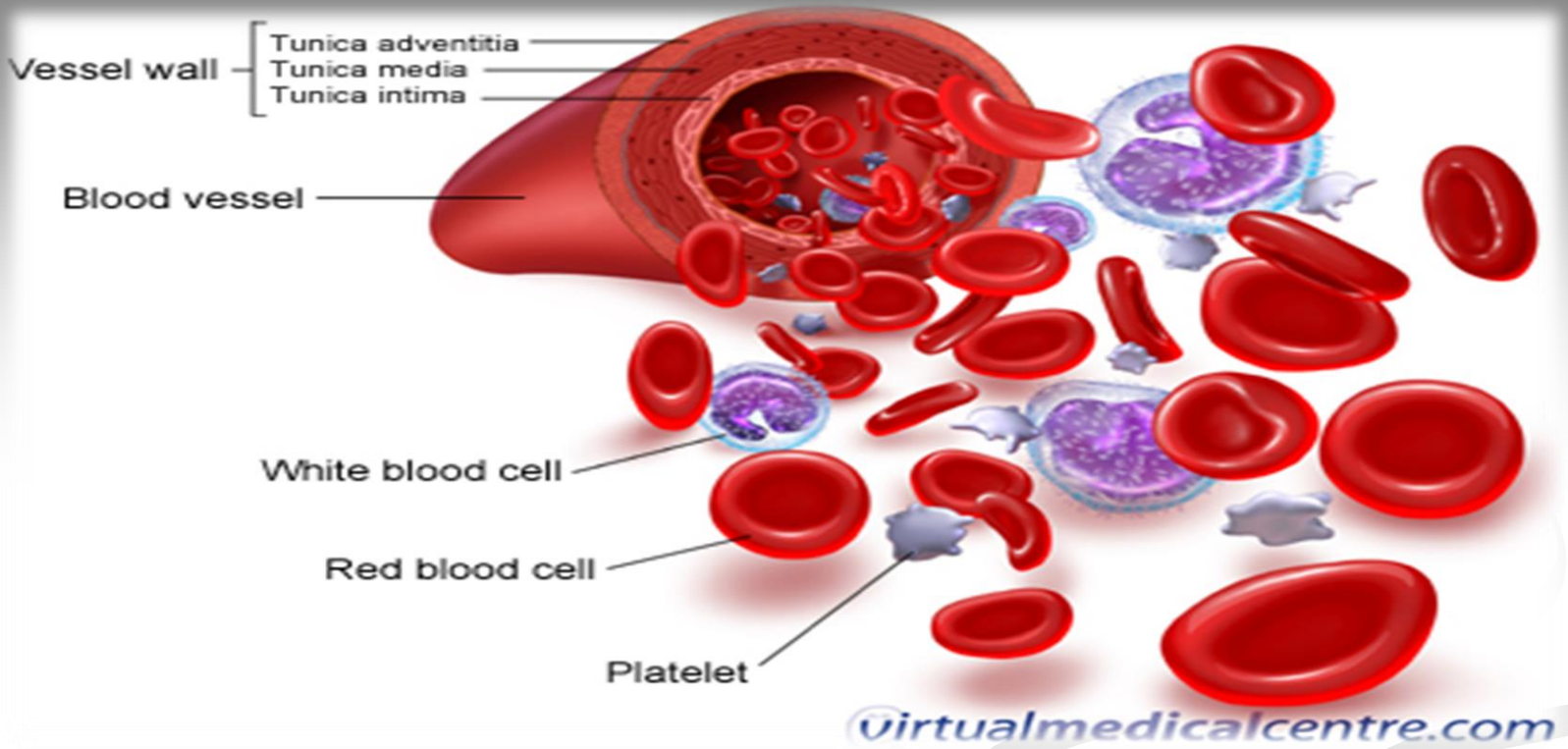


Blood

Esraa Keewan

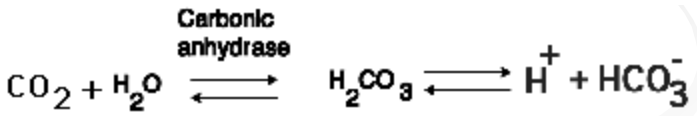
- Cells need a constant supply of O_2
- Co_2 must be removed continuously
- Cells can survive and function only within a narrow pH and temperature
- Cells must be protected against disease causing microorganism

Blood Contributes to Homeostasis

- Blood serving as vehicle for transporting materials to and from the cells
- Buffering change in pH
- Carrying excess heat to the body surface for elimination
- Play a major role in the body's defense system

Functions of the Blood

- Transportation:
  - Transports gases *O2/CO2*, nutrients, hormones and metabolic wastes
- Regulation
  - pH "Buffering" : 7.35 – 7.45
  - Body temperature

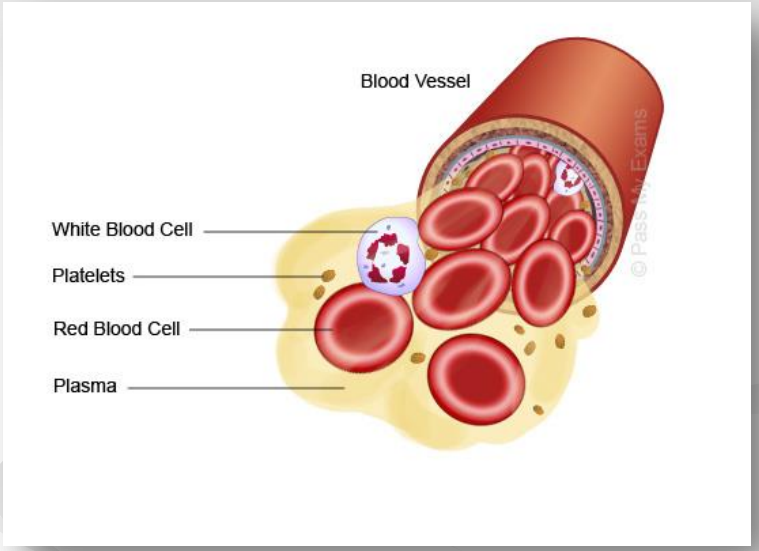


- Protection
  - Clot formation; minimize blood loss when a blood vessel is damaged
  - Protection against foreign substance

Blood

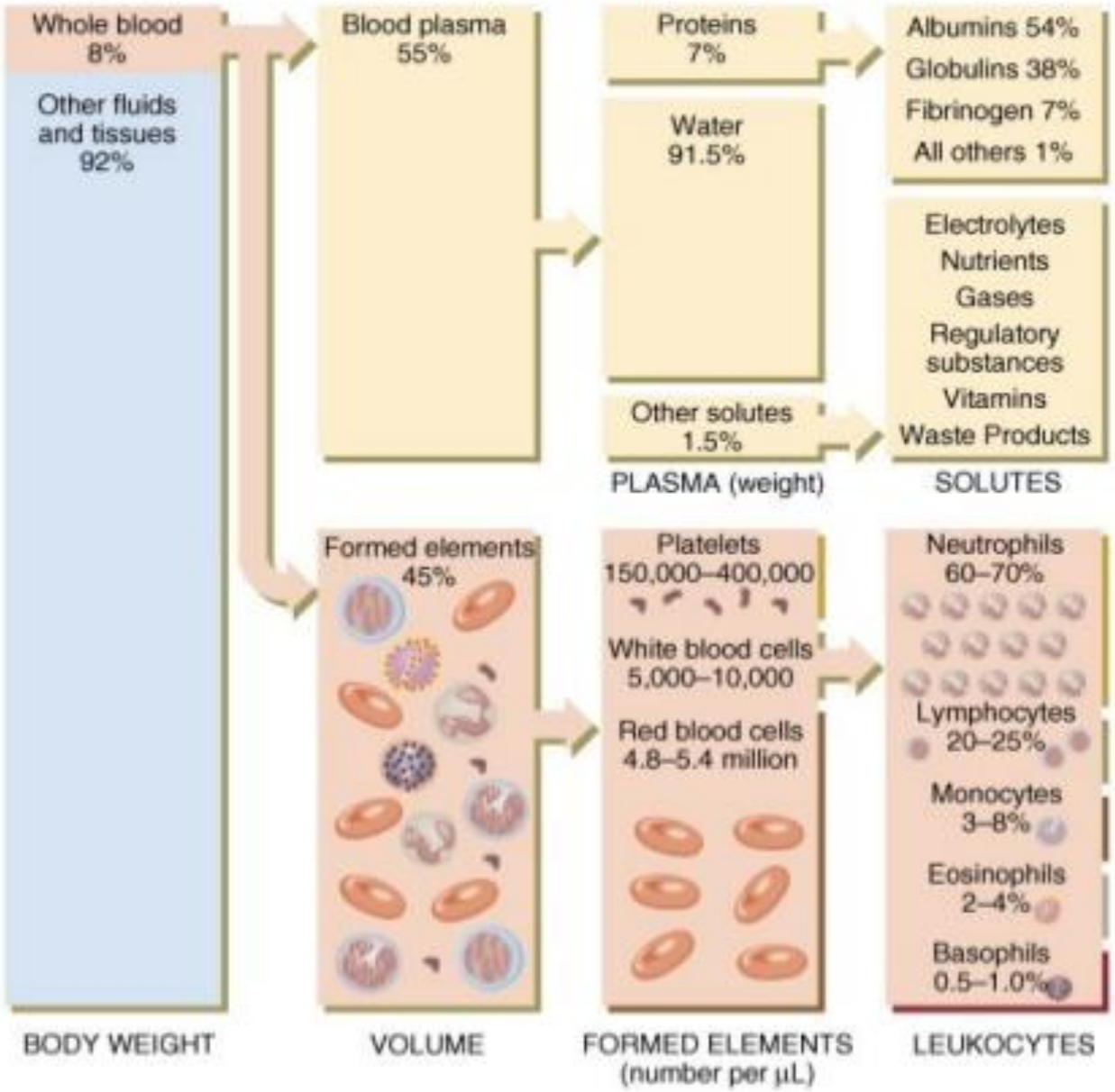
- Blood accounts for 8% of total body weight

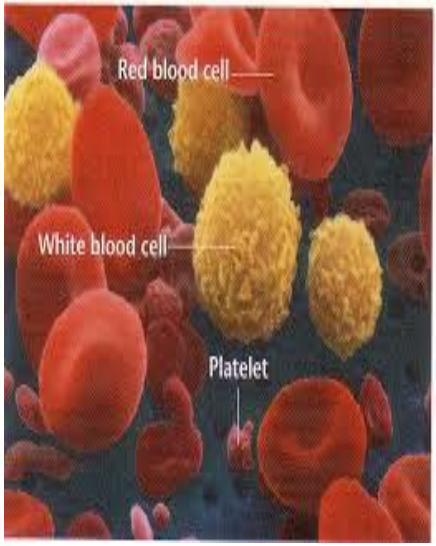
- Blood volume:
  - Males: 5 – 6 liters
  - Females: 4 – 5 liters



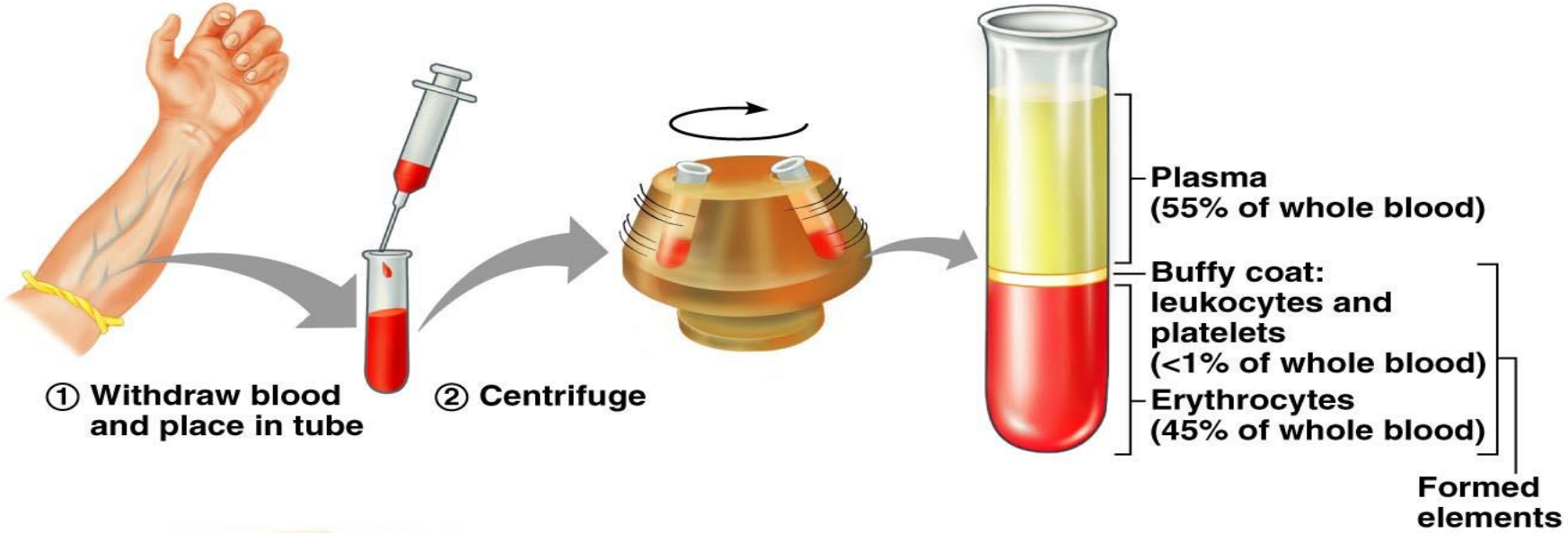
- Consists of cellular and liquid elements
  - Blood cells – formed elements
    - Erythrocyte (Red Blood Cells RBCs)
    - Leukocytes (White Blood Cells WBCs)
    - Thrombocytes (Platelets)
  - Plasma – fluid portion

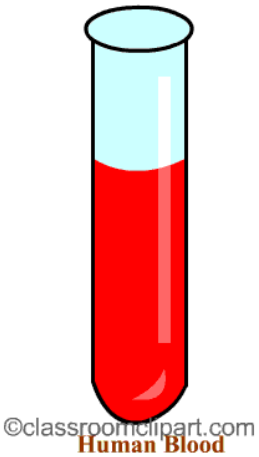
Blood component



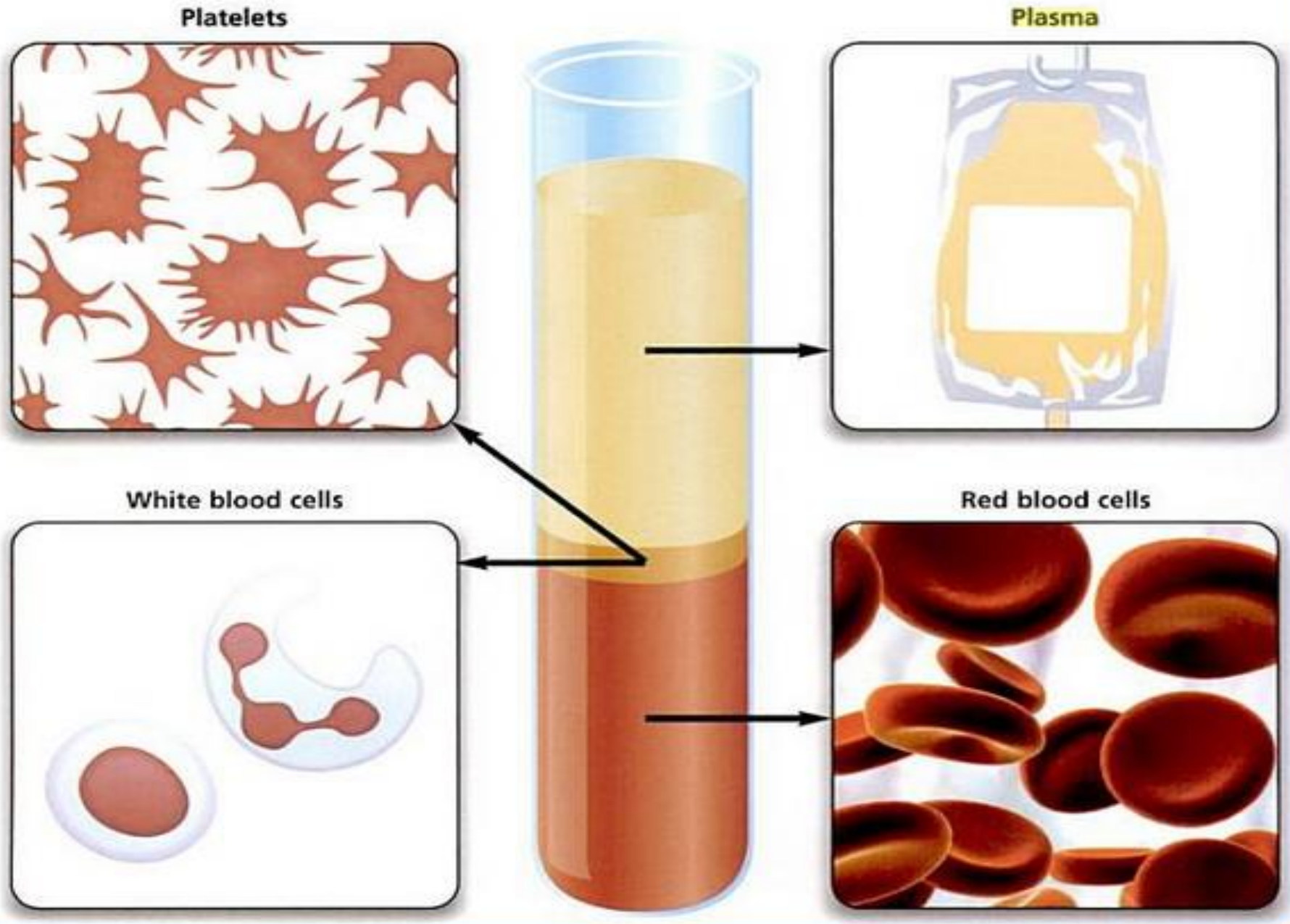


Composition of Blood



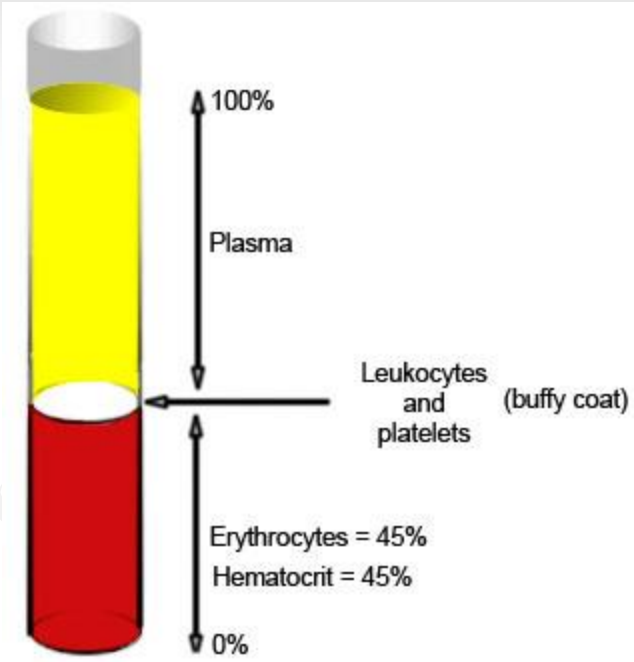


The Blood

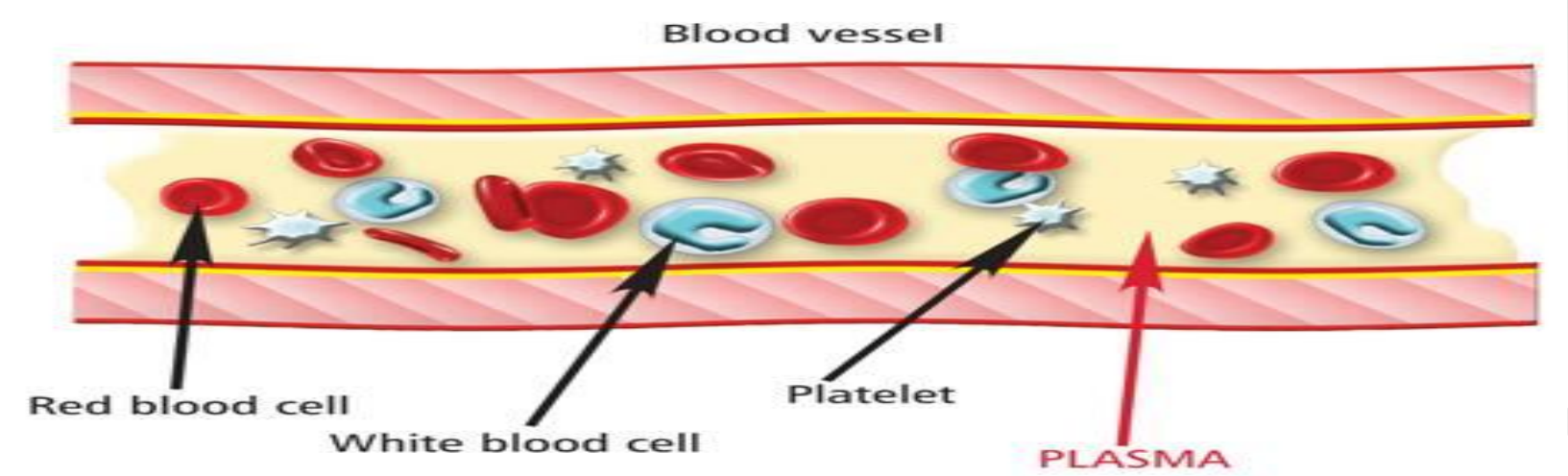


Hematocrit, Packed Cell Volume (PCV)

- (Hematocrit, packed cell volume PCV)– measure of % RBC in the total blood volume
  - Males: 47% ± 5%
  - Females: 42% ± 5%



Plasma
Liquid Element of the Blood



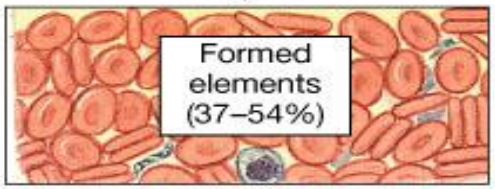
Plasma
Liquid Element of the Blood

Sample of whole blood

consists of

Plasma (46–63%)

+



Formed elements (37–54%)

PLASMA COMPOSITION	
Plasma proteins	7%
Other solutes	1%
Water	92%
Transports organic and inorganic molecules, formed elements, and heat	

PLASMA PROTEINS	
Albumins (60%)	Major contributors to osmotic pressure of plasma; transport lipids, steroid hormones
Globulins (35%)	Transport ions, hormones, lipids; immune function
Fibrinogen (4%)	Essential component of clotting system; can be converted to insoluble fibrin
Regulatory proteins (<1%)	Enzymes, proenzymes, hormones

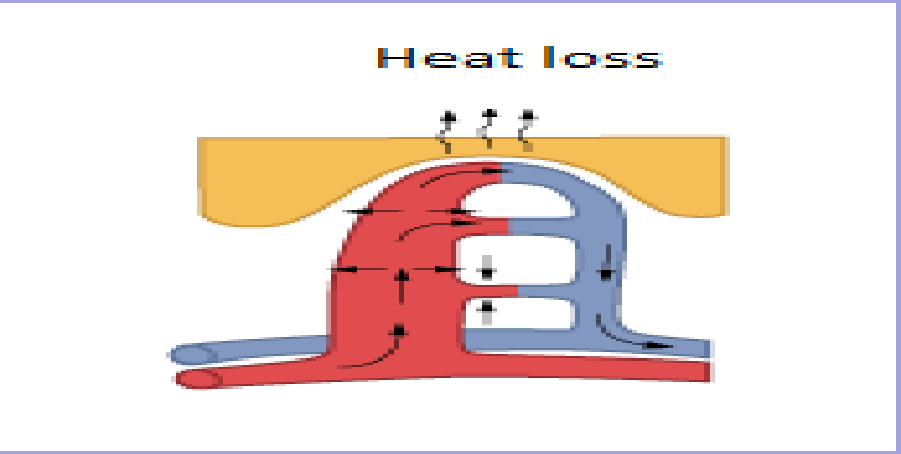
OTHER SOLUTES	
Electrolytes	Normal extracellular fluid ion composition essential for vital cellular activities. Ions contribute to osmotic pressure of body fluids. Major plasma electrolytes are Na^+, K^+, Ca^{2+}, Mg^{2+}, Cl^-, HCO_3^-, HPO_4^{2-}, SO_4^{2-}
Organic nutrients	Used for ATP production, growth, and maintenance of cells; include lipids (fatty acids, cholesterol, glycerides), carbohydrates (primarily glucose), and amino acids
Organic wastes	Carried to sites of breakdown or excretion; include urea, uric acid, creatinine, bilirubin, ammonium ions

(b)

Plasma

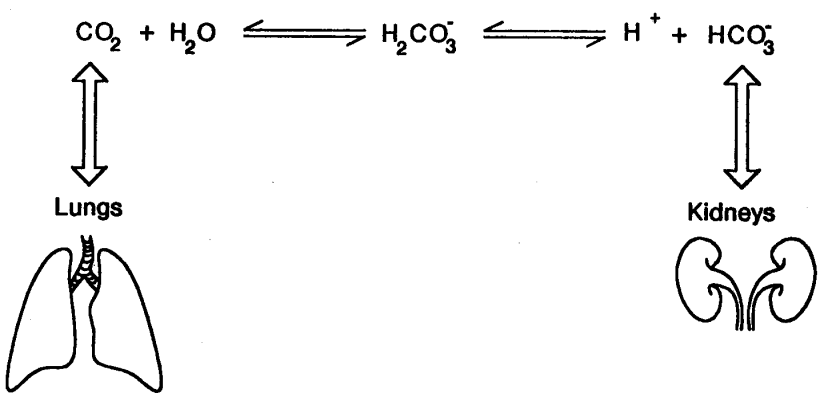
- plasma water:
  - 90% of plasma
  - Transport medium: for materials being carried in the blood

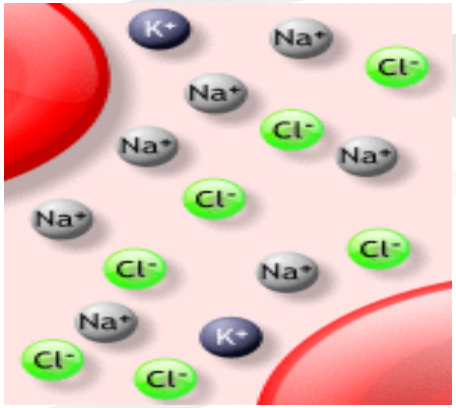
  - Carries heat: plasma absorb and distribute much of the heat generated metabolically within tissues, as blood travels close to the surface of the skin



Plasma

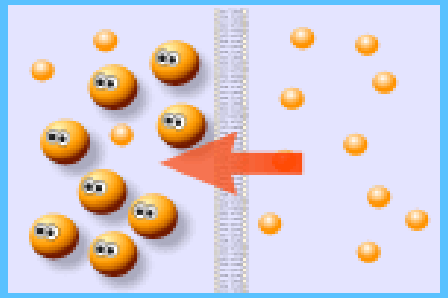
- Functions of electrolytes in the plasma:
  - Membrane excitability
  - Osmotic distribution of fluid between ECF and ICF
  - Buffering system (H2CO3 : HCO3 -)





Plasma

- Functions of proteins in the plasma:
  - Colloid osmotic effect to distribute fluid of ECF between plasma and ISF (force preventing excessive loss of fluid from capillaries into ISF so helps maintain plasma volume

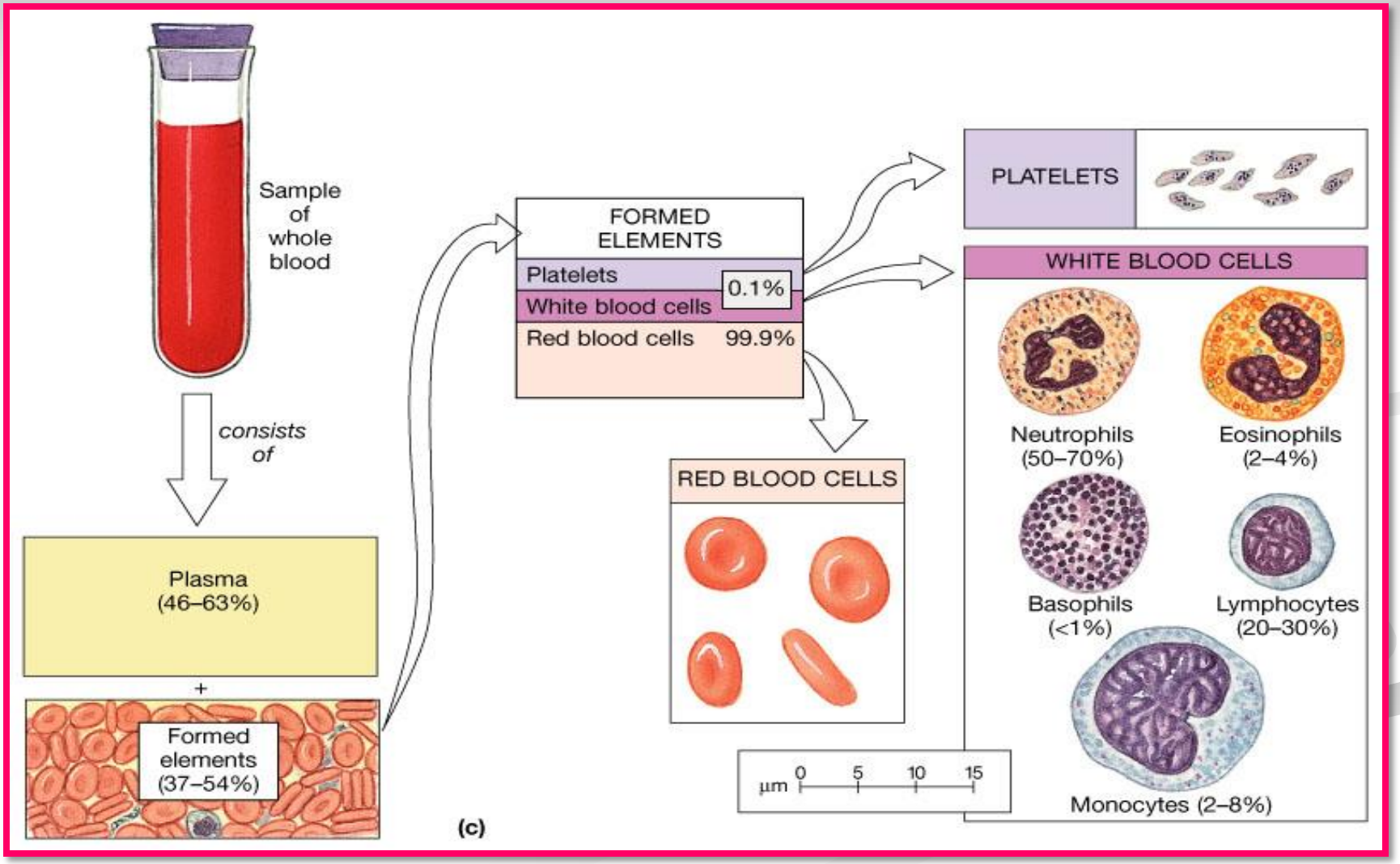


  - Buffering
  - Transport medium (transport substances that's poorly soluble in plasma ; thyroid hormone's, cholesterol and iron)
  - Clotting
  - Antibodies; gamma globulins

Formed Elements

- **Red blood cells (erythrocytes):**
- **White blood cells (leukocytes):**
  - Granulocyte:
    - Neutrophils
    - Eosinophils
    - Basophils
  - Agranulocyte:
    - Lymphocyte
    - Monocyte
- **Platelets (Thrombocyte)**

Composition of Blood



Erythrocytes – Red Blood Cells (RBCs)

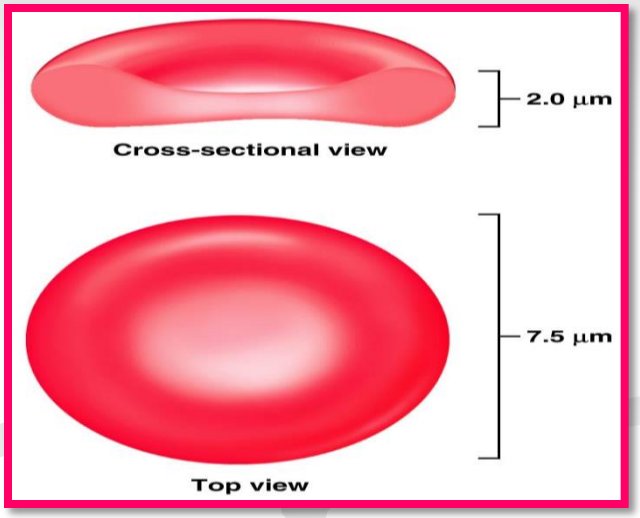
- Most numerous of the formed elements
  - Females: 4.3 – 5.2 million cells/cubic millimeter
  - Males: 5.2 – 5.8 million cells/cubic millimeter

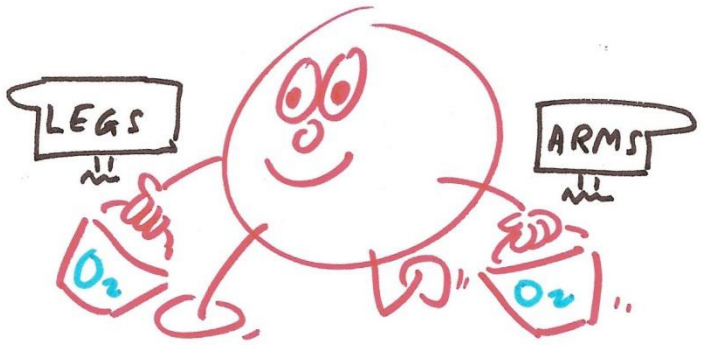
- Made in the red bone marrow in long bones, cranial bones, ribs, sternum, and vertebrae

- Average lifespan 100 – 120 days

RBC Structure

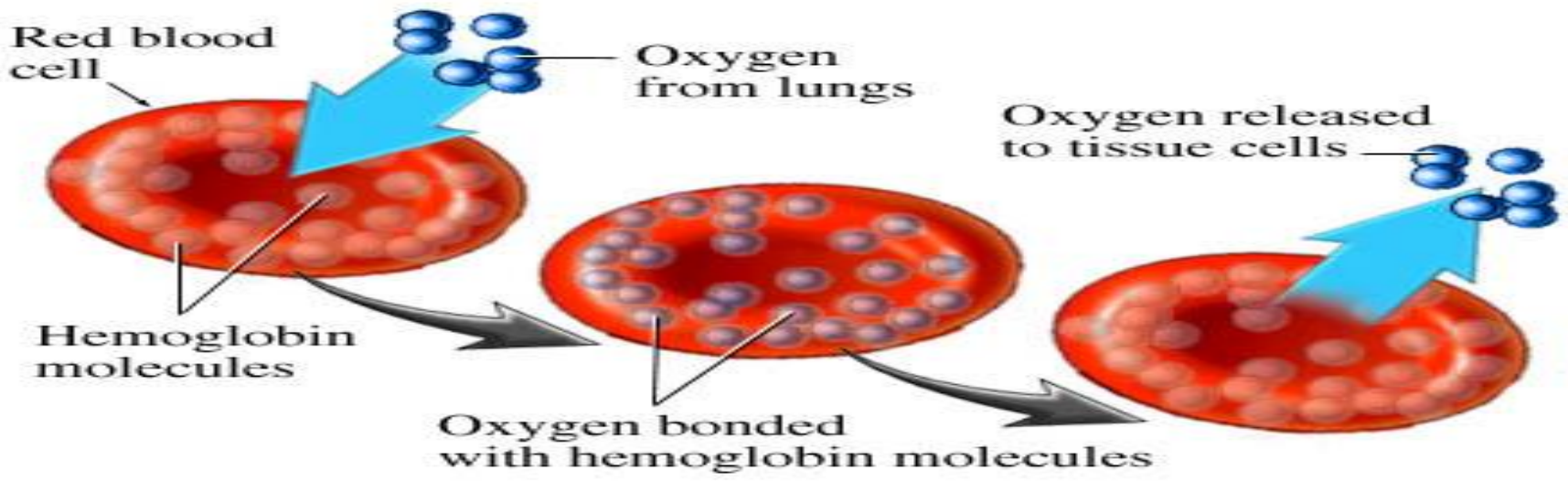
- Oxygen-transporting cells
  - 7.5 μm in diameter (diameter of capillary 8 – 10μm)
  - Biconcave shape – 30% more surface area
  - Have no organelles or nuclei
  - Contains **hemoglobin**





RBC Structure

- Primary Function = Transport oxygen from the lungs to the cells of the body & assist with CO_2 removal
- 98.5% of O2 carried in the blood is bound to hemoglobin (Oxyhemoglobin)
- 30 % of CO2 carried in the blood is bound to hemoglobin (carbamino hemoglobin)



Hemoglobin

- Hemoglobin – oxygen carrying protein
  Each RBC has about 280 million hemoglobin molecules

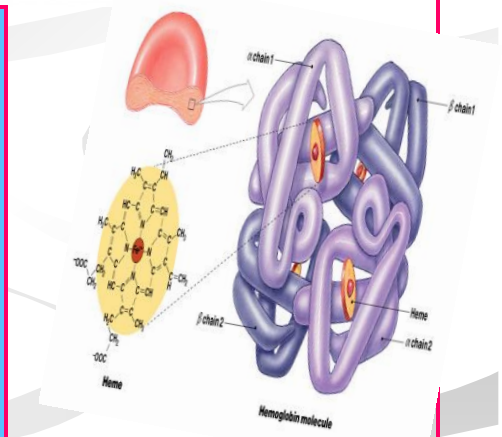
HEMOGLOBIN

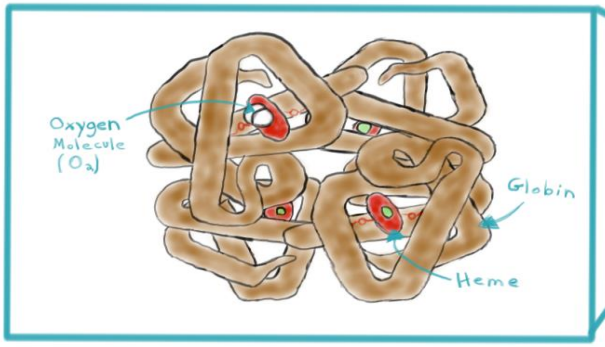
HEME=IRON

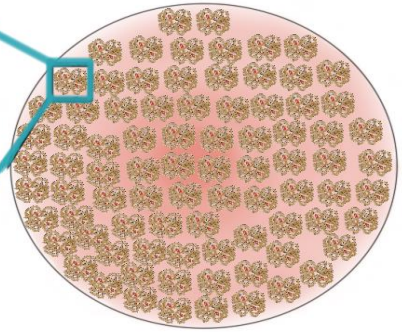
GLOBIN= PROTIEN

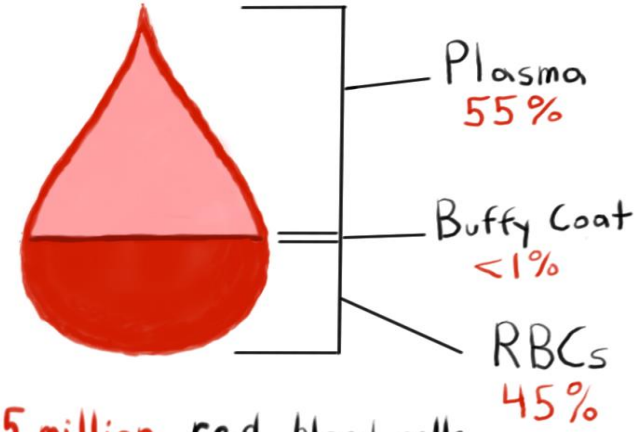
Heme= iron containing non- protein group (4 in one hemoglobin molecule, each one binds reversibly with one O2)

Globin : a protein (made up of 4 highly folded polypeptide chains)





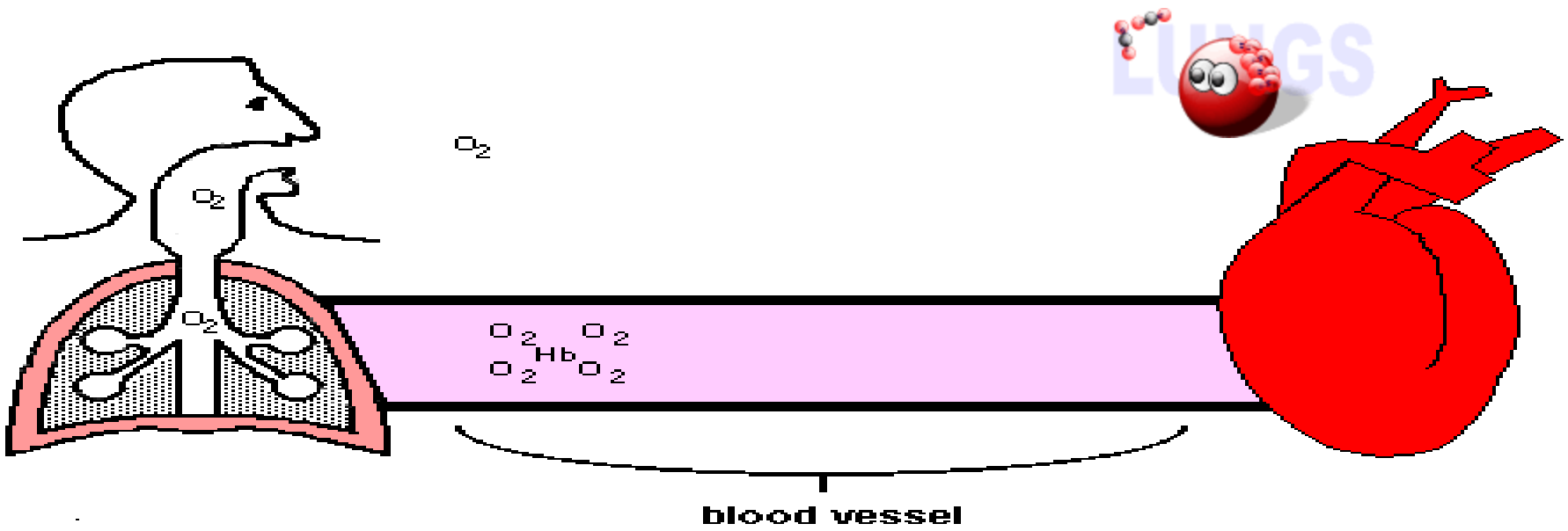




4 oxygen molecules in hemoglobin

250 million hemoglobins per red blood cell

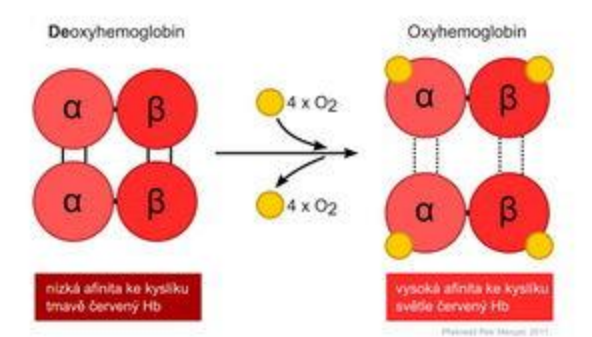
5 million red blood cells per drop of blood (1 mcL)

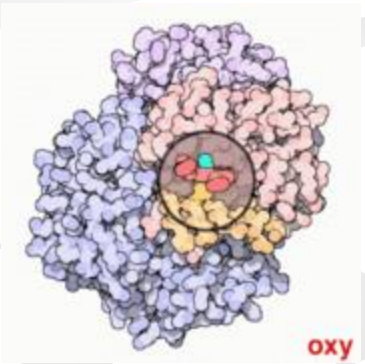


Hemoglobin

- Hemoglobin can bind to:
  - O2 ; reversibly:

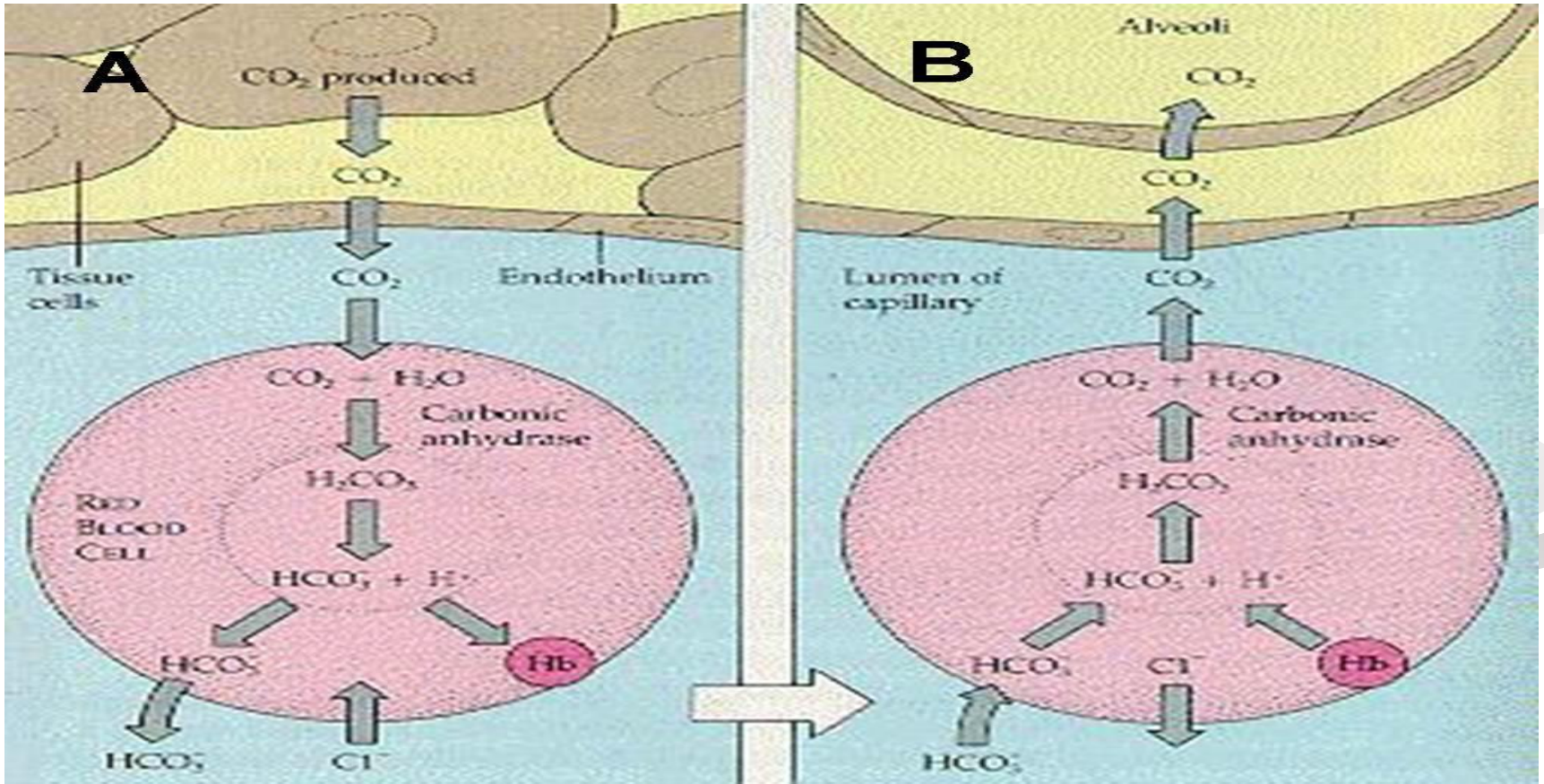
  transport it from lung to tissue (Heme)
  - CO2; reversibly: so transport it from tissue to lung (Globin)
  - H^+ ; reversibly
  - CO (toxic gas); irreversibly it has a huge affinity to bind to hemoglobin thus replacing O2
  - NO(vasodilator); reversibly: bind in the lung, released in tissues
    - Ensure that the O2 rich blood can make its vital round
    - Helps stabilize blood pressure





RBCs

- Contain large quantity of carbonic anhydrase which catalyze the reaction between water and CO2 to form carbonic acid (H2CO3)
- 60% of CO2 carried in the blood is transport as HCO3-

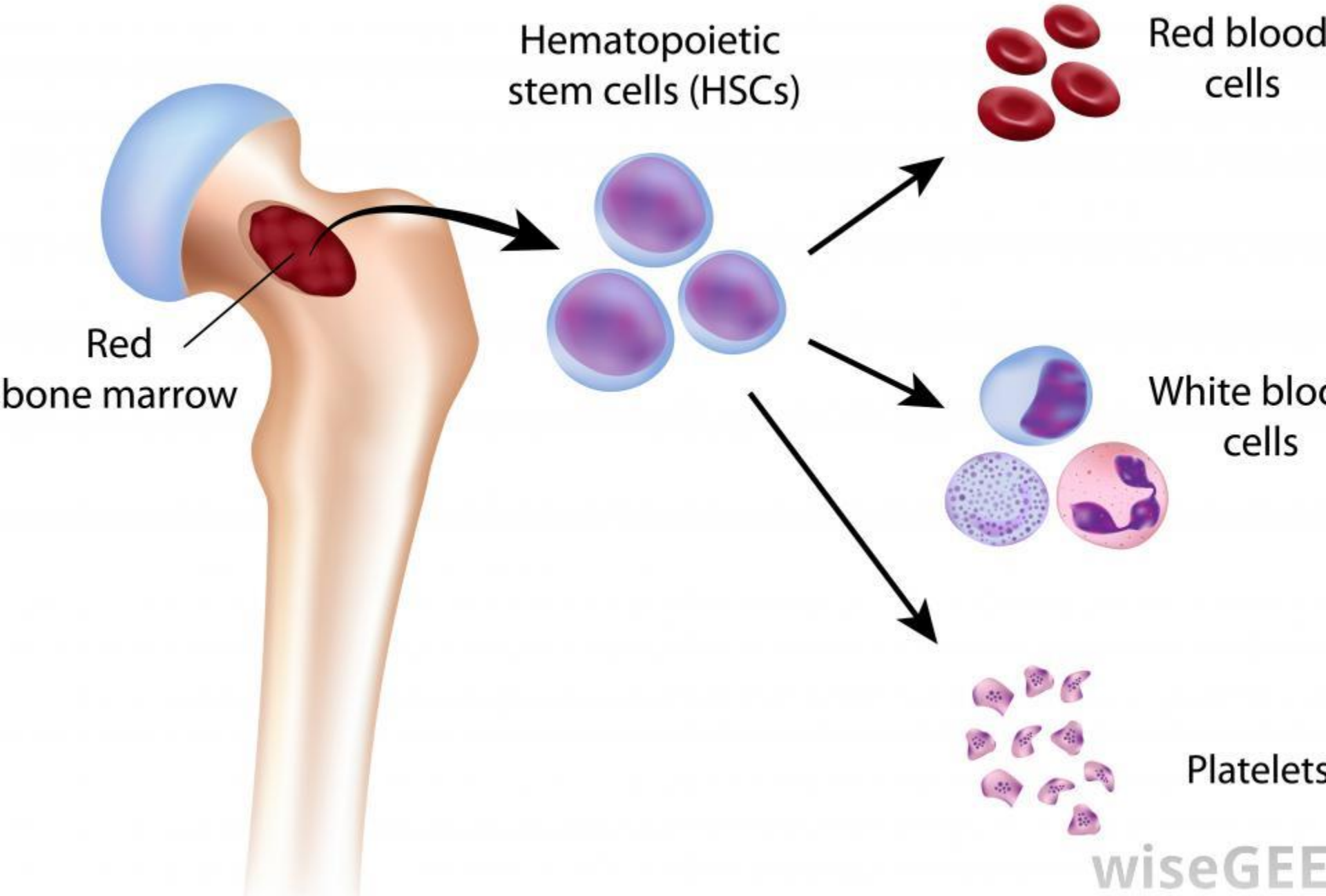


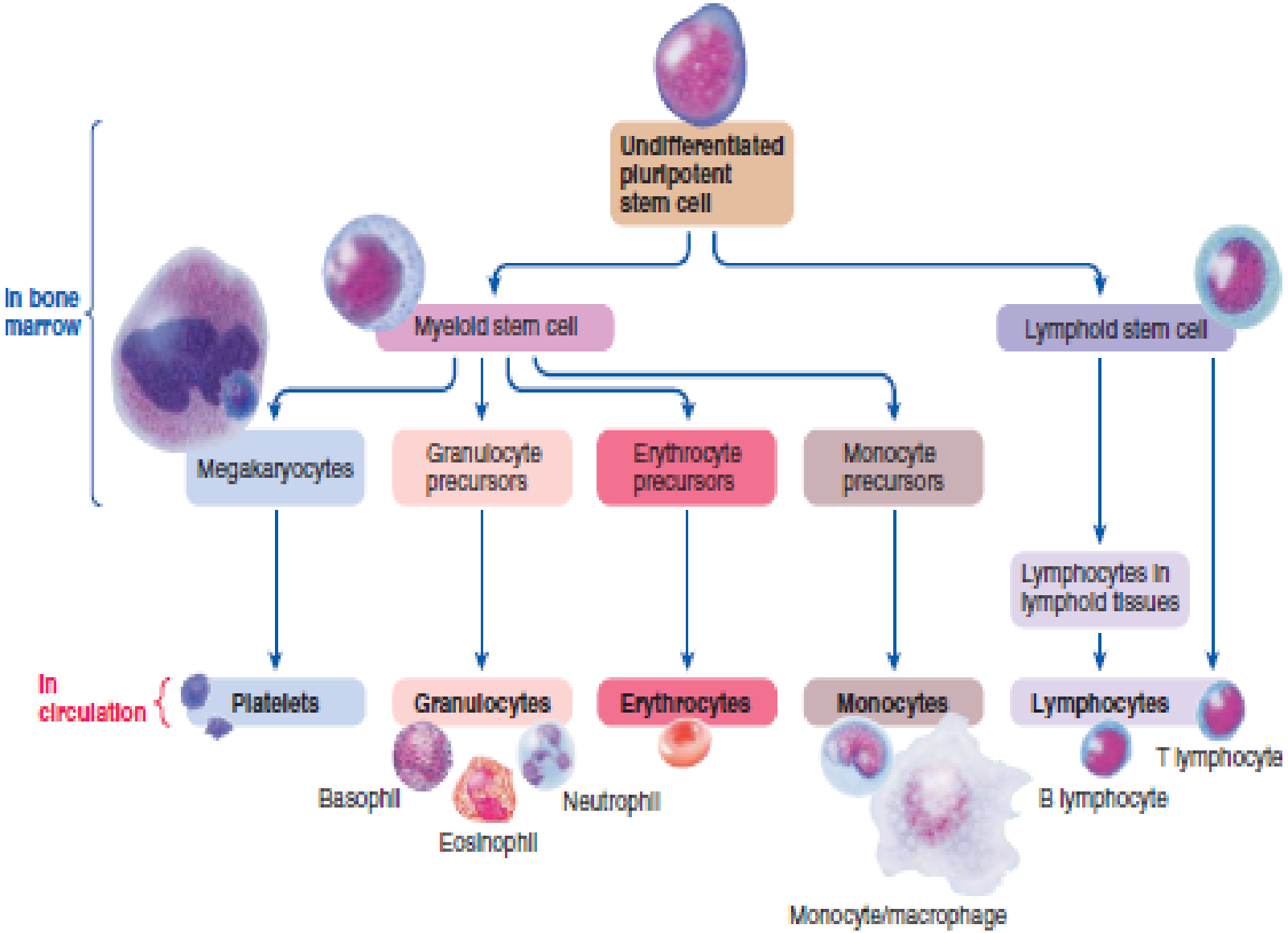
RBCs

- Lack intracellular organelles necessary for cellular repair, growth, division

- Short Life Span (~120 days)
  - Aged RBC
  - Fragile - prone to rupture
- Ruptured RBC's are destroyed in spleen
  - Phagocytic WBC's "clear the debris"

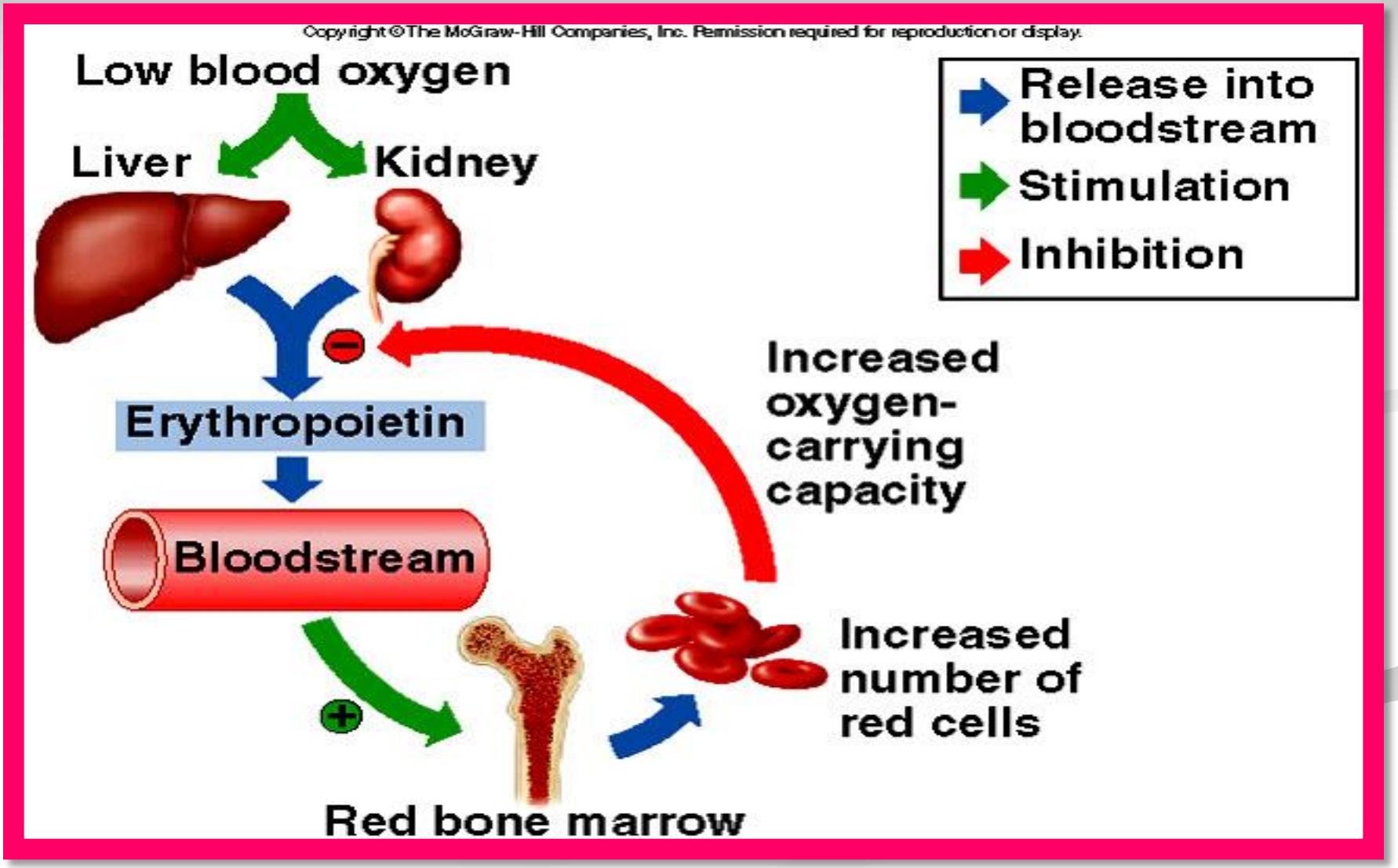
- New erythrocyte are produced in bone marrow by **ERYTHROPOIESIS**


Hematopoietic
stem cells (HSCs)
Red blood
cells
Red
bone marrow
White bloo
cells
Platelets



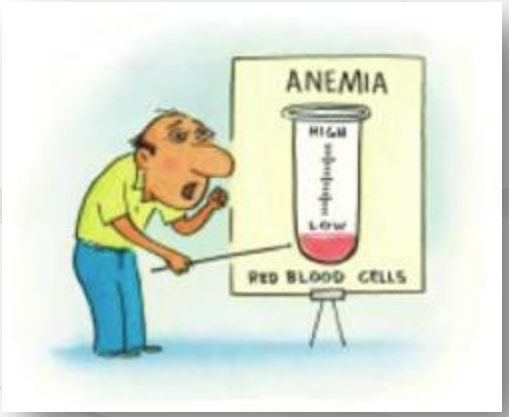
● **FIGURE 11-9 Blood cell production (hemopoiesis).** All the blood cell types ultimately originate from the same undifferentiated pluripotent stem cells in the red bone marrow.

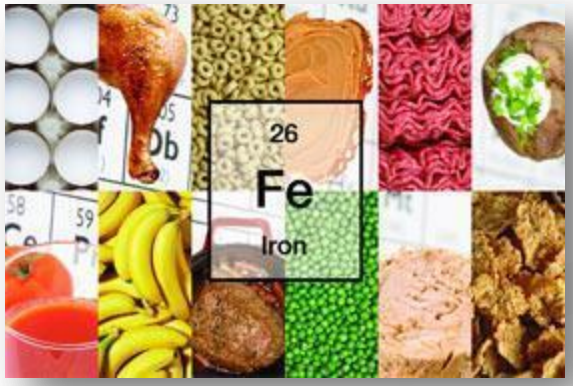
Control of Erythropoesis



Anemia
(below normal O2 carrying capacity
Low hematocrit)

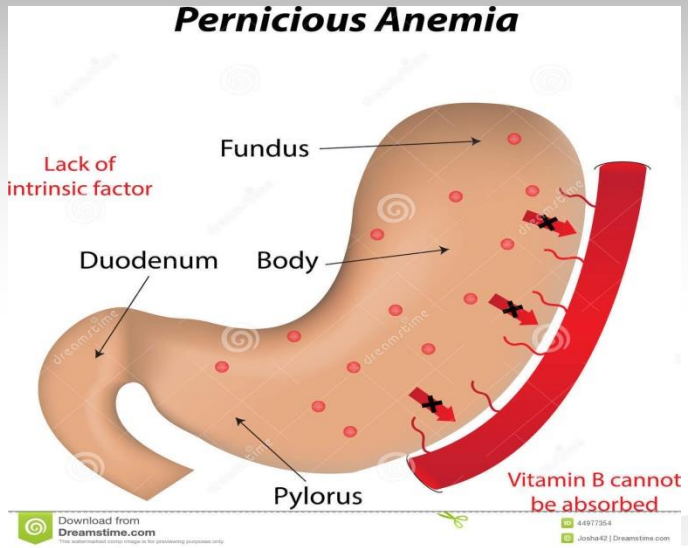
- Nutritional Anemia: caused by a dietary deficiency of a factor needed for erythropoiesis
  - Iron deficiency anemia occurs when not enough iron is available for synthesis of hemoglobin



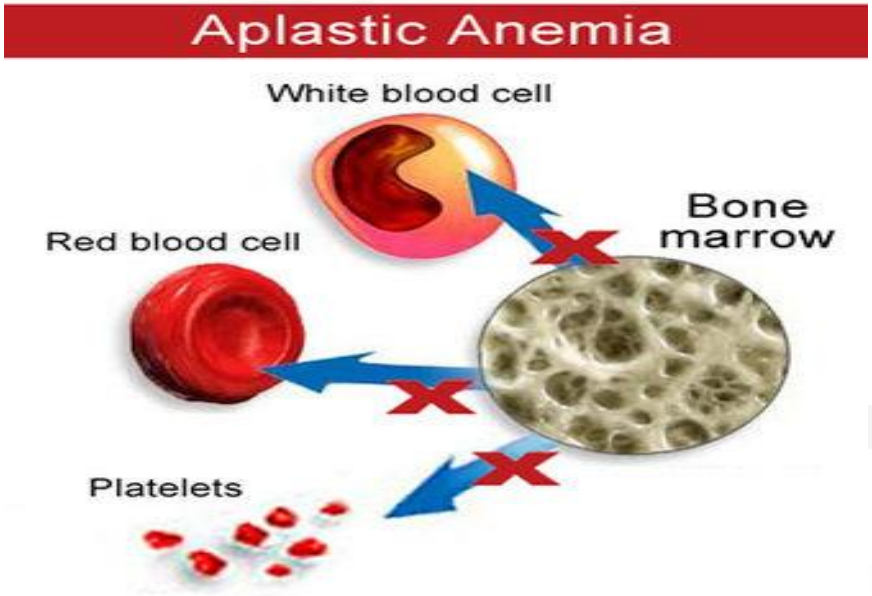


Anemia

- Pernicious Anemia: caused by inability to absorb enough ingested vitamin B12 from the digestive tract
  - Deficiency of intrinsic factor

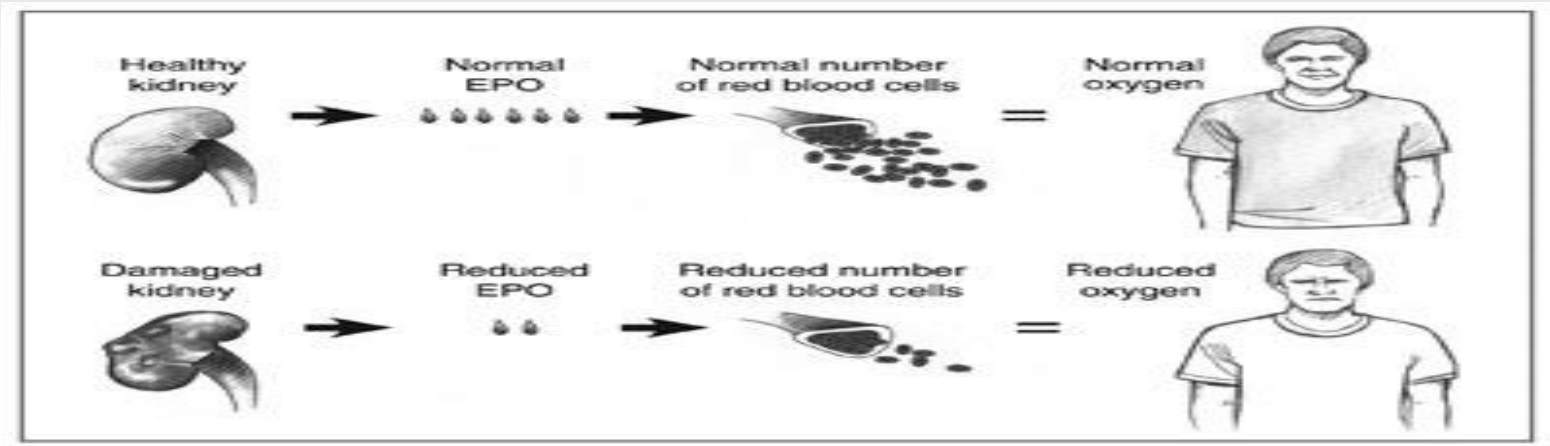


- Aplastic Anemia:



Anemia

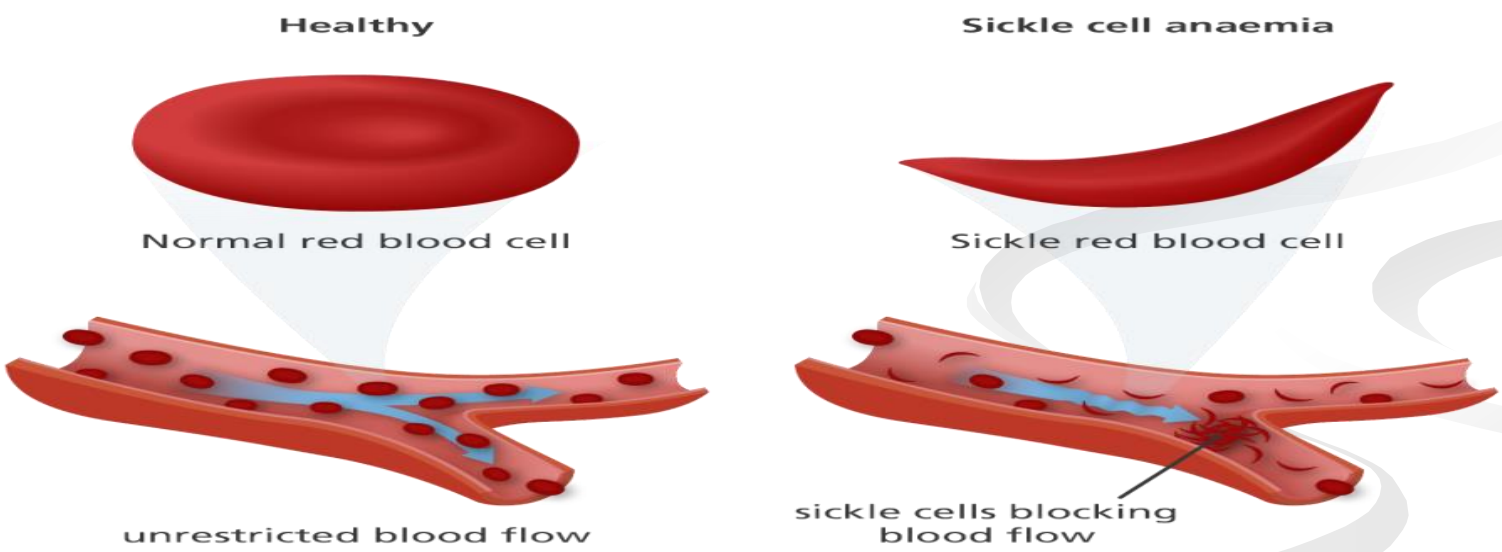
- Renal Anemia:



- Hemorrhagic anemia:

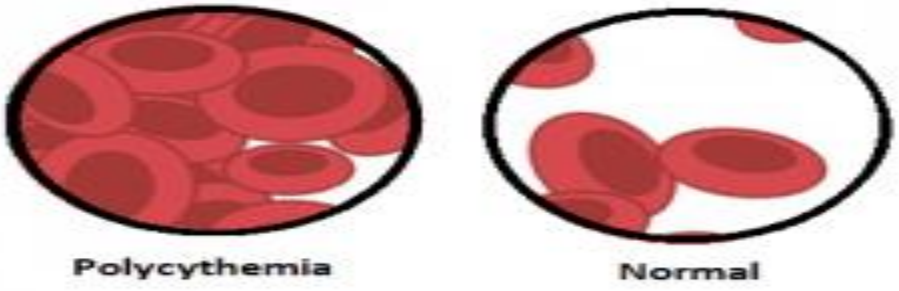
Anemia

- Hemolytic Anemia:



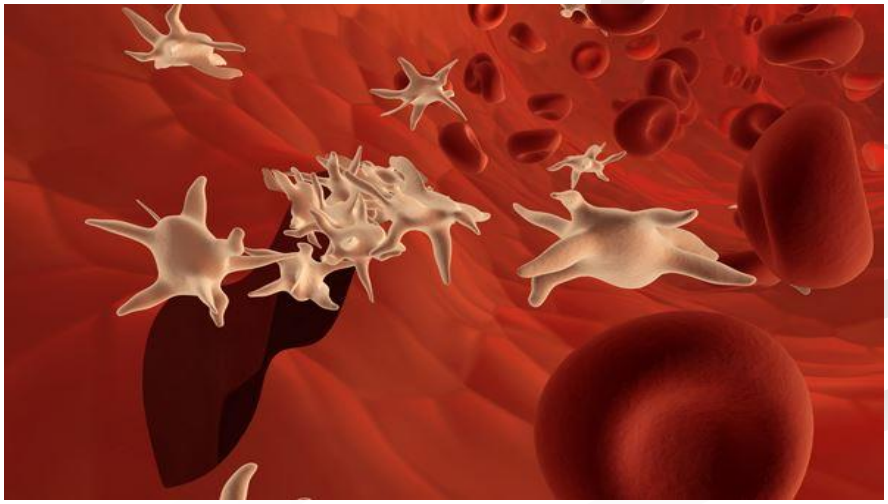
Polycythemia
Excess of circulating RBCs

- Primary Polycythemia: is caused by a tumor like condition of the bone marrow in which erythropoiesis proceeds at an excessive, uncontrolled rat
- Secondary Polycythemia: is an appropriate erythropoietin induced adaptive mechanism to improve blood's O2 carrying capacity in response to a prolonged reduction in O2 delivery to the tissues
  - Occurs normally in people living in high altitudes
  - People with chronic lung disease or cardiac failure



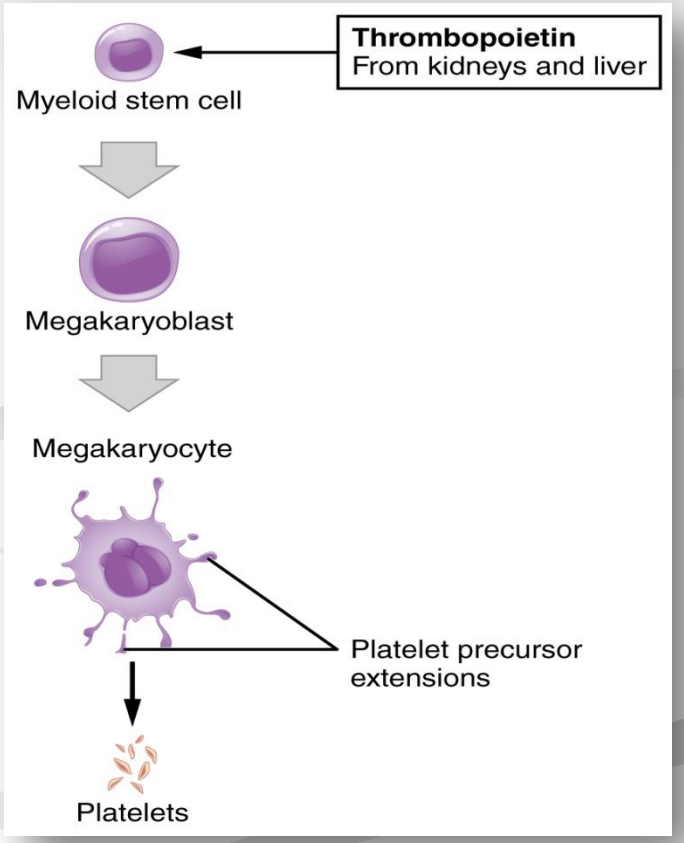
Platelets

- Normally (150,000-350,000 platelets/mm3).
- Platelets are not whole cells, but small fragments
- Involved in stopping bleeding when a blood vessel is damaged; Process is called hemostasis
- Contain several clotting factors – calcium ions, ADP, serotonin
- Platelets contain high concentration of **Actin** & **Myosin**, which enables them to contract.



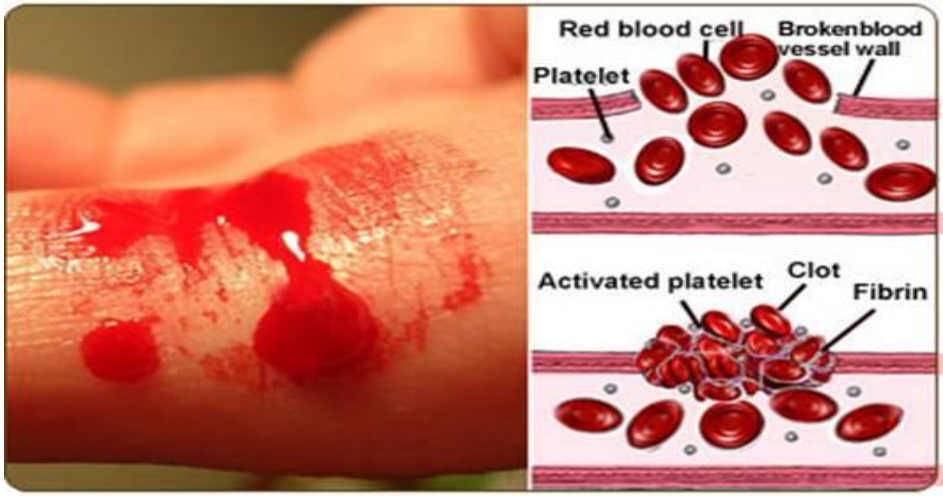
Platelets

- Origin: **Megakaryocytes** (large cells in the bone marrow each one produces >1000 Platelets)
- Platelets remain functional for an average of 10 days
(Removed afterwards by macrophages, especially in spleen & liver)
- Platelets production is stimulated by the hormone **Thrombopoietin**, that's synthesized in the **Liver**.



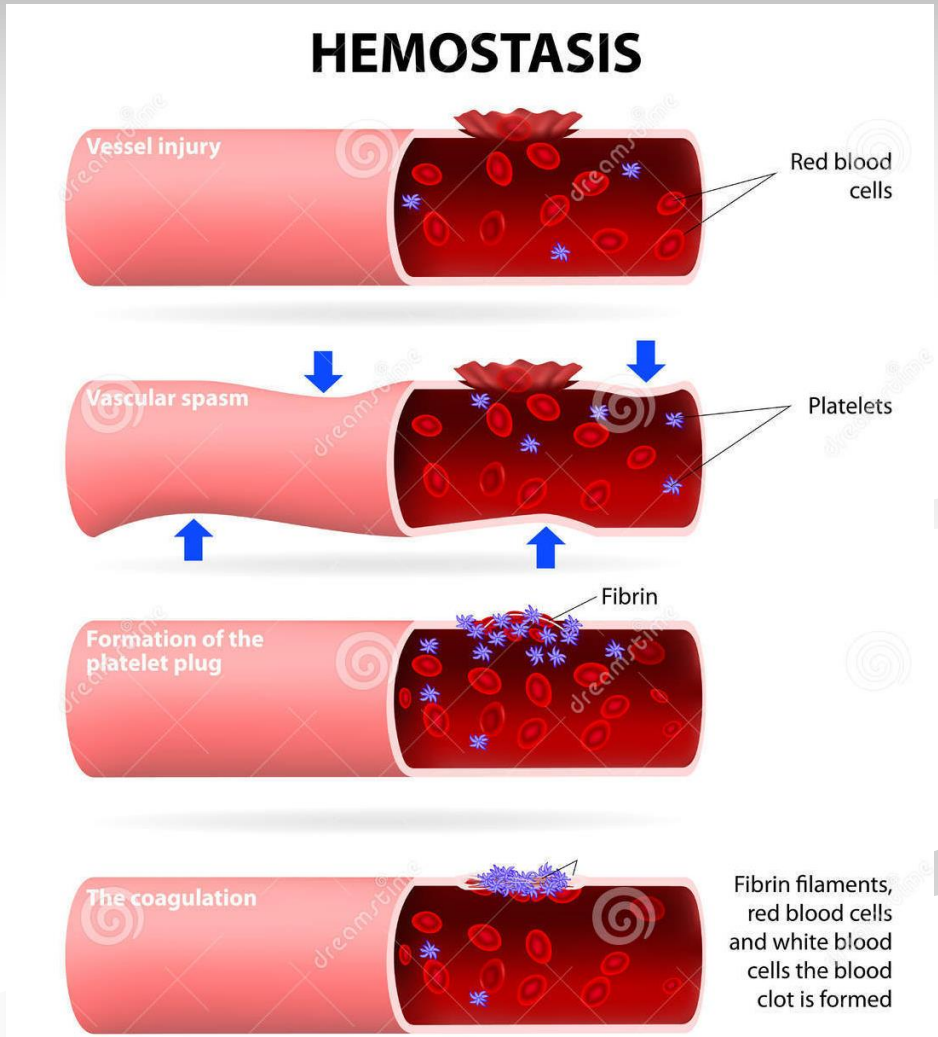
Hemostasis

• The process of stopping bleeding from broken blood vessel (stopping of hemorrhage)



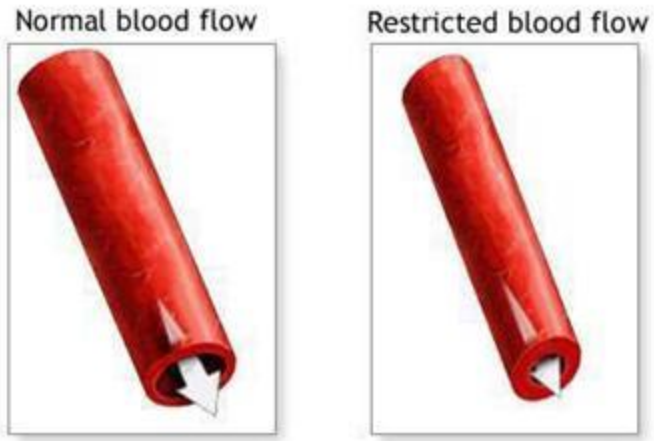
Hemostasis

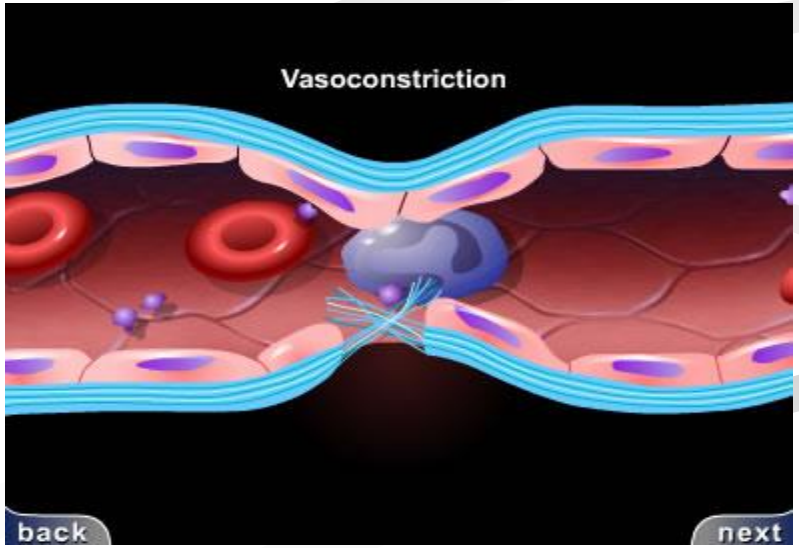
- involves 3 major steps:
  - Vascular spasm
  - Formation of platelet plug
  - Blood coagulation (clot formation)



Hemostasis

- **Vascular spasm:**
  - A cut blood vessel will immediately constrict.
  - Intrinsic response of the endothelium
  - slows blood flow through the defect and thus minimize blood loss.
  - Make the vessel wall sticky & adherent. to each other, further sealing off the damaged vessel

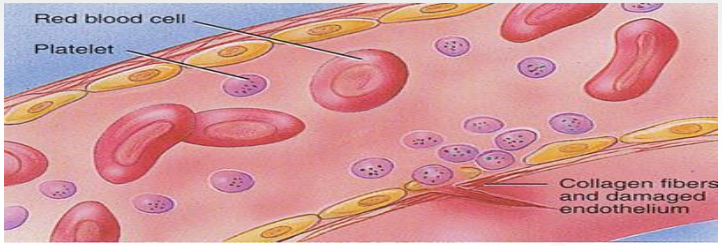


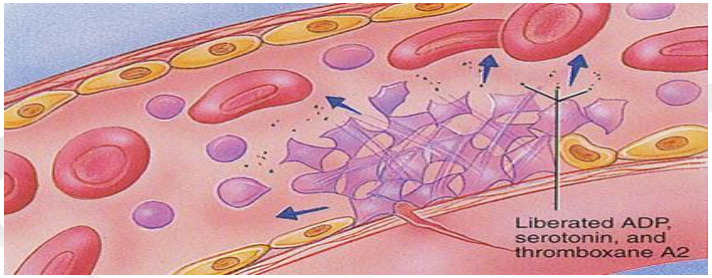


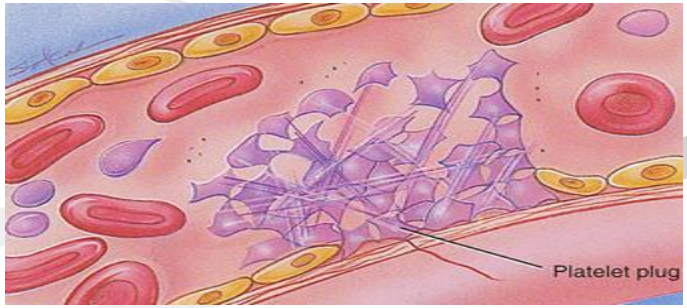
Hemostasis

- **Platelet plug formation steps:**

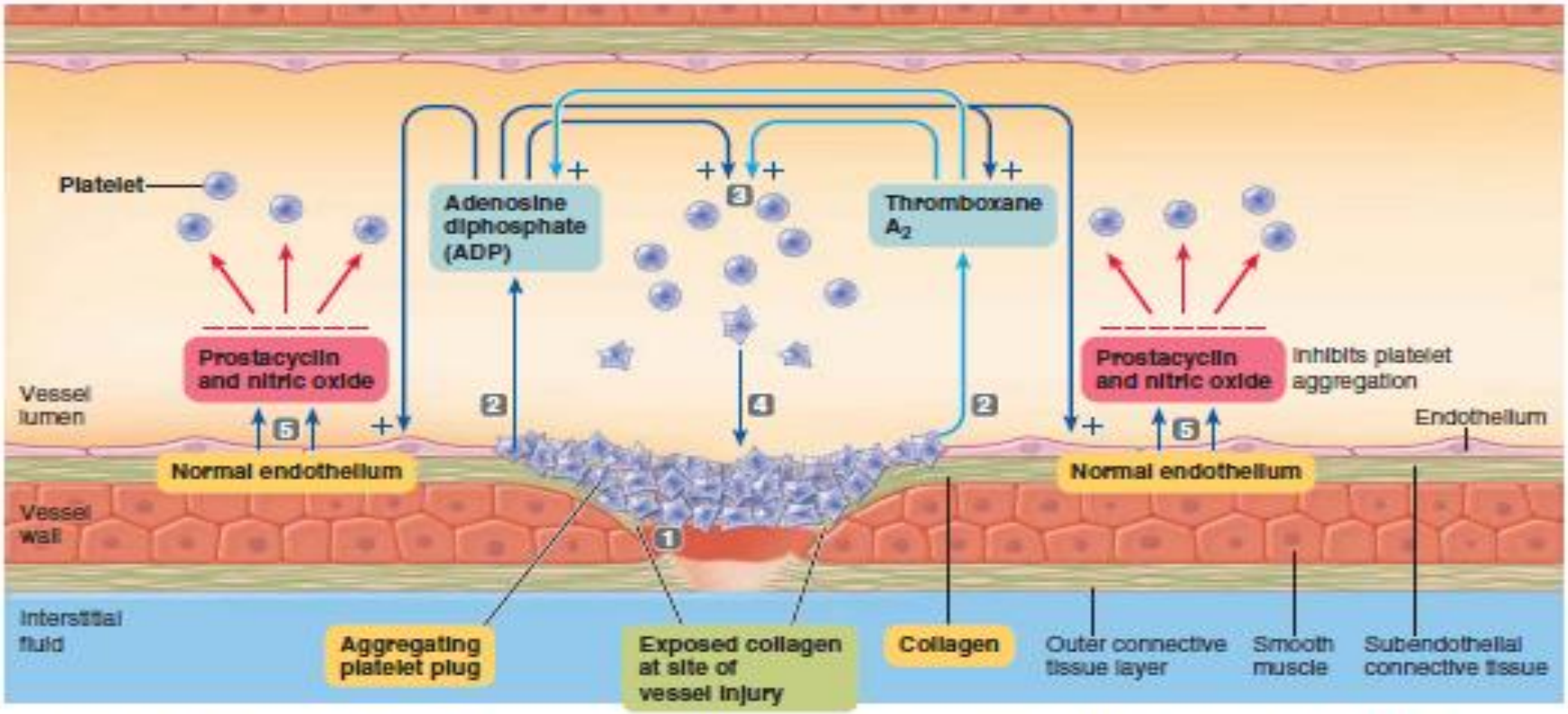
1. Platelets Adhesion: Platelets stick to exposed collagen of vessel (platelets do not stick to smooth endothelial surface)
2. Platelet Release Reaction: Platelets release Thromboxane A2, Serotonin & ADP activating other platelets
3. Platelet Aggregation: Activated platelets stick together and activate new platelets to form a mass called a platelet plug, Plug reinforced by fibrin threads formed during clotting process

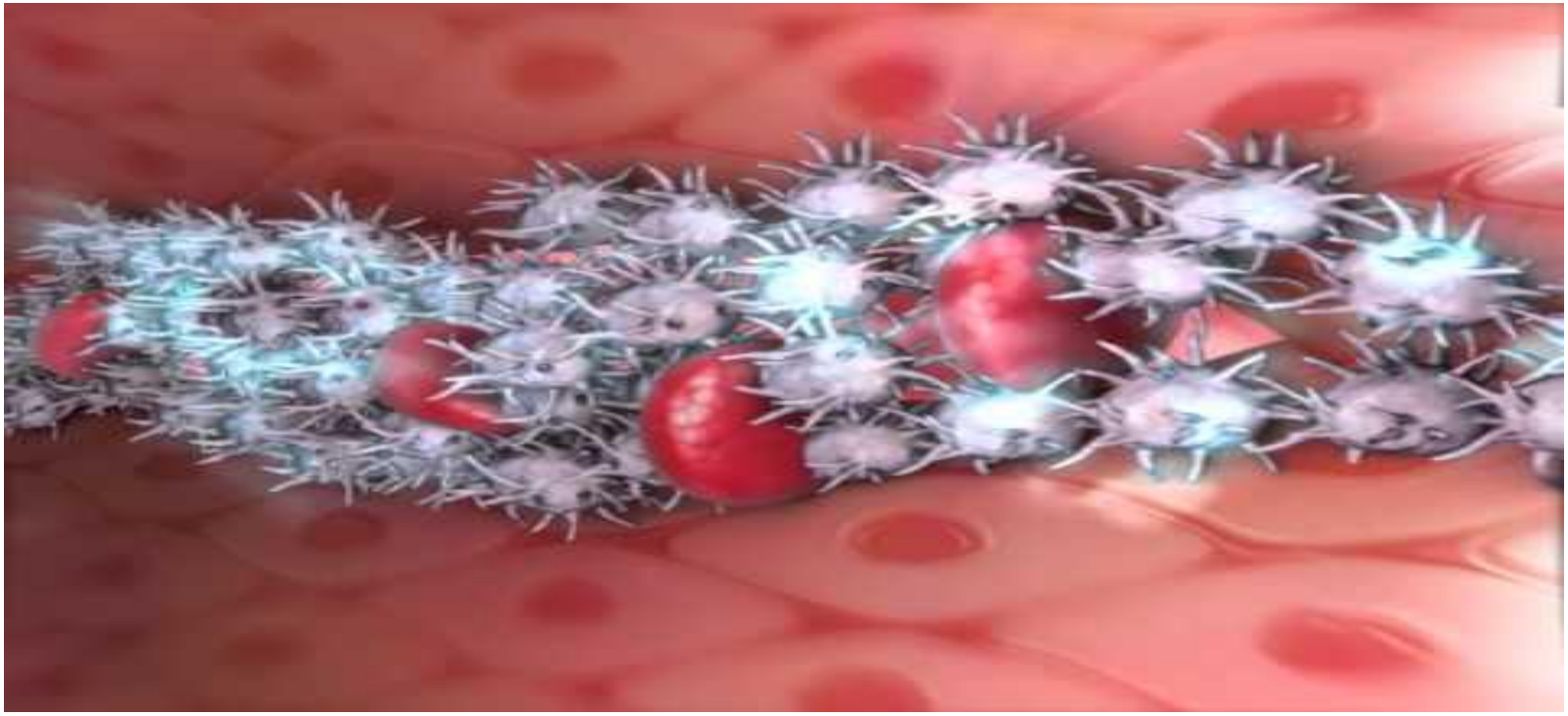






Platelet Plug is limited to the defect and dose not spread to the nearby undamaged vascular tissue, WHY?

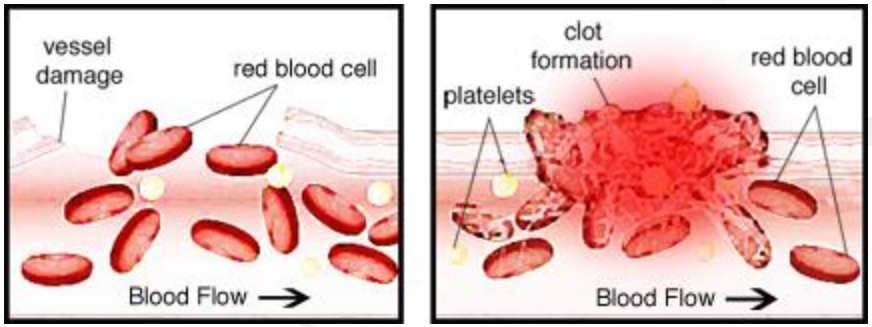




- Platelet plug functions:
  - Seals the defect
  - Actin-Myosin complex within the aggregates will strengthen the plug → so more sealing
  - The plug releases a powerful vasoconstrictor → enhancing the initial vascular spasm
  - The plug also releases other chemicals that enhance blood coagulation.

Clot formation

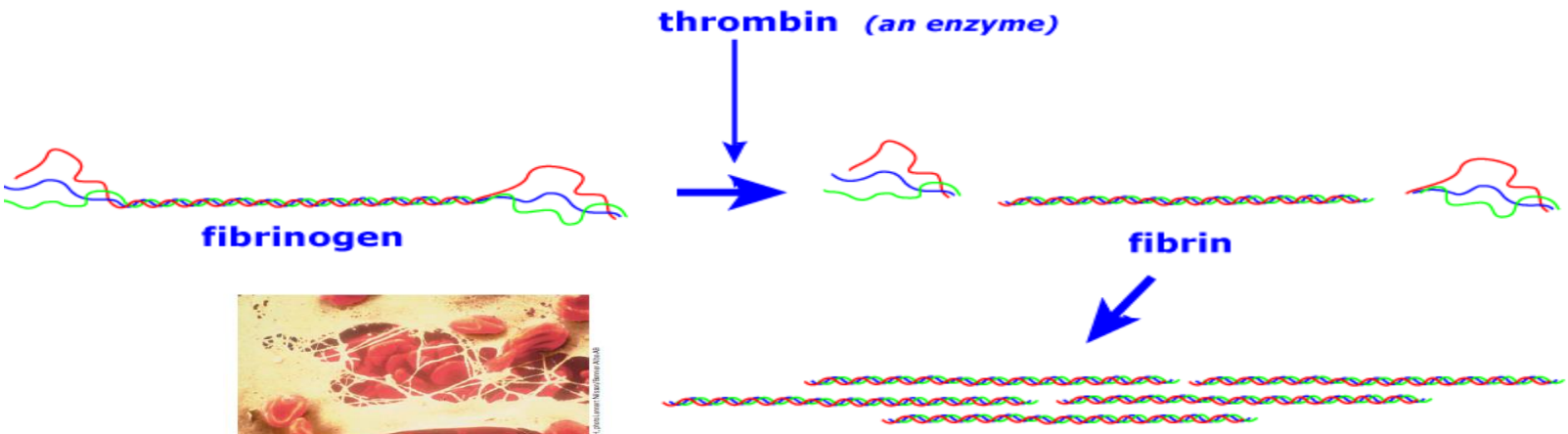
- **Blood coagulation,** or **clotting,** is the transformation of blood from a liquid into a solid gel.
- Formation of a clot on top of the platelet plug strengthens and supports the plug, reinforcing the seal over a break in a vessel.



CLOT FORMATION

• The ultimate step in clot formation is the conversion of **fibrinogen** into **fibrin** by the enzyme **thrombin** at the site of the injury.

• Fibrin molecules adhere to the damaged vessel surface, forming a loose, netlike meshwork that traps blood cells, including aggregating platelets. The resulting mass, or **clot**



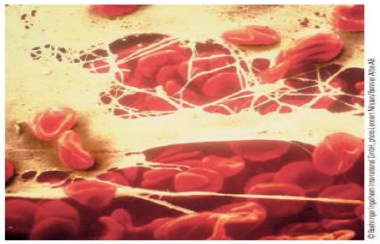
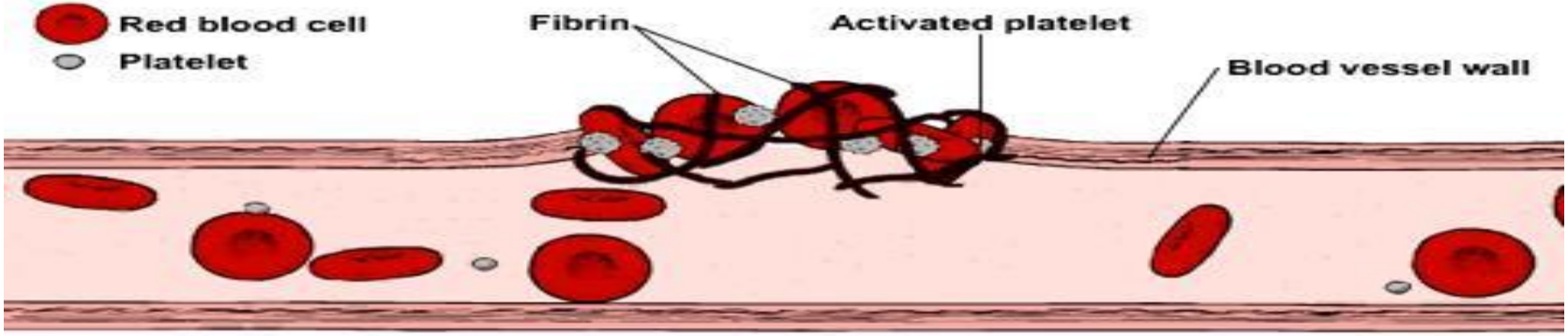
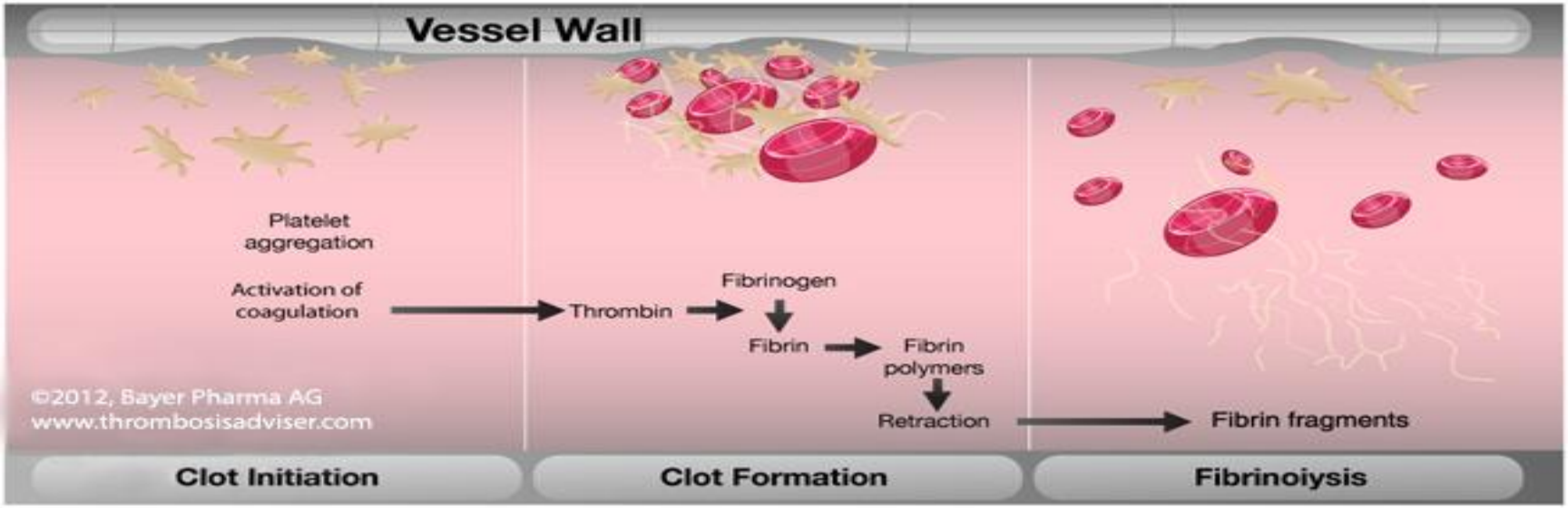
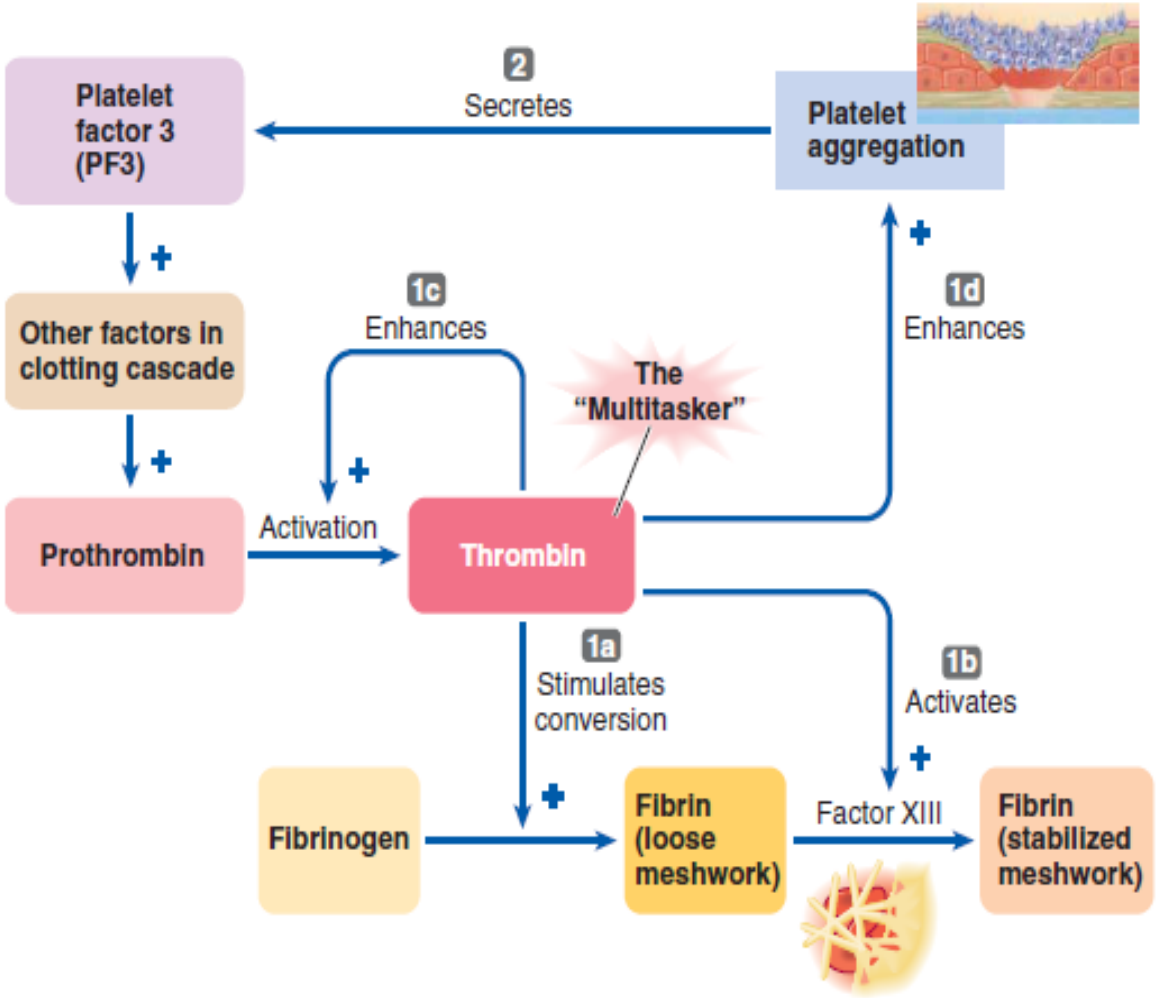


FIGURE 11-12 Erythrocytes trapped in the fibrin meshwork of a clot.


Red blood cell
Platelet
Fibrin
Activated platelet
Blood vessel wall


Vessel Wall
Platelet aggregation
Activation of coagulation
Thrombin
Fibrinogen
Fibrin
Fibrin polymers
Retraction
Fibrin fragments
©2012, Bayer Pharma AG
www.thrombosisadviser.com
Clot Initiation
Clot Formation
Fibrinoiysis

Roles of Thromobin



1 Thrombin, a component of the clotting cascade, plays multiple roles in hemostasis:

- 1a stimulates conversion of fibrinogen to fibrin
- 1b activates factor stabilizing fibrin meshwork of clot
- 1c enhances activation of more prothrombin into thrombin through positive feedback
- 1d enhances platelet aggregation

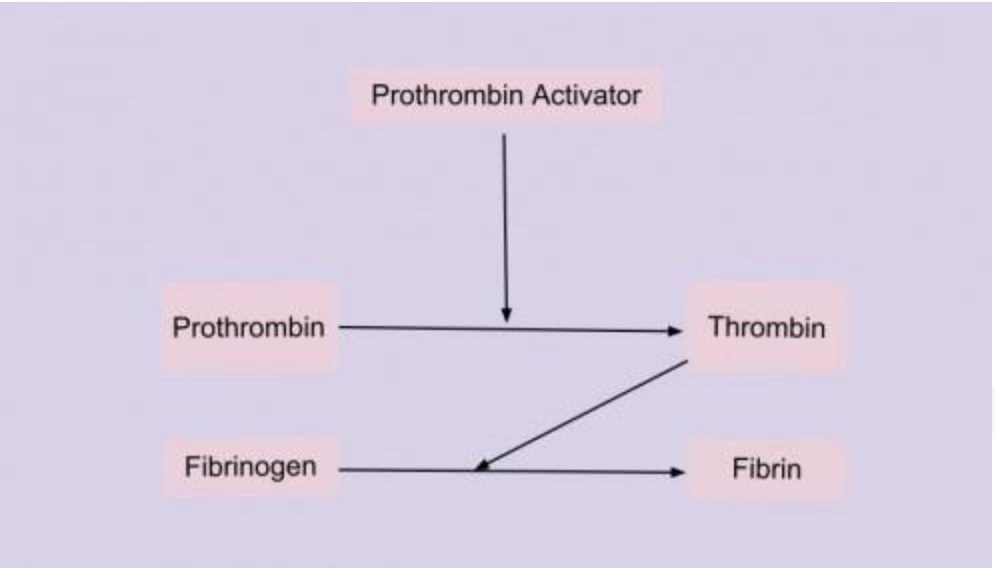
2 Through positive feedback, aggregated platelets secrete PF3, which stimulates clotting cascade that results in thrombin activation.

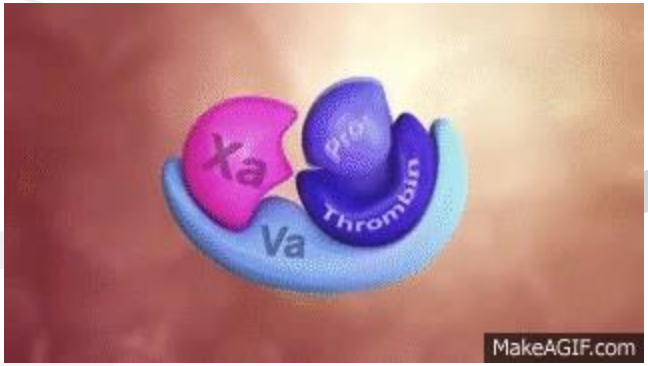
● **FIGURE 11-13** Roles of thrombin in hemostasis.

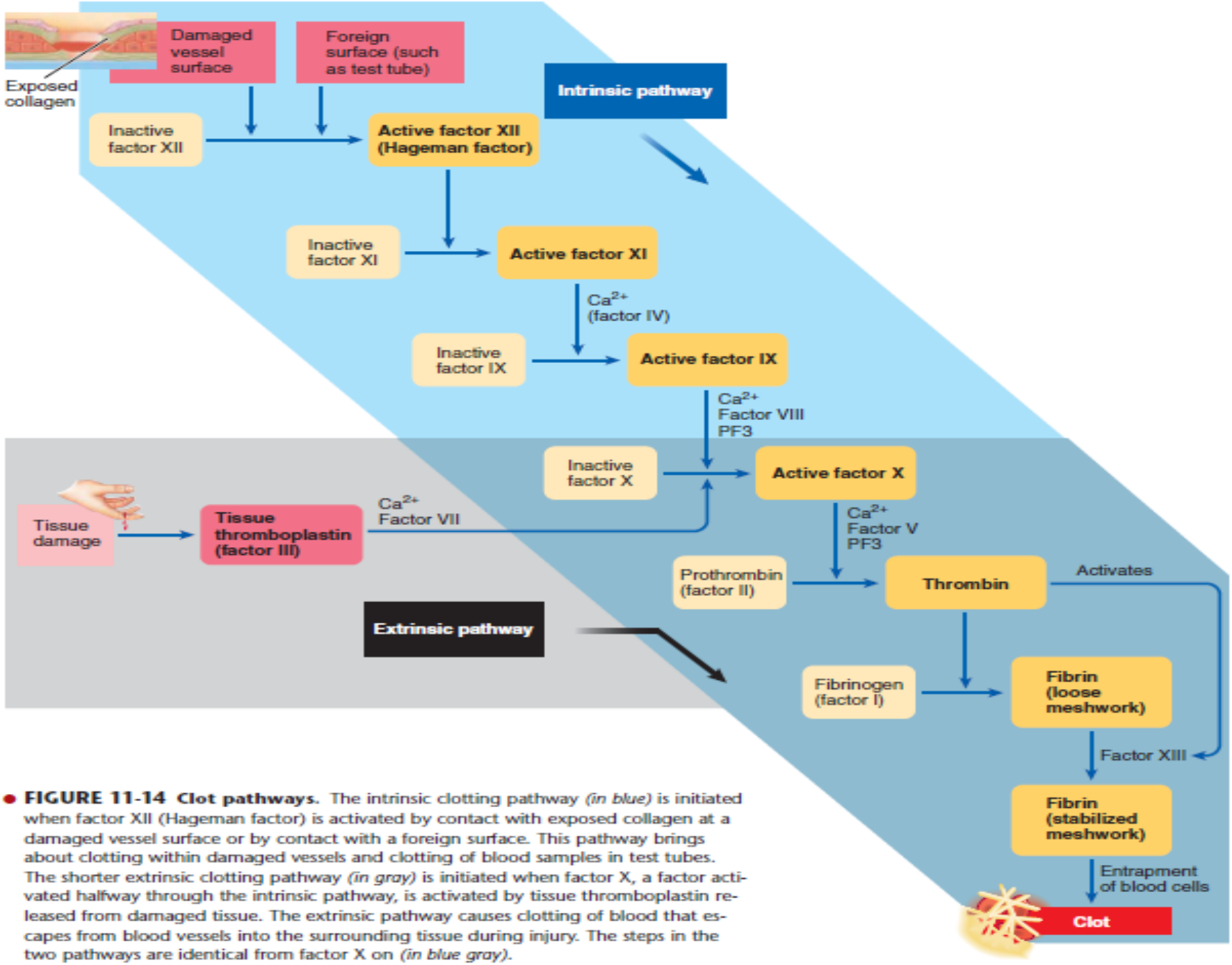
• Because thrombin converts the fibrinogen molecules in the plasma into fibrin, thrombin must normally be absent from the plasma except in the damaged vessel otherwise, blood would always be coagulated

How can thrombin normally be absent from the plasma?
thrombin's existence in the plasma in the form of an inactive precursor called prothrombin.

•prothrombin converts into thrombin **ONLY** when blood clotting is desirable and This conversion involves the clotting cascade.







● **FIGURE 11-14 Clot pathways.** The intrinsic clotting pathway *(in blue)* is initiated when factor XII (Hageman factor) is activated by contact with exposed collagen at a damaged vessel surface or by contact with a foreign surface. This pathway brings about clotting within damaged vessels and clotting of blood samples in test tubes. The shorter extrinsic clotting pathway *(in gray)* is initiated when factor X, a factor activated halfway through the intrinsic pathway, is activated by tissue thromboplastin released from damaged tissue. The extrinsic pathway causes clotting of blood that escapes from blood vessels into the surrounding tissue during injury. The steps in the two pathways are identical from factor X on *(in blue gray)*.

Hemostatic is a complementary mechanisms , HOW??
Hemostatic mechanisms reinforce each other., The aggregated platelets secrete platelet factor 3 (PF3), which is essential for the clotting cascade that in turn enhances further platelet aggregation

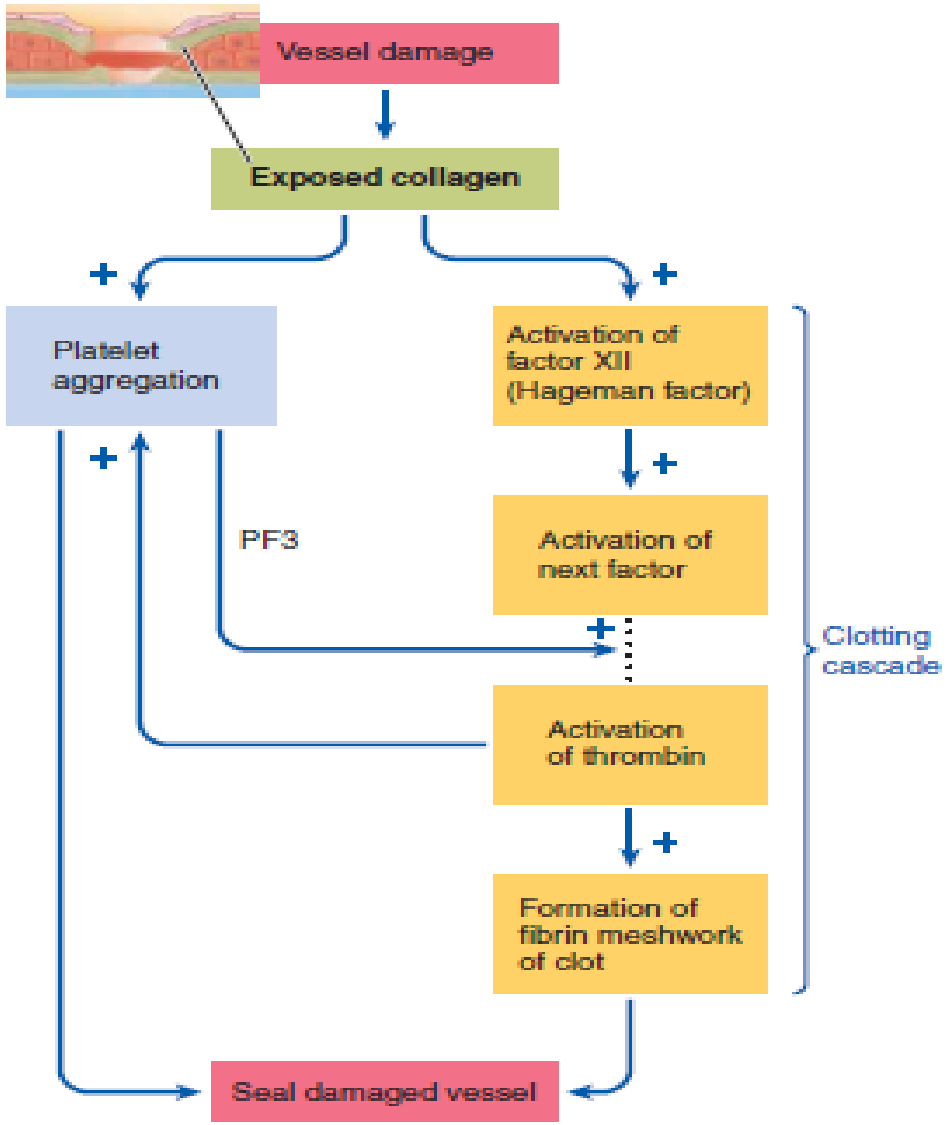


FIGURE 11-15 Concurrent platelet aggregation and clot formation. Exposed collagen at the site of vessel damage simultaneously initiates platelet aggregation and the clotting cascade. These two hemostatic mechanisms positively reinforce each other as they seal the damaged vessel.

Clot Dissolution

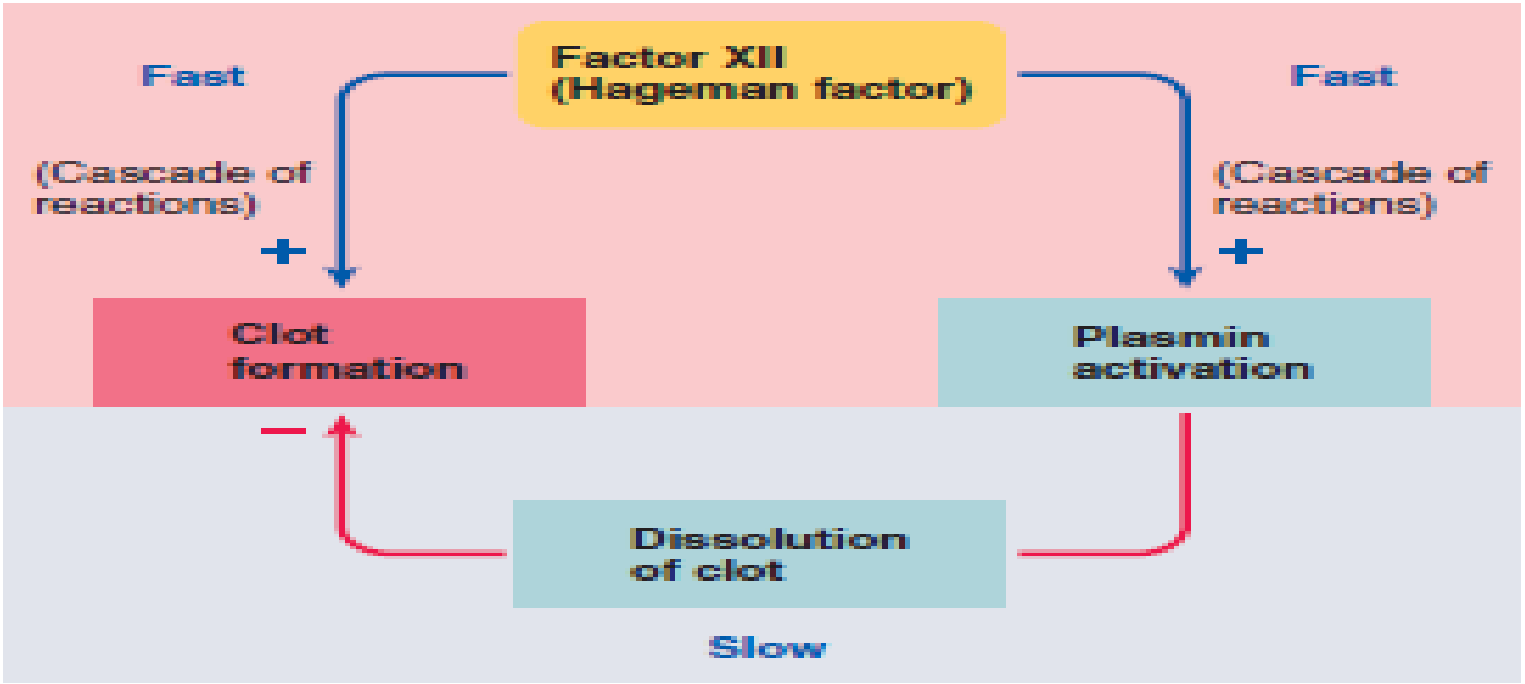
• Clot is dissolved slowly by a fibrinolytic (fibrin-splitting) enzyme called **plasmin**

• Plasmin, like the clotting factors, is a plasma protein produced by the liver and present in the blood in an inactive precursor form, **plasminogen.**

• **Plasmin is activated in a fast cascade** of reactions involving many factors, among them factor XII (Hageman factor)

• Activated plasmin becomes trapped in the clot and later dissolves it by slowly breaking down the fibrin meshwork.

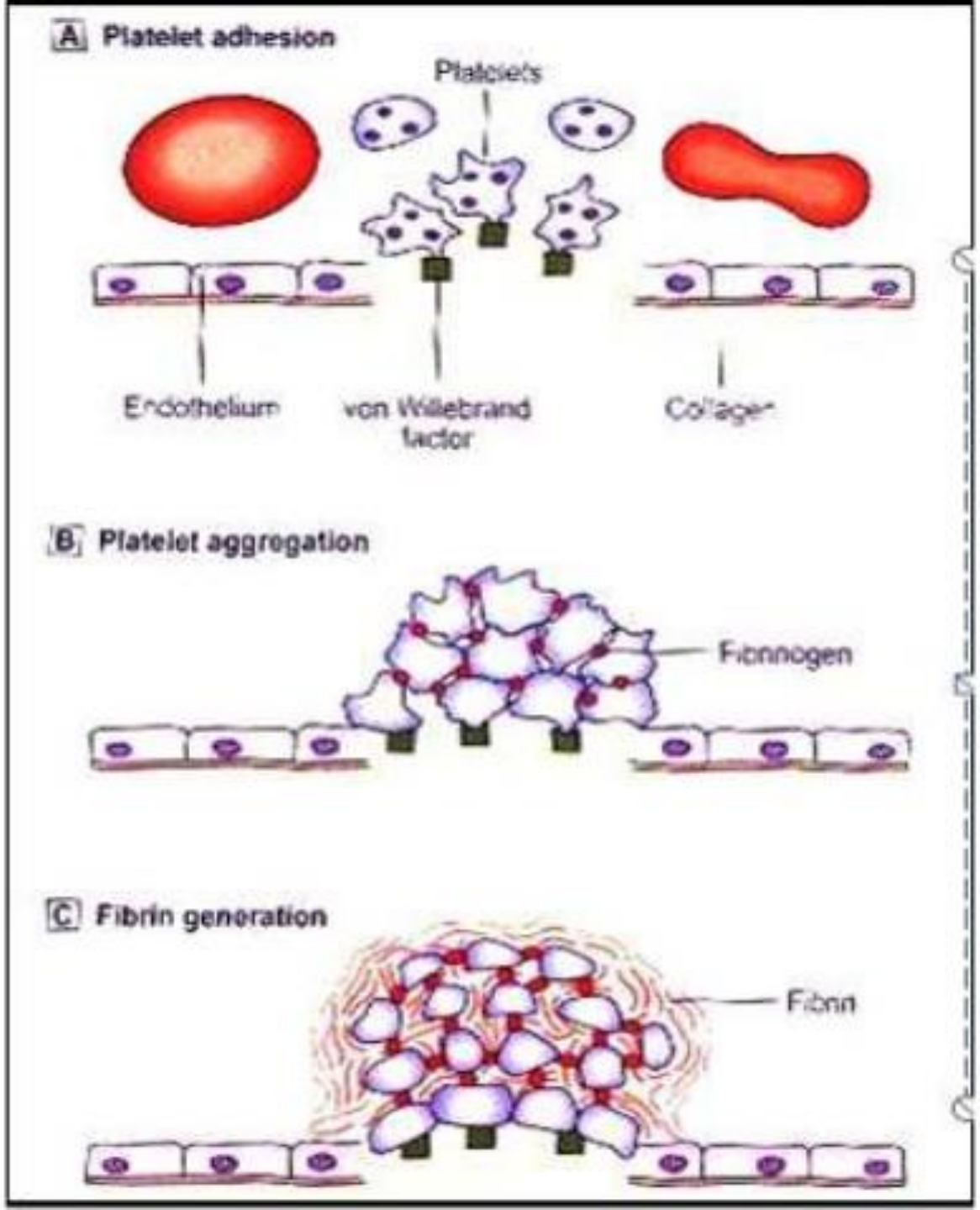
Role Of Factor XII In Clot Formation And Dissolution.



- **FIGURE 11-16 Role of factor XII in clot formation and dissolution.** Activation of factor XII (Hageman factor) simultaneously initiates a fast cascade of reactions that result in clot formation and a fast cascade of reactions that result in plasmin activation. Plasmin, which is trapped in the clot, subsequently slowly dissolves the clot. This action removes the clot when it is no longer needed after the vessel has been repaired.

Haemostasis:

- Vasoconstriction
- Platelet activation
- Haemostatic plug
- Coagulation
- Stable clot formation
- Clot dissolution

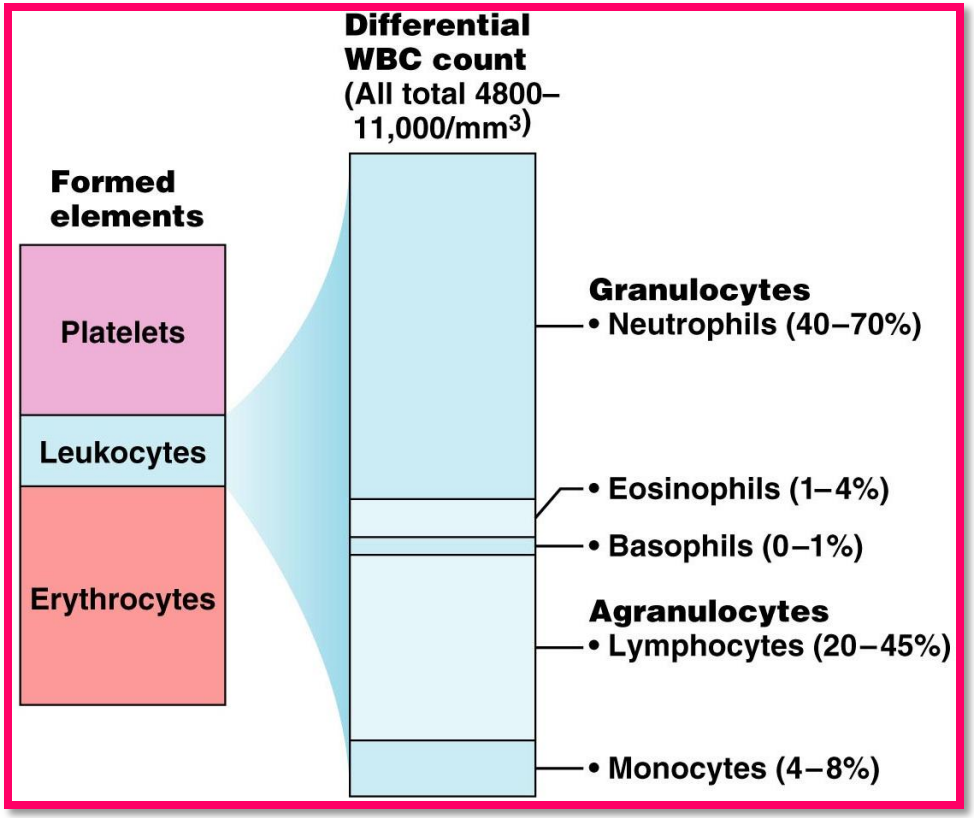


Leukocytes – White Blood Cells (WBCs)

- Mobile unit of immune system
- Colorless (because lack to hemoglobin)
- 4,800 – 11,000/cubic millimeter
- WBCs have a nucleus and are larger than RBCs
- Most produced in bone marrow

Leukocytes – White Blood Cells (WBCs)

- Two types of leukocytes
  - Granulocytes
  - Agranulocytes
- Differential WBC Count
  - Never
  - Let
  - Monkeys
  - Eat
  - Bananas

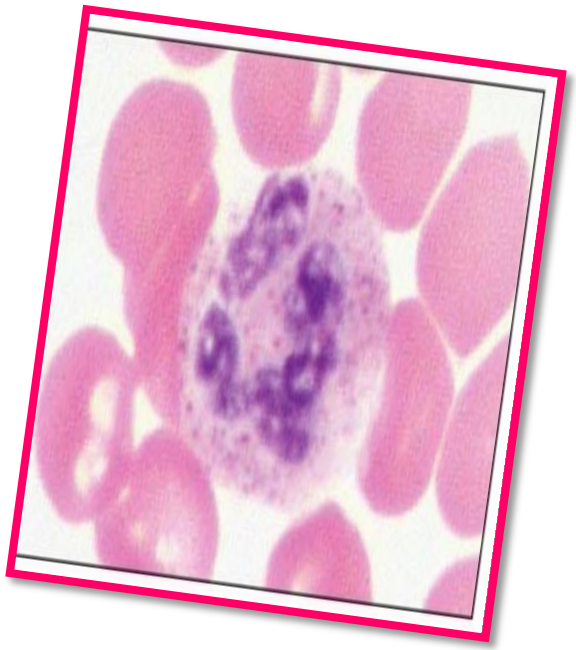


White Blood Cells

Type Of White Blood Cells	% By Volume Of WBC	Description	Function
Neutrophils	60 – 70 %	Nucleus has many interconnected lobes; blue granules	Phagocytize and destory bacteria; most numerous WBC
Eosinophils	2 – 4 %	Nucleus has bilobed nuclei; red or yellow granules containing digestive enzymes	Play a role in ending allergic reactions
Basophils	< 1 %	Bilobed nuclei hidden by large purple granules full of chemical mediators of inflammation	Function in inflammation medication; similar in function to mast cells
Lymphocytes (B Cells and T Cells)	20 – 25 %	Dense, purple staining, round nucleus; little cytoplasm	the most important cells of the immune system; effective in fighting infectious organisms; act against a specific foreign molecule (antigen)
Monocytes	4 – 8 %	Largest leukocyte; kidney shaped nucleus	Transform into macrophages; phagocytic cells

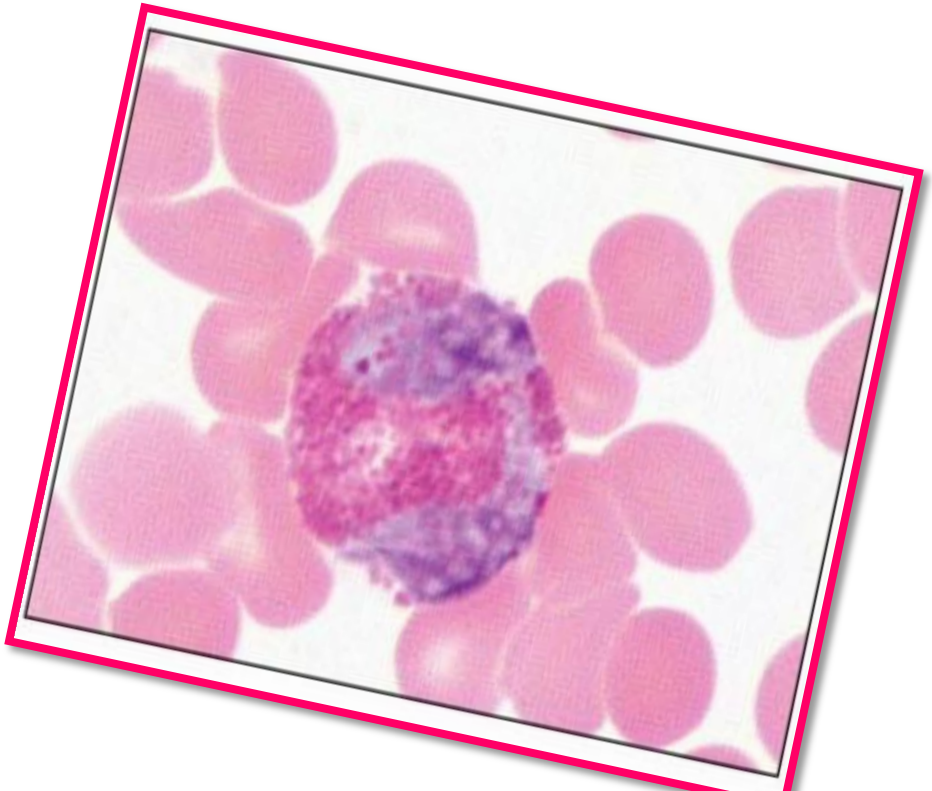
Granulocytes

- Neutrophils – most numerous WBC
  - Phagocytize and destroy bacteria
  - Increased with acute bacteria infection
  - Nucleus – has two to six lobes
  - Granules pick up acidic and basic stains



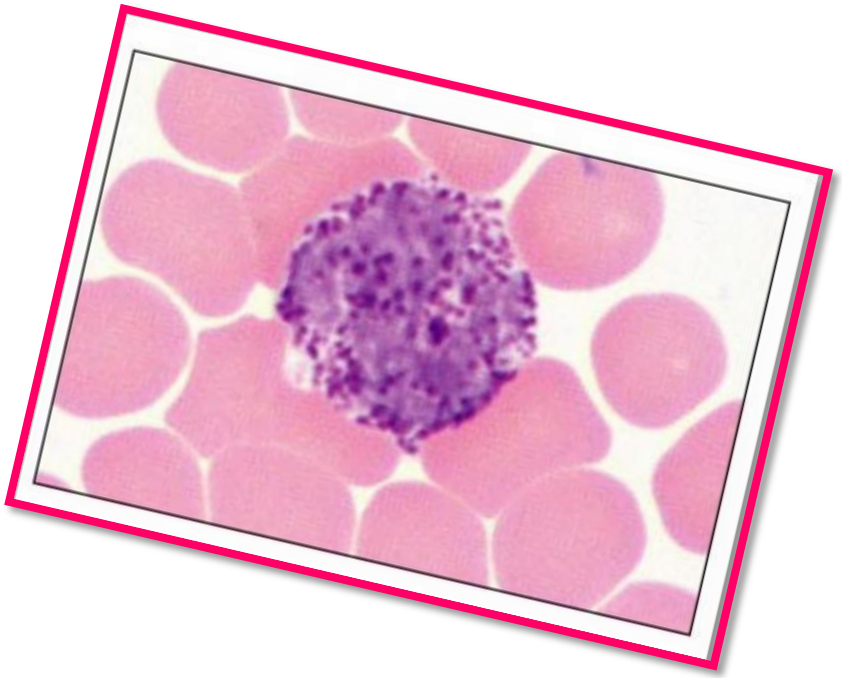
Granulocytes

- Eosinophils – compose 1 – 4% of all WBCs
  - Play roles in ending allergic reactions, parasitic infections
  - Red acidic dye eosin



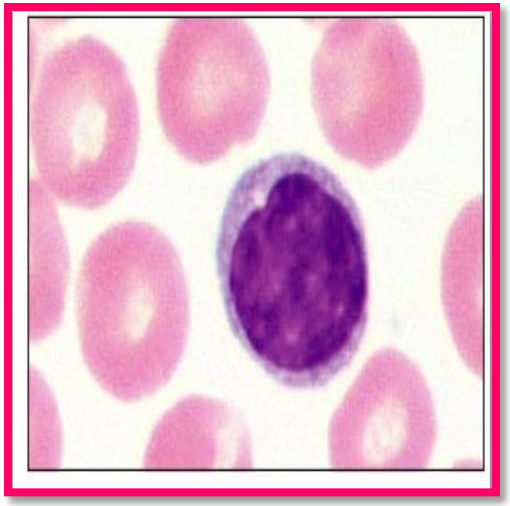
Granulocytes

- Basophils – about 0.5% of all leukocytes
  - Nucleus – usually two lobes
  - Synthesize and store histamine and heparin
  - Basic dye (methaline blue)



Agranulocytes

- Lymphocytes – compose 20 – 45% of WBCs
- Two main classes of lymphocyte
  - T cells – attack foreign cells directly
  - B cells – produce antibody which circulate in blood and bind with specific kinds of foreign matter and destroy it



Agranulocytes

- Monocytes – compose 4–8% of WBCs
  - The largest leukocytes
  - Nucleus – kidney shaped
  - Transform into macrophages
    - Phagocytic cells

Summary of Formed Elements

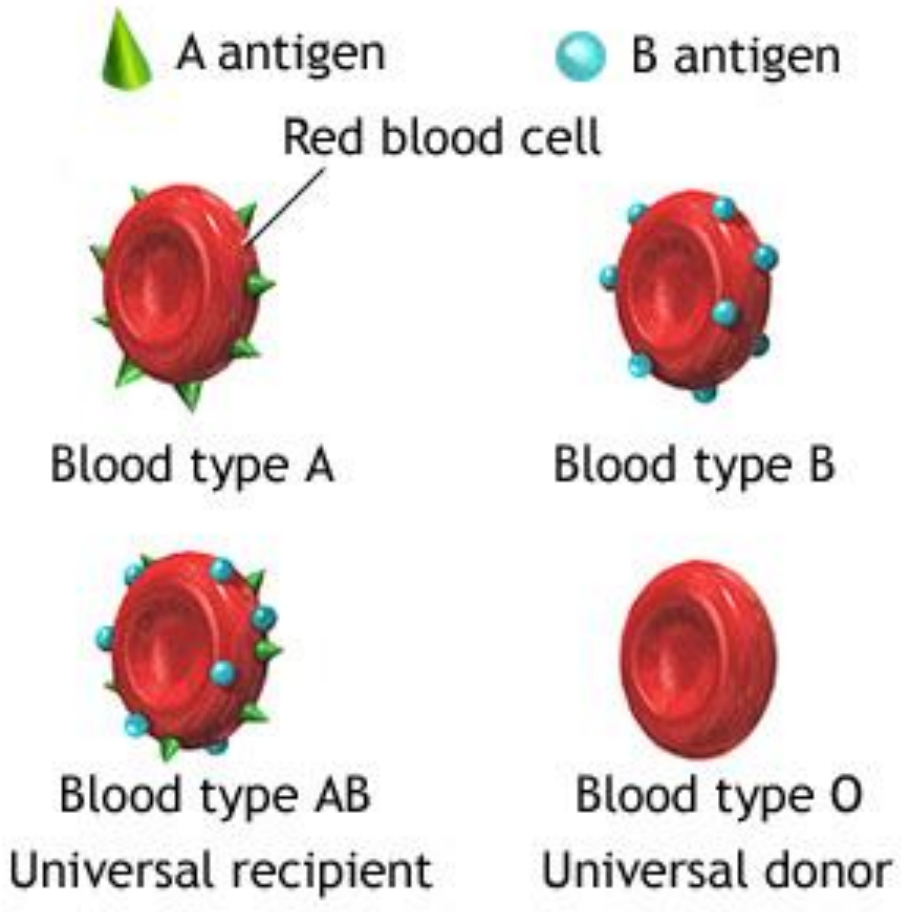
TABLE 17.1 Summary of Formed Elements of the Blood

Cell Type	Illustration	Description*	Number of Cell per mm^3 (μl) of Blood	Duration of Development (D) and Life Span (LS)	Function
Erythrocytes (red blood cells; RBCs)		Biconcave, anucleate disc; salmon-colored; diameter 7–8 μm	4–6 million	D: 5–9 days LS: 100–120 days	Transport oxygen and carbon dioxide
Leukocytes (white blood cells, WBCs)		Spherical, nucleated cells	4800–11,000		
Granulocytes					
• Neutrophils		Nucleus multilobed; inconspicuous cytoplasmic granules; diameter 12–14 μm	3000–7000	D: 7–11 days LS: 6 hours to a few days	Destroy bacteria by phagocytosis
• Eosinophils		Nucleus bilobed; red cytoplasmic granules; diameter 12–15 μm	100–400	D: 7–11 days LS: about 5 days	Turn off allergic responses and kill parasites
• Basophils		Nucleus bilobed; large blue-purple cytoplasmic granules; diameter 10–14 μm	20–50	D: 3–7 days LS: a few hours to a few days	Release histamine and other mediators of inflammation
Agranulocytes					
• Lymphocytes		Nucleus spherical or indented; pale blue cytoplasm; diameter 5–17 μm	1500–3000	D: days to weeks LS: hours to years	Mount immune response by direct cell attack (T cells) or via antibodies (B cells)
• Monocytes		Nucleus U- or kidney-shaped; gray-blue cytoplasm; diameter 14–24 μm	100–700	D: 2–3 days LS: months	Phagocytosis; develop into macrophages in tissues
Platelets		Discoid cytoplasmic fragments containing granules; stain deep purple; diameter 2–4 μm	150,000–500,000	D: 4–5 days LS: 5–10 days	Seal small tears in blood vessels; instrumental in blood clotting

*Appearance when stained with Wright's stain.

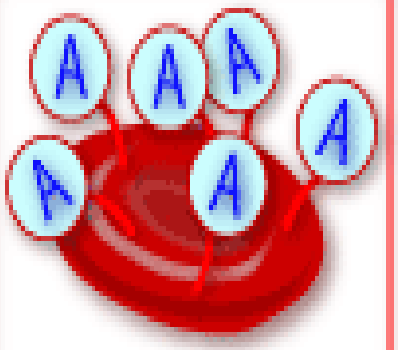
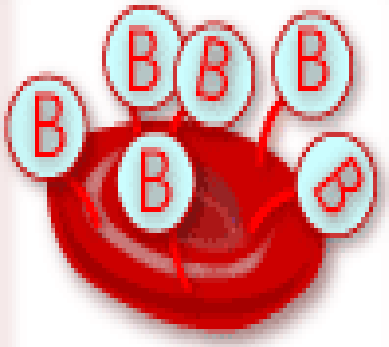
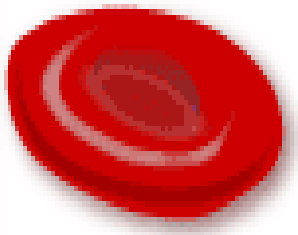
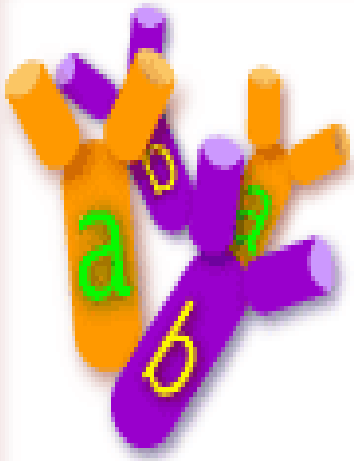
Blood Typing

What does blood types mean?



Different blood types have different SURFACE PROTEINS on their RBCs

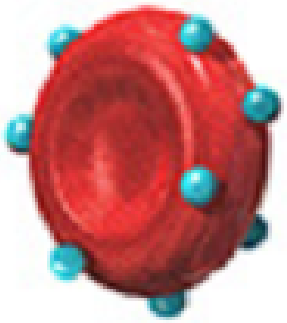
The ABO Blood System

Blood Type (genotype)	Type A (AA, AO)	Type B (BB, BO)	Type AB (AB)	Type O (OO)
Red Blood Cell Surface Proteins (phenotype)	 A agglutinogens only	 B agglutinogens only	 A and B agglutinogens	 No agglutinogens
Plasma Antibodies (phenotype)	 b agglutinin only	 a agglutinin only	 No agglutinin	 a and b agglutinin

ABO System…

- Antibodies (agglutinins) in plasma are considered naturally occurring; that it produced without any known exposure to Antigen
- agglutinins are gamma globulins, as are almost all antibodies, produced by bone marrow and lymph gland cells
- Most of them are IgM and IgG immunoglobulin molecules.

Rh Factor



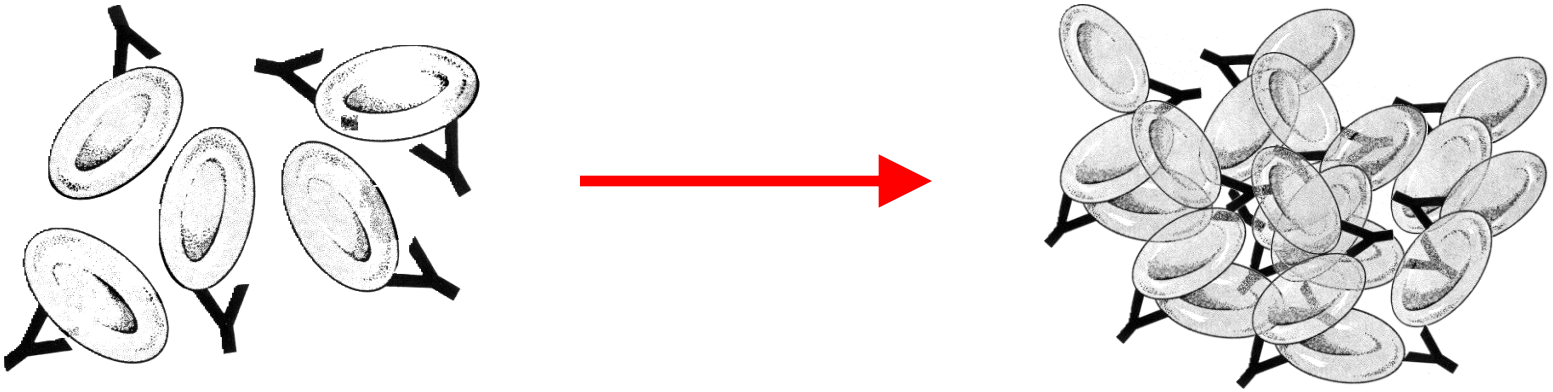
If your blood does contain the Rh protein, your blood is said to be Rh positive (Rh+)

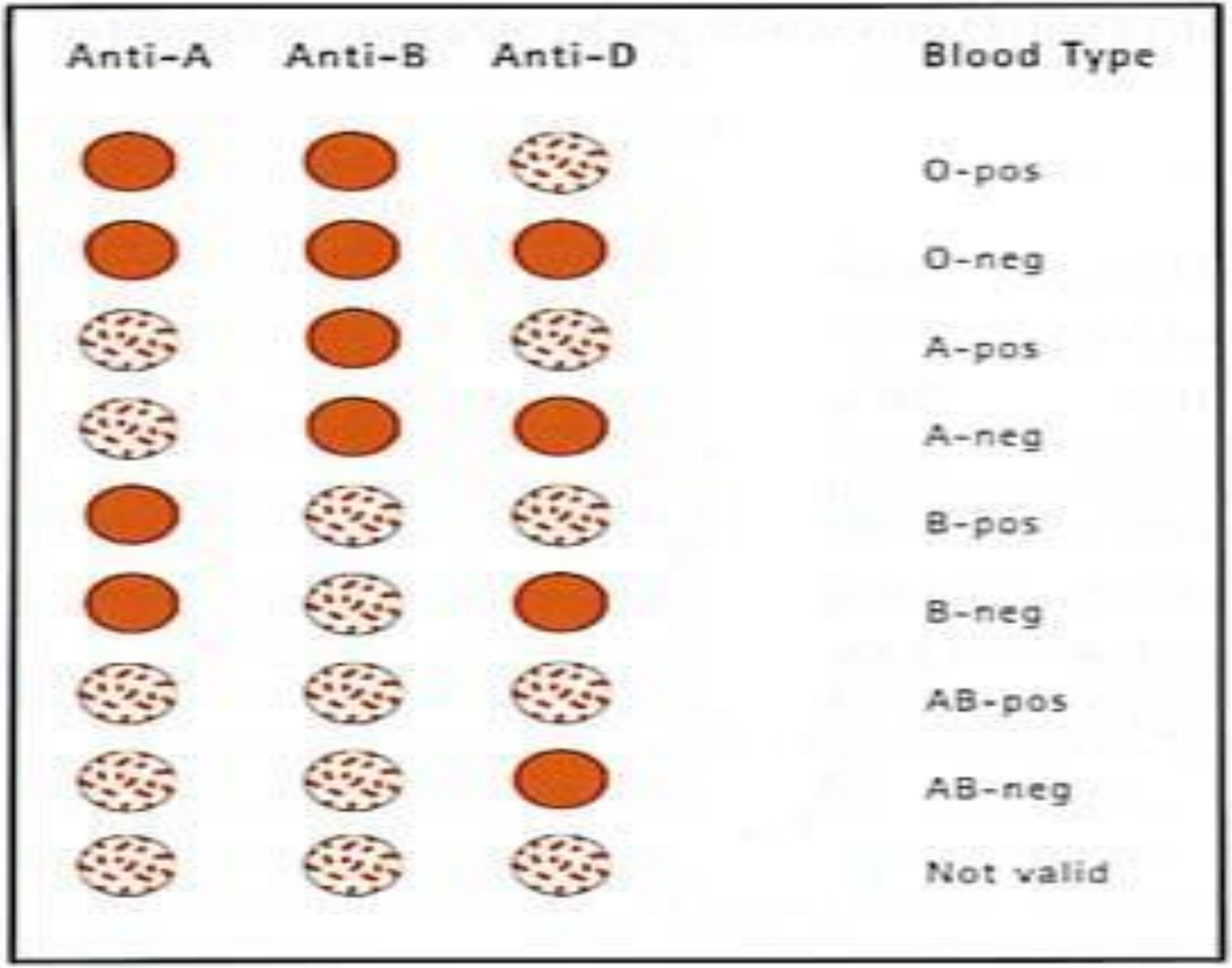
If your blood does NOT contain the Rh protein, your blood is said to be Rh negaitive (Rh-)

Rh System

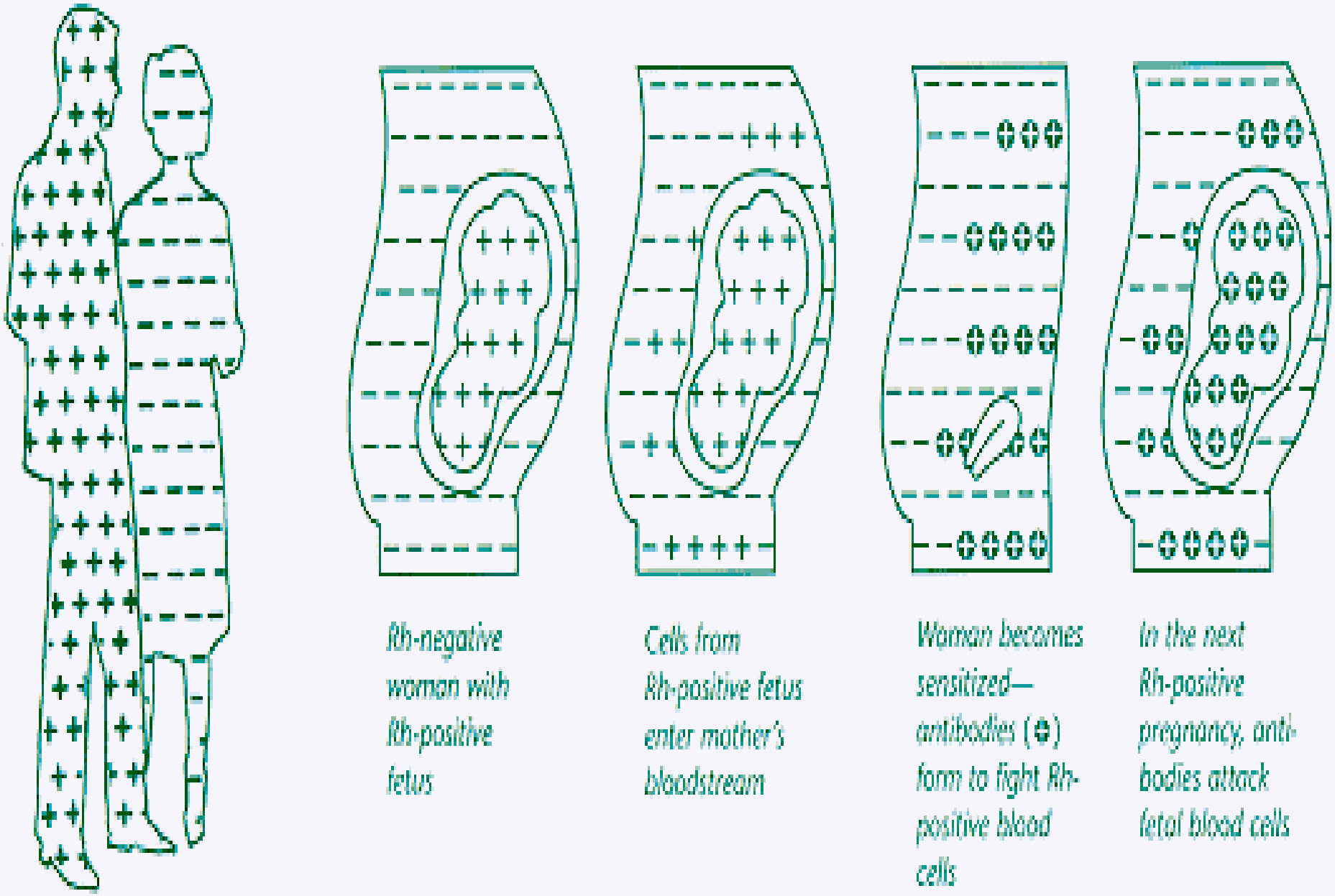
- Antibodies to rhesus factor only develop in two circumstances:
  1. transfusion of Rh +ve cells to Rh –ve person
  2. The presence of Rh +ve fetus in Rh –ve mother

Agglutination




Anti-A
Anti-B
Anti-D
Blood Type
O-pos
O-neg
A-pos
A-neg
B-pos
B-neg
AB-pos
AB-neg
Not valid

Rh factor is of particular medical important



How Rh sensitization occurs.