

## **The Blood**

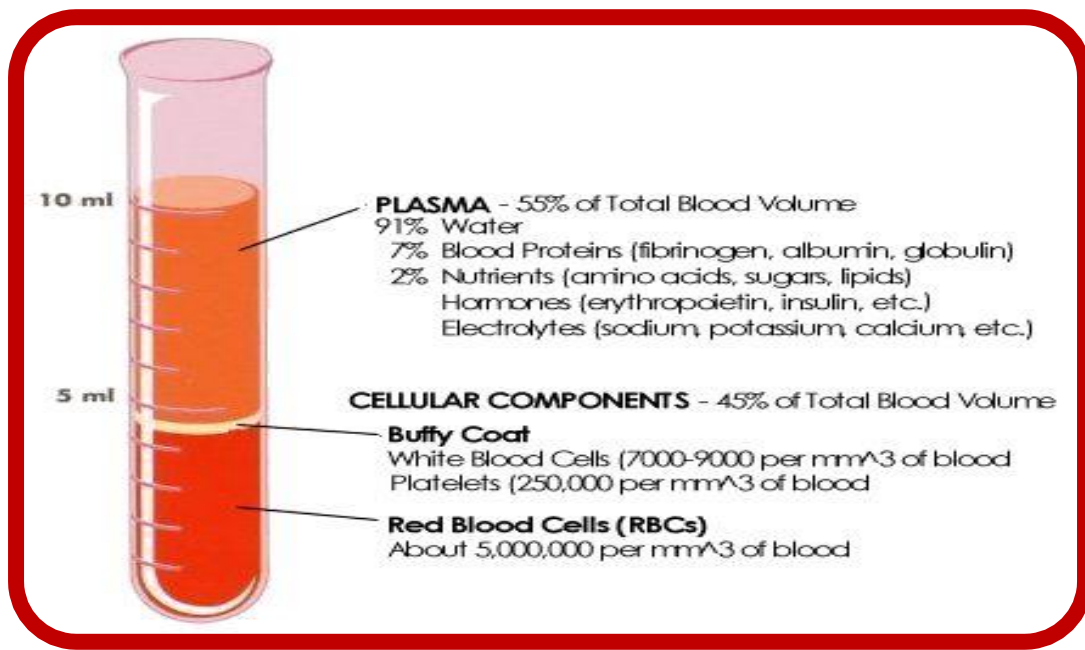
- Blood is a fluid connective tissue. It circulate continually around the body, allowing constant communication between tissues distant from each other.
- Blood makes up about 7% of body weight (about 5.6 liters in a 72 Kg man). This proportion is less in women, while in children is greater (gradually decreasing until the adult level is reached).

### **Functions of the Blood**

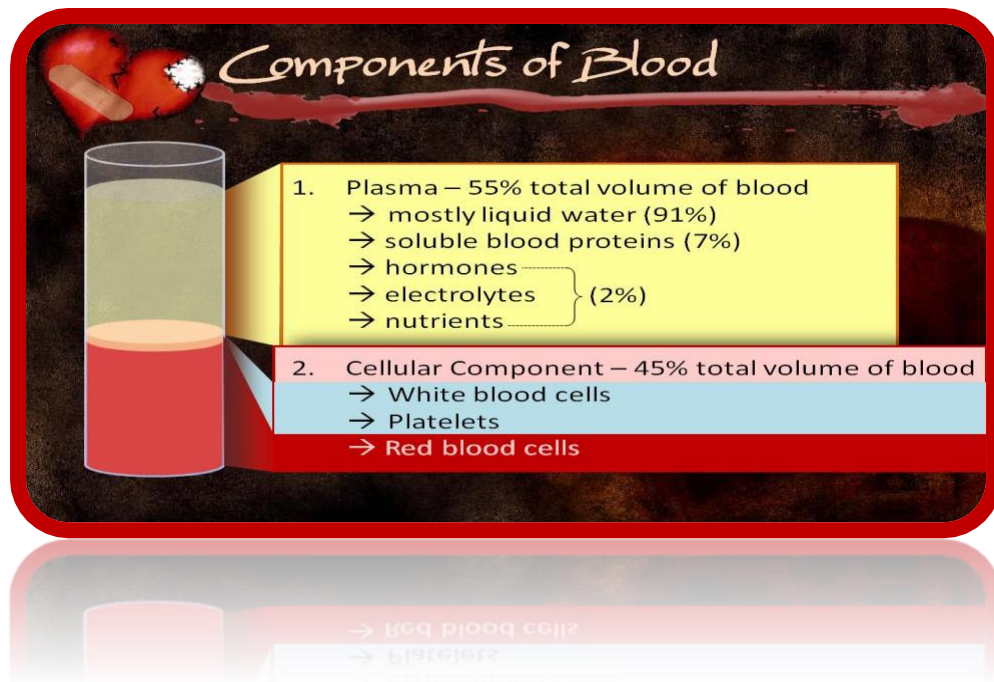
1. The main function of the blood is to maintain intracellular homeostasis by:
  - a). Carries O<sub>2</sub> and nutrients (glucose, amino acids, lipids, and vitamins) to the cells.
  - b). Carries CO<sub>2</sub> and other wastes (nitrates, creatine, nucleic acid) away from the cell.
2. Providing intercellular communication in the body: carries hormones (secreted by endocrine glands) to the target organs.
3. Protection and defense: it allows cells and immunological proteins to transport from place to place where need them.
4. Self repair mechanism: clotting cascade.

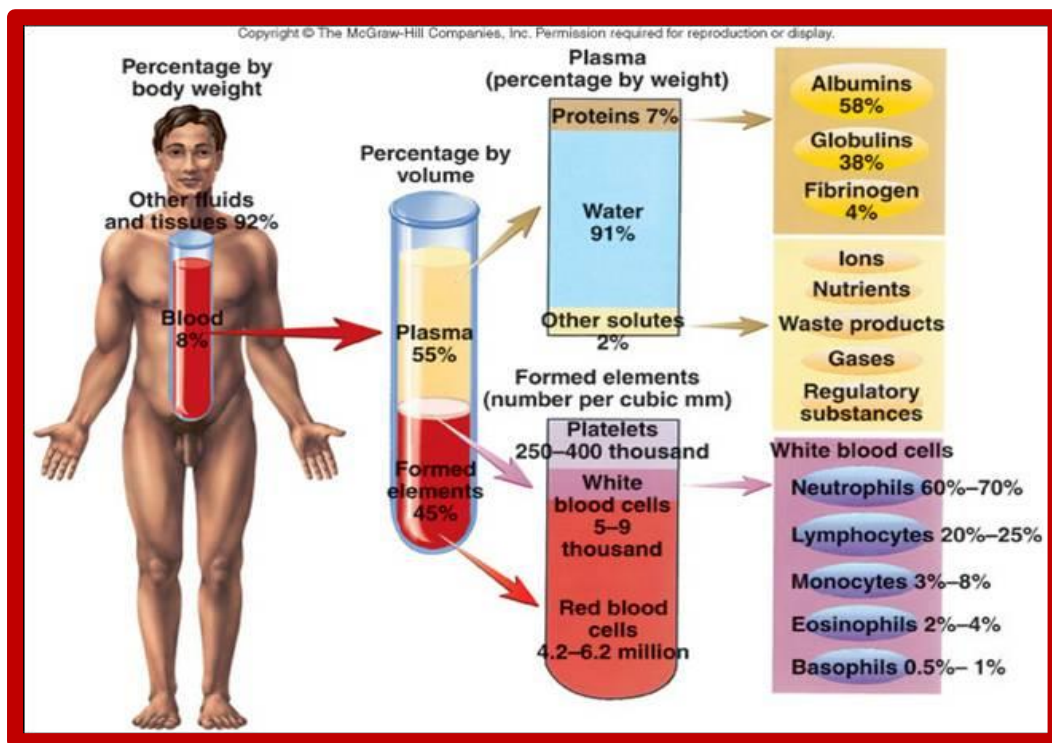
### **Blood Components**

- Blood is composed from 2 fractions:
  1. Plasma
    - Non living extracellular matrix
    - composes about 55% of total blood volume.
  2. Formed elements (living cells)
    - composes about 45% of total blood volume.
- The two frictions of blood can be separated by spinning.



Hematocrit tube with blood after centrifugation  
 Plasma forms the supernatant, buffy coat forms the middle layer and the red blood cells form the sediment





## Plasma

- the constituents of plasma are:

1. **Water** (90-92%)

2. **Plasma proteins:** make up about 7% of plasma.

- **Albumins** (about 60% of total plasma protein) They are responsible for maintain normal plasma *osmotic pressure*. Albumins also act as *carrier molecules* for free fatty acids, some drugs and steroid hormones.

- **Globins** their main functions are: as *antibodies (immunoglobulins)*, *transportation of some hormones and mineral salts* (e.g. thyroglobulin carries the hormone thyroxin and transferrin carries the mineral iron. And inhibition of some proteolytic enzymes (e.g. macroglobulin inhibits trypsin activities)

- **Clotting factors.** These are responsible for *coagulation of blood*.

3. **Inorganic salts** (electrolytes) like Ca, Na, Po<sub>4</sub> which are responsible for muscle contraction, transmission of nerve impulses, --ect.

4. **Nutrients:** glucose, amino acid, fatty acids and glycerol.

5. **Waste products** like urea, creatinine and uric acid they are carried in the blood to the kidney for excretion.

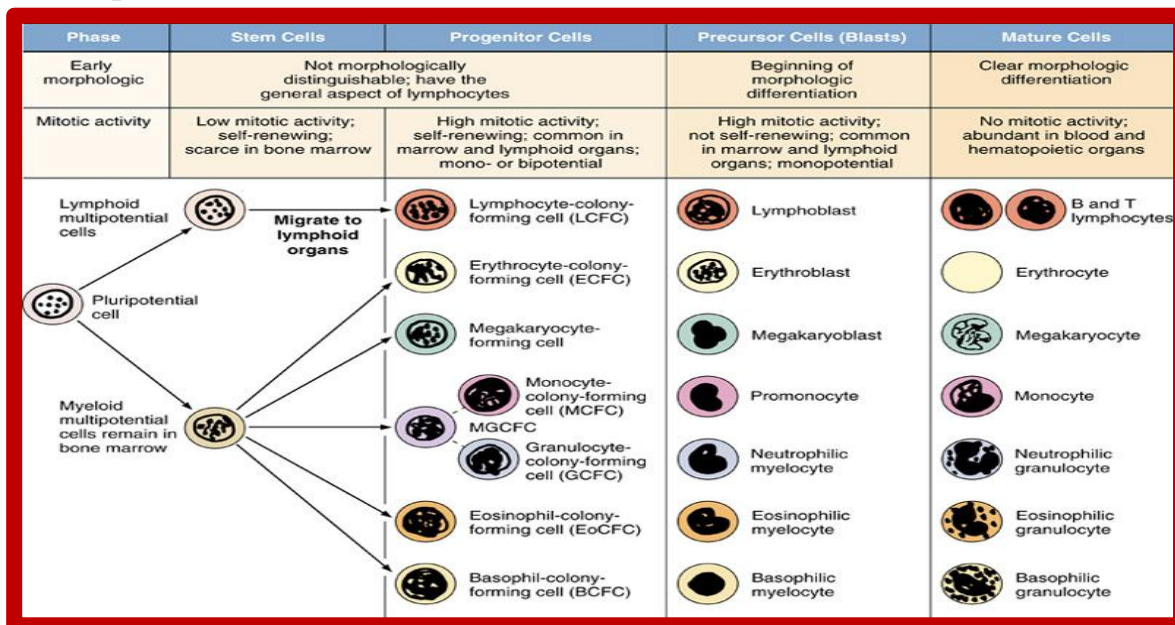
6. **Hormones and gases**

## Formed Elements (Cellular Content of Blood)

- There are three types of blood cell:
  - Erythrocytes** (Red Blood Cells =RBC).
  - Platelets** (thrombocytes)
- Leukocytes** (white blood cells = WBC) they include monocytes, lymphocytes, neutrophils, eosinophils, and basophils

## Source of Blood Cells

- Mature blood cells have a relatively short life span.
- Blood cells are synthesised mainly in the red bone marrow.
- Some lymphocytes, additionally are produced in lymphoid tissue.
- The organ or system responsible for synthesis blood cells are called hematopoietic system and the process of blood cell formation is called hematopoiesis.



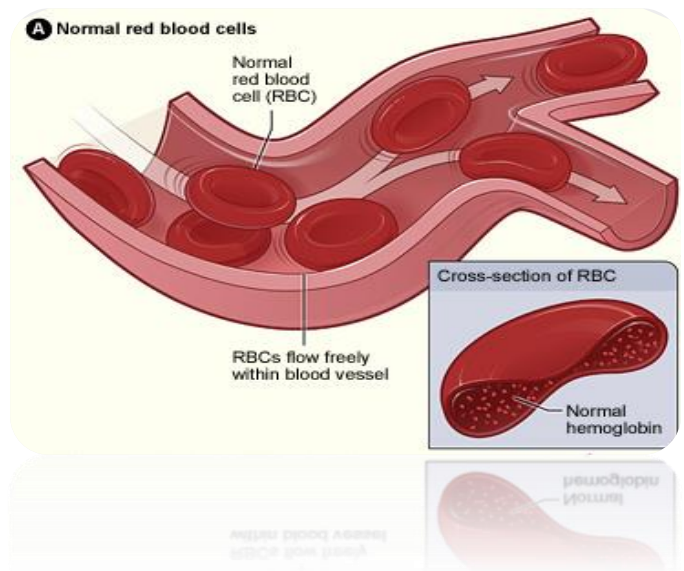
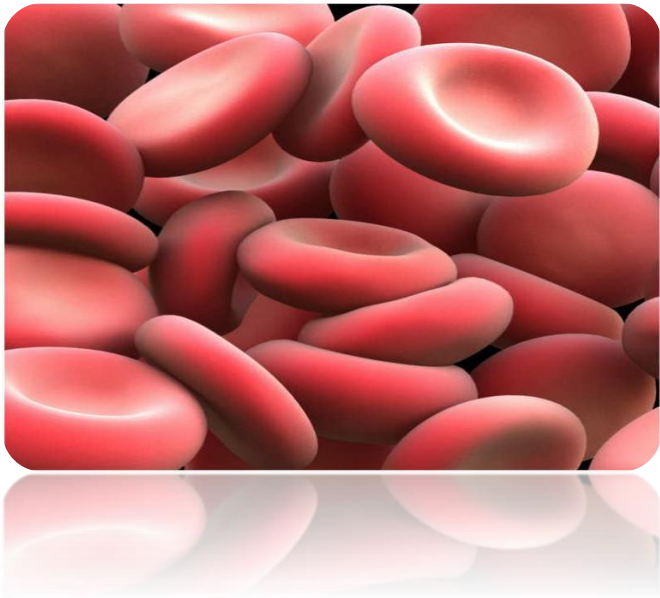
## Hematologic System

- Erythrocytes = Red Blood Cells**
  - Red blood cells are biconcave discs, they have no nucleus and cytoplasmic organelles. They contain a red coloured protein called hemoglobin. Their

main function is in gas transport, mainly of O<sub>2</sub> but they also carry some CO<sub>2</sub>.

- Human erythrocytes are 7.5 µm in diameter, 2.6 µm thick at the rim and 0.8 µm thick in the center.
- The biconcave shape increases their surface area for gas exchange, and the thinness of the central portion allows fast entry and exit of gases.
- The cells are flexible so they can squeeze through narrow capillaries.

The normal concentration of erythrocytes in blood is approximately 3.9- 5.5 million per microliter in women and 4.1-6 million per microliter in men



## Biconcave shape of RBC

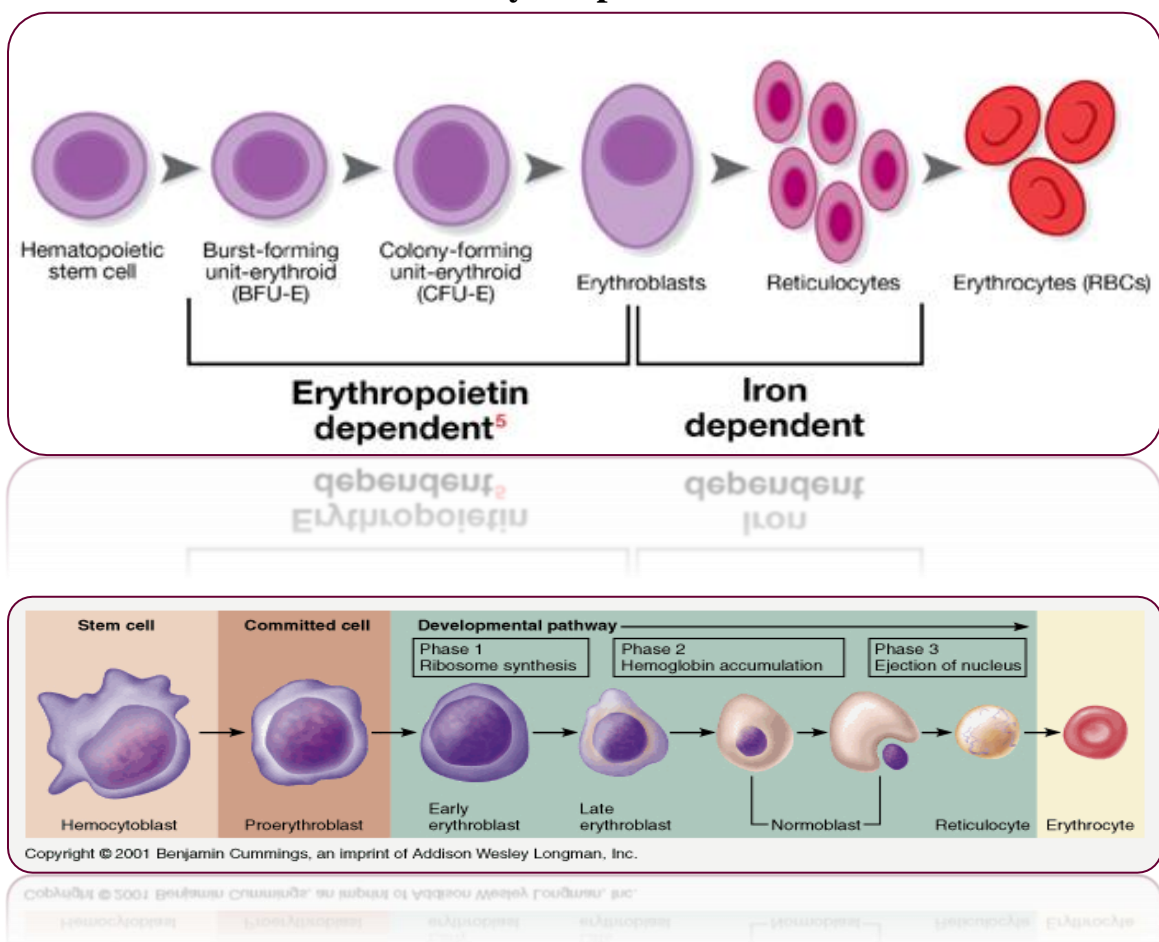
### Life Span and Formation of Red Blood Cells

- Erythrocytes are produced in red bone marrow (in the ends of long bones and in flat and irregular bones).
- They pass through several stages of development before entering the blood.
- Their life span in circulation is about 120 days.
- The process of RBC development from stem cells takes about 7 days and is called erythropoiesis.



- The immature cells are released into the blood stream as reticulocytes and then mature into erythrocytes over 1-2 days within circulation. During this time, they lose their nucleus and therefore become incapable of division.
- The hormone erythropoietin and substances such as iron, folic acid, and vitamin B12 are essential for the production of erythrocytes.
- Erythropoietin hormone is a glycoprotein hormone produced in the kidneys and stimulates the production of globin (the protein component of Hb), enhances the release reticulocytes in the circulation and enhances reticulocytes maturation to mature RBC.

### Erythropoiesis



### Physiological Factors influencing RBC number

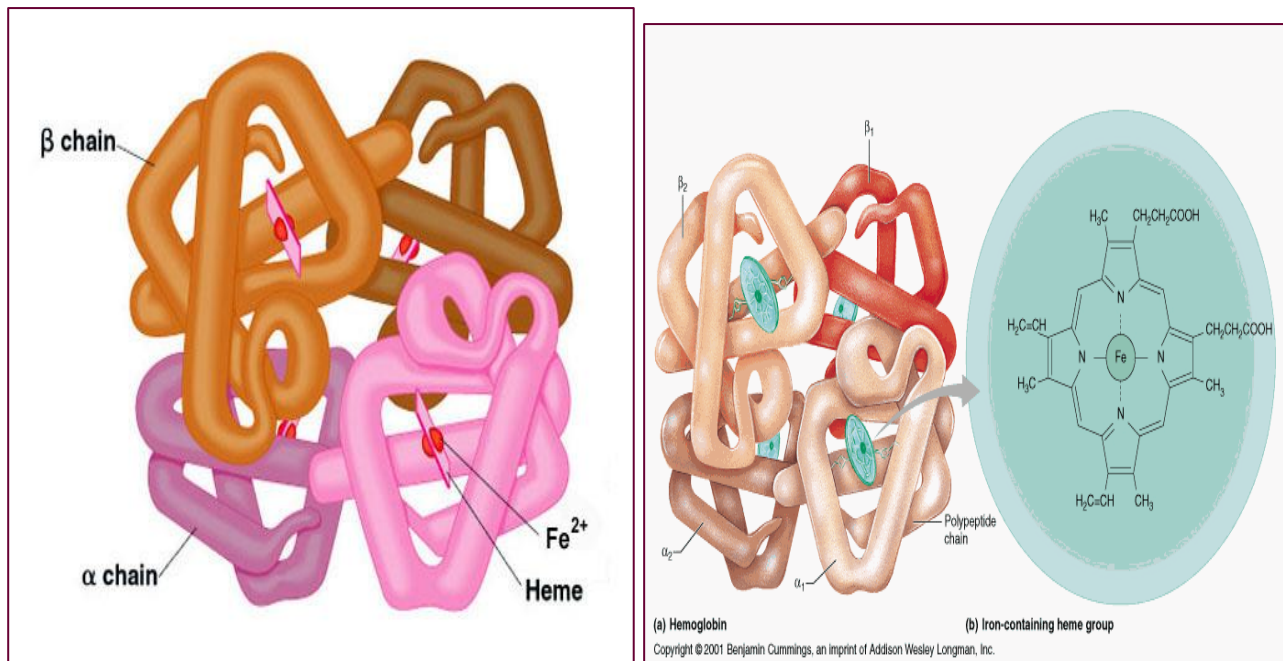
- RBC count is very high at birth (8-10 million/mm).
- The count is higher in children than in adults.
- RBC count is raised at high altitude, in warm temperature, during excitement.

- In women RBC count is relatively low during pregnancy.  
A fall in RBC count is seen low altitude.

## Hemoglobin (Hb)

- Hb is the most important constituent of red blood cells. It is responsible for transport of O<sub>2</sub> from lungs to tissues and CO<sub>2</sub> from tissues to lungs.
- The normal value in a normal male adult is **13-18 g\100ml** and in female is **11.5- 16.5 g\100ml**.
- Molecules of hemoglobin is large and complex. They are made up of **heme** and **globin**.
- **Heme** is made up of **iron** (in ferrous form) and **porphyrin**.
- **Globin** is a protein that has **4 polypeptides chains** (2 *alpha* and 2 *beta*).
- Each unit of Hb contains **4 units of heme** that are united together by the alpha and beta chains of globin.
- Each unit of heme can combine with one molecule of O<sub>2</sub>. So one molecule of Hb can carry **4 molecule of O<sub>2</sub>**.
- Each RBC carries **about 280 million Hb molecules**, therefore each RBC has ability to carry **over a billion O<sub>2</sub> molecules**.
- Hb with O<sub>2</sub> is called **oxyhemoglobin**, and Hb without O<sub>2</sub> called deoxyhemoglobin.

## Hb Structure



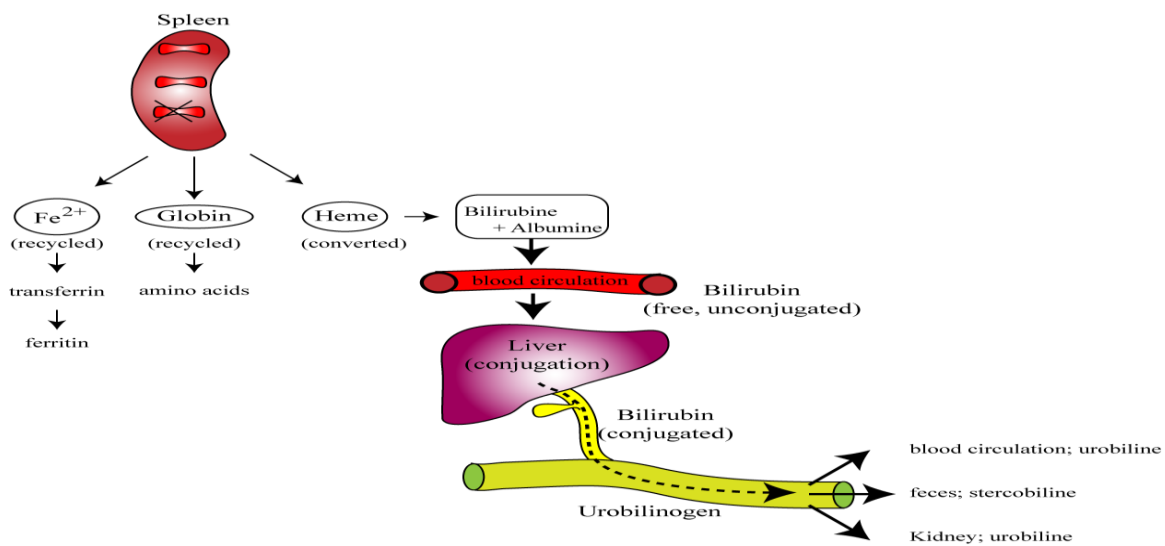
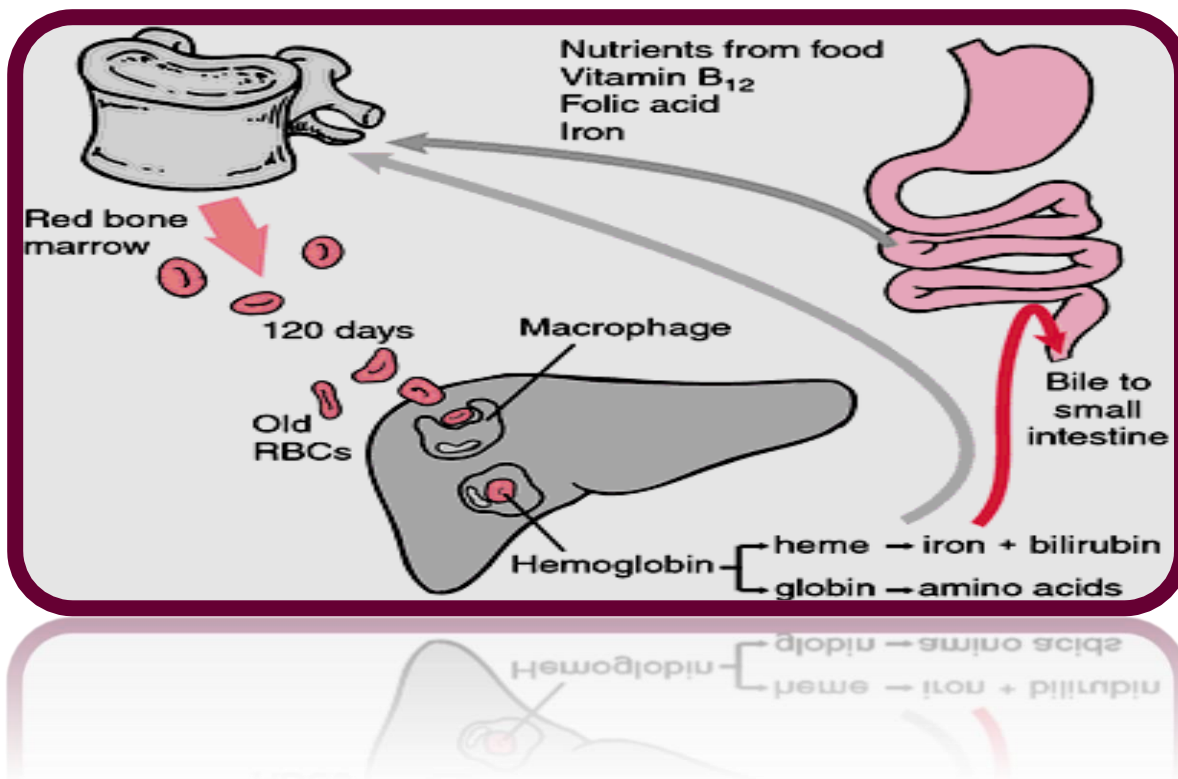
## Types of Normal Hb

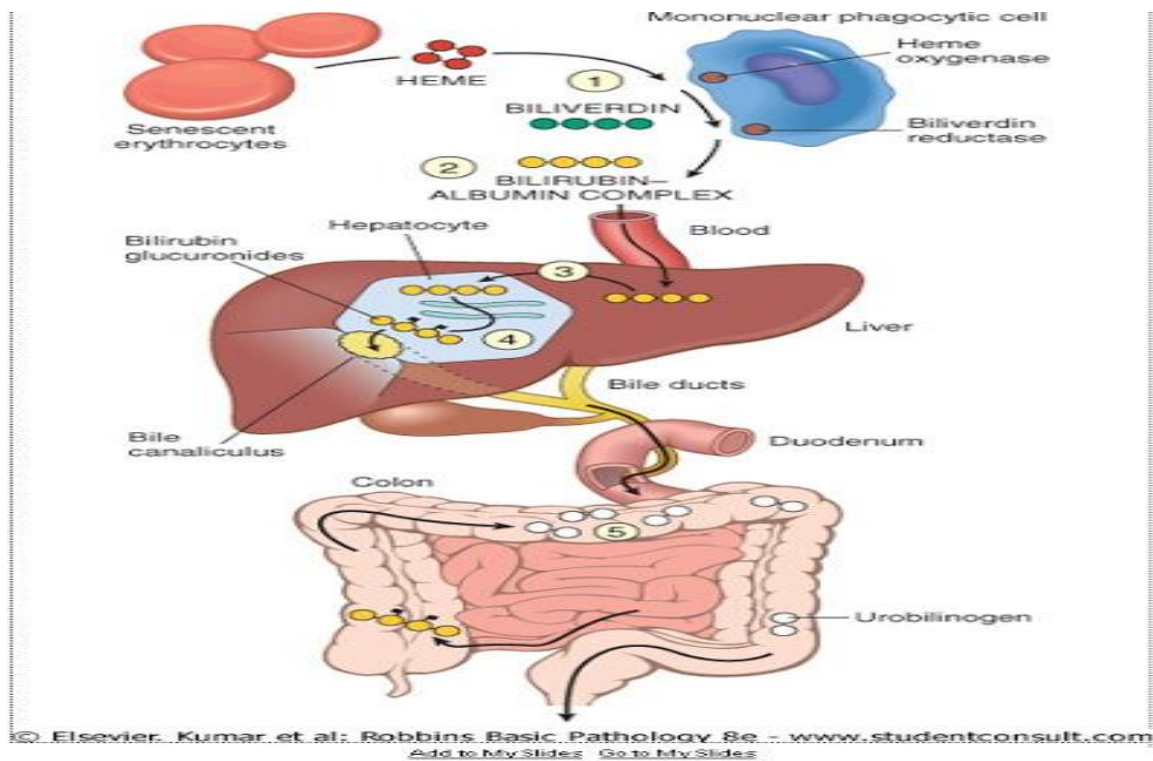
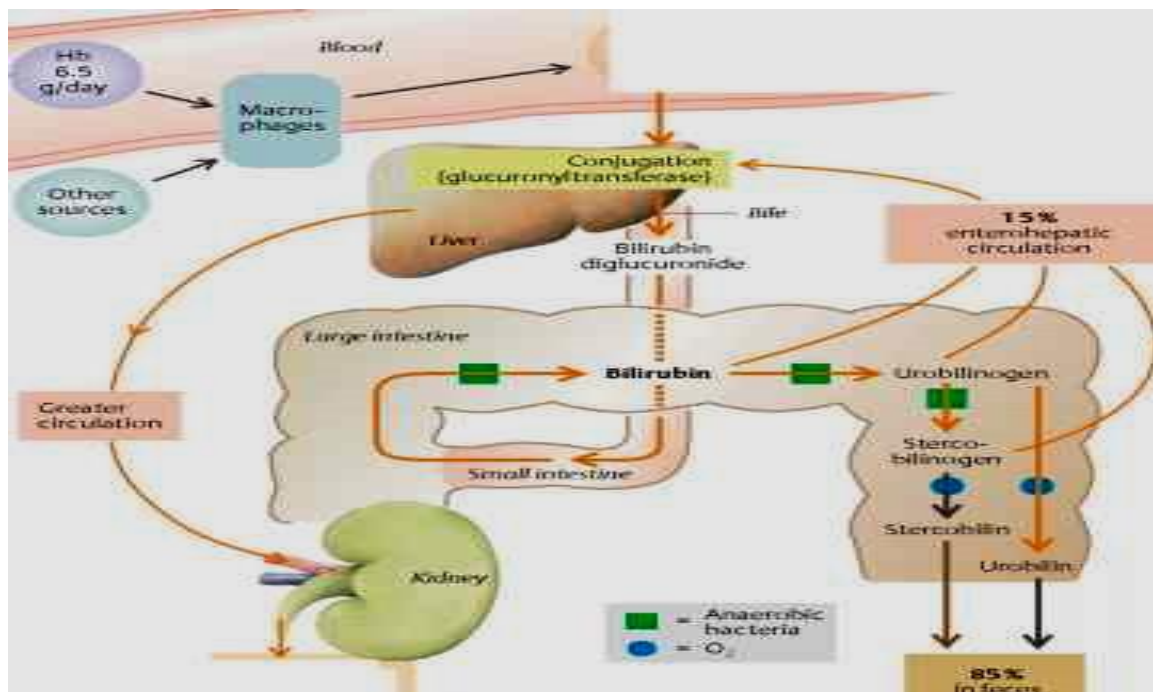
- **Fetal hemoglobin Hb F** ( $\alpha_2$  and  $\gamma_2$ ): presents in the fetus during the last seven months of development in the uterus. and replaced by adult Hb within 6 month after birth.
- **Adult hemoglobin Hb (Hb A)** consists of :
  - HbA ( $\alpha_2 \beta_2$ ) 95%
  - Hb A2 ( $\alpha_2 \delta_2$ ) 1.5- 3%
  - Very small amounts of Hb F ( $\alpha_2 \gamma_2$ )

## Recycling RBC

- At the end of erythrocytes life span, their constituents (Hb) are broken down (to **heme** and **globin**) and *reused to form new erythrocytes*.
- **Iron** released from heme is carried by **transferrin protein** into the blood and then to various tissues (bone marrow, liver)
- **Porphyrin** released from heme is converted into a yellow pigment called **bilirubin**.
- **Bilirubin** is insoluble (unconjugated form). It is taken by liver cells changed to soluble form (conjugated form) and excreted into bile.
- In the large intestine conjugated bilirubin is converted into **stercobilinogen** (by action of bacteria) and then into **stercobilin** which is responsible for brown color of feces
- Some **stercobilinogen** is absorbed into blood and excreted into urine which called **urobilinogen** exposure to air converts into **urobilin**.



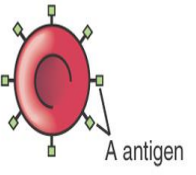





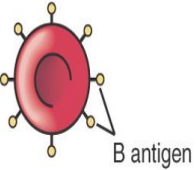

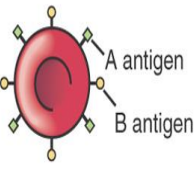










## Blood Groups

- The plasma membrane of erythrocytes are composed of lipids and proteins.

- Several types of proteins are present including A, B proteins (antigens) and Rh (D) factor responsible for person's blood group.
- Individuals make antibodies to these antigens but not to own type of antigen
- Persons of blood group A have antigen of type A on their red blood cells. Their serum contains antibodies of type B.
- Persons of blood group B have antigen of B on their red blood cells. Their serum contains antibodies of type A.
- Persons of blood group AB have antigens of both types A and B. they do not have type A or type B antibodies.
- Persons of blood group O have neither A nor B. antibodies of both types A and B are present.
- Rh factor or antigen (Rhesus factor), about 85% of people have this antigen on their own cell membrane of RBC.

Blood Type	Antigen (RBC membrane)	Antibody (plasma)	Can receive blood from	Can donate blood to	ABO Blood Groups				
A (40%)	 A antigen	Anti-B antibodies 	A, O	A, AB	Antigen (on RBC)				
B (10%)	 B antigen	Anti-A antibodies 	B, O	B, AB					
AB (4%)	 A antigen B antigen	No antibodies	A, B, AB, O	AB	Antibody (in plasma)				
O (46%)	 No antigen	Both Anti-A and Anti-B antibodies 	O	O, A, B, AB					
					Blood Type	Type A Cannot have B or AB blood Can have A or O blood	Type B Cannot have A or AB blood Can have B or O blood	Type AB Can have any type of blood Is the universal recipient	Type O Can only have O blood Is the universal donor

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## Leucocytes = White blood cells (WBC)

- Leucocytes are the largest blood cells.
- They account for only about 1% of the blood volume.

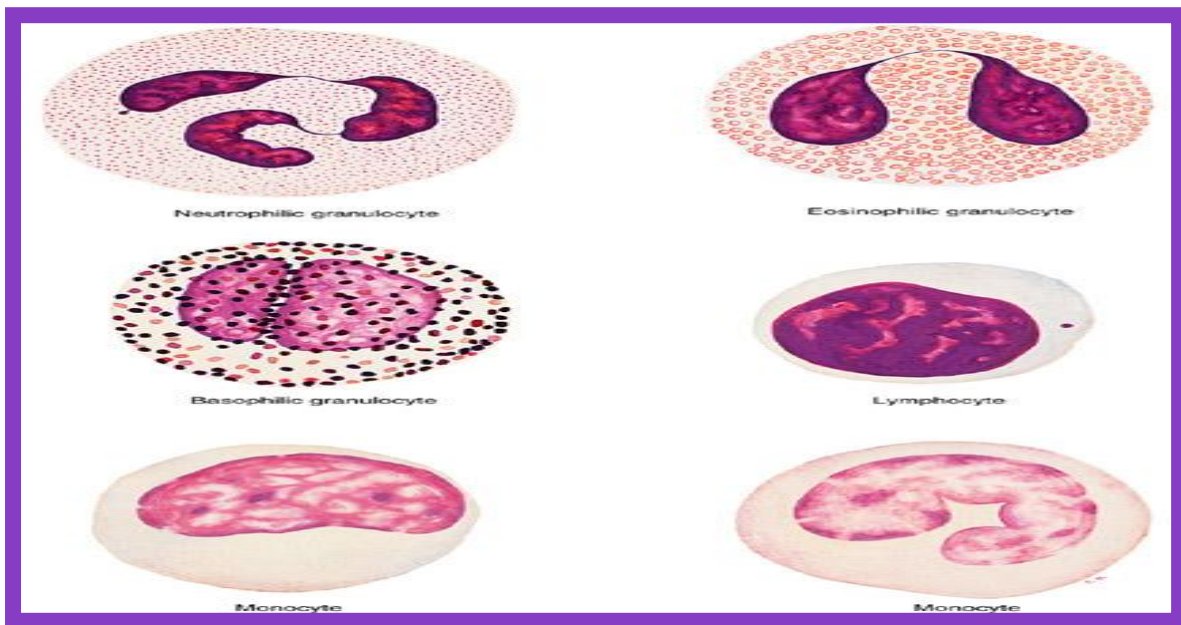
- **Leucocytes are different from erythrocytes in several ways:**

1. They are true cells, each leucocyte having a nucleus, mitochondria, and other organelles.
2. They do not contain Hb.
3. Leucocytes can actively move while erythrocytes do not have mobility of their own.
4. Normally erythrocytes do not leave the vascular system but leucocytes can leave vessels and enter the surrounding tissue.
5. Most leucocytes have a relatively short life span.

### **Types of WBC**

- There are two main types:
  1. **Granulocytes** which contain granules in their cytoplasm and they *Neutrophils, eosinophils* and *basophils*.
  2. **Agranulocytes**
    - *Monocytes* and *lymphocytes*.
- There are about 7500  $\mu\text{l}$  (range 5000-10000  $\mu\text{l}$ ).
- **Neutrophils** represent **60-70%** of total WBC. And about **20-30% lymphocytes**. While **eosinophils** are about **3%**, **basophils 1%** and **monocytes** about **5%**.

The 5 types of human leukocytes. Neutrophils, eosinophils, and basophils have granules that stain specifically with certain dyes and are called granulocytes. Lymphocytes and monocytes are agranulocytes; they may show azurophilic granules, which are also present in other leukocytes



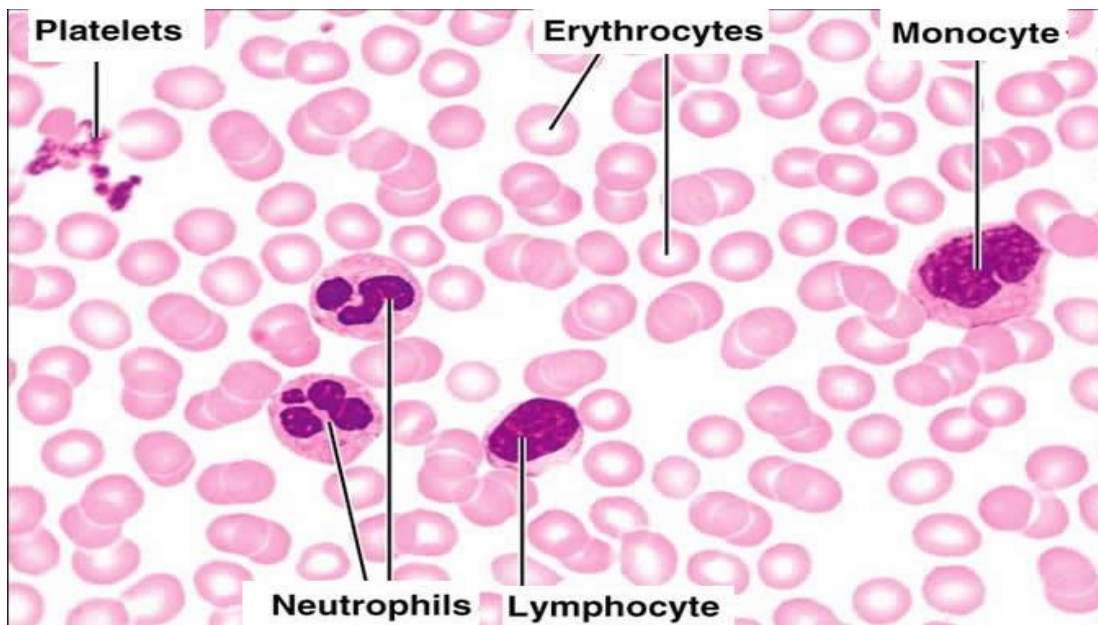
## Granulocytes

### 1. Neutrophil

#### Neutrophils (Polymorphonuclear leukocytes)

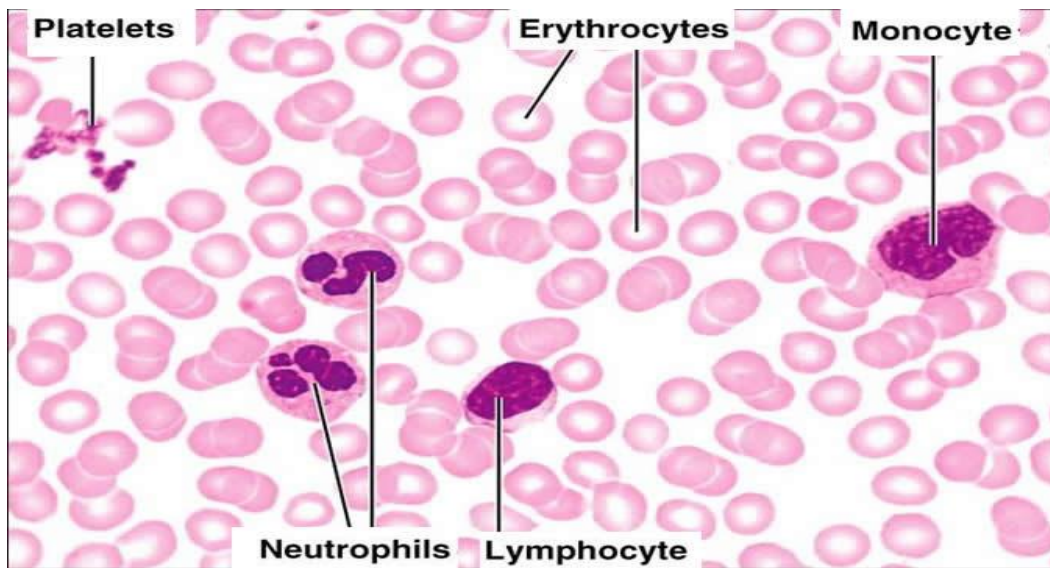
- Constitute 60-70% of circulating leukocytes.
- They are 12-15  $\mu\text{m}$  in diameter with nucleus consisting of 2-5 lobes.
- The cytoplasm of the neutrophil contains 2 main types of granules (**specific granules** and **azurophilic granules**).
- **Specific granules** are small granules and contain *alkaline phosphatase, collagenase, lactoferrin, lysozyme* and several *non enzymatic antibacterial proteins*.
- **Azurophilic granules** are lysosomes and contain *acid phosphatase,  $\alpha$ -monosidase, myeloperoxidase, lysozyme, cationic antibacterial proteins, collagenase, elastase, nucleotidase* and others.
- Neutrophils have short half life 6-7 hours in blood and 1-4 days in the tissues.
- Neutrophils have phagocytic activity against bacteria and other small particles.
- During phagocytosis, superoxide ( $\text{O}_2^-$ ) and hydrogen peroxide ( $\text{H}_2\text{O}_2$ ) are formed that kill microorganisms.
- Myeloperoxidase with  $\text{O}_2^-$  form a powerful killing system.
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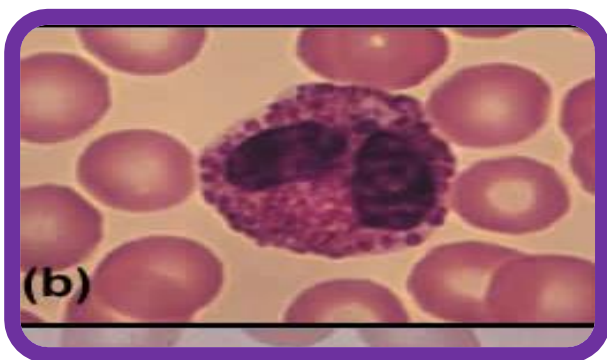


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## 2.Eosinophil



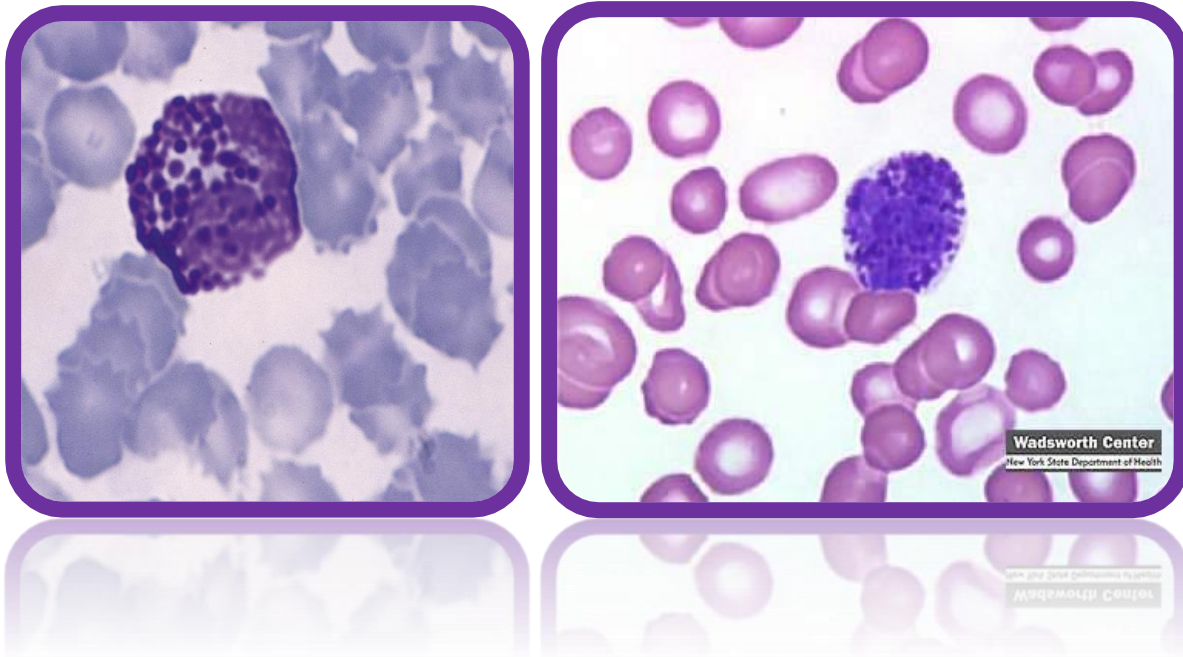
## 2-Eosinophils

- Eosinophils constitute 2-4% of leukocytes in normal blood.
- Life span in circulation is about 10 hours and 10 days in tissues.
- These cells have bilobed nucleus.
- The cytoplasm of eosinophil contains large granules that are stained by eosin.

- The granules contain many types of enzymes e.g. *peroxidase*, *RNAase*, *phospholipase*, and others, additionally the granules contain a protein called the **major basic protein**. This protein has ability to kill parasitic worm.
- An increase in the number of eosinophils in the blood is associated with **allergic reaction** and **parasitic infection**.

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### 3. Basophils

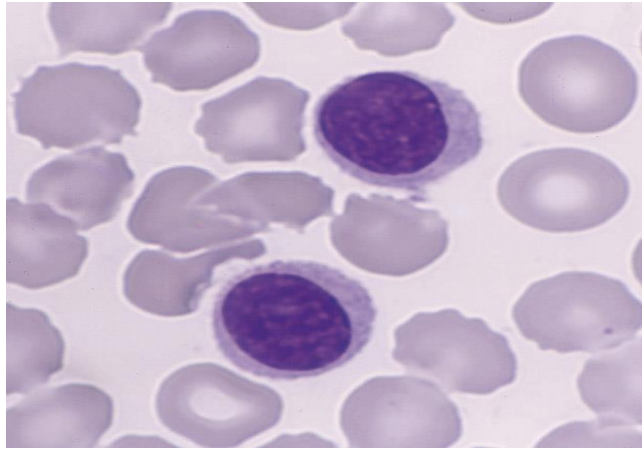


- Basophils make up less than 1% of blood leukocytes.
- There are about 12-15  $\mu\text{m}$ .
- The nucleus is divided into irregular lobes or S shaped.
- The cytoplasm contains very large granules that are stained with basic dye.
- The granules contain mainly **histamine** and **heparin**.

These cells play an important role in the **allergy**

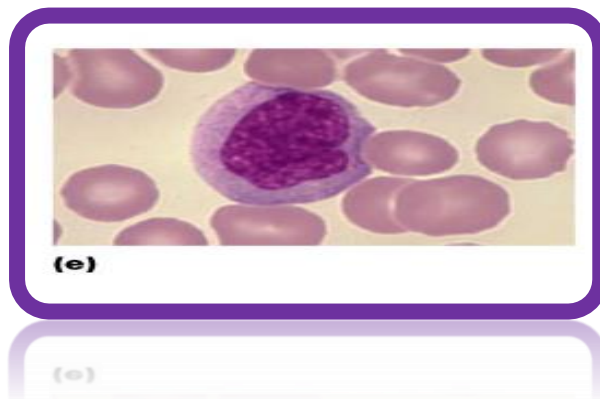
### Agranulocytes

#### 1. Lymphocyte



- Lymphocytes are spherical cells
- There are small lymphocytes with diameter of 6-8  $\mu\text{m}$  and large lymphocytes with diameter up to 18  $\mu\text{m}$ .
- The nucleus of lymphocyte are large and rounded.
- The cytoplasm of the small lymphocytes is scanty and in blood smear it appears as a thin rim rounded the nucleus. And it is slightly basophilic.
- Lymphocytes vary in life span; some live only a few days and other survive for many years.
- Lymphocytes are classified according to their function to; **B lymphocyte**, **T lymphocyte**, and **Natural Killer cell**.
- All types of lymphocytes are related to immune reactions in **defending against invading microorganisms, foreign macromolecules, and cancer cells**.
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## 2. Monocyte

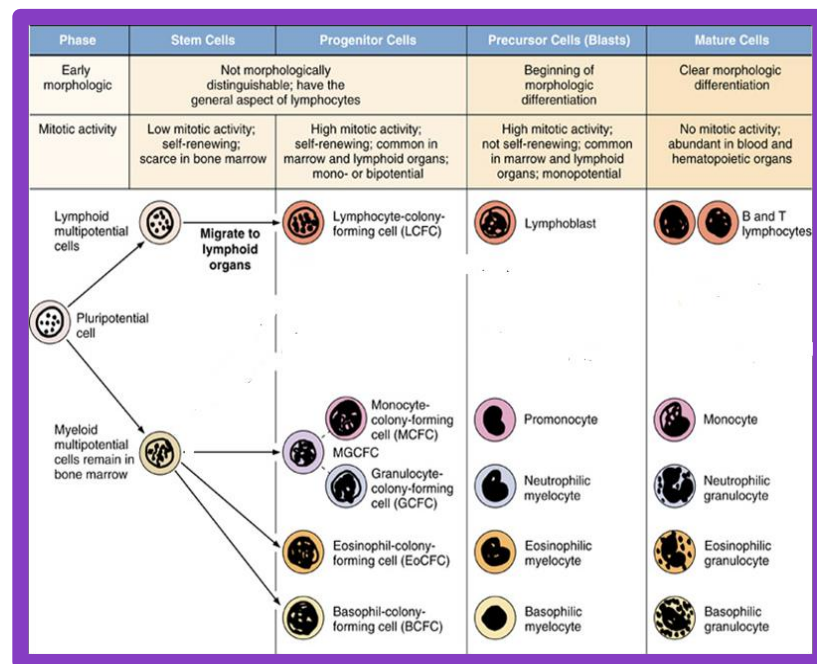


**Monocytes**



- These are the largest of the white blood cells.
- The nucleus is horseshoe- or kidney-shaped.
- The cytoplasm of monocyte is basophilic and contains very fine azurophilic granules (lysosomes).
- Blood monocytes migrate into the tissues and develop into macrophages.
- Macrophages engulf large particles and pathogens (large cell eater).
- The life span in the circulation is few days but 60-120 days in the tissues.
- They account 4-11%
- The main function monocyte is phagocytosis but also has ability to secret certain substances like interleukins e.g. interleukin 1 (IL-1).
- Macrophages have important functions in inflammation and immunity.

## Leukopoiesis



**Thrombocytes = Platelets**

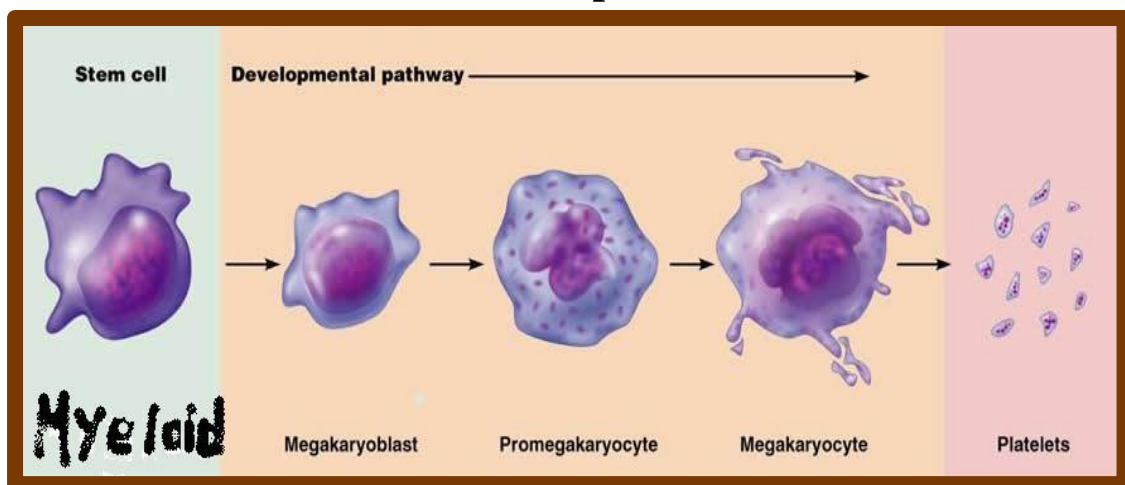


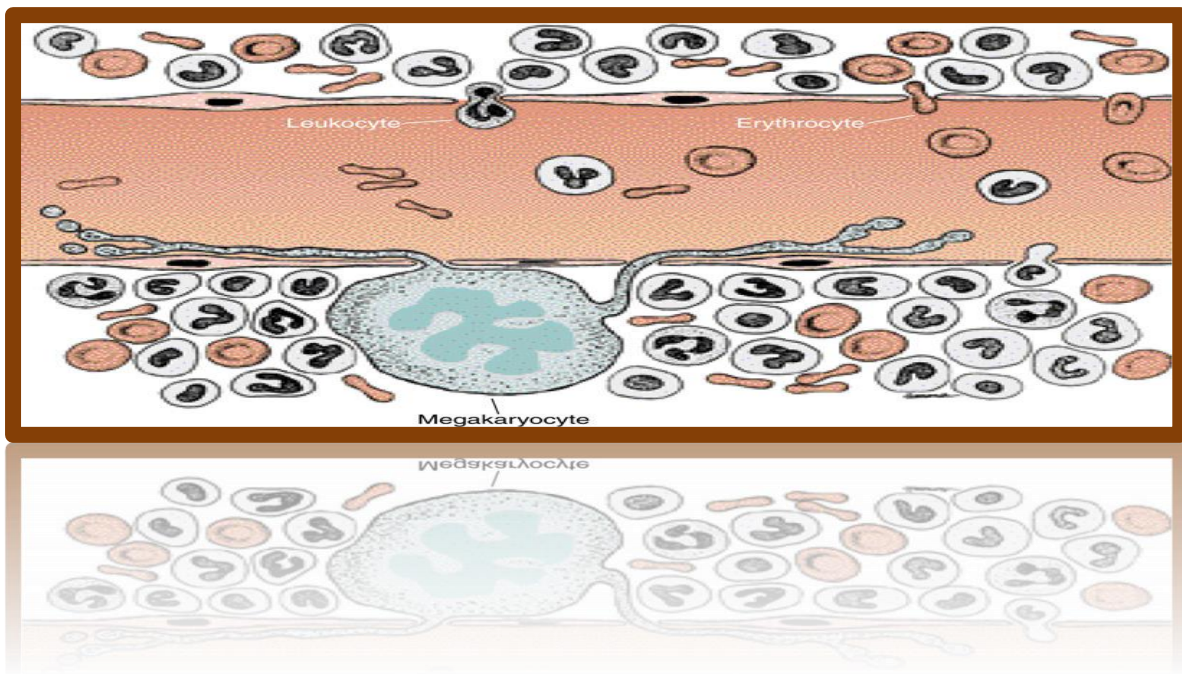
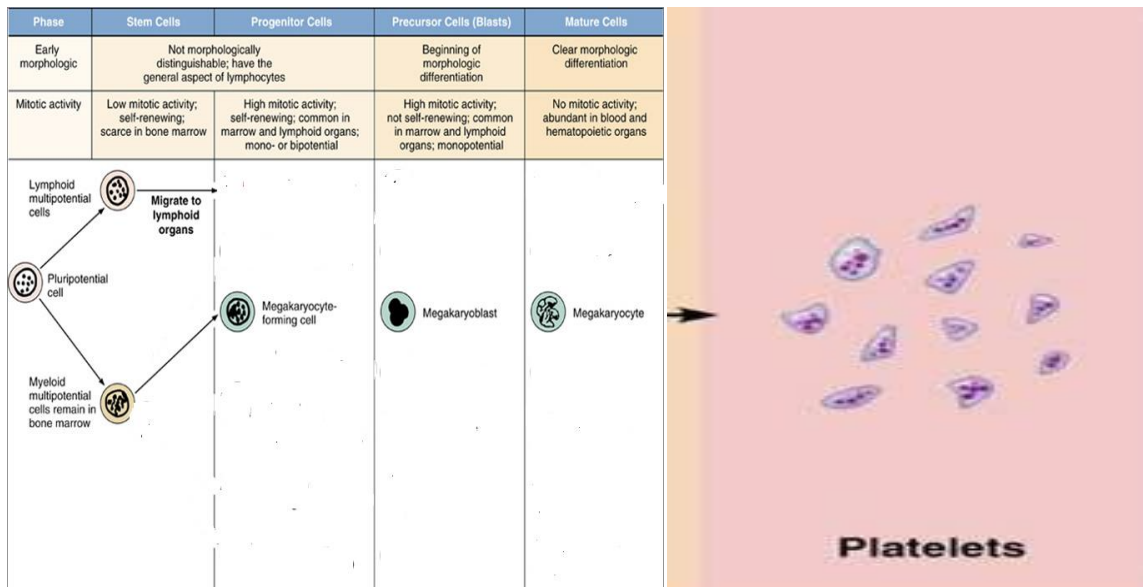
- Blood platelets are non-nucleated disc like cell fragments 2-4  $\mu\text{m}$  in diameter.  
Platelets are not true cells. They originate from fragments of megakaryocyte cytoplasm that reside in the red bone marrow.
- Each platelet has a peripheral light blue stain transparent zone the hyalomere and a central zone containing granules called the granulomere.
  - Platelets granules contain calcium ions, ADP, ATP, serotonin, pyrophosphate, hydrolytic enzymes, P- selectin, fibrinogen, platelet-derived growth factor, coagulation factor V and XIII and other substances.
  - Platelets are very sticky so appear under light microscope as clumps of cells.
- Platelets promote blood clotting and help repair gaps in the walls of blood vessels, preventing loss of blood.
- Normal platelets counts range from 200,000- 400000 per microliter of blood.

**Thrombopoietin** released by kidneys has ability to stimulate platelets synthesis.

- Platelets have a life span of about **10 days**.
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### Thrombopoiesis





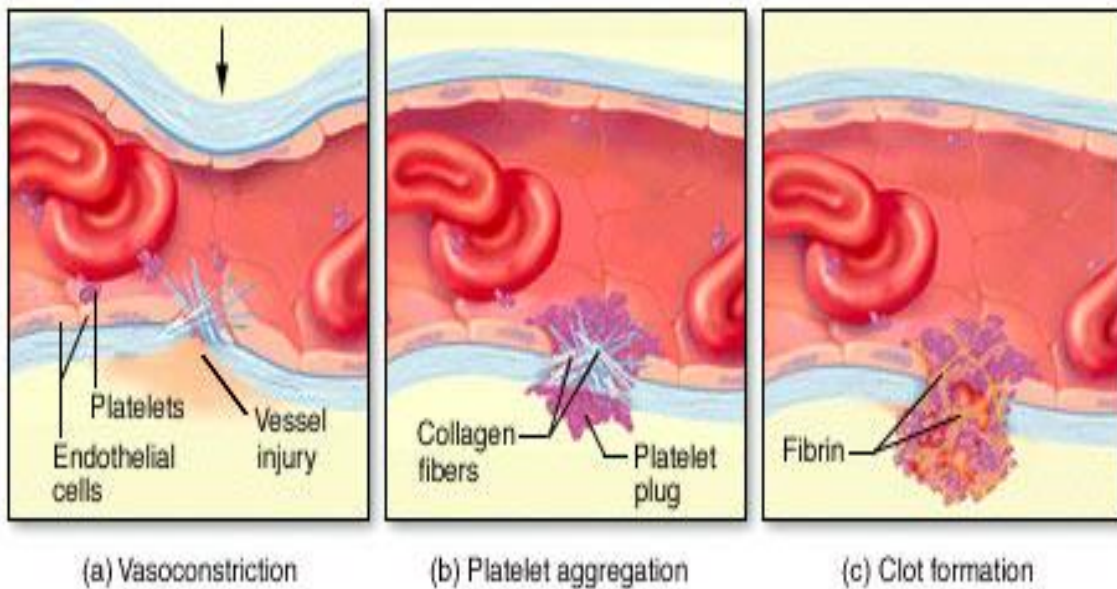
Drawing showing the passage of erythrocytes, leukocytes, and platelets across a sinusoid capillary in red bone marrow. Because erythrocytes (unlike leukocytes) do not have sufficient motility to cross the wall of the sinusoid, they are believed to enter the sinusoid by a pressure gradient that exists across its wall. Leukocytes, after the action of releasing substances, cross the wall of the sinusoid by their own activity. Megakaryocytes form thin processes that cross the wall of the sinusoid and fragment at their tips, liberating the platelets.

## Haemostasis= Hemostasis

### Steps of Haemostasis

1. Vascular spasm
2. Platelets plug formation
3. Coagulation (blood clotting)

Fibrynolysis

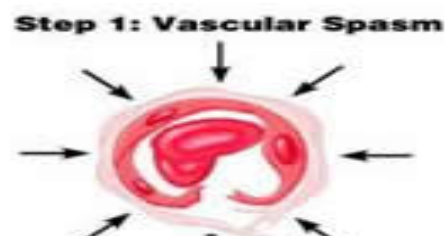
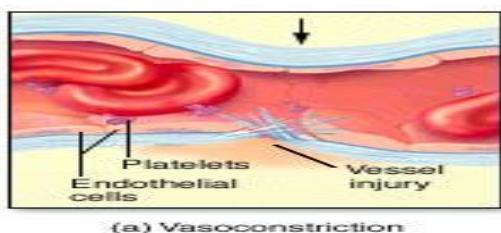


### 1. Vascular spasm

Cause by:

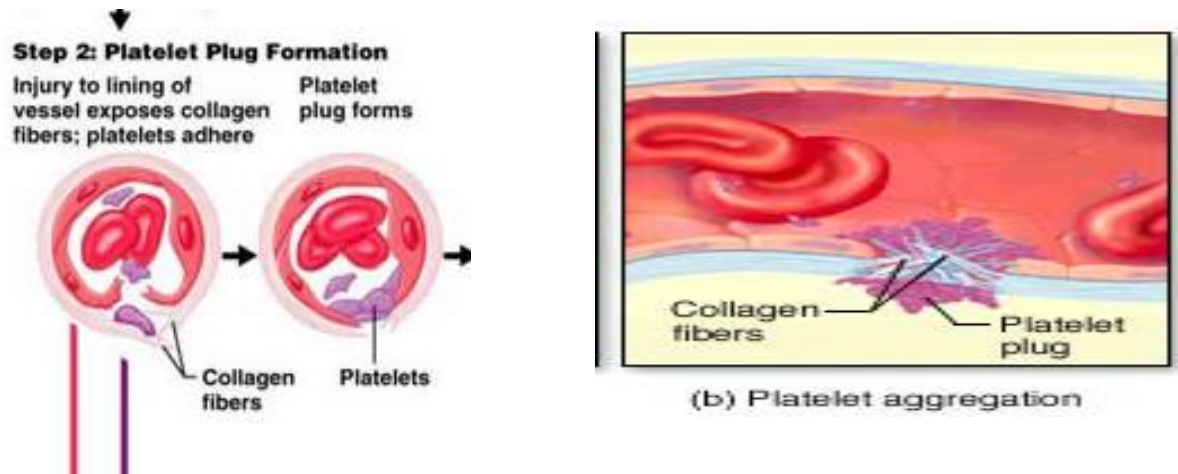
- **Direct injury** (vasoconstriction specially in the area where damage took place).
- **Chemical substances** (like **serotonin** produced by platelets that aggregate on damaged blood vessel and **thromboxanes** released by damaged vessel).

**Pain reflex**



## Platelets plug formation

1. **Primary aggregation:** discontinuities in the endothelium are followed by platelets aggregation to exposed collagen. Thus, a platelet plug is formed at a first step to stop bleeding.
2. **Secondary aggregation:** platelets in the plug release an adhesive glycoprotein and ADP. Both are potent platelet aggregation, increasing the size of the platelets plug.



## 3. Coagulation (blood clotting)

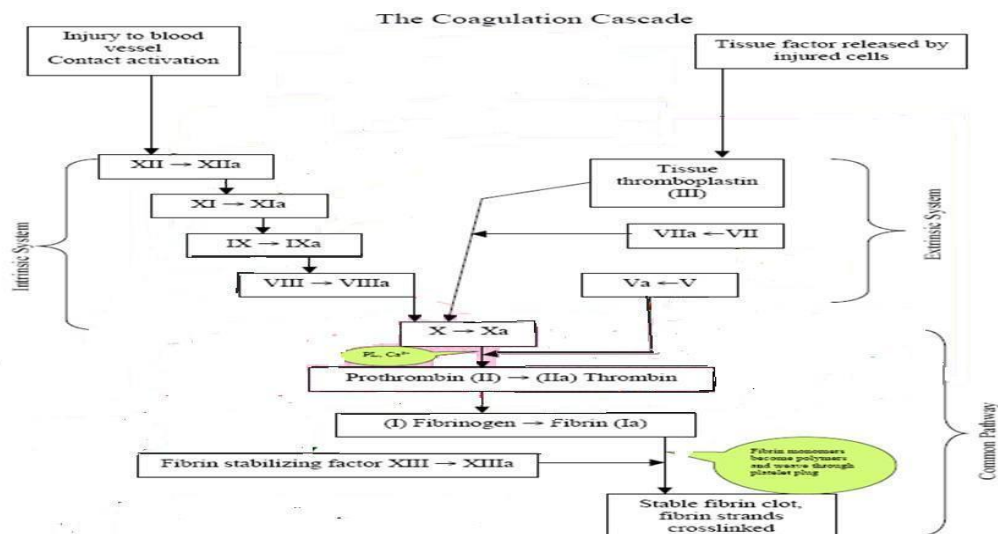
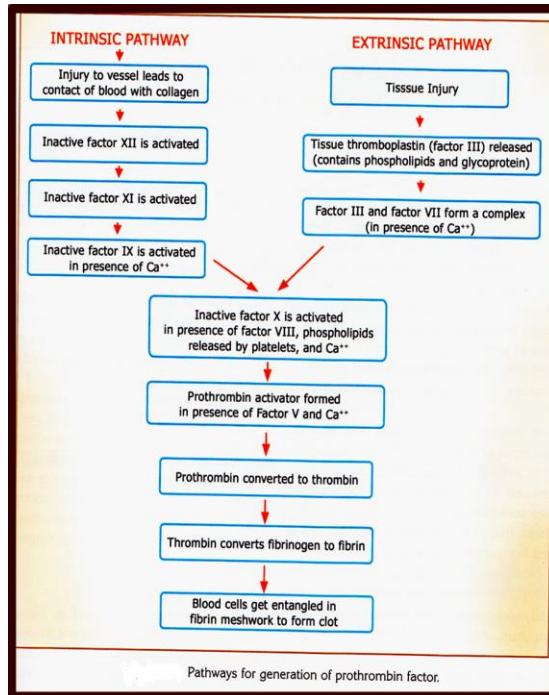
- Coagulation of blood is very important for stoppage of bleeding from an injured blood vessel. The process of coagulation is complex and involves many steps and many factors (most of which are proteins). The factors are identified by roman numerals (I – XIII), and also given names as shown in the next slide.
- These clotting factors activate each other in specific order resulting in the formation of **prothrombin activator**.
- **Prothrombin activator** is the first step in the *final common pathway* of blood coagulation.
- In the final common pathway, the prothrombin activator converts **prothrombin** (present in the plasma) to **thrombin** (an enzyme).
- Thrombin acts on the plasma protein **fibrinogen** and converts it into insoluble fibers of **fibrin** these fibers form a meshwork in which blood gets entangled to form a solid clot.



- The final common pathway can be initiated by two processes (pathways):

1. Extrinsic pathway occurs due to tissue damage.
2. Intrinsic pathway occurs due to damage to endothelial cells.

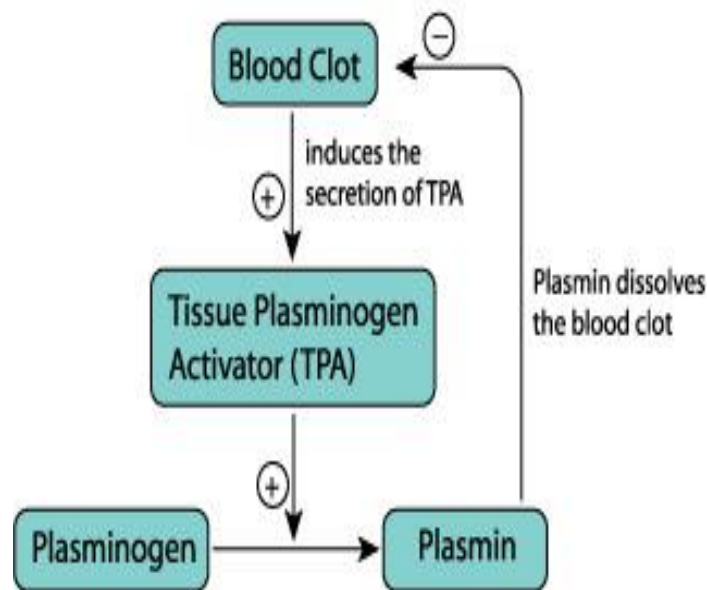
Each pathway consists of a number of steps that are shown in the next slides.





## Fibrinolysis

- After the clot has formed the process of removing it and healing the damaged blood vessel begins.
- Fibrinolysis (breakdown of the clot) is the first step of healing.
- Plasminogen is converted to the plasmin.
- Plasmin initiates the breakdown of fibrin to soluble.
- As the clot is removed the healing process restores the integrity of the blood vessel wall.



## Control of Coagulation

- The body control and limit the coagulation cascade; otherwise once started the clotting process would spread throughout the circulatory system. The main controls are:
  1. The perfect smoothness of normal endothelial cells of the blood vessel (means that platelets do not adhere to it).
  2. The presence of natural anticoagulants, e.g. heparin in the blood which inactivate clotting factors.