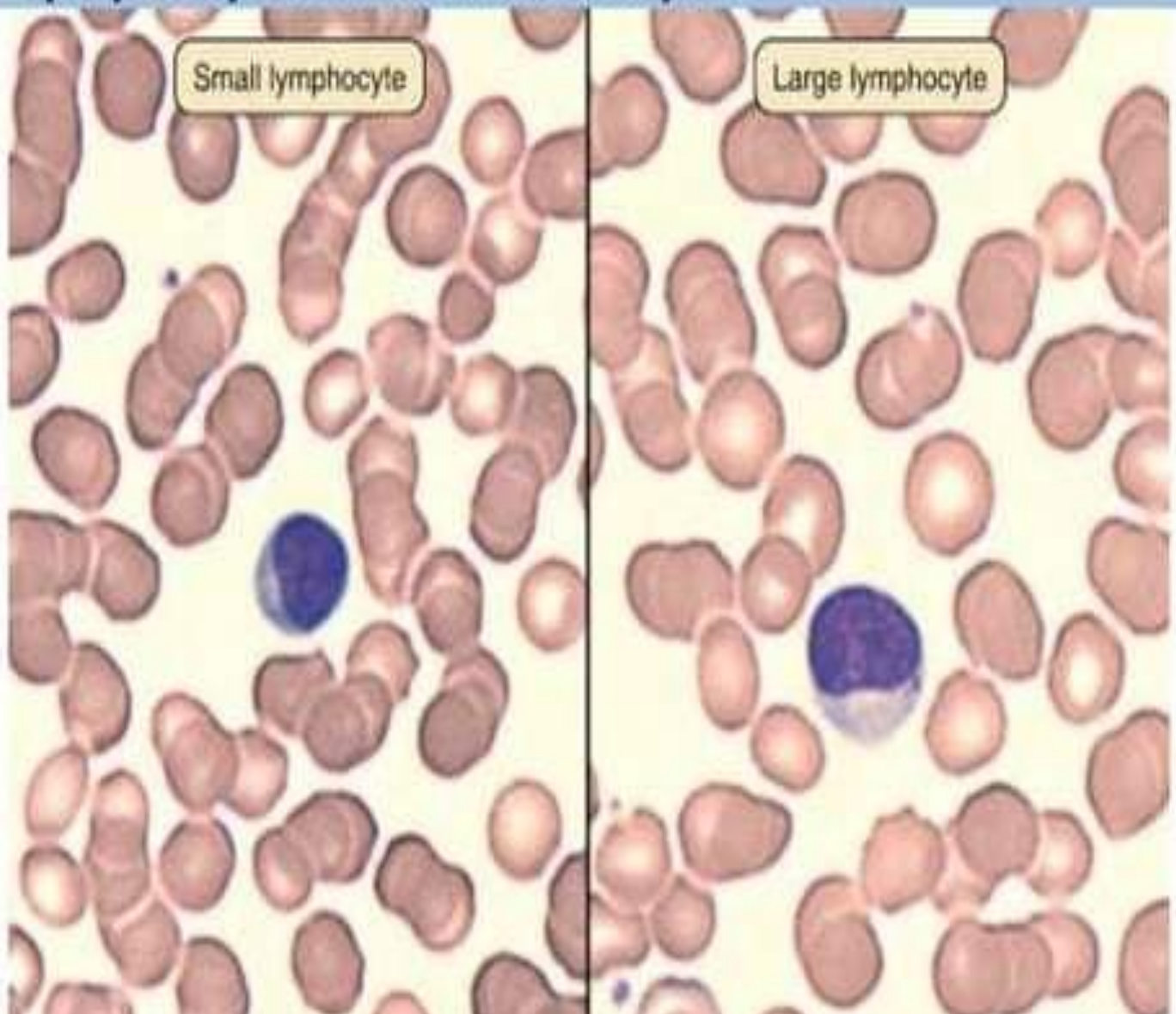
**Function:**

- Mediate immune responses, antigen-antibody reactions.
- **B cells** develop into plasma cells, which secrete antibodies.
- **T cells** attack invading viruses, cancer cells and transplanted tissues
- **NK cells** attack wide variety of infectious microbes

# Lymphocyte under microscope

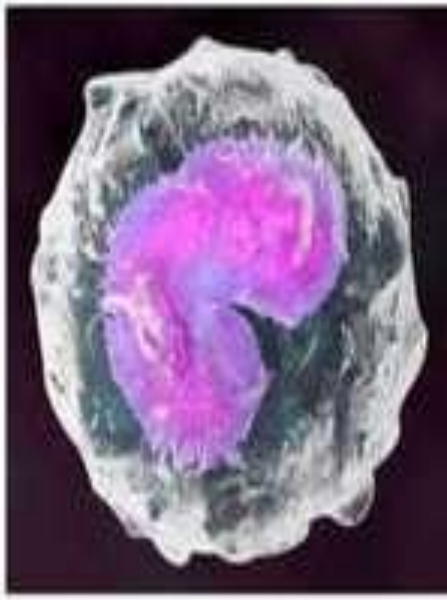






# Monocyte

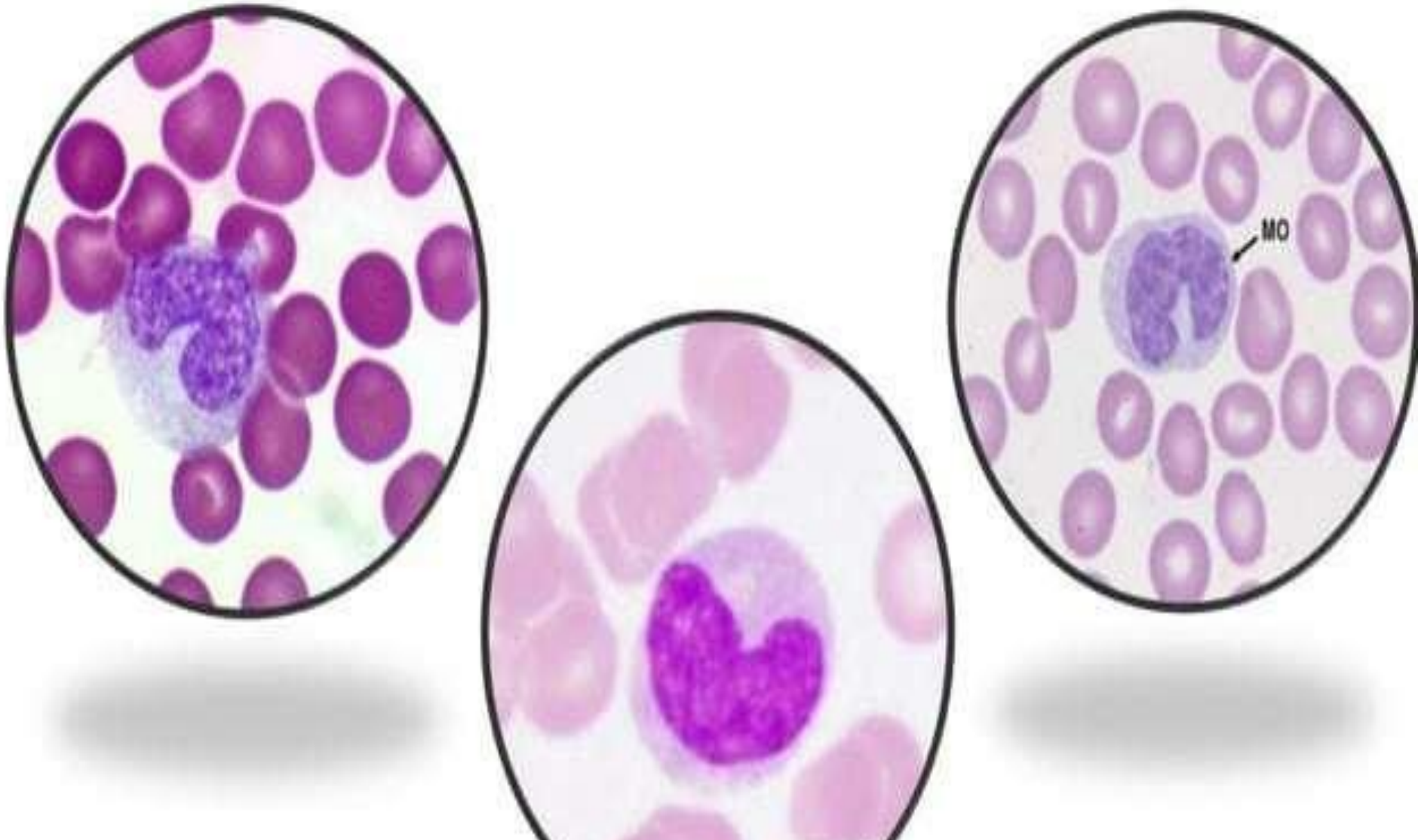
- Nucleus is usually kidney- shaped or horseshoe- shaped
- Cytoplasm is blue- grey and has a foamy appearance due to very fine granules (lysosomes)
- Largest WBCs accounts for **100-700 per $mm^3$** (2 – 8% of all leukocytes)
- Monocytes develop in **macropahges**



## Functions

- Phagocytosis after transforming to macrophages
- Produces ***Interleukin 1*** which:
  - + acts on the hypothalamus causes increase in body temperature during microbial infection.
  - + Stimulate globulin production by liver

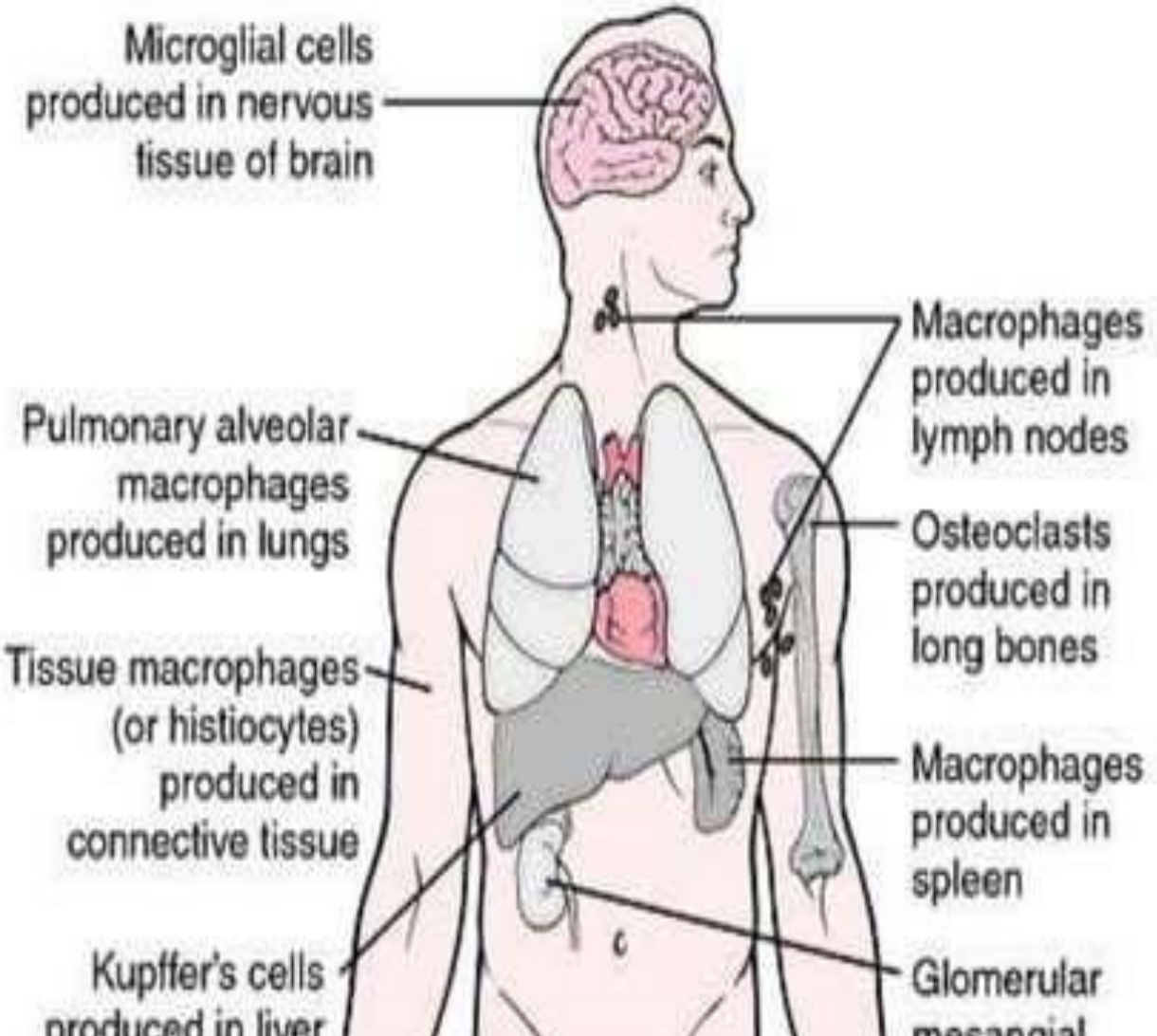
# Monocyte under microscope



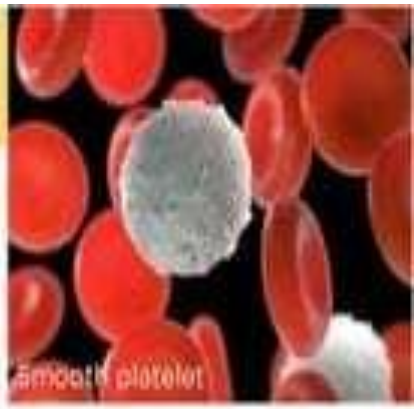
# The Reticuloendothelial system *(The Monocyte- macrophage system)*

- Consist of body's complement of monocytes and macrophages
- Some macrophage are mobile and some are fixed.
- The macrophages provide effective defence at key body locations.
- The collection of fixed macrophages are shown in the **figure** in the next slide.
- Macrophages produce chemicals called ***cytokines***, ***interleukin 1.***

# The Reticuloendothelial system *(The Monocyte- macrophage system)*



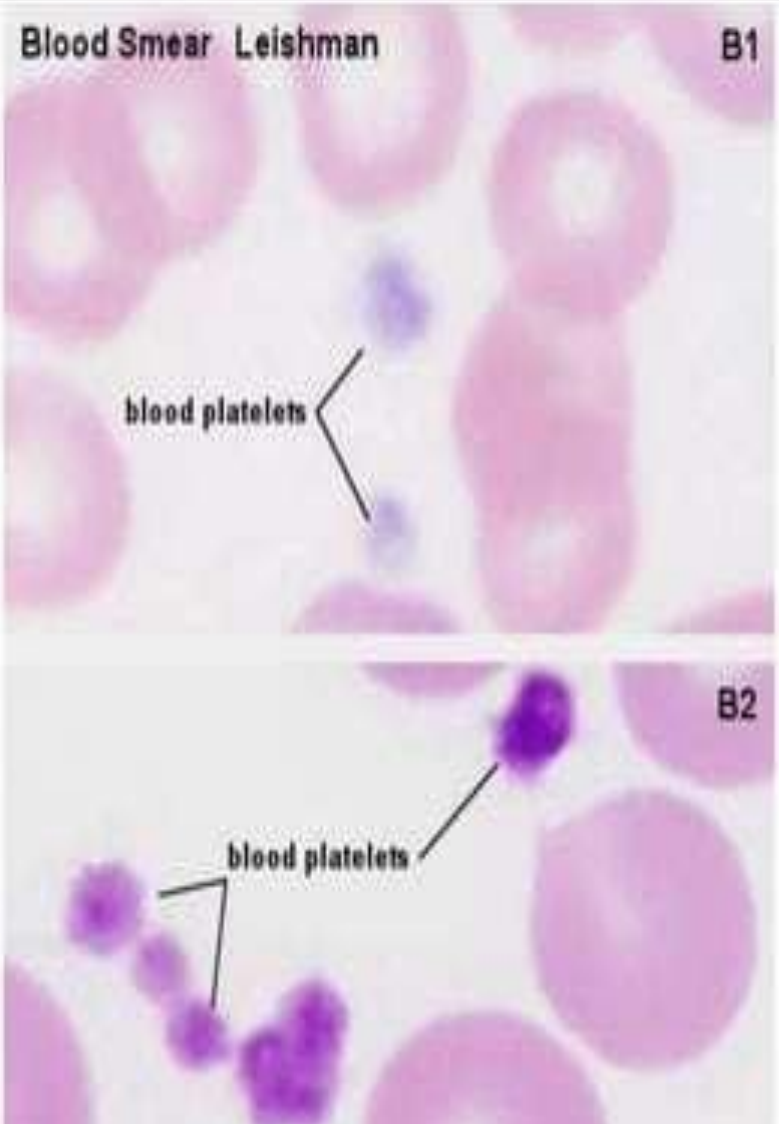
# Platelets (Thrombocytes)

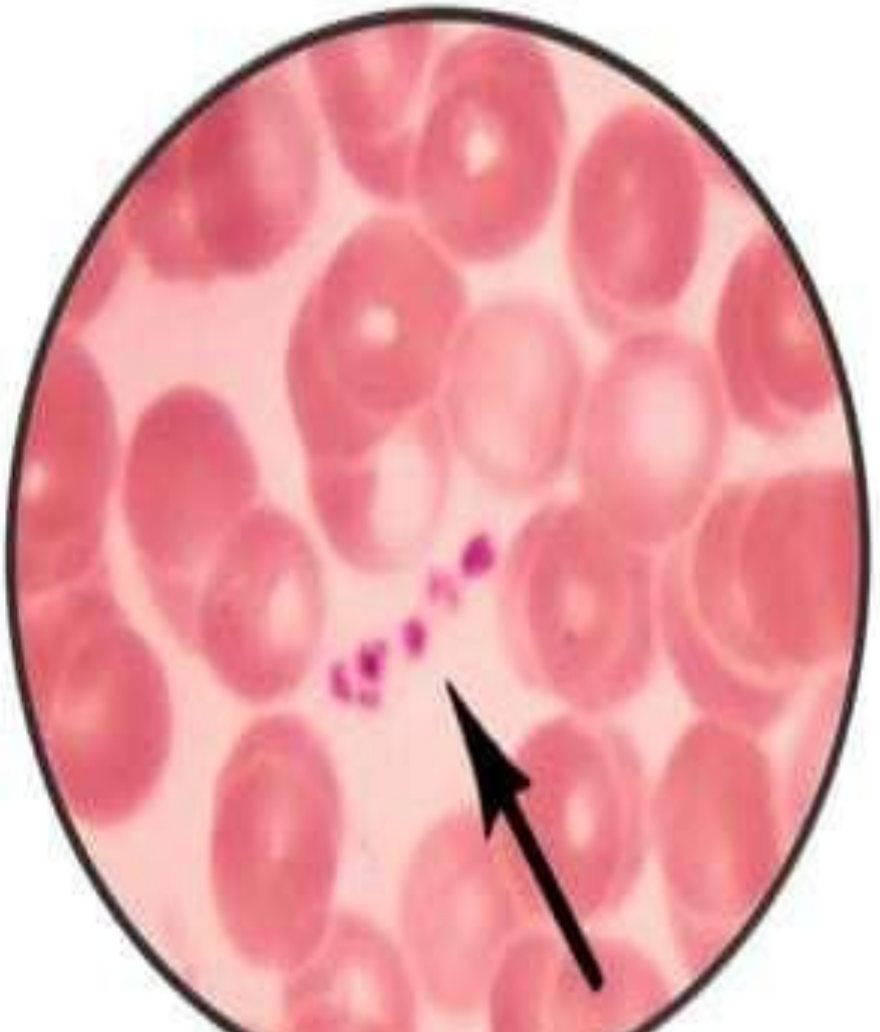


- Irregular disc shaped cells
- 2 – 4 µm in diameter
- Does not have nucleus
- Cytoplasm is packed with granules containing substances which help in clotting.
- Cessations or Ending of bleeding is called ***haemostasis***.
- Normal count: **1,50,000 to 4,00,000 per $mm^3$**

- The hormone ***thrombopoietin*** from the liver stimulates platelet production.
- Life span : **8 – 11 days** (unused platelets destroyed by macrophages in the spleen)

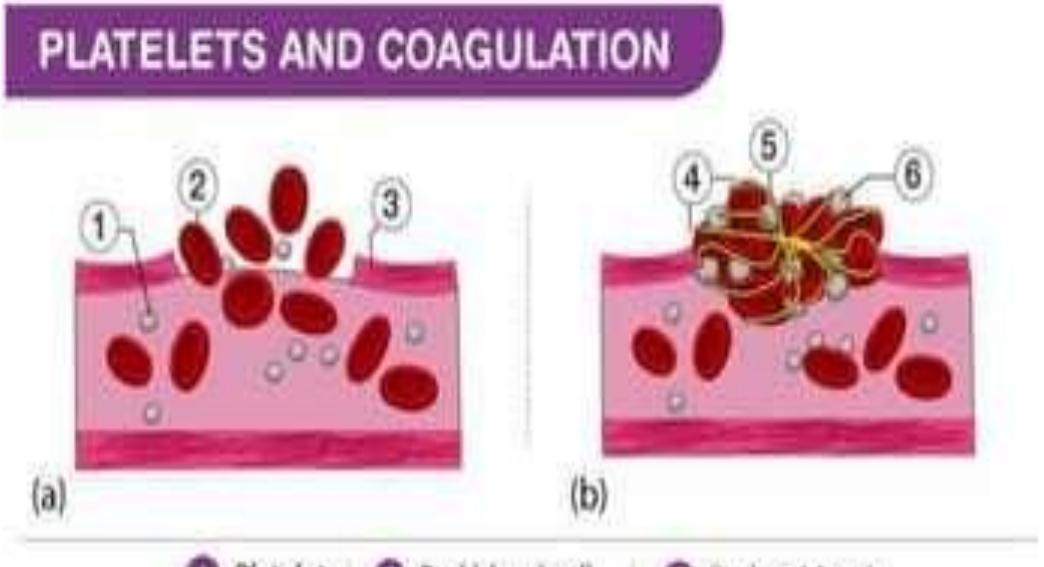
# Platelets under microscope



# **Haemostasis** : The stopping of blood flow

- When a blood vessel is damaged, there will be loss of blood.
- This loss of blood is stopped and healing of the damaged vessel takes place through stages.
- Platelets play an important role in haemostasis through **coagulation** or **blood clotting.**




Stages of Haemostasis:

1. Vasoconstriction
2. Platelet plug formation
3. Coagulation (Blood clotting)
4. Fibrinolysis

# 1. Vasoconstriction

Platelets come in contact with damaged blood vessel

↓

Platelets become sticky and adhere to the damaged walls

↓

Platelets release ***Serotonin***

↓ causes

Constriction (narrows) of blood vessel

↓

Reduces or stopping blood flow

## 2. Platelet plug formation

Adherent platelet clump together

↓ releases

**Adenosine Diphosphate** (ADP) and other substances

↓ causes

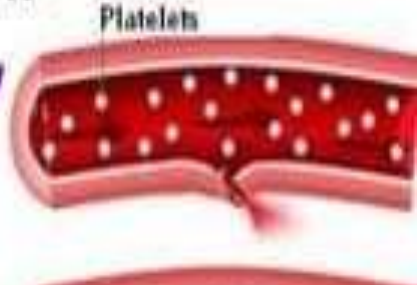
Attraction of more platelets to the injured site

↓ positive feedback

More platelets accumulate at site of vascular damage

↓ within 6 minutes of injury

Forms a temporary seal **(Platelet plug)**



## 3. Coagulation (Blood Clotting)

- This is a complex process that also involves a positive feed back system.
- Coagulation is aided by **12** clotting factors.

- There are **three** pathways for coagulation
  - Extrinsic pathway (activated within seconds)
  - Intrinsic pathway (activated in 3 -6minutes)
  - Common pathway (activated after Ext and Int pathway)

# CLOTTING FACTORS

| NUMBER* | NAME(S) | SOURCE | PATHWAY(S) OF ACTIVATION |
|---|---|---|---|
| I | Fibrinogen. | Liver. | Common. |
| II | Prothrombin. | Liver. | Common. |
| III | Tissue factor (thromboplastin). | Damaged tissues and activated platelets. | Extrinsic. |
| IV | Calcium ions ($Ca^{2+}$). | Diet, bones, and platelets. | All. |
| V | Proaccelerin, labile factor, or accelerator globulin (AcG). | Liver and platelets. | Extrinsic and intrinsic. |
| VII | Serum prothrombin conversion accelerator (SPCA), stable factor, or proconvertin. | Liver. | Extrinsic. |
| VIII | Antihemophilic factor (AHF), antihemophilic factor A, or antihemophilic globulin (AHG). | Liver. | Intrinsic. |
| IX | Christmas factor, plasma thromboplastin component (PTC), or antihemophilic factor B. | Liver. | Intrinsic. |
| X | Stuart factor, Prower factor, or thrombokinase. | Liver. | Extrinsic and intrinsic. |
| XI | Plasma thromboplastin antecedent (PTA) or antihemophilic factor C. | Liver. | Intrinsic. |
| XII | Hageman factor, glass factor, contact factor, or antihemophilic factor D. | Liver. | Intrinsic. |

# STAGES OF BLOOD CLOTTING

Thromboplastin released by damaged tissue cells enters the blood

Platelets adhere to damaged blood vessel lining

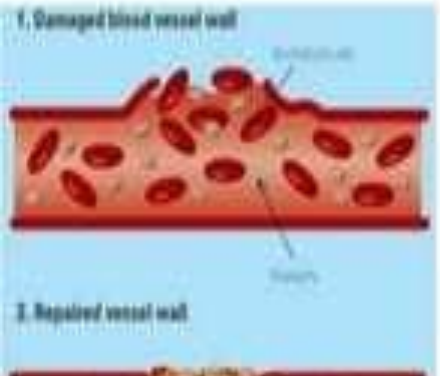
**Extrinsic Pathway**

**Intrinsic Pathway**

Prothrombin activator

Prothrombin → Thrombin

Fibrinogen → Loose fibrin threads



# SUMMARY OF CLOTTING PROCESS

Injury or damage

- Injury/ rupture to blood vessel

Vessel contracts

- Blood vessel around wound constrict - reduce blood flow to the damaged area.
- Activated Platelets stick to injury site

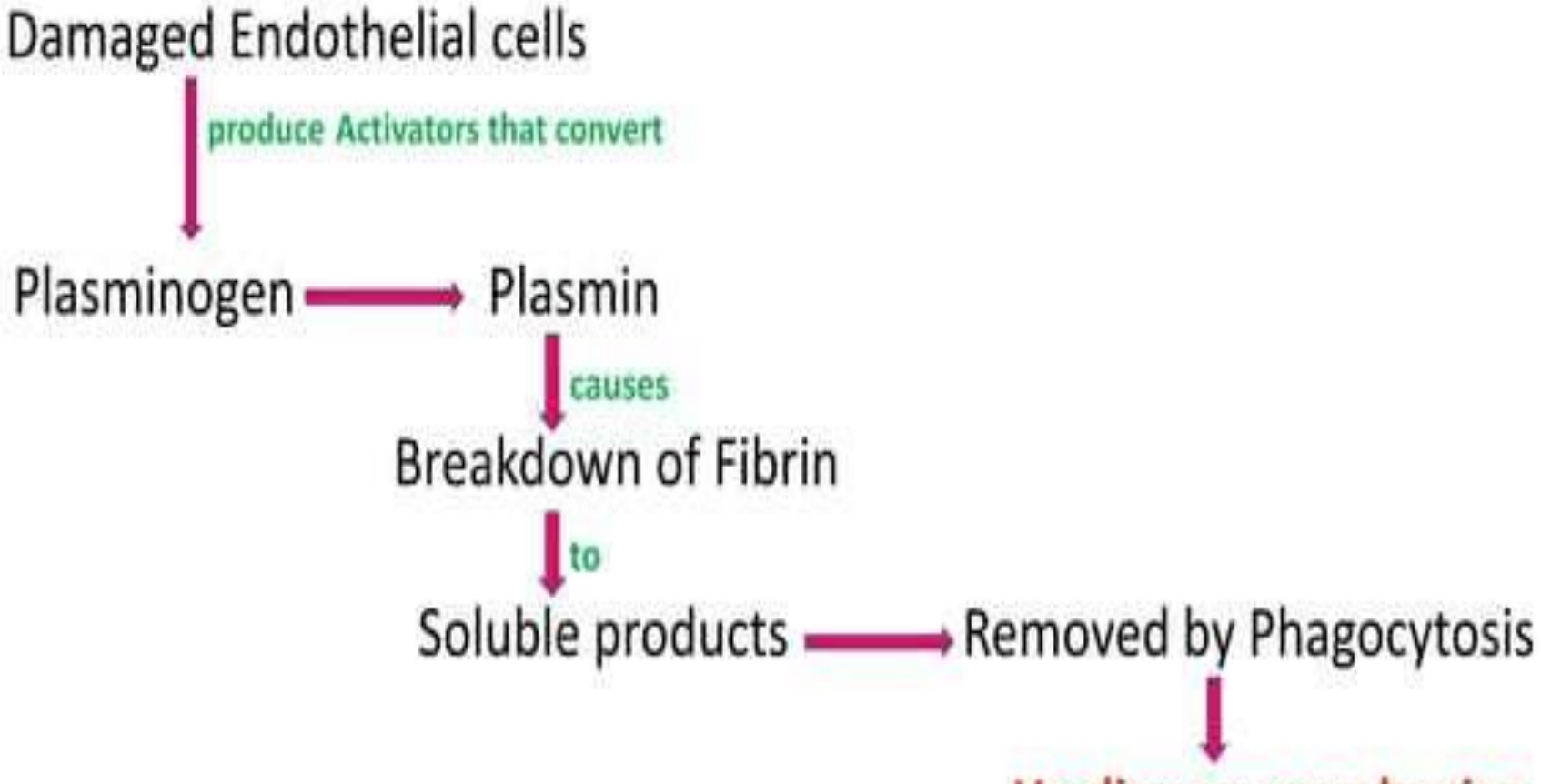
Platelet plug

- Platelets become sticky and clump together to form platelet plug.
- Platelets & damaged tissue release clotting factors (eg.Factor VIII)

- Blood clotting mechanism to form Fibrin

## 4. Fibrinolysis:

- The process of removing the clot and healing of the damaged blood vessel begin.
- The breakdown of clot is known as fibrinolysis



# Blood Groups

- The surface of erythrocytes contain a genetically determined collection of antigens made up of glycoproteins and glycolipids.

- The presence or absence of various antigens, blood is categorized into different groups.

- There are at least 24 blood groups and more than 100 antigens.

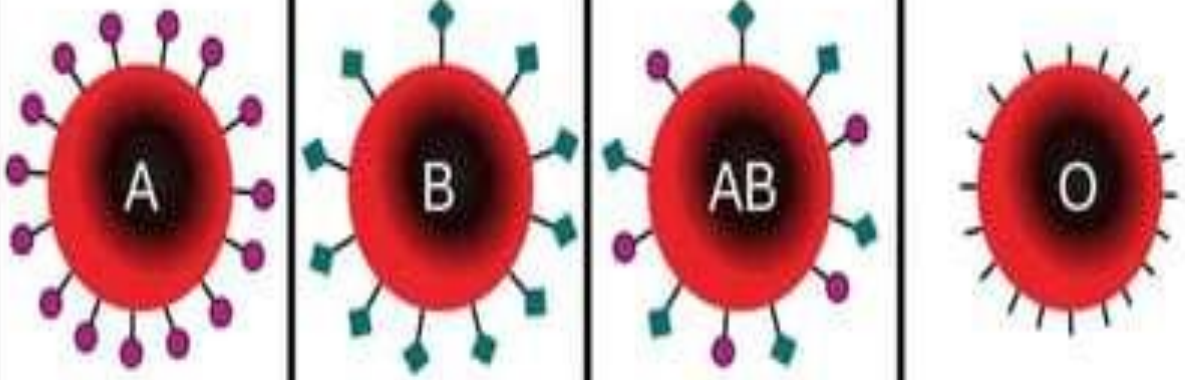
- The **two** major blood groups are

  - ABO Blood group
  - Rh Blood group

# ABO Blood Group

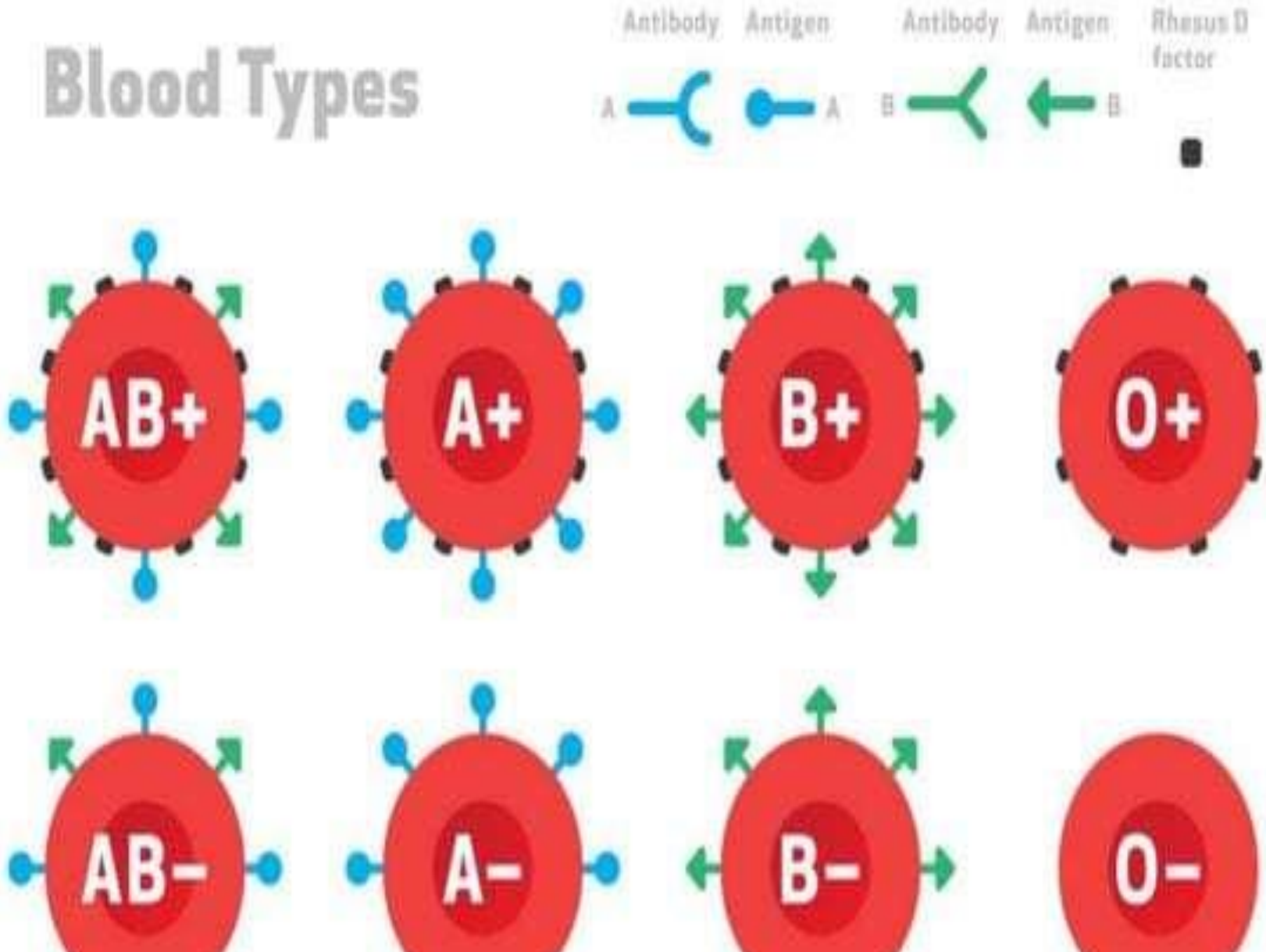
- It is based on two glycolipid antigen called **A** and **B**
- People whose RBCs have only antigen A have **type A blood**
- People having antigen B are **type B blood**
- People with both antigen A and B are **type AB blood**
- Who neither antigen A nor antigen B are **type O blood**

- Blood plasma usually contains antibodies called **agglutinins** that react with A or B antigen if the two are mixed

| | Group A | Group B | Group AB | Group O |
|---|---|---|---|---|
| Red blood cell type |   | | | |
| Antibodies in plasma |  Anti-B |  Anti-A | None |  Anti-A and Anti-B |
| Antigens in red blood |  | | | |

# Rh Blood Group

- It is due to the presence of Rh antigen called **Rh factor**.
- It was first found in the blood of ***Rhesus monkey***.
- People whose RBCs have Rh antigen are $Rh^+$ (Rh Positive)
- People whose RBCs lack Rh antigen are $Rh^-$ (Rh negative)


Blood Types
Antibody
Antigen
Antibody
Antigen
Rhesus D factor
A
A
B
B
AB+
A+
B+
O+
AB−
A−
B−
O−

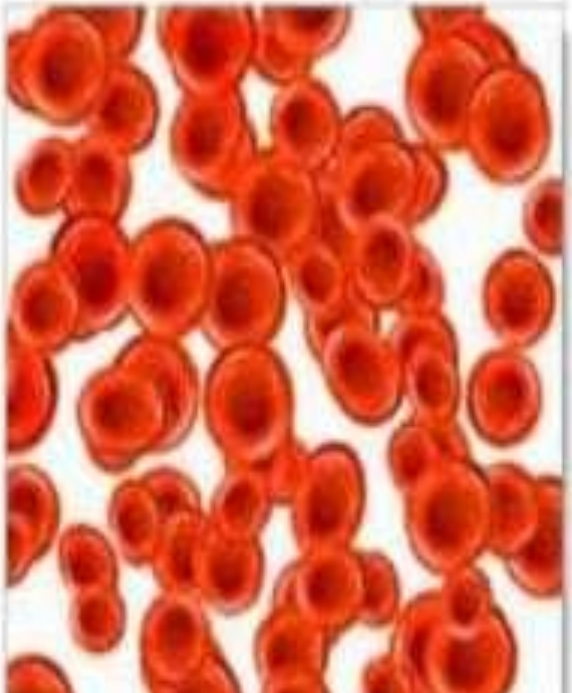
| TYPE | YOU CAN GIVE BLOOD TO | YOU CAN RECEIVE BLOOD FROM |
|---|---|---|
| A+ | A+, AB+ | A+, A-, O+, O- |
| O+ | O+, A+, B+, AB+ | O+, O- |
| B+ | B+, AB+ | B+, B-, O+,O- |
| AB+ | AB+ | EVERYONE |
| A- | A+, A-, AB+, AB- | A-, O- |
| O- | EVERYONE | O- |
| B- | B+, B-, AB+, AB- | B-, O- |

Whom can you donate blood or receive blood from ?

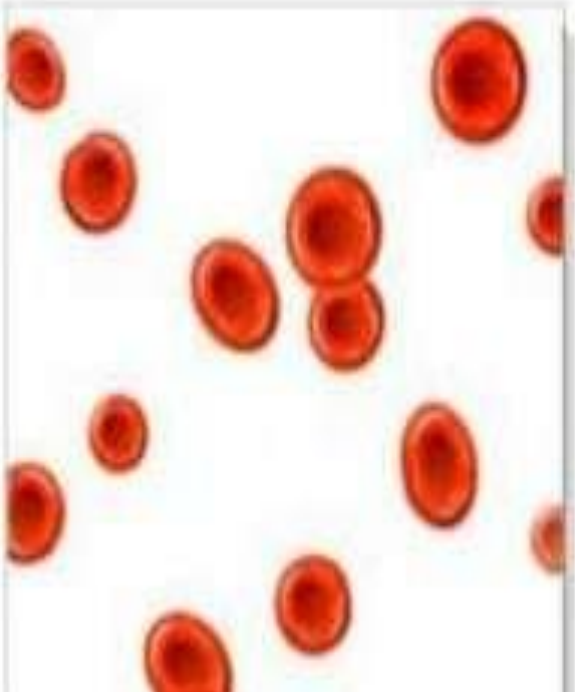
# Disease conditions associated with blood

# ERYTHROCYTE DISORDERS

Normal amount of red blood cells

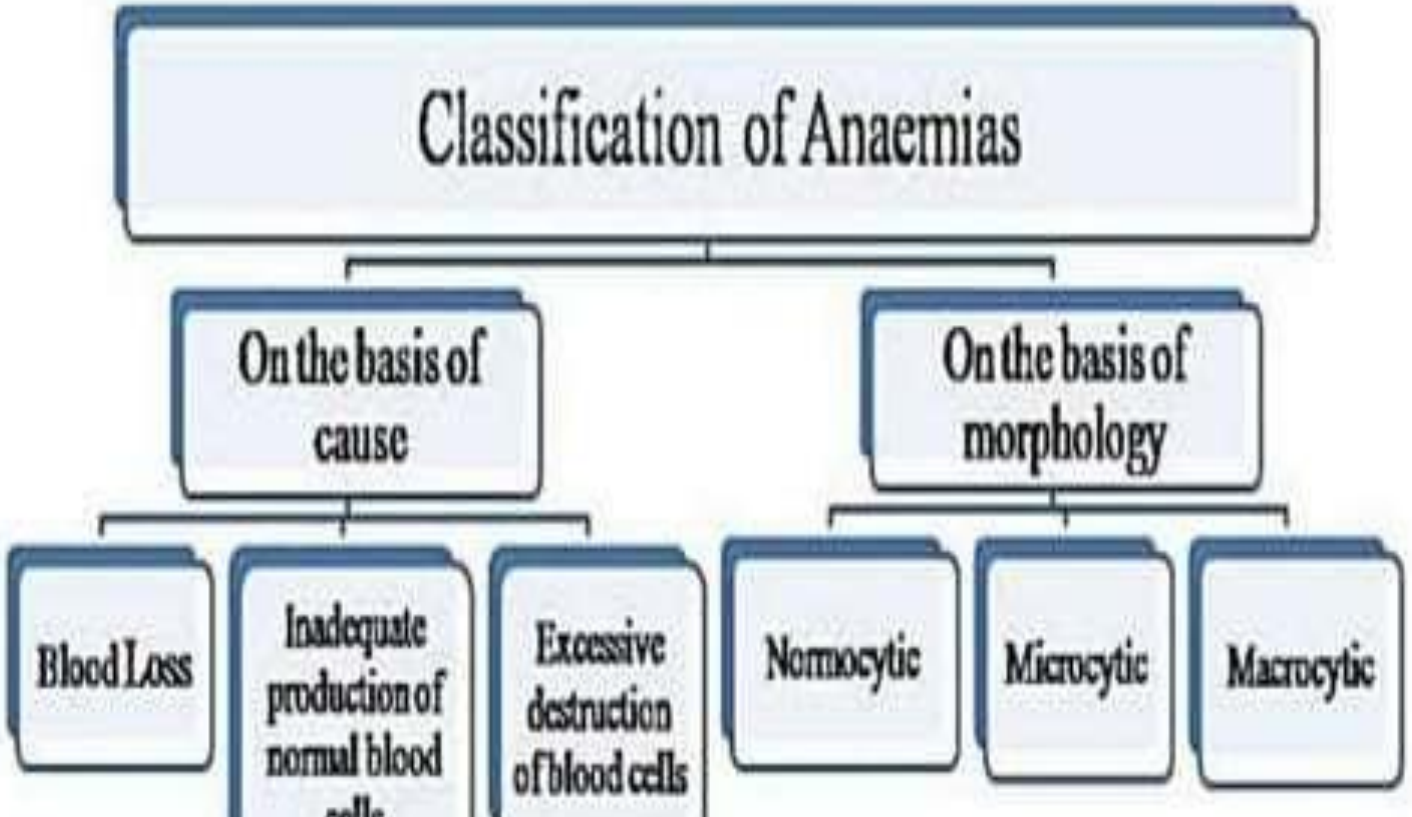


Anemic amount of red blood cells



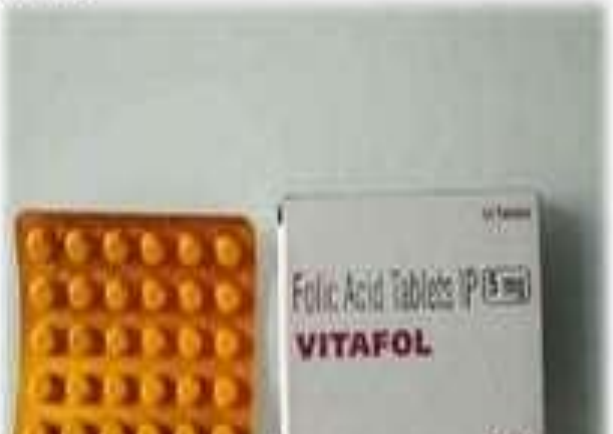
# Anaemias

- Anaemia is the inability of the blood to carry enough oxygen to meet body needs, because of low levels of haemoglobin in the blood.



# Nutritional deficiency anaemia


- Iron deficiency anaemia
- Vitamin $B_{12}$ deficiency anaemia: Pernicious anaemia
- Folic acid deficiency anaemia



# Other types

- **Aplastic anemia**:

This occurs when the bone marrow does not produce enough red blood cells, and treatment may involve transfusions. Certain medicines, toxins, and infectious diseases can cause aplastic anemia.

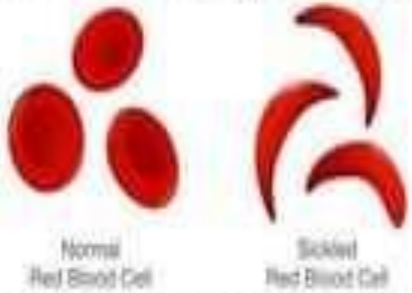

- **Haemolytic anaemia:**

These occurs when circulating erythrocytes are destroyed or are removed prematurely from the blood because the cells are abnormal or the spleen is overactive. The life span of RBCs is shortened considerably from 120 days.

# Congenital Haemolytic Anaemias

- **Sickle cell anaemia:**

It is an inherited group of disorders, red blood cells change shape into a sickle shape. The cells die early, leaving a shortage of healthy red blood cells (sickle cell anaemia) and can block blood flow causing pain (sickle cell crisis).




- **Thalassaemia:**

Thalassemia is an inherited blood disorder characterized by less oxygen-carrying protein (haemoglobin) and fewer red blood cells in the body than normal.

- **Haemolytic disease of new born:**

(**HDN**) is a blood disorder in **newborn** babies. It occurs when the new born's red blood cells break down at a fast rate. It's also called ***erythroblastosis fetalis***. **Hemolytic** means

# Acquired Haemolytic Anaemias

- **Chemical agent associated anaemias**: e.g. sulphonamides, toxins by microbes, chemicals at work places.

- **Autoimmune anaemia:**

It occurs when body make antibodies to their own red cell antigens, causing haemolysis. e.g: Carcinoma, viral infection etc.

- **Blood transfusion reaction anaemia.**

When an individual receives blood transfusion carrying antigen different from their own, the immune system will recognize them as foreign body, make antibodies and destroy them

# Polycythemia

- It is the abnormally large number of erythrocytes in the blood.
- There is abnormal increase in number of RBCs, more than normal
- This causes increased blood viscosity, slow blood flow and risk of intravascular clotting, ischemia and infarction.

# Leukocyte disorders

- **Leukopenia**: In this condition, the total blood leukocyte count is less that 4000/$mm^3$


- **Granulocytopenia** (Neutropenia):

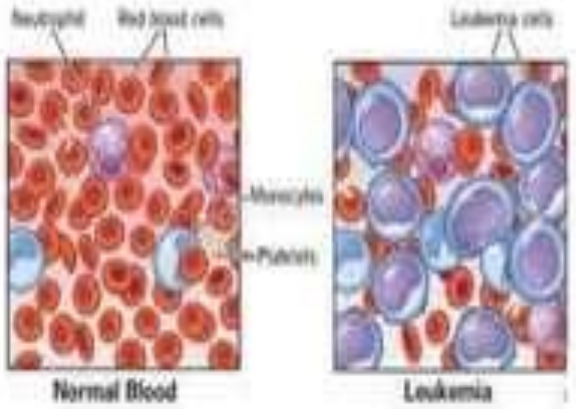
Abnormal reduction in number of circulating granulocytes.

- **Leukocytosis:**

An increase in the number of circulating leukocytes, occurs as a normal protective reaction especially in infection.

# Leukemia

- Leukaemia is a malignant proliferation of white blood cell. It results in the uncontrolled increase in the production of leukocytes.




- Causes: Ionising radiation, Chemicals, genetic factors

- **Types:**

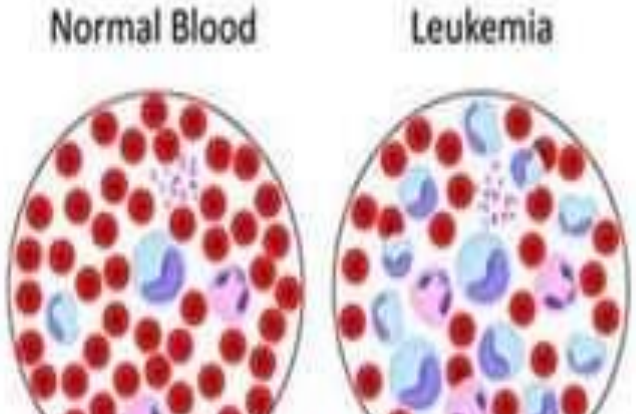
  - **Acute Leukemia**

    Acute myeloblastic leukemia (AML)

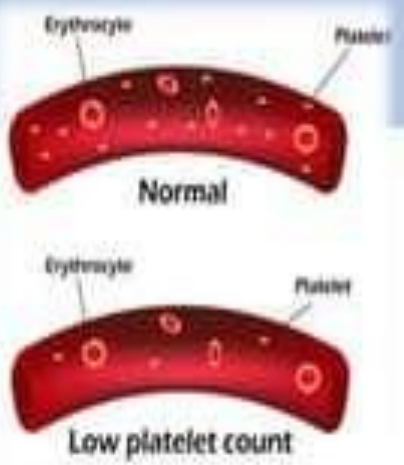
    Acute lymphoblastic leukemia (ALL)

  - **Chronic Leukemia**

    Chronic myeloid leukemia (CML)



# Thrombocytopenia




- This is defined as blood platelet count below 1,50,000 / $mm^3$
- Bleeding occurs when count falls below 30000/ $mm^3$
- It maybe due to reduced platelet production or increased platelet destruction

# Vitamin K Deficiency

- Vitamin K is required by the liver for the synthesis of many clotting factors, therefor deficiency of vitamin K can lead to abnormal clotting.

# Disseminated Intravascular Coagulopathy (DIC)

- Disseminated intravascular coagulation (**DIC**) is a condition in which blood clots form throughout the body, blocking small blood vessels. Symptoms may include chest pain, shortness of breath, leg pain, problems speaking, or problems moving parts of the body.

# Haemophilias

- Haemophilia is an inherited bleeding disorder where **blood doesn't clot** properly. It is caused when blood does not have enough clotting factor. A clotting factor is a protein in blood that controls bleeding.

There are two types of haemophilia. Both have the same symptoms:

- **Haemophilia A** is the most common form and is caused by having reduced levels of clotting factor VIII (8).
- **Haemophilia B**, also known as Christmas Disease, is caused by having reduced levels of

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- https://ashpublications.org/blood/article/116/4/511/27471/A-day-or-5-in-a-neutrophil-s-life

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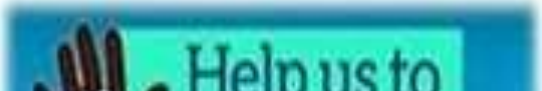
# THANK YOU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